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Kuwait Foundation for Advancement of Sciences (K.F.A.S.)

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Vol. 2

Proceeding of The Second International Conference on

Islamic Medicine

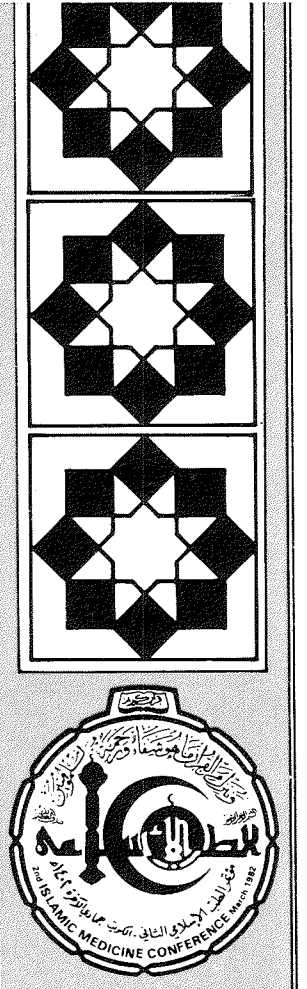
No. V

Applied Studies in Islamic Medicine and Advantages of Herbal Treatment

Supervised by
H.E. Dr. Abdul Rahman Abdullah Al-Awadi
The Minister of Public Health and
President of Islamic Medicine Organization

Edited by
Dr. Ahmed Ragai El-Gindy
Hakeem Mohammad Zahoorul Hasan

Jumada Al-Thani 1402/March-April 1982
State of Kuwait



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PART SEVEN

STUDIES ON THERAPEUTIC MEASURES MENTIONED IN HOLY QURAN AND HADITH AND USED BY MOSLEM PHYSICIANS.

Part Seven: *Studies on Therapeutic Measures Mentioned in Holy Quran or Hadith and Used by Moslem Physicians.*

CHAPTER ONE

(Papers Presented)

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2. OPENING REMARKS.
   Dr. Ibrahim Jameel Badran.
3. HONEY REGIMEN IN MANAGING CHRONIC NON-SPECIFIC DIARRHOEA.
   Dr. Salem Najam Salem, et al.
4. USE OF HONEY IN THE TREATMENT OF CHRONIC BILHARZIAL ULCER.
   Dr. Fahim Abdul Rahim, et al.
5. A CLINICAL STUDY OF THE TOPICAL USE OF BEE HONEY IN THE TREATMENT OF SOME OCULAR DISEASES.
   Dr. Mohammed H · Emarah.
6. SOME PHARMACOLOGICAL PROPERTIES OF SOME CONSTITUENTS OF NIGELLA SATIVA L. SEEDS: THE CARBONYL FRACTION OF THE ESSENTIAL OIL.
   Dr. Mohammed El-Dakhakhany.
7. FASTING IN ISLAM — MEDICAL ASPECTS.
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9. MENSTRUAL HYGIENE: AN EXPERIMENTAL STUDY CONCERNING QURANIC FACTS AND THE JEWISH FALLACIES.
   Dr. Mohammed Abdel Latif.
10. GENERAL DISCUSSION.

REPORT ON THE FIRST SESSION

This session was held from 08.30 a.m. to 11.00 a.m., under the chairmanship of Prof. Dr.Ibrahim Jameel Badran and Dr. Ahmed Shawki Ibrahim acted as moderator. In this session seven papers were presented by the famous clinicians and scientists on "STUDIES ON THERAPEUTIC MEASURES, MENTIONED IN HOLY QURAN OR HADITH AND USED BY MOSLEM PHYSICIANS". Then general discussion was allowed, in which maximum number of delegates took part and expressed their skillful views.

Editors.

OPENING REMARKS OF THE CHAIRMAN

Prof. Ibrahim Badran

The litle of this session is 'Studies on therapeutic measures mentioned in Holy Quran or Hadith and used by Moslem physicians'. The first chapter of the bases of this task is to be classified, because every work has to have a foundation. Such is this medicine, which differentiates between an atheist and a Moslem. Those living in this area have to benefit from the experience of their predecessors, who have done the research in this medicine in accordance with Holy Quran and Hadith. Every respect is to be offered to those who have done their part in this kind of research before us.

HONEY REGIMEN IN MANAGING CHRONIC NON-SPECIFIC DIARRHOEA

Prof. S.N. Salem, Mr. M.A. Hasan and Mr. Jamal El-Din

EGYPT

There is no contradiction between Islamic teachings and sciences. Moreover, Islam urges his followers to think over and look deeply into scientific matters.[1] Medicine is no exception as our gracious Prophet Muhammad (ﷺ) threw lights on some medical problems in order to get benefit and to set up examples for us to follow his steps.[2] In Hadith Sahih, He (ﷺ) said:

> *" There is a[3] remedy for every disease. If one gets the sound remedy the disease will be eradicated. "*

He, (ﷺ), also said:

> *" If there is any goodness in your methods of treatment, that will be in lancet incision, honey or cautery. "*

In a previous work we have used honey for treatment of upper gastro-intestinal disease with good results and presented a paper.[4] In that paper we have quoted the Hadith on diarrhoea and how the Prophet Muhammad (ﷺ), had advised Honey for its treatment. In this work we have applied honey regimen for treatment of non-specific chronic diarrhoea and in patient suffering from mild ulcerative colitis with chronic diarrhoea.

PATIENTS AND METHODS

Thirty women aged 18-45 years (mean 28 years) and 23 men aged 31-55 years (mean 39 years) were studied during 7-months' period (Feb. -Aug, 1981). They were known to us to have chronic nonspecific diarrhoea with the following criteria:[2,6]

1. The patient should have at least 3 motions per day for more than 3 weeks and/or recurrent of diarrhoea.
2. There were association of gastro-intestinal symptoms such as diffuse or localised abdominal pain, flatulence, dyspepsia, anal irritation with or without upper gastro-intestinal symptomatology.
3. Absence of systemic diseases.
4. Stool examination (smear and culture) showed no pathogens.
5. Barium enema with double air contrast.
6. Sigmoidoscopy and rectal biopsy examinations ruled out Schistosomal amoebic, infective or parasitic infestations but may show non-specific inflammation.
7. No, or poor response to different types of chemotherapy and/or dietary regimen.

All the subjects were outpatients. They were instructed to administer three tablespoonfuls (45ml.) of fresh honey, before breakfast and at bed-time. No drug were used and the patients were allowed bland diet. This regimen lasted for 3 weeks and they were followed up for 4 months during which if relapses took place they were advised to repeat the honey regimen for 1-3 weeks.

RESULTS

Fifty three patients, their age groups and sex distribution are illustrated in table-1. It is observed that the majority of them belonged to the 3rd decade among females and a decade older in males. Table-2, shows presentation of the patients where it is seen that, besides diarrhoea, many lower and upper gastro-intestinal symptoms are present. Weight loss and abnormal sigmoidoscopic pictures with his-

tological changes of rectal mucosa are seen in nine patients with mild ulcerative colitis. Response to treatment was achieved in 83% of the series (table-3). However, relapses took place in one third of the patients when followed for 4 months, but again responded to fresh courses of honey. It is of great interest that ulcerative colitis group showed marked improvement, not only clinical but also sigmoidoscopic and histological pictures that went back to normal at the end of the follow-up period (table-4).

DISCUSSION

The results of this study showed that honey regimen was effective in managing Chronic non-specific diarrhoea. The patients included in this series were related mostly to the gastro-intestinal disease called "the irritable bowel syndrome."[5,6]

However, nine patients were suffering from non-specific ulcerative colitis who showed a good response to honey regimen. In a previous study, we employed honey rectal enemata for treating ulcerative colitis patients. Nevertheless, our success was limited and we face difficulties over the matter.[4] Now it is pretty evident that the oral honey is very useful in this group. The present series is small and we shall take the matter further to include large number of cases so that our conclusions will be sound.

It is observed that other symptoms, including psychological ones, had been improved and those who manifested loss had regained their losses. The patients who relapsed have responded to a fresh course of honey. They are feeling well relieved and happy because, for months and even years they used to receive repeated courses of anti-diarrhoeal, anti-amoebic, anti-cholenergic, anti-biotics and other drugs, either continuous or intermittent with none or poor response. They were subjected to toxic and side-effects of such chemotherapy. In addition, they suffered the heavy cost of medicine and economical losses because of repeated sick leaves spending them miserably at home. On the other hand, honey is delicious, cheap, nutritious, easily available, safe and which carries no side effects.[7]

It is not clear how the honey works in diarrhoea. It is known that honey contains 40% dextrose. It also has bacteriostatic property.[7] It also modifies the secretory functions of alimentary tract and for sure it reduces gastric Hcl secretion and perhaps inhibits gastric and other intestinal hormones. Consequently, the motility of the gut may be modified towards the regulation of bowel habit. However, we feel that this study should be extended to include the patho-physiology of diarrhoea and identify the role of honey in its control.

TABLE — 1

PATIENTS: AGE & SEX

Age Group	Female	Male	Total
Under 20 years	4	—	4
Under 20-30 years	13	5	18
Under 31-40 years	8	11	19
Over 40 years	5	7	12
TOTAL	**30**	**23**	**53**

TABLE — 2
PRESENTATION

Symptoms and Signs	Female	Male	Total & %
Diarrhoea	30	23	53 (100%)
Diffuse abd. pain	20] 28	9] 17	45 (85%)
Localised abd. pain	8]	8]	
Flatulence	19	12	31 (58.9%)
Distension	16	7	23 (43%)
Anal irritation	15	7	22 (41%)
Nausea & vomiting	13	4	17 (32%)
Weight loss	4	3	7 (13%)
Abd. Sigmoidoscopy	5	6	11 (20%)
Abn. rectal biopsy	7	8	15 (28%)

TABLE — 3
REPONSE TO THE TREATMENT

Response	Patients		Total	And %
	Female	Male		
Good	15	13	28	(53%)
Moderate	10	6	16	(30%)
Poor	5	4	9	(17%)
TOTAL	**30**	**23**	**53**	**(100%)**

TABLE — 4
FOLLOW-UP (4-Ms.)

Response	Patients		Total	And %
	Female	Male		
Relapse	4	5	9	(17%)
Intermittence	5	2	7	(13%)
Abn. Sigmoidoscopy - 2 out of 7 Abd. rectal biopsy - 2 out of 11				

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USE OF HONEY IN THE TREATMENT OF CHRONIC BILHARZIAL ULCER BLADDER

(Preliminary Study)

Dr. Fahim Abdel Rahim, Dr. Farouk Al-Gyoshi and Mr. M. Mansour Al-Kinani.

EGYPT

INTRODUCTION

God said in the Holy Quran[1] in Sorat al-Nahl (Bees) paragraph 68 & 69 what means:

> *GOD HAS SENT A HOLY MESSAGE TO BEES TO MAKE USE OF THE MOUNTAINS, TREES AND SPREADING FRUITS AND GO THROUGH ALL THE ROUTES THAT GOD HAS FACILITATED. OUT OF THEIR BELLIES GETS A SYRUP (HONEY) IN DIFFERENT COLOURS; IT GIVES CURE TO PEOPLE. IN THIS, THERE IS A VIRTUAL EXAMPLE TO THINKING PEOPLE.*

The Holy Quran paragraph and many of the Sayings of the prophet Mohamed (ﷺ) explain the benefits of honey. As an example of the Prophet sayings in this respect:

> *"Take these two curatives: honey and the Quran."* [6]

Also, His sayings in this respect:

> *" That who takes honey thrice a month will not contract a severe illness."*[6]

He (ﷺ) also said:

> *" Cure is in three: drink of honey, wet cupping and cautery and I do not recommend the latter."*

Going along the religious program in al-Azhar Faculty of Medicine and bearing in mind the prevalence of urinary bilharziasis amongst the Egyptian farmers, we suggested this work. Ulcers of the bladder are common complications or urinary bilharziasis. We tried the use of Honey in the treatment of chronic bilharzial bladder ulcers.

REVIEW OF LITERATURE:

In Egypt, we get three types of Honey: Honey of citreons (Oranges & Lemons), Honey of clover, Honey of cotton.[4]

Honey is usually collected twice a year in June and in August or September. In the citreon rich fields a third collection can be got in April.

Composition of Honey:

Water	17.7%
Fructose	40.5%
Sucrose	1.9%
Glucose	34.02%
Minerals, Acids & unidentified	4.2%

It contains also vitamins as B_1, B_6, C, K, E, etc. It includes enzymes as Diastase, Invertase, Catalase, Peroxidase, etc... Minerals in honey include Calcium, Sodium, Potassium, Magnesium, Iron, Phosphorus, Sulfur, Iodine and Radium in certain types. Antibiotics, Antiviruses and cytotostatics[3,8] have been identified in it.

Therapeutic use of Honey:

Since very long times honey has been widely used in the treatment of many diseases and wounds. Hippocrates[12] used it since 2500 years for treating wounds as also did Avicenna,[13] D. Antaky,[5] Ibn al--Bitar[2] and others. M. Pollman[14] dressed wounds with honey and observed rapid healing. This is attributed to the privileges of honey:

a) Bactericidal due to its hygroscopic action.

b) The dressing remains wet and does not stick to the growing granulation tissue.

c) It is nontoxic and nonirritant.

d) It contains glucose, fructose, vitamin and minerals essential for rapid regeneration of tissues.

Y. Krentsky[15] ascribed the rapid healing of wide wounds after application of honey to the increase production of glutathione in the tissues. Glutathione stimulates oxidation and hence activates cell growth and multiplication.

In urology, honey has been used widely since long times by al-Samarkandi[4] and Ibn al-Nafis.[7] Avicenna[13] used it with some herbs in treating bladder ulcers. Nafis[7] applied it with barley for treating bladder swelling. Rhaziz,[16] Antaky[5] and others[17] combined it with other medicines to control urinary calculi.

Honey is used also for diseases of the gastrointestinal tract, skin, eye, heart, blood, respiration, psychoneurosis and intoxications.

MATERIAL AND METHODS

Eighty patients with chronic bilharzial bladder ulcers were selected from al-Azhar University Hospital's outpatients.They underwent these investigations:

- History and clinical examination.
- Urinalysis, culture and sensitivity both before and after the treatment.
- Cystoscopic examination of the bladder with detailed description of any changes, site, size and shape of the ulcer. This was repeated after completing the course of treatment.
- Radiographic examination of urinary tract: Plain and in certain cases I.V.U.
- A course of antibilharzial treatment (antimony compound) I.M. was given to every patient before the trial.

Then the patients were divided into groups:

Group I : 50 patients, each was given one table-spoonful (15 ml.) of Honey (80% in water) orally daily for two months. 40 m. of Honey (50% in sterile water) were instilled into the bladder through a catheter twice per week. The patients were instructed to keep the solution in the bladder for two hours.

Group II : 10 patients of whom were found to have urinary bacterial infection, were given antibiotics according to the urine culture and sensitivity, a full course for 10 days and then a suppressive dose for 50 days.

Group III: (Control): 20 patients had a tablespoonful of 50% sucrose in water orally daily for two months. 40 ml. of normal saline 0.9 % was instilled in the bladder and kept for two hours, twice weekly for two months.

RESULTS

The cases, selected, included 71 men from 20 to 39 years old and 9 females, 18 - 32 years old.

Most patients were complaining of the usual symptoms of cystitis as burning micturition, referred pains and of frequency of micturition.

Clinical examination showed suprapubic tenderness in 12 cases and on the prostate and bladder base in 28 cases.

Sign of fibrosis in the spermatic cord were detected in four patients.

Urinalysis: The constituents were within normal except an excess in R. B. C. in 64% of cases and excess W. B. C. in 48%.

Urine culture: At the onset of treatment 59 cases (74 %) had sterile urine and 26% showed significant bacteriurio (Bacterial counts more than 10).[6] Organisms found included:

Organisms	No. of cases
E. coli	15
Staphylococci	5
Ps. aeruginosa	1

Cystoscopy: All cases showed chronic bilharzial cystitis with one or more chronic bilharzial ulcers.

Urography: was performed for 33 patients. 21 cases showed bilharzial calcification of the bladder and lower ureters. One had a small stone in the left kidney.

I.V.U.: showed dilatation in the lower ureters in 7 cases (5 unilateral and 2 bilateral).

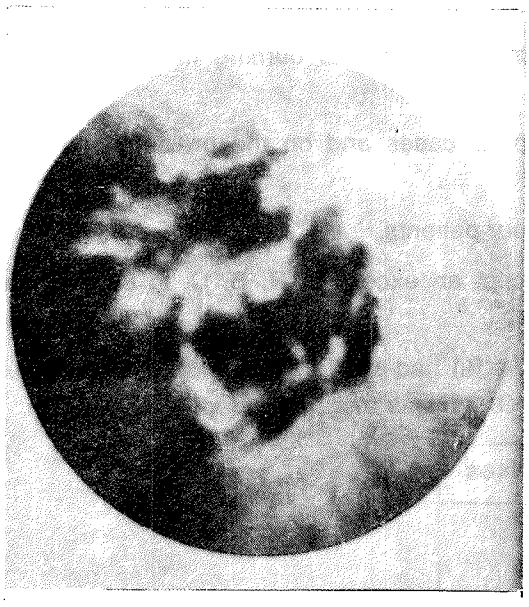
FOLLOW-UP:

Group I : The use of honey caused improvement of the condition of the patients and ameliorated their symptoms in a large number of cases.

Table I

Complaint	Before Treatment	After Treatment	Percentage Improved
Burning micturition	50	22	56%
Post-mictur. pain	44	16	63%
Suprapubic pain	20	8	60%
Perineal pain	10	—	100%
Urethral pain	8	—	100%
Frequency (extreme $\frac{20}{10}$)	16	6	62%
Frequency (moderate $\frac{10}{6}$)	26	14	46%

The ratio of R.B.C. and W.B.C. in the urine dropped in most cases.



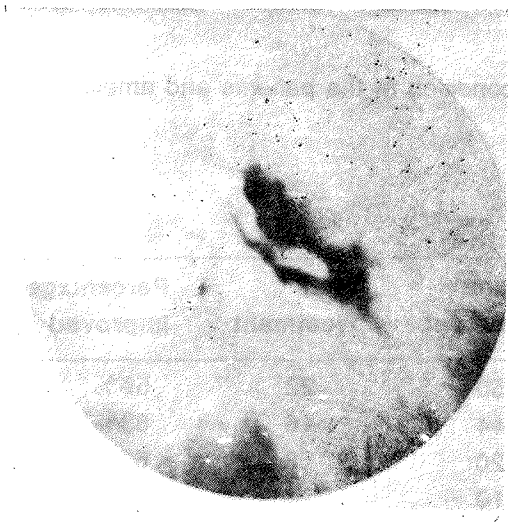


Table II

No. of Cells.	No. of cases before trt.	Cases Cured	percentage
R.B.C.: 100 H.P.F.	4	4	100%
10-100	28	12	43 %
W.B.C.: 100 H.P.F.	4	4	100%
10-100	20	8	40%

N.B. Some of the severe cases changed to moderate.

This group included 16 patients with positive urine culture. After treatment 10 of these including one with pyocyaneus showed sterile culture. But two cases who had sterile culture before treatment developed staphylococci positive cultures after treatment.

Cystoscopy showed marked improvement in 43 out of 50 cases and 28 ulcers healed completely. Fig. 1 & 2. Table III

Table III

Cystoscopy	Before Trt.	Healed	% of healing
Chr. superficial U.B.	50	28	56%

Group II : (Cases receiving antibiotics) included 10 cases of whom 5 had positive urine cultures. They received: chloramphenicol 3, cephalosporin 2, according to culture and sensitivity and sulfamethoxazole for the sterile cases, 5. At the end of treatment, 2 cases improved and showed drop in the number of W.B.C. in the urine, but not to the normal level. In 3 cases cystoscopy showed improvement in the bladder musosa but the ulcers remained the same, only one ulcer was reduced in size.

Group III: (Control) One of 20 cases showed symptomatic improvement for some time, but later these were exacerbated and the R.B.C. and W.B.C. in urine did not change, except in two improving cases. In one case in which symptoms became distressing. W.B.C. in the urine increased.

Cystoscopy: We found the same picture in 17 cases. In one case the size of the ulcer increased and in two cases it became less.

DISCUSSION

God said in the Holy Quran what means:

IN IT (HONEY) THERE IS CURE TO PEOPLE.

These Holy words did not specify the disease or diseases and laid freedom to human thinking and experimentation in this respect. Also from the words of prophet Mohamed (ﷺ) and following the

routes of the old moslem scientists we carried out this work to treat a common disease in Egyptians.

many moslem authors[2,4,5,7, & 10] mentioned the value of Honey in treating ulcers of the stomach and duodenum. Samarkandi[4] used it for bladder ulcers, oral or through the urethra. Nafis[7] used honey with barley water for bladder swellings. It has been used in old times and recently as antibacterial and antiviral agent and for dressings of wounds, burns and abscesses. Polman[14] ascribed its value to its hygroscopic properties and that its dressings do not stick to the wound and remains moist protecting the growing tissues.

There is a good ratio of the constituents of honey of unidentified nature. It contains biological substances, vitamins, hormones, enzymes and cell activators.

In Egypt and in some other countries due to bilharzial infection patients develop ulcer of the bladder. Chronic bilharzial bladder ulceration is a disabling disease. It results from fibrosis and ischemia of the submucosal tissues which lead to necrosis of the mucosa and ulceration.

The effective treatment for these ulcers up till now is surgical excision of the ulcer and the surrounding part of the whole thickness of the bladder wall.

In our department two groups of research workers tried two drugs for these ulcers:

1. Prostaglandins PGF_2x and PGE_2 (18) and
2. Honey

The first drug gave encouraging results but the rate of cure did not reach that attained with honey which has biological and cell activator properties.

Using honey orally and intravesically for two months resulted in improvement of the patient's complaints and disappearance of some symptoms as burning micturition in 56%, urethral and perineal pain in 100% of cases. The ratio of R. B. C. in the urine (sign of ulcer activity) dropped. Also the pyuria improved and bacteria disappeared from 62% of cases in spite of the use of urethral catheterization twice weekly, for the drug instillation.

Cystoscopy showed improvement in most cases and complete healing of the ulcers in 56%. This is a rather high ratio if evaluated against the relatively short period of drug application. If a longer trial is made we may get better results. There are as well other bilharzial complications as bladder neck stenosis or ureteric strictures which may be responsible for persistence of some symptoms.

The use of antibiotics in chronic bilharzial ulcers of the bladder did reduce some of the symptoms due to the associated secondary infection but could not give cure of the ulcers. The preliminary use of antibilharzial treatment did not markedly affect the course of chronic ulcers. The improvement was marked with the use of honey.

CONCLUSIONS & RECOMMENDATIONS

Honey is one of the natural drugs which prove valuable in the treatment of many diseases.

In this work, honey was used both orally and intravesically for the treatment of chronic bilharzial bladder ulcers in a group of patients.

Two other control groups were compared. The results showed honey to be effective in ameliorating pains and in the healing of a good percentage of cases.

We suggest giving honey more chances in managing this disease and other. It is also advisable to use it for longer periods. Critical chemical analysis to define the effective constituents of honey is welcome.

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A CLINICAL STUDY OF THE TOPICAL USE OF BEE HONEY IN THE TREATMENT OF SOME OCULAR DISEASES

Dr. Mohamed H. Emarah

EGYPT

The author got the idea of using honey in the treatment of some external ocular diseases from Sourat el-Nahl in the Holy Quran:

> *AND THY GOD INSPIRED THE BEES, TO BUILD CELLS IN HILLS, ON TREES AND IN HABITATIONS, THEN TO EAT THE NECTAR OF FLOWERS OF FRUITS, AND FIND WITH SKILL THE SPACIOUS PATHS OF THY GOD: THERE ISSUES FROM WITHIN THEIR BODIES, A DRINK OF VARYING COLOURS, WHEREIN IS HEALING FOR MANKIND: VERILY IN THIS IS A SIGN FOR THOSE WHO GIVE THOUGHT*
>
> (S.16: V.68,69)

The author employed honey, for the first time clinically, in the treatment of a patient who presented with dense post-herpetic corneal stromal reaction. The patient named (A.A.) was a male, aged 30 years, who had a recurrent dendritic corneal ulcer with intense stromal reaction. The patient had four previous recurrences. In the last recurrent, the cornea was erroneously treated by the local instillation of cortico--steroid drops prescribed by a local doctor to suppress the stromal antigen-antibody reaction. Later, the patient was sent to me for consultation and on examination a large amaeboid corneal ulcer in a fairly white eye was found (Fig.1). The patient was then advised to stop immediately all local steroids and was asked to commence with specific antiviral therapy, I.D.U. drops hourly during the day, and Vidarabine ointment at night in addition to ancillary treatment in the form of atropine drops q.i.d., pad and bandage (Emarah, 1978). After 15 days complete re-epithelialization of the cornea occured and no staining with fluorescein could be demonstrated (Fig.2.) In spite of this effective conventional therapy, the patient's visual acuity did not substantially improve because of the dense stromal reaction. This situation was very critical because the topical use of corticosteroids which is known to suppress the viral antigen-antibody reaction in the corneal stroma will inevitably enhance virus replication in the corneal epithelium making the condition very much worse, while the delay in resolving the stromal reaction will result in permanent corneal damage through scar tissue formation.

This led the author to prescribe Bee Honey topically twice daily to test its efficacy in such critical situations.

The repeated ocular examinations once weekly revealed definite resolution of most of the stromal reaction within six weeks (Fig.3).

This fascinating result encouraged the author to conduct a clinical study to find out the efficacy of the topical use of Bee Honey in the treatment of external ocular problems.

MATERIAL AND METHODS

Selection of Patients:

Patients presenting, at the University Hospital or my private consultation office, with an external ocular trouble were examined clinically in a systematic fashion. All positive findings necessary to make the diagnosis on clinical grounds recorded. All patients with external ocular inflammations had a swab taken from the conjunctival sac and sent to laboratory for culture and sensitivity test to available antibiotics. Epithelial scrapping was also done in selected cases to assist the diagnosis.

After making the final diagnosis based on clinical observations and laboratory investigations, the appropriate conventional line of treatment was recommended for each patient . Patients who did not

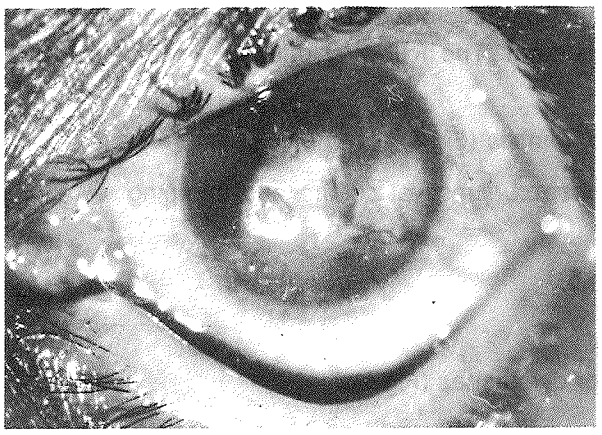

Fig.1

Large Amaeboid Herpetic Corneal Ulcer.

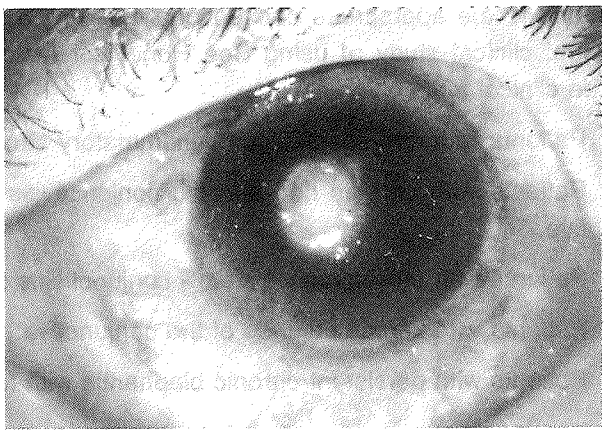

Fig.2

Post-herpetic Corneal scarring fifteen days after treatment.

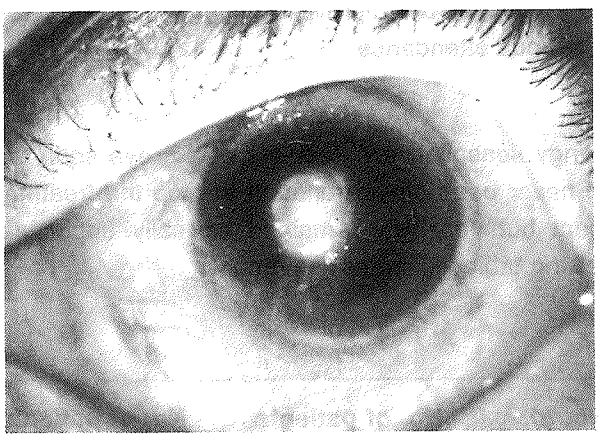

Fig.3

Post-herpetic Corneal scarring six weeks after treatment showing resolution of the Stromal reaction

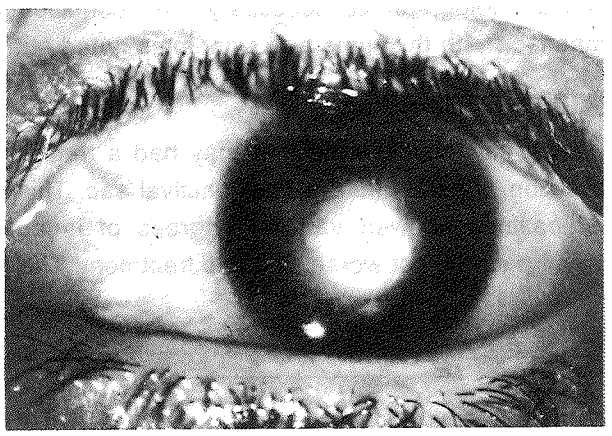

Fig.4

Non-specific Post - inflammatory Stromal Keratitis

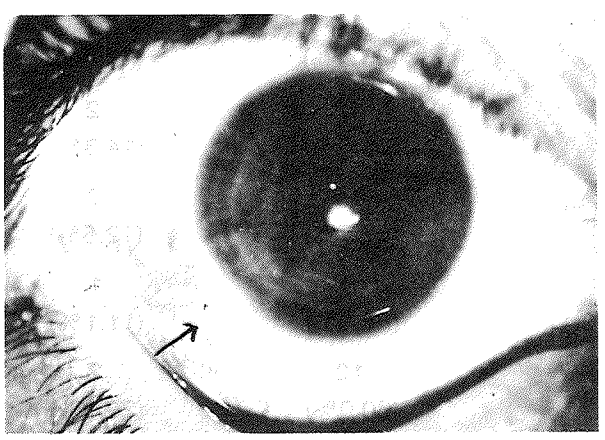

Fig.5

Phyctenular Keratoconjunctivitis the arraw points to the site of the Phlycten.

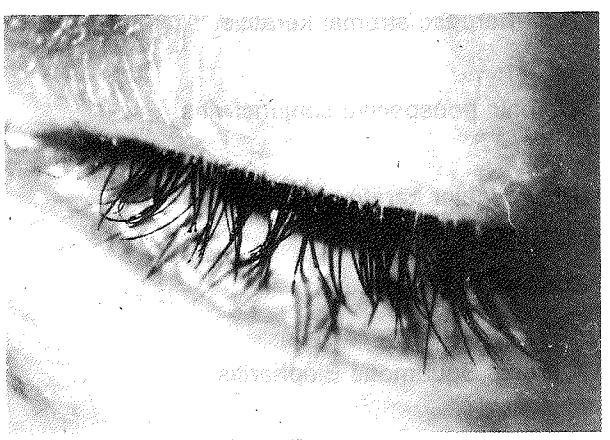

Fig. 6

Squamous Blepharitis showing scales at the root of the lashes.

respond to the appropriate conventional therapy, e.g. post-herpetic stromal keratitis, were admitted to the present clinical study of using Bee Honey for their treatment. The following patients were also included in the clinical trial:

1. Patients with non-specific post inflammatory stromal keratitis (Fig.4) .
2. Patients with chronic non-specific conjunctivitis whose conjunctival culture and scraping were negative.
3. Patients with phlyctenular kerato - conjunctivitis (Fig.5).
4. Patients with xerotic patches of the conjunctiva.
5. Patients with persistent chronic blepharitis with fall of eye lashes (Fig.6).

Method of Application

Pure oriental Bee honey was applied with a glass rod into the inferior conjunctival fornix, just like any eye ointment, 2-3 times daily depending on the ocular condition. The patient was reviewed once weekly recording all the signs and symptoms of the ocular condition, in addition to drawing a sketch or taking a photograph as necessary. The condition was judged to be improved, unchanged or worse in comparison with the signs and symptoms noted at the previous attendance.

RESULTS

Most patients reported that they had a transient stingy sensation and redness of the eye soon after application of honey into the conjunctival sac. This had never been severe enough to stop the treatment. Most patients showed variable degrees of improvement but very few remained clinically unchanged. None of patients got worse with this treatment. The following table illustrates the results.

Ocular Conditions Treated	Total No. of Patients	No. of patients improved	No. of patients unchanged
Non-specific stromal keratitis	30	26 (86.7%)	4 (13.3%)
Post-herpetic stromal keratitis	18	15 (83.3%)	3 (16.4%)
Chronic nonspecific conjunctivitis	14	12 (85.7%)	2 (14.3%)
Phlyctenular kerato-conjunctivitis	16	14 (87.5%)	2 (12.5%)
Xerosis of conjunctiva	9	8 (88.9%)	1 (11.1%)
Chronic Squamous Blepharitis	15	12 (80.0%)	3 (20.0%)

DISCUSSION

Honey is the sweet viscid yellow fluid, the nectar of flowers collected by Bees. The results obtained in the present study after the topical use of Bee Honey in the treatment of some external ocular dis-

eases are indeed very encouraging.

The mode of action of Bee Honey in the resolution of the afore-mentioned external ocular conditions is very intriguing. One may speculate that the hyperaemia induced by the irritant effect of Honey flushes the affected area with non-specific antibodies combating the diseases process. Also, Bee Honey may contain some enzymes which activate the specific and non-specific body defensive mechanisms to protect itself against the undue harmful effects of the invading micro-organisms. This mode of action will obviously have no dangerous side effects on the human body and will not induce any iatrogenic disorder. These speculations, being based on purely clinical observations, may require some laboratory biochemical and pathological confirmatory evidences. The biochemical assays may take years and years of painstaking research work before one discovers, if God wills, the actual active ingredients in Bee Honey, the unique Holy medicine.

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SOME PHARMACOLOGICAL PROPERTIES OF SOME CONSTITUENTS OF NIGELLA SATIVA L SEEDS: THE CARBONYL FRACTION OF THE ESSENTIAL OIL

Dr. Mohamed El-Dakhakhany

EGYPT

The carbonyl fraction of the essential oil of *Nigella sativa L.* seeds was shown to be effective in protecting Guinea pigs against histamine induced bronchospasm. It possessed very low toxicity; there was no effect on heart or blood pressure. It diminished the effect of histamine on the isolated bronchial muscle and ileum of the Guinea pig. It also counteracted the stimulatory effect of adrenaline on the isolated rabbit uterus. This fraction possessed also a uricosuric activity when tried in rats. It also possessed a choleretic activity increasing the flow of bile with an increase in total solids in dogs.

Nigella sativa L. is an annual of the Ranunculacea herbaceous plant growing in countries bordering on the Mediterranean Sea. The seeds and oil have been used since centuries for the treatment of different diseases by most of the common people. It has been reported that Prophet Mohamed (ﷺ) said:

"The black seed is a remedy for every disease except death".

It has been also reported in David's Prescription that the seeds can cure some chest diseases, cough, respiratory oppression, nausea, ascites, as a diuretic, as an anthelmintic, as a preservative for food and for many other purposes. These uses were later assured by some European authors e.g.Mattiolus and Bock [1] .

Mahfouz and El-Dakhakhany [2] isolated a crystalline active principle from the essential oil of *Nigella Sativa L.* which was proved later to be the dimer of thymoquinone [3] . El-Dakhakhany found later [4] that the carbonyl fraction isolated from the volatile oil was polythymoquinone and it possessed lower toxicity than thymoquinone itself. So it was thought to study some of the pharmacological actions of polythymoquinone i.e. toxicity, uricosuric activity, choleretic activity and protective action against histamine induced bronchospasm in order to reach a drug with low toxicity.

EXPERIMENTAL

The pharmacological investigations carried out were: toxic tests, uricosuric activity, choleretic activity, protective action against histamine-induced bronchospasm and anti-inflammation effect.

The carbonyl fraction (polythymoquinone) used was the one isolated from the carboxylic acid fraction of the volatile oil of Nigella Sativa L. seeds by Girard reagent [2] . Thymoquinone itself-used sometimes for comparison was isolated from the essential oil of *Nigella Sativa L.* seeds by the use of silica gel column chromatography [3] .

1. *Toxicity tests:* Male rats, weighing from 250-300 grams were used. The carbonyl fraction and thymoquinone were injected intraperitoneally dissolved in propylene glycol in doses varying from 5 mg.up to 160 mg./kg. body weight. The mortality rate of the rats were recorded against a control group which received only same amount of propylene glycol and was kept under the same condition. The LD_{50} was then obtained using the same method described by Gaddum [5] .
2. *Uricosuric activity:* This was studied on male rats, 250-300 in weight. Every two rats were placed in a metabolic cage. Food given was milk and bread. The urine was collected every 24 hours and uric acid was determined colormetrically by the method of Benedict and Frank [6] . The uric acid in urine was recorded as mg. uric acid per day per cage. After establishing an average starting level for uric

acid excretion over a period of 12 days, the drug under investigation was intramuscularly injected (4mg./kg. body weight in propylene glycol) for succesive five days. Each drug was given to 20 rats. Control experiments were also carried out where the animals were only in with 0.2ml. of propylene glycol.

3. *Choleretic activity:* Dogs weighing 10-14kg. were used. After initial anaesthesia with ether, barbitone sodium was given (0.22 gm./kg. , body weight) intravenously through the femoral vein. An upper median abdominal incision was made and the liver, gall bladder, common bile duct, cystic duct and hepatic duct were exposed. The cystic duct was tied to exclude completely the gall bladder. The common bile duct was then ligated just before entering the duodenum and L. cannula was introduced so as to collect all the bile coming from the liver, through the hepatic duct. Bile was collected in special containers every 30 minutes, the volume was recorded and total solids were determined.

   Bile was collected at first during a period of 2-3 hours which represented normal secretion. The carbonyl fraction or thymoquinone was then slowly intravenously administered followed by a small volume of warm saline (about 5ml.). Control experiments were carried out, only propylene glycol was injected. For each drug about 10 dogs were done.

4. *Protective action against histamine induced bronchospasm:* Guinea pigs (200-250 grams) were chosen to be of the same sex and same body weight. The carbonyl fraction and thymoquinone were intraperitoneally injected (in propylene glycol) in different groups of animals. After about 2 hours, the animals together with controls (receiving only propylene glycol) were placed in a glass container and exposed to histamine mist (0.25% sol. of histamine acid phosphate sprayed under a pressure of 0.5 kg./sq.cm). The time elapsing before the onset of dyspnoic convulsions was taken as a measure for the degree of protection imparted by the drug administered. When 10 minutes passed without the animal showing obvious signs, this was considered as complete protection.

5. *Anti-inflammatory effect:* This was carried out according to Selye [7] . To each group of 10 rats (about 200 grams weight) a cotton piece was inserted under the skin to act as a foreign body. A daily dose of the carbonyl fraction and thymoquinone of 5mg/kg body weight was administered intramuscularly for seven days. Control experiments were carried out where the rats received only propylene glycol and in another group the rats received a daily dose of a standard anti-inflammatory agent namely 5mg./kg. body weight of prednisone. The granuloma formation was determined in all the rats by weighing the cotton pellet.

RESULTS AND DISCUSSION

The toxicity tests showed that LD_{50} of the carbonyl fraction is 150mg/kg. body weight and is far less than that of thymoquinone itself which is 10 mg./kg. body weight.

The carbonyl was found to possess a favourable uricosuric activity (Table I). In some rats the uric acid excretion was doubled during the first days of treatment followed by a steep decrease which dropped sometimes below normal. The maximum uric acid excretion brought about by the carbonyl fraction was on the third day of treatment (Table II). The drug was only injected for five days, as in previous experiments [4] , it was shown that the uric acid excretion dropped below normal despite administration of the drug. This can be accounted for by the limited stores of uric acid in rats. However, the uric acid level in urine started to return gradually to normal levels after stopping the drug during few days. The uricosuric activity of the carbonyl fraction was almost the same as that of thymoquinone (Table I, II), but the carbonyl fraction, far less toxic, may favour its use as a uricosuric drug.

The carbonyl fraction and thymoquinone possessed also a choleretic activity, but thymoquinone was found to be active in this respect. Both of them caused an increase in volume and total solid of the bile (Table III). It was found that the increase in volume of bile persisted for several hours while that of total

solids was only for 1-2 hours and was maximal during the first 30 minutes after i.v. injection of both drugs. In the control experiments, it was observed that the collected bile was gradually less in volume and total solids. The total solids were approximately halved after about 6 hours. It was also noted, that the increase in volume and total solids after administration of the carbonyl fraction or thymoquinone was more obvious in dogs with low control bile volume and total solids i.e. in cases of hypofunction. In comparison to sodium taurocholate, it was previously found [8] that its effect started immediately after i.v. injection, reached maximum secretion in about 15 minutes and continued for a period of less than one hour.

The carbonyl fraction and thymoquinone protected Guinea-pigs against histamine induced bronchospasm (Table IV), yet a higher dose of thymoquinone was required to impart this protective action. Consequently, all the Guinea-pigs receiving thymoquinone died few hours after the experiment. The mechanism of this action is not yet fully clear although a direct action on the bronchial muscle has been previously proposed [9]. Mahfouz et al [10] observed an increase in the histaminopexic power in sera of asthmatic patients after treatment with the carbonyl fraction. An anti - inflammatory effect was not possessed by both drugs as the "granuloma-pouch" experiments showed that the drugs did not diminish the weight of the pellet than those of the control group.

Although the carbonyl fraction (polythymoquinone) and thymoquinone are close in structure, yet they differed to some extent in their pharmacological properties; thymoquinone being sometimes more active but always more toxic. Polymerisation of thymoquinone with subsequent separation of the carbonyl fraction lowered to a great extent the toxicity of thymoquinone without appreciable loss of activity.

The carbonyl fraction may prove to be of favourable therapeutic value in cases of hepatic insufficiency, gout and in some cases of bronchial asthma. Preliminary reports are encouraging assuring the use of the carbonyl fraction for the above-mentioned conditions; it was used in very low dosage i.e. 6-10mcg/kg. body weight daily without showing any side effects even for long term therapy.

SUMMARY

The pharmacological properties of the carbonyl fraction (polythemoquinone) isolated from the volatile oil of Nigella sativa L.seeds were studied. It was found that it possessed a uricosuric, choleretic and protective activity against histamine induced bronchospasm. On the other hand, it was devoid from any anti - inflammatory activity and possessed very low toxicity than the parent substance thymoquinone. This supports its use for the many purposes, the Nigella Sativa L.seeds are reputed for by the common people, preferably without the other ingredients.

ACKNOWLEDGEMENTS

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TABLE I
URIC ACID EXCRETION DAILY BEFORE AND THREE DAYS AFTER I.M. ADMINISTRATION OF THE DRUG

DRUG	MEAN URIC ACID EXCRETED ± S. E. MG / CAGE / DAY		
	Before drug	3 days after drug	
Thymoquinone (4 mg/kg. bdy wt.) 20 rats	1.46 ± 0.02	2.4 ± 0.08	☆
Carbonyl fraction (polythymoquinone, 4mg / kg / bdy / wt.) 20 rats	1.4 ± 0.05	2.6 ± 0.07	☆
Control 20 rats	1.33 ± 0.05	1.25 ± 0.01	

☆ significant change.

TABLE III
EFFECT OF THE CARBONYL FRACTION AND THYMOQUINONE ON THE EXCRETION OF BILE IN DOGS (I.E. IMG/KG. WEIGHT)

DRUG	AVERAGE BILE EXECRETED IN 30 MINUTES ± S.E.				
	BEFORE DRUG		AFTER INJECTION OF DRUG 30 MINUTES		
	Vol. ml.	T.S. g	Vol. Ml.	T.S. g	
Thymoquinone (10 dogs)	1 ± 0.03	0.12 ± 0.01	2 ± 0.06	0.14 ± 0.02	☆
Carbonyl fract. (10 dogs)	1.6 ± 0.05	0.09 ± 0.015	2 ± 0.05	0.11 ± 0.01	☆
Control (5 dogs)	2.2 ± 0.10	0.11 ± 0.01	2 ± 0.04	0.093 ± 0.01	

TABLE II

URIC ACID EXCRETION IN RATS BEFORE, DURING AND AFTER INTRAMUSCULAR ADMINISTRATION OF THE DRUGS IN PROPYLENE GLYCOL

DRUG	AVERAGE URIC ACID (MG / CAGE / DAY)														
	BEFORE TREATMENT					DURING TREATMENT					AFTER TREATMENT				
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
Thymoquinone 4 mg./kg. bdy. wt.	1.4	1.6	1.5	1.4	1.4	1.5	2.8	2.4	2.3	1.8	1.4	1.5	0.9	0.95	1.0
Carbonyl Fraction 4 mg./kg. bdy wt.	1.6	1.4	1.5	1.3	1.2	2.1	2.4	2.6	2.2	1.8	1.6	0.7	0.58	0.25	0.7
Control 0.1 ml propylene glycol.	1.6	1.5	1.3	1.0	1.25	1.5	1.55	1.25	0.88	1.25	1.0	0.88	0.75	1.0	1.35

TABLE IV

THE EFFECT ON INHALATION OF HISTAMINE MIST[1] ON GUINEA PIGS RECEVING AN I.P. INJECTION OF THYMOQUINONE, THE CARBONYL FRACTION. CONTROL ANIMALS WERE INJECTED WITH PROPYLENE GLYCOL. (0.1 ml.)

No. of Experiment.	TIME (IN MINUTES AND SECONDS) ELAPSING BEFORE THE ONSET OF CONVULSIONS		
	Control Animals	Thymoquinone 80 mg./kg	Carbonyl Fraction 50 mg./kg.
1.	1'20''	C.P.[2,3]	C.P.
2.	1'10''	C.P.	C.P.
3.	55''	C.P.	C.P.
4.	1'08''	7 45''	C.P.
5.	1'07''	C.P.	C.P.
6.	1'0''	C.P.	C.P.
7.	1'12''	C.P.	6'30''
8.	1'05''	C.P.	C.P.
9.	1'17''	C.P.	C.P.
10.	1'05''	C.P.	C.P.
11.	1'08''	C.P.	C.P.
12.	1'	C.P.	C.P.
13.	1'07''	C.P.	C.P.
14.	1'12''	C.P.	C.P.
15.	1'17''	C.P.	C.P.

(1) 0.25% aqueous histamine acid phosphate; sprayed under a pressure of 0.5 Kg/sq. cm.

(2) C.P. complete protection, i.e. no obvious signs in 10 mins.

(3) all animals injected with thymoquinone died in the course of few hours.

FASTING IN ISLAM - MEDICAL ASPECTS

Dr. Hassam Gareeboo

MAURITIUS

O YOU WHO BELIEVE! FASTING IS PRESCRIBED TO YOU AS IT WAS PRESCRIBED TO THOSE BEFORE YOU THAT YOU MAY LEARN SELF--RESTRAINT.

(Quran S.2: V.183)

God has ordered us to fast between sunrise and sunset for one lunar month every year. This is one of the five pillars of Islam.

BUT IF ANY OF YOU IS ILL, OR ON A JOURNEY THE PRESCRIBED NUMBER SHOULD BE MADE UP FROM DAYS LATER.

(Quran S.2: V.184)

God tells us that if we are ill, it is not compulsory for us to fast during the month of Ramadhan. Of course, should one recovers one's health, one should fast to make up the number of days that one has not fasted during that month.

The word "ILL" may be rather vague; it can be anything from a mild headache to a widespread cancer in a dying patient. There is no doubt that fasting can be a contra-indication for certain illnesses; there are however, other illnesses where fasting may be therapeutic. In this paper, I hope to go through extensively these 2 categories of illnesses. But first of all, let us consider the physiology of fasting.

All the organs in the body must necessarily participate in the physiological changes that occur during fasting. However, we will consider the important ones:

1. *Metabolic:* - (a) Carbohydrate Metabolism: For homeostasis, the blood glucose must at all times be kept above a certain level i.e. above 80 mg %. In fasting, after the carbohydrate absorbed from the G.I. tract has been used up, metabolically, the blood glucose is maintained by glycogenolysis i.e. glycogen stored in the liver is metabolized and converted to Glucose by the Pathway: - Glycogen --- Glucose 6 phosphate -- Glucose.

It is essential that the blood glucose be maintained above 80mg% otherwise the clinical signs of hypoglycaemia sets in. An organ like the brain does not metabolize anything but glucose for its energy supply and hense any drop in blood sugar will affect adversely the proper functioning of the brain. This mobilization of glycogen in the liver is set off by the liberation of certain hormones like Adrenaline mainly but also the corticosteroids. The glucose liberated by this process is passed into the blood to maintain the level of blood glucose above 80mg%.

Glycogen is also present in muscles. This glycogen will also be metabolized in physically active people who are fasting. During the breakdown of glycogen in muscles, glucose cannot be formed because of lack of glucose 6 phosphatase in muscles. However energy can be generated by metabolism of stored glycogen by muscles. In vigorous physiological activity, anaerobic glycolysis occurs and lactic acid is produced. This escapes in the blood and is converted into glucose and glycogen by the liver.

Liver in a 70kgm. man stores about 100gm. of glycogen, which can provide the glucose requirement of his tissues for about 6 hours. Total amount of glucose in blood is only 5gm.

After the glycogen depot have been exhausted, gluconeogenesis takes place for the production of glucose from non carbohydrate sources especially from animo acids.

In fasting, once the glycogen stores in muscles are depleted, the muscles will start using stored fat as a source of energy. In people who are very active physically and who are fasting, metabolism of fat

to produce energy and gluconeogenesis must take place.

(b) Fat Metabolism: Fat is obtained from dietary sources and from fat depot. It is hydrolysed to glycerol and long chain fatty acids in the liver. Glycerol is metabolised to glucose and long chain fatty acids to Acetyl CO A and Carbondioxide and water. Some ketone bodies are produced and this can be metabolized by certain tissues. Ketosis, of course, can be dangerous in certain diseases where acidosis is already present e.g. uncontrolled diabetes mellitus, renal failure etc.

In summary, the metabolic changes during fasting include glycogen mobilization from liver depot, glycogen metabolism in muscles, fat oxidation, to provide energy, with some resulting ketosis and gluconeogenesis from aminoacid that are antiketogenic or glucogenic. These metabolic changes are already taking place at a very slow rate in normal non-fasting people. Fasting merely accelerates and increases the magnitude of the reagents in these re-actions. This metabolic overhaul during fasting serves to sharpen the body's re-actions to any forms of stress. It is a form of spring cleaning of our metabolism.

2. *Gastro Intestinal:* - During fasting there is a slowing down of the movements of the gut on the one hand and on the other very little gastric, intestinal and pancreatic secretions are produced. With the slowing down of the alimentary tract, there is an increased daily rest for the gastro-intestinal tract. As rest is an important physiological necessity, this increased rest for the gastro intestinal tract must therefore be beneficial to the human body.

All the gastro intestinal secretions must also decrease in amount as for a longer period every day, there will be no food in the upper alimentary tract. This is so because (a) the cephalic phase of salivary and gastric secretions will be decreased if one fasts with true spiritual fervour so that one does not give thought to food when one is fasting. (b) The other phase of secretion in the alimentary tract depends upon the presence of food in the alimentary tract and obviously this will be decreased in relation to fasting as there will, after some time, be no food in the upper alimentary tract. Decreased secretions of the alimentary canal again allow the glands concerned to have an increased period of rest every day.

3. *Cardiac:* - 10% of the cardiac output goes to the alimentary tract during digestion and there is a tremendous decrease of this part of the cardiac output when there is no digestion during fasting. This decrease in the cardiac output means less work for the heart and consequently some degree of rest.

On the Metabolic side, because of the slight risk of Ketosis, any disease where this is likely to be harmful it is prudent not to fast, e.g. diabetics who are ketotic, or who are taking biguanide antidiabetics (because of the risk of lactic acidosis), patients with chronic renal failure. Also in this particular condition a plentiful and constant supply of fluid is required to maintain an adequate urine flow and fasting by decreasing the fluid intake will aggravate renal failure. Any other conditions where increased fluid intake is required e.g. recurrent renal calculi, pyelonephritis, diabetes insipidus etc. are contra-indications to fasting.

On the positive side, obese people may find fasting a helpful step towards slimming as long as they do not overeat for Iftar or Suhur. Also the practice of fasting will help them to get used to eating less even when they are not fasting. Diabetics who are well controlled on Insulin may find it difficult to fast because of the risk of hypoglycaemia. However, 2 doses of soluble Insulin before Suhur and Iftar may be quite satisfactory for their diabetic control. Of course, diabetic patients who are well controlled on oral hypoglycaemic drugs will be able to fast as long as they avoid the biguanides as hypoglycaemic agents.

In gastro-intestinal diseases, gastritis is the disease, par excellence, which is helped by fasting, again as long as the patient with gastritis who fasts, does not undo the good work by indulging in excessive intake of food or in food prohibited for these patients when they break their fast.

Patients with duodenal ulcers may be harmed by fasting as they require regular meals to help the

ulcers to heal. Patients with chronic acute diarrhoeal diseases or diseases where vomiting occurs should refrain from fasting as the risk of dehydration is always present if adequate fluid intake is not observed.

Fasting and rest can do tremendous good to patients with cardiac disease. Of course, if the patient is seriously ill or needs constant medication during the day, then fasting is forbidden. There is a decrease in the frequencies of their chest pain while fasting and that is because there is a decrease of 10% of the cardiac output during fasting.

Patients who are ill enough to be admitted to hospital or who need medication either oral or injection during the day should refrain from fasting.

As far as psychiatric illnesses are concerned, most if not all of the so called neurotic illnesses are relieved by fasting. The idea of fasting apart from the spiritual aspect, is the total abstinence from every physical necessity of life viz. food, drink and sex. Consequently, by regulating the physical necessities of our body to a sub-conscious level, the mind automatically has to be exercised in the active control of the body so that the pangs of hunger and thirst are not agonizing.

Now, the neurotic illnesses that give rise to physical symptoms, the so called psychosomatic illness would be relieved, if fasting permits the patient's mind to exert a positive control over his body. If the person who fasts does so with religious fervour then the other neurotic psychiatric illnesses e.g. depression, anxiety and mania can be relieved by fasting. This is achieved by the observation that fasting has a streamlining effect on the ruffled mind. The disturbed state of mind in the psychiatric illnesses mentioned above is soothed and the mood is elevated.

Migraine is one of those illnesses where fasting may seem to be a contra-indication but in fact it may be therapeutic. A number of patients with migraine get acute attacks if they fast. These patients are usually obsessional characters who develop anxiety symptoms if something is not right and they strive very hard to set it right. In fasting the pain of hunger is not right sub-consciously for them because they know that it can be relieved by eating. However, patients with migraine can fast and derive benefit from it if they do it in the right way. Hunger can stop being a trigger for their migraine if they learn to relax and accept the pain of hunger as a normal physiological fact and not try to fight it.

People who indulge in cigarette smoking and want to give it up will find fasting a good training ground for this exercise. The abstinence from smoking between sunrise and sunset will be enough to produce mild withdrawal effects from this particular craving. In time, during the month of Ramadhan, the craving can become very weak and will enable to smoker to give it up completely.

Pregnant mothers are advised not to fast because the increased metabolic demands from the foetus may produce ketosis which is obviously deleterious to the foetus. Lactating women will find that their milk supply will be decreased during fasting especially in hot weather and the baby will necessarily have to suffer from this insufficient supply of milk. Women who are menstruating or who have post partum lochia should not fast as they are considered unclean from the Islamic point of view. In the Quran it is said.

> *THEY ASK THEE CONCERNING WOMEN'S COURSES. SAY: THEY ARE A HURT AND A POLLUTION.*
>
> (S.2: V.222)

Postponement of menstruation in women during the month of Ramadhan is not unlawful (by the use of drugs).

In this paper I have considered the physical and mental benefits accuring from fasting. The spiritual bonus is beyond the scope of this paper. But it must be borne in mind that we fast because by doing so we are obeying the commands of God and not primarily to derive any physical or mental benefit from it. God in his wisdom has deemed it necessary for us to fast and therefore we accept this blindly but God

also tells us that it is good for us:

FAST-IT IS BETTER FOR YOU, IF ONLY YOU KNOW

(Quran S.2: V.184)

May be with modern knowledge we have now a faint idea as to why "IT IS BETTER FOR US TO FAST".

THE EXPRESSION OF DERMATOGLYPHICS AND ITS ROLE IN THE ISLAMIC MEDICINE

Dr. Abdulbari Bener

SAUDI ARABIA

INTRODUCTION

The inheritance of dermal patterns originally has been found and utilized by Francis Galton (1882). The scientific classification of dermatoglyphic patterns, palms, and fingertips was formulated by Francis Galton (1882) in his classic work on Finger Prints. In fact, there is some indication concerning finger prints in the Quran before Francis Galton.

بلى قادرين على أن نسوي بنانه

NAY, WE ARE ABLE TO PUT TOGETHER IN PERFECT ORDER THE VERY TIPS OF HIS FINGERS.

(S. 75 - V 4)

Recent studies on the inheritance of dermatoglyphic patterns of fingertips, palms and soles notably by Bener (1978, 1979, 1980a, 1980b. 1980c. 1980d) have proposed a number of chromosomal genes that control the development of pattern form on specific digit and on sequences of digit. It has not been possible thus to determine whether intrinsic non-chromosomal factors, such as the cytoplasm, may also play a role in the specification of pattern.

The science of finger prints developed in human genetics to the art of medical diagnosis for unraveling the precise nature of developmental and chromosomal disorders, and the scientist with an authoritative interpretation of the quantitative genetics of dermatoglyphics in normal populations.

We still do not know how the patterns formed by the dermal ridges on fingers, palms, and soles and toes are inherited, but in the past twenty years advances have been made in our knowledge of the genetics of other features of ridged skin. This has come about largely in two ways: from studies of quantitiative traits, particularly in families, and more recently from comparative studies of the dermal prints of persons with chromosomal aberrations, those of their relatives and control populations. During the past few years there has been increased interest in dermatoglyphics, deriving from the growth in fundamental research on fingerprint and allied features on palms and soles. The subject is beginning to play an increasingly important role in human genetics, largely due to its value in the study of chromosomal aberrations.

The hand has great diagnostic value in bedside medicine only to be enriched now by clinical dermatoglyphics. The finger prints and ridge counts measure resemblance between twins in the determinations of twin zygosity; the hands of newborns detect latent neurological abnormalities; and the hands of children reveal characteristic patterns of chromosomal anomalies and congenital defects since the factors that determine the growth of the hands and feet at the time of ridge formation produce dermatoglyphic distortion. Dermal patterns are grouped into three major types despite their great diversity but pattern combinations and frequencies are more significant than pattern types. Gross distortion of the dermal pattern can occur in association with malformations of the limbs whether genetic or nongenetic in origin. The flexion creases, the heart, head and life lines of palmistry are not dermal ridges but are formed at the same time during the third fetal month, and effect the course of the dermal ridges. Clearly, flexion creases may themselves be determined by the same forces that effect ridge alignment.

CHARACTERISTICS OF DERMAL RIDGES

Dermal ridges have various notable characteristics which make them important, not only for personal identification, but also in human biology.

1. Unlike most human traits, dermal ridges and the configurations formed by them are not affected developmentally by age.
2. Throughout post-natal life they are not affected by environment.
3. The detailed structures of individual ridges are extremely variable.
4. Although the patterns formed by the ridges vary in size, shape and detailed structure, they can be classified into several main types.

Ridge differentiation takes place in the foetus during the third and fourth months of foetal life. The initial stage begins when the hand is about 3.5 mm in length and is completed when it is approximately 15.6 mm long. After this time there seems to be no change in pattern during the period of intrauterine growth. Secondary ridges which sometimes occur, are not formed, however, until the fifth and sixth foetal months. The dermal papilae develop during the seventh pre-natal month, by which time the epidermal ridges are complete in every respect.

From birth throughout life and indeed until decomposition of the skin takes place after death, no developmental changes occur either in the detailed structure of the ridges or in the ridge patterns. The only changes are those in size, the growth of the ridges keeping pace with the growth of hands and feet Environmental factors can only have effect in the uterus during the period of ridge formation Scars, resulting from injuries, can be formed at any time, but are easily recognised.

As dermal ridge arrangements are determined in early foetal life, they supply records of growth disturbances taking place at this time. It is now well established that such disturbances cause modifications of the ridge arrangements palmar patterns in particular are sensitive indicators of developmental anomalies. Moreover, it is known that ridge configurations show significant distortion in cases where chromosomal abnormalities are present.

METHODS OF RECORDING DERMATOGLYPHICS

A number of methods for recording dermatoglyphics exist. The methods vary in their requirements for equipment, time and experience and in the quality of the prints produced.

Dermatoglyphic patterns are usually recognizable by the naked eye. A simple magnifying lens, preferably with a light source such as is found in an otoscope, helps greatly in scanning dermatoglyphics, especially in infants and small children whose pattern are very fine. The scan alone often gives the investigator sufficient data for most medical purposes but permanent impressions or prints are necessary for quantitative analysis of dermatoglyphics.

A- *Standard Methods:*

The methods described in the following section have been designed primarily to obtain prints of ridged skin for dermatoglyphic analysis. All methods described here are relatively easy to use, rapid, and inexpensive. However, the methods vary somewhat in the quality of the prints obtained. Any of these printing techniques may become a method of choice of an individual investigator, based on his preference of the features that each method offers.

1. Ink Methods.
2. Inkless Methods
3. Transparent Adhesive Tape Method
4. Photographic Method

B- *Special Methods:*

The methods listed below are not widely used to obtain dermatoglyphic prints. However, there may be some advantages that the standard methods can not offer, such as allowing the study of the correlation between the epidermal patterns and the underlying bone structures (radiodermatography), study of sweat pores (hydrophotography), or study of the special shape of the ridged skin areas (plastic mold method). These methods may be useful to the investigator interested in special, rather than standard, dermatoglyphic features.

1. Hydro-photography
2. Radio-dermatography
3. Plastic Mold
4. Automatic Pattern Recognition
5. Magma Brush Technique in Dermatoglyphic Research

APPLICATION TO DERMATOGLYPHICS DATA

Dermatoglyphics offer at least two major advantages as an aid to the diagnosis of medical disorders:

1. the epidermal ridge patterns on the hands and soles are fully developed at birth and thereafter, remain unchanged for life;
2. scanning of the ridge patterns or recording their permanent impressions (i.e., prints) can be accomplished rapidly, inexpensively, and without any trouble.

Our knowledge of the genetics of dermatoglyphics tests has increased considerably in recent years, yet, inspite of these advances, many problems still await solution, some of these concern the location of genes on the chromosomes, information on gene location can be obtained in two ways:

1. From linkage studies, and
2. from the analysis of the dermal prints of patients with aberrant chromosomes and those of their close relatives.

Widespread material interest in epidermal ridge formations by inspection of skin ridges, therefore, promised to provide a simple, inexpensive means for determining whether a given patient had a particular chromosome pattern repeat. It is possible to draw conclusions about ridge abnormalities in groups of patients. Unusual ridge configurations have been shown to exist not only in patients with chromosomal defects but also in patients with single gene disorders and in some in whom the genetic basis of the disorder is unclear.

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MENSTRUAL HYGIENE

AN EXPERIMENTAL STUDY CONCERNING QURANIC FACT AND THE JEWISH FALLACIES

Dr. Mohammed Abdel-Latif

EGYPT

INTRODUCTION

It would be expected that a cyclic phenomenon, such as menstruation, should have produced a vast store of folklore, fancies and superstitions mingled with few facts throughout the course of recorded history.

The age-old concept, held by Ancient Egyptians considered menstruation as a deliterious process and a woman during the flow to be unclean and toxic.*

Hippocrates, Galen and succeeding physicians of the middle ages elaborated the same idea, (Lawrence, 1943).[1]

The concept of uncleanliness and toxicity of a woman during menstruation was held by Jews. The old Jewish Law, so called Tawrah, provided for abstinence during menstruation or for 5 days whichever is the shorter) and for 7 days afterwards, making a total of 12 days in any one cycle. That consideration extends to every aspect either marital or otherwise. Any touch to the woman during that period or even using a utensil handled by her is prohibited. This old Jewish code did not differentiate, in its judgement, between menstruation and other types of vaginal bleeding.

Several authors, however, Guatier (1900)[2] and Bourcet (1900)[3], tried to find out inorganic poisons such as arsenic and iodine in the body excreta of menstruating women.

Macht (1943),[4] claimed that he had previously found in the sweat, saliva and circulating blood of menstruating women, a substance toxic to plant growth and the touch of a menstruating woman to vegetables caused their tilting and prevented their preservation.

Other investigators, (Smith and Smith; 1940-1950)[5-12], attributed the death of laboratory animals, after their injection with minimal doses of menstrual discharge , to the presence of a highly toxic euglobin, the so-called menotoxin, in that material.

It was proved later that those animals died from bacteraemia rather than toxaemia (Zondek; 1953).[13]

Arabs considered menstruation as a device and frustration of nature for the periodic excretion of accumulated harmful products and in a sense a method of purgation and elimination of toxins from the body of menstruating women. They used to call that woman:

١ ـ عارِكٌ ـ ٢ ـ فَارِكٌ ـ ٣ ـ دَارِسٌ ـ ٤ ـ كَابِرٌ ـ ٥ ـ طَامِسٌ ـ ٦ ـ طَامِثٌ ـ ٧ ـ ضَاحِكٌ ـ ٨ ـ حَائِضٌ .

With the exception of the latter, all these terms bear Arab's concept. The latter term is the one used by the Glorious Quran in the statement 222 from Albakarah, which says:

ويسألونك عن المحيض قل هو أذى فاعتزلوا النساء في المحيض ، ولا تقربوهن حتى يطهرن ،
فإذا تطهرن فاتوهن من حيث أمركم الله ، ان الله يحب التوابين ويحب المتطهرين .

THEY ASK THEE, CONCERNING WOMEN'S COURSES SAY: THEY ARE. A HURT AND A POLLUTION: SO KEEP AWAY FROM WOMEN, IN THEIR COURSES, AND DO NOT APPROACH THEM UNTIL THEY ARE CLEAN. BUT

★ They recorded; retardation in growth, and death, of implanted seeds, irrigated by water contaminated with menstrual blood when compared to seeds irrigated by pure water.

WHEN THEY HAVE PURIFIED THEMSELVES, YE MAY APPROACH THEM. IN ANY MANNER, TIME, OR PLACE.

ORDAINED FOR YOU BY GOD FOR GOD LOVES THOSE WHO TURN TO HIM CONSTANTLY AND HE LOVES THOSE WHO KEEP THEMSELVES PURE AND CLEAN.

(S2 : V222)

It is note-worthy to record that; when Jews at Medina, were informed by this statement they complained that "that man should never leave any one code of ours without its contradiction".

The term used by Quran, points to the "time", the "site" and, in the meantime, to the "act", warning that it is harmful. Thus the prohibition is limited to avoidance of coitus at that particular time of the flow.

The allowance for regaining marital relations is provided for, by complete cessation of the flow, then douching the vagina with clean water.

In Hadith, after Prophet Mohammed (ﷺ), douching the vagina is carried on thricely by clean water, then rubbing its walls by a piece of wool soaked in misk, from above downwards, tracing the direction of the blood flow.

In contrast to the Jewish Law, Islamic Religion differentiated between menstruation and vaginal bleeding due to any other cause, which has another judgement.

Coitus is the sole aspect which is prohibited, as ruled by the glorious Quran during menstrual flow. The acts of love, fantacies and fine behaviour towards a menstruating woman offered by the husband, are encouraged by Islam, rather than prohibited, as provided in the Jewish Law.

These items inferred that menstruation, from the Islamic point of view, is considered neither deliterious, nor toxic. Sound Islamic understanding may lead one to conclude that the problem of menstrual hygiene lies in the field of microbiology.

Jeffcoate (1967)[14] wrote: "In some countries, young girls are taught to douche the vagina at the end of each menstrual period. This again is a relic of the old idea of uncleanliness. Vaginal douching as a hygienic measure at the end of a period, or at any other time, is unnecessary and is potentially harmful in that it washes away the natural protective discharges".

He also wrote: "It is remarkable that this old code (Jewish code) provided for abstinence during what is now recognised as a safe period, and allowed resumption of marital relations at the optimum time for conception".

Jeffcoate added, "medical arguments against the practice of coitus during menstruation are that sexual excitement may cause uterine congestion and may increase the menstrual flow, and that the more vascular and friable vaginal walls may be injured. These are theoretical considerations of little practical significance. If there is chronic or latent infection in the genital tract of either male or female there is danger of causing salpingitis if coitus is practised during menstruation, but in a healthy couple there is no sound medical reason for advising against it. The only real objection is the obvious aesthetic one, and even this can be overcome if the woman first douches the vagina and then temporarily contains the uterine discharge by inserting "Dutch Cap".

AIM OF WORK

The prospective aim of this work is to find out sound scientific explanation for menstrual hygiene as extracted from Quranic fact and to throw light on the Jewish fallacies concerning the subject.

In order to reach this goal, the variations in the vaginal flora and pH, during the menstrual cycle are studied.

MATERIAL AND METHOD

In the present study, 27 nulliparous women and 23 multiparous ones, were examined and proved to be free, medically as well as gynaecologically. They used neither pills nor drugs, and were instructed not to experience coitus or vaginal douche 24 hours prior to their visit. They attended to the outpatient clinic at Galaa Maternity Hospital, Cairo, Egypt, in 4 visits, during the premenstrual, menstrual, post-menstrual and midmenstrual cycle.

In each visit, a mid-stream urinary sample, centrifuged and cultured for organisms, a lower vaginal swab, an upper one were taken and cultured on different media, the pH of the vagina was measured, a hanging drop for trichomonas and an endometrial specimen was taken, prepared, stained and examined for dating the phase. Bacterial count was performed for the specimens.

RESULTS

The results obtained from our work were recorded on a sheet titled "Vaginal Flora During the Menstrual Cycle". Then were tabled in 3 tables and were represented in 5 diagrammatic plates.

Table 1: Represents the incidence (No. of participants and percentage) of most important organisms encountered in the upper and lower vaginae of fifty women during the four phases of the menstrual cycle, with the pH of every phase.

Table 2: Represents the incidence (No. of participants and percentage) of most important organisms encountered in the upper and lower vaginae of twenty-seven nulliparous women during the four phases of the menstrual cycle, with the pH of every phase.

Table 3: Represents the incidence (No. of participants and percentage) of most important organisms encountered in the upper and lower vaginae of twenty-three multiparous women during the four phases of the menstrual cycle, with the pH of every phase.

PLATE I: Represents, diagramatically from above downwards, in the menstrual phase, concentration of glycogen (the nearer the vertical lines, the more is the concentration) and a curve showing the count of the organisms in relation to pH, phase of the cycle and dating.

PLATES II & III: Illustrate, diagramatically, the bacterial counts of the most important organisms encountered in the lower vaginae of women, in relation to; dating of the cycle, endometrial changes and glycogen concentration.

PLATES IV & V: Illustrate, diagramatically, the bacterial counts of the most important organisms, encountered in the upper vaginae of women, in relation to dating of the cycle, endometrial changes and glycogen concentration.

The results obtained from study are summed up in the following points:

1. A "Vaginal Flora Cycle" not independent from the ovarian hormonal cycle, was found to occur. The Lactobacillus acidophilus (safe-guard of the vagina) and the pathogenic organisms, go in asyncronous curves. During menstruation the pathogens prevail and were met with in immense numbers, meanwhile the lactobacillus was absent.
2. Pathogens, during menstruation, were met with in the lower vaginae, while the upper vaginae seemed to be almost sterile.
3. Other types of pathogens, rather than those already encountered in the vaginae of our participants, were met with during the menstrual phase. These came from the urethra anteriorly (B. Proteous) and from the anus posteriorly (B. Coli).
4. A non-pathogenic organism (Staph. Albus) was found (in some cases) to be reverted during menstruation to pathogenicity, so called staph. albus var aureous.

5. Trichomonas vaginalis was found to flourish and multiply during the menstrual phase. At that phase it was found to inhibit the fornices instead of the lower part of the vagina.
6. The incidence and bacterial counts, of pathogens were noticed to be more or less in nulliparous women, than in multiparous ones. Also the pH readings were more acidic in nulliparae than in multiparae. The reverse was met with as regards Lactobacilli.

VAGINAL FLORA DURING THE MENSTRUAL CYCLE

No. **Name:** **Age:** **Parity:**

Pre-menstrual phase

Lower vaginal swab:
Upper vaginal swab:
Urinary deposits:
Other techniques:
Hanging drop (Trichomonas):
Endometrial biopsy:

pH of the vagina:

Menstrual phase

Lower vaginal swab:
Upper vaginal swab:
Urinary deposits:
Other techniques:
Hanging drop (Trichomonas):
Endometrial biopsy:

pH of the vagina:

Post-menstrual phase

Lower vaginal swab:
Upper vaginal swab:
Urinary deposits:
Other techniques:
Hanging drop (Trichomonas):
Endometrial biopsy:

pH of the vagina:

Mid-menstrual phase

Lower vaginal swab:
Upper vaginal swab:
Urinary deposits:
Other techniques:
Hanging drop (Trichomonas):
Endometrial biopsy:

pH of the vagina:

Remarks:

	PRE-MENSTRUAL				MENSTRUAL				POST-MENSTRUAL				MID-MENSTRUAL			
PH.	PH: 4.6				PH: 7.1				PH: 4.3				PH: 4.3			
SITE.	U.V.		L.V.		U.V.		L.V.		U.V.		L.V.		U.V.		L.V.	
INCIDENCE	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
LACTO-BACILLI	48	96	42	96	7	14	9	18	50	100	50	100	50	100	50	100
E. COLI.	9	18	16	32	11	22	25	60	6	12	12	24	6	12	12	24
STR. FAECALIS	5	10	7	14	3	6	20	40	3	6	5	10	2	4	5	10
OTHER COLIFORM	7	14	9	18	1	2	11	22	5	10	8	16	6	12	7	14
STAPH. ALBUS.	5	10	7	14	1	2	9	18	4	8	6	12	3	6	6	12
NIESSERIAE.	0	0	1	2	0	0	2	4	0	0	1	2	0	0	1	2
MIMEAE.	0	0	3	6	1	2	5	10	0	0	2	4	1	2	2	4
PNEUMO-COCCI.	1	2	3	6	0	0	5	10	0	0	1	2	0	0	1	2
DIPHTHEROID	0	0	4	8	0	0	5	10	1	2	4	8	1	2	3	6
B. PROTEUS.	0	0	1	2	0	0	4	8	0	0	0	0	0	0	0	0
STR. HAEMOL.	1	2	2	4	0	0	3	6	0	0	1	2	0	0	1	2
STR. ANAER.	1	2	0	0	3	6	3	6	1	2	1	2	2	4	0	0
TRICHOMONAS	9	18	0	0	11	22	0	0	10	20	0	0	8	16	0	0
CANDIDA.	4	8	4	8	1	2	3	6	2	4	2	4	2	4	2	4
URINE (PROTEUS)	4— 8%				4— 8%				4— 8%				4— 8%			
STAPH. AUREUS.	0	0	1	2	0	0	3	6	0	0	2	4	0	0	2	4

TABLE I.

The incidence of Vaginal Flora encountered in the upper and Lower vaginae (U.V. & L.V.) of fifty Participants at 4 phases.

PHASE.	PRE-MENSTRUAL				MENSTRUAL				POST-MENSTRUAL				MID-MENSTRUAL			
PH.	PH: 4.3				PH: 7.1				PH: 4.1				PH: 4.1			
SITE	U.V.		L.V.		U.V.		L.V.		U.V.		L.V.		U.V.		L.V.	
INCIDENCE.	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
LACTOBACILLI.	26	96.29	26	96.29	5	18.52	7	25.92	27	100	27	100	27	100	27	100
E. COLI.	3	11.11	7	25.92	5	18.52	13	48.15	2	7.41	6	22.22	2	7.41	6	22.22
STR. FAECALIS.	2	7.41	3	11.11	1	3.760	9	33.33	1	3.70	2	7.41	0	0	2	7.41
OTHER COLIFORM.	3	11.11	4	14.81	0	0	5	18.52	2	7.41	3	11.11	3	11.11	3	11.11
STAPH. ALBUS.	2	7.41	3	11.11	0	0	4	14.81	1	3.70	2	7.41	1	3.70	2	7.41
STAPH. AUREUS.	0	0	0	0	0	0	1	3.70	0	0	1	3.70	0	0	1	3.70
NIESSERIAE.	0	0	0	0	0	0	1	3.70	0	0	0	0	0	0	0	0
MIMEAE.	0	0	1	3.70	0	0	2	7.41	0	0	1	3.70	0	0	1	3.70
PNEUMO-COC.	0	0	1	3.70	0	0	2	7.41	0	0	0	0	0	0	0	0
DIPHTHEROID	0	0	1	3.70	0	0	2	7.41	0	0	1	3.70	0	0	1	3.70
B. PROTEUS.	0	0	0	0	0	0	1	3.70	0	0	0	0	0	0	0	0
STREPT. HAEM.	0	0	1	3.70	0	0	1	3.70	0	0	0	0	0	0	0	0
STR. ANAEROBE	1	3.70	0	0	2	7.41	2	7.41	1	3.70	1	3.70	1	3.70	0	0
TRICHOMONAS	4	14.81	0	0	5	18.52	0	0	4	14.81	0	0	3	11.11	0	0
CANDIDA.	1	3.70	1	3.70	0	0	1	3.70	1	3.70	1	3.70	1	3.70	1	3.70

TABLE II.

U.V. = UPPER VAGINA, L.V. = LOWER VAGINA.

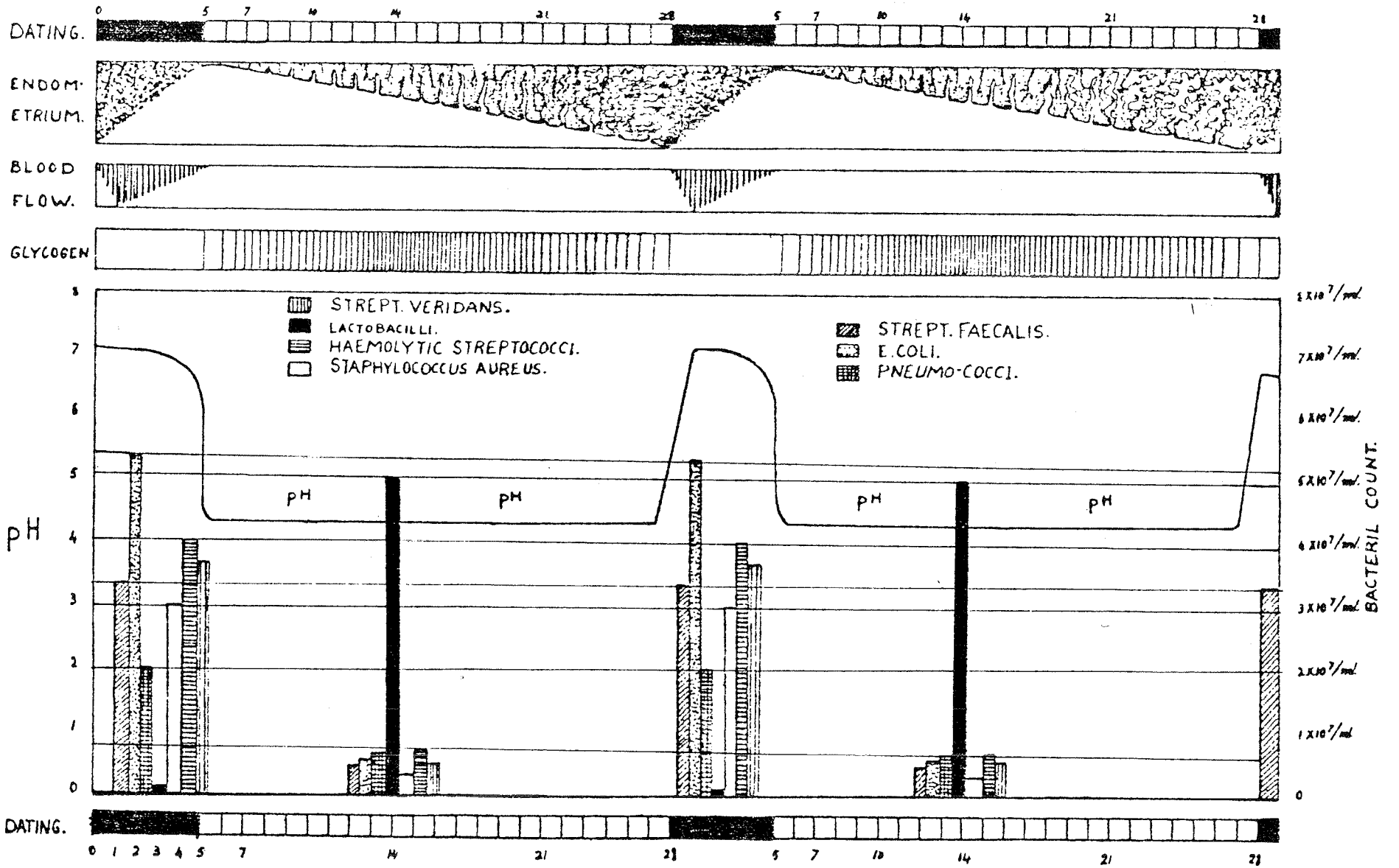
Vaginal Flora encountered in the vaginae of 27 nulliparae at the four phases of the menstrual cycle & their incidence.

PHASE.	PRE-MENSTRUAL				MENSTRUAL				POST-MENSTRUAL				MID-MENSTRUAL			
PH.	PH: 4.8				PH: 7.1				PH: 4.6				PH: 4.6			
SITE.	U.V.		L.V.		U.V.		L.V.		U.V.		L.V.		U.V.		L.V.	
INCIDENCE.	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
LACTO-BACILLI.	22	95.85	22	95.85	2	8.69	2	8.69	23	100	23	100	23	100	23	100
E. COLI.	6	26.08	9	39.13	6	26.08	12	52.17	4	17.39	6	26.08	4	17.39	6	26.03
STREPT. FAECAL.	3	13.04	4	17.39	2	8.69	11	47.83	2	8.69	3	13.04	2	8.69	3	13.04
OTHER COLIFORM	4	17.39	5	21.74	1	4.35	6	26.08	3	13.04	5	21.74	3	13.04	4	17.39
STAPH. ALBUS.	3	13.04	4	17.39	1	4.35	5	21.74	3	13.04	4	17.39	2	8.69	4	17.39
STAPH. AUREUS.	0	0	1	4.35	0	0	2	8.69	0	0	1	4.35	0	0	1	4.35
NIESSERIAE.	0	0	1	4.35	0	0	1	4.35	0	0	1	4.35	0	0	1	4.35
MIMEAE.	0	0	2	8.69	1	4.35	3	13.04	0	0	1	4.35	1	4.35	1	4.35
PNEUMO-cocci.	1	4.35	2	8.69	0	0	3	13.04	0	0	1	4.35	0	0	1	4.35
DIPHTHEROIDS.	0	0	3	13.04	0	0	3	13.04	1	4.35	3	13.04	1	4.35	2	8.69
B. PROTEUS.	0	0	1	4.35	0	0	3	13.04	0	0	0	0	0	0	0	0
STR. HAEMOLYT.	1	4.35	1	4.35	0	0	2	8.69	0	0	1	4.35	0	0	1	4.35
STR. ANAEROB.	0	0	0	0	1	4.35	1	4.35	0	0	0	0	1	4.35	0	0
TRICHOMONAS.	5	21.74	0	0	0	26.08	0	0	6	26.08	0	0	5	21.74	0	0
CANDIDA.	3	13.04	3	13.04	1	4.35	2	8.69	1	4.35	1	4.35	1	4.35	1	4.35

TABLE: III.

U.V. = UPPER VAGINA, L.V. = LOWER VAGINA.

Vaginal Flora encountered in the vaginae of 23 multiparae at the four phases of the menstrual cycle & their incidence.


DATING.
0 5 7 10 14 21 28 5 7 10 14 21 28
ENDOM-
ETRIUM.
BLOOD
FLOW.
GLYCOGEN
STREPT. VERIDANS.
LACTOBACILLI.
HAEMOLYTIC STREPTOCOCCI.
STAPHYLOCOCCUS AUREUS.
STREPT. FAECALIS.
E. COLI.
PNEUMO-COCCI.
pH
pH
pH
pH
pH
8
7
6
5
4
3
2
1
0
5X10⁷/ml.
7X10⁷/ml.
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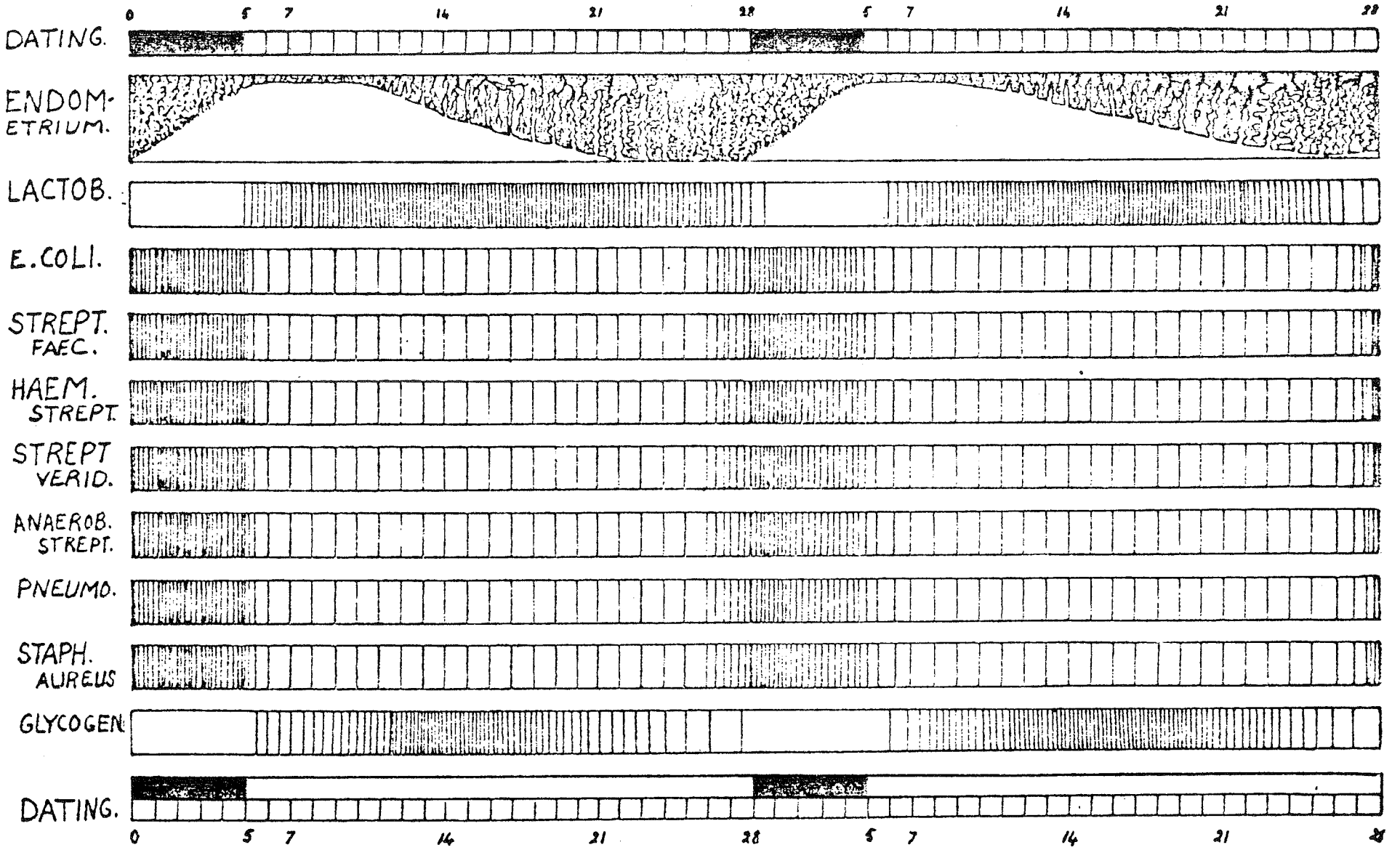
BACTERIL COUNT.
DATING.
0 1 2 3 4 5 7 14 21 28 5 7 10 14 21 28

PLATE I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STREPT.
STREPT
VERID.
ANAEROB.
STREPT.
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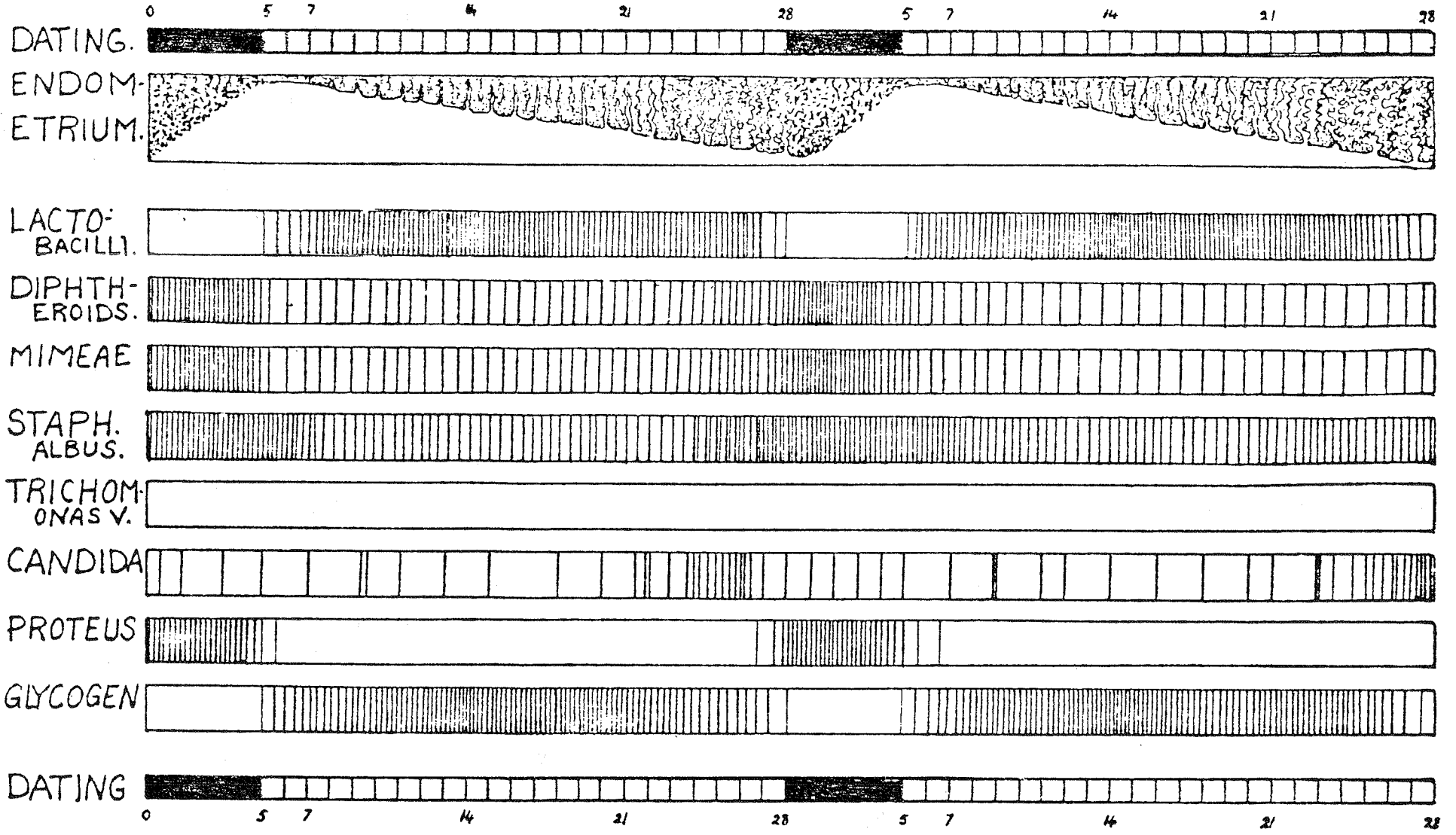
STAPH.
AUREUS
GLYCOGEN
DATING.
0 5 7 14 21 28 5 7 14 21 28

PLATE II.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ONAS V.
CANDIDA
PROTEUS
GLYCOGEN
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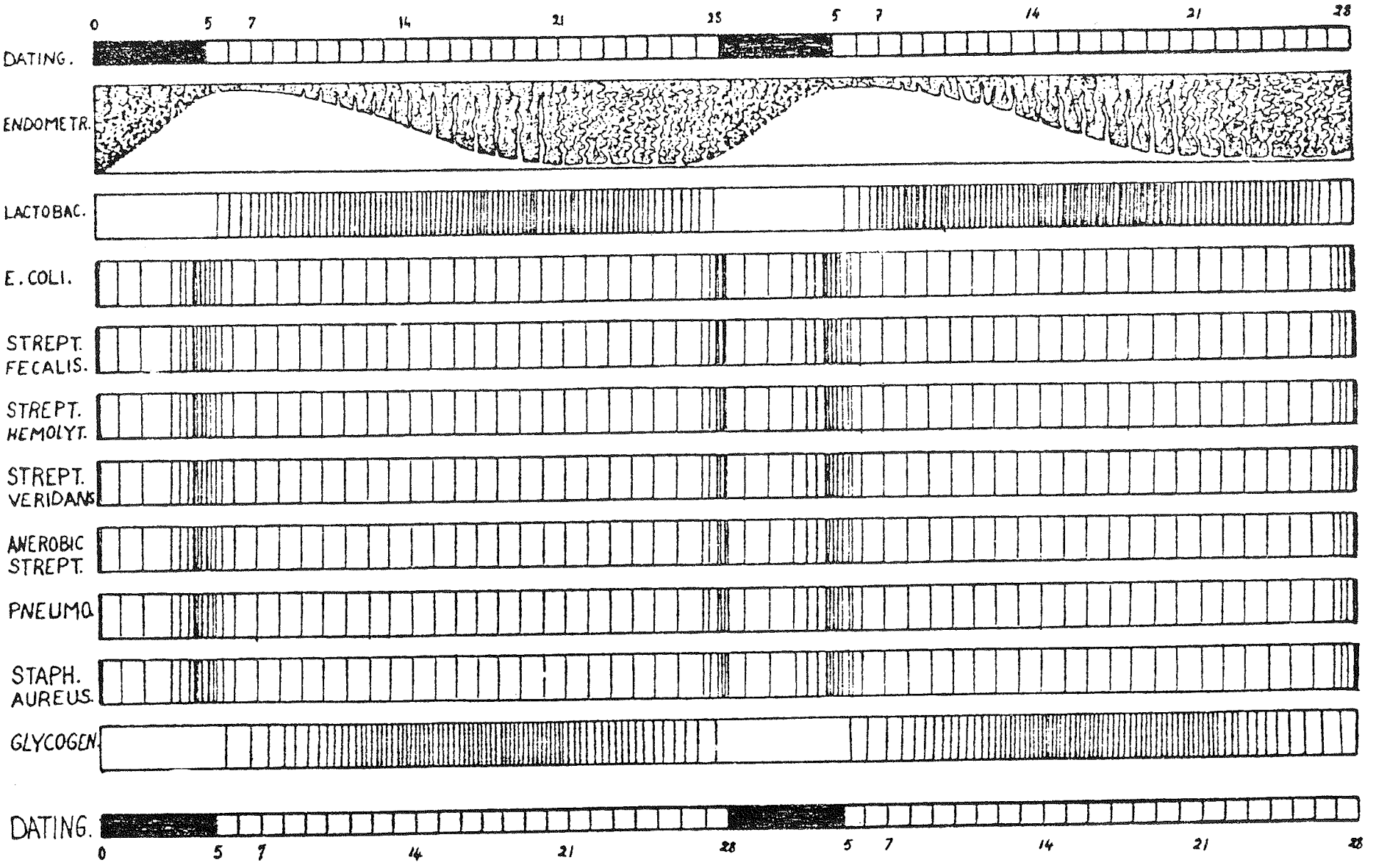
PLATE III.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LACTOBAC.
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STREPT. FECALIS.
STREPT. HEMOLYT.
STREPT. VERIDANS
ANEROBIC STREPT.
PNEUMO.
STAPH. AUREUS.
GLYCOGEN.
DATING.
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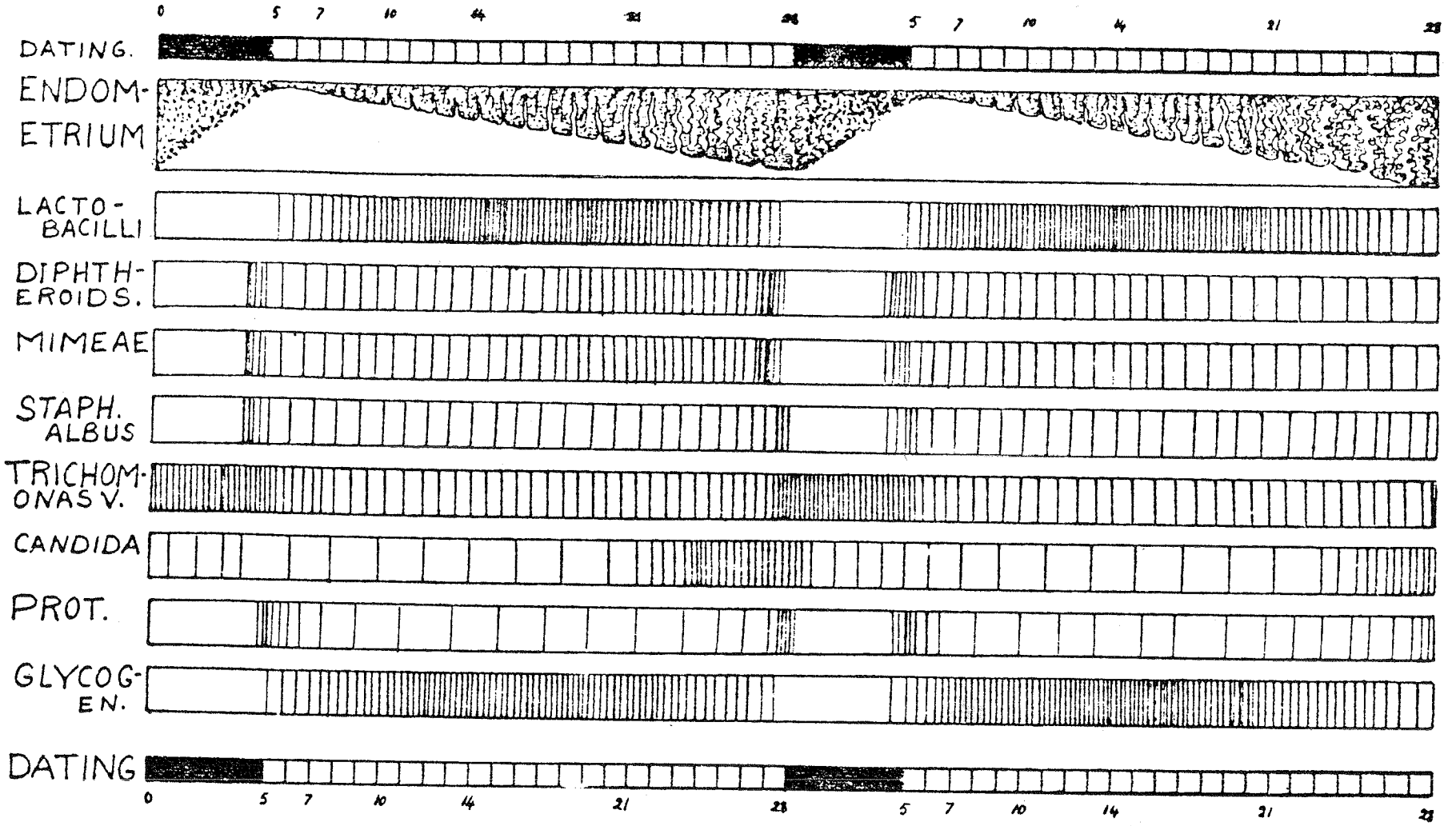
PLATE IV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EROIDS.
MIMEAE
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ALBUS
TRICHOM-
ONAS V.
CANDIDA
PROT.
GLYCOG-
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PLATE V

DISCUSSION

Although several scientists, the world over, have spent generations to prove the toxicity of menstruation and the uncleanliness of a menstruation woman, yet all their efforts have not reached a fruitful goal and in consequence the concept held by Jews was scientifically dropped almost completely.

Sound understanding to Quranic Fact and the selection of the term "Flow" rather than other terms, used by Arabs thereupon, together with items explained in Hadith after Prophet Mohammad (ﷺ) inferred that:

> *Neither menstruation is a toxic phenomenon, nor a menstruating woman is unclean.*

The prohibition, ruled by Quran is specified, and coitus is the sole aspect that is prohibited during the flow, inferring that, its harmful effects lie locally in the vagina.

The vagina is lined by stratified squamous epithelium, devoid of cilia, does not secrete and possess no peristaltic movements. The only defence mechanism of the vagina against bacterial invasion to the female genital system and to the peritoneal cavity, lies in the bacteriological balance.

The "safe-guard" of the vagina is the Lactobacillus acidophilus.* This organism possesses a bactericidal action through its production of lactic acid by fermenting glycogen impregnated inside the exfoliated vaginal epithelium cells. (Huvi, 1961)[15] and bacteriostatic action through inhibiting the growth of other patogens (Berger and Karovic, 1961).[16]

The vaginal mucosa and the ovarian function on one hand and the cytology of the vaginal smear, its glycogen content, and its concentration during the menstrual cycle on the other hand influence the growth of Lactobacilli and their flourishing (Eyer, 1961).[17]

The proliferation of vaginal epithelium reaches its peak at the mid-menstrual cycle (Sammour, 1963).[18] The glycogen content inside the cells, also reaches its peak at the ovulatory period at the mid-menstrual phase (Bamforth, 1950).[19]

Accordingly, at the mid-menstrual period, the glycogen containing cells are increased both in number and in their glycogen content, furnishing a good culture medium for the growth and multiplication of Lacto-bacilli; a fact prominently realised in this study, as regards the highest bacterial count ($5x10^7$/ml) its presence in 100% of our case, during that phase.

Immediately before the onset of the flow, and as a result of withdrawal of hormones, the glycogen diminishes, the activity of Lactobacillus ceases and it is attenuated. Instead of being harboured in 100% of our cases during the midmenstrual phase, it was found to be harboured in 96% in the premenstrual phase, and the count was found to be 3×10^7/ml.

With the onset of the flow the lactobacillus dies, as it cannot withstand the high alkalinity (pH 7.1) of the menstrual discharge, and with the establishment of the flow, the organism is scavengered, hence it was met with in 14% and 18% only, in the upper and lower vaginae respectively in this series. The higher incidence in the lower vagina is due to the current flow from above downwards. The bacterial count was found to be conclusive. In the cases harbouring the organism during the menstrual phase, bacterial count did not exceed 0.1×10^7/ ml, and even those cases were in the first day of the flow.

The pH readings were 4.3 in the post menstrual and mid-menstrual phases. Meanwhile, in the premenstrual phase it was found to be 4.6, due to diminution in count and activity of lactobacilli. With the onset of the flow, pH was found to be 7.1.

It was found that, the reverse to lactobacilli exactly occurs to pathogenic organisms. These were

* Doderlein, A. (1892) was the first to describe it, also called Doderleins bacillus.

encountered occasionally and in minute numbers in the lower vaginae of participants. Mean-while, the upper vaginae were almost sterile.

With the start of the flow, the pH reverts to alkalinity and the safe-guard is absent, they multiply, flourish, activate and invite others from their neighbourhoods (Coliforms from the anus and perineum posteriorly and B. Proteus (from the urethral meatus and vestibule anteriorly).

Strept. Faecalis was encountered in 40% during menstruation, instead of 10% before.

B. Proteus was met with only in the menstrual phase, in 8% of our cases, who were harbouring it in their urines.

During that time of flow, and as a result of withdrawal of hormones, the endometrium is denuded in several areas, its integrity is broken, the vagina and surrounding structures are fragile. The only natural barrier against bacterial invasion to these tissues; is the current flow of blood from above downwards, as was evidenced by comparing the upper vaginal specimens with the lower ones. The formers were nearly almost sterile.

Trichomonas vaginalis was found to flourish. Every one trichomonous gives four trichomona during the menstrual phase, and they creep to inhabit the fornices instead of the lower vagina.

At the end of the flow, the menstrual discharge ceases, the alkalinity is no longer encountered, the activity of pathogenic organisms diminish and they become attenuated. But there is no flow from above downwards to wash them, hence the indication of vaginal douching at the end of every period, to permit harbouring the lactobacilli again. Accordingly Jeffcoate's suggestions are fallacious, except for the point of douching the vagina at any time rather than after the period.

"A Vaginal Flora Cycle" was found to occur. The lactobacillus (safe-guard or policeman of the vagina) and pathogenic organisms go in asyncronous curves.

It appeared that marital relations if carried on during the flow, would be harmful for both the female by subjecting her friable pelvic tissues, at that particular time, to the invasion of pathogens and the liability of their spread to the endometrium, tubes and peritoneal cavity and for the male through exposing the penile urethra to catch the Trichomonas vaginalis harbouring the fornices, at that time, and waiting for this opportunity.

Jeffcoate* suggested that: "sexual intercourse at the time of menstruation is probably more frequent than is generally realised". This is not true. The common belief considers it dangerous, and there is no reason for uprooting the common belief (Curts and Hoffman, 1950).[20]

It appeared that; the two items provided by Quran for regaining marital relations after menstruation are, by far, the most sound hygienic principles, from the scientific point of view considering the "Vaginal Flora Cycle".

Marital relations are not postponed after that, as held by Jews, in order not to deprive a woman from her menstrual end peak sexual desire, (Undry 1969).[21]

No prohibition, by Quran, as held by Jews, for other sympathies of marital relations during that time, which are important to alleviate psychic depression accompanying the phenomenon.

The suggestion held by Jeffcoate that: "the Jewish law provided for abstinence during what is now recognised as a safe period, and allowed marital relations only at the optimum time for conception", does not hold for good. Hence the Jewish law did not differentiate, in its judgement, between menstruation and other vaginal bleedings, as ruled by Quran. Also it is known that ovulation may occur at any time, even during menstruation.

* The author of "Principles of Gynaecology", a text book studied by undergraduate and postgraduate medical students, the world over.

Applying the Jewish law to a menstruating woman, deprives her from her menstrual end-peak sexual desire and adds psychic troubles to those already accompanying the phenomenon, on no basis.

Needless to say that every woman should have a lesson in personal hygiene during her menstruation extracted from Quran and every husband must learn from Islamic items, how to treat his wife during that particular time.

CONCLUSION

The lesson extracted from Quran is, by far, the most sound scientific base, concerning menstrual hygiene.

The Jewish codes, are no more than old fallacies ideas inherited, perhaps, from ancient Egyptians.

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GENERAL DISCUSSION

Dr. Fouad Hifnawi,

In fact, following what has been said this morning in this meeting, I was tremendously happy, because we have started carrying out our experimental studies and this in itself is a good achievement of the goals of these kinds of Conferences. In the beginning, I thought that we will be merely confining ourselves to repetition and to what was done in the past and this, of course is not sufficient. To bring about the necessary revival in our scientific studies, a new phase of new, studies should be started, and new approaches should be decided upon, in view of creating new, modern physicians of the same calibre as, Ibn Sina and al-Zahrawi. I want to say here is, to keep our own Islamic traditions and at the same time to be wearing a modern hat that is using the modern innovations and its relevants.

Dr. Ahmed Shawky Al-Fangari,

I have a very brief observation regarding the speech of Dr. Hassam Gareeboo. He has said that fasting helps to reduce our weight and in fact, many people came to visit me and they told me that they gained weight during Ramadan and after which they find that they do not manage to lose weight during Ramadan. In fact, the reason is that, the 'Sunna', the tradition of Prophet (ﷺ) is not followed, because Jaber said that the Holy Prophet (ﷺ) when he started eating after the day's fasting, used to eat a few dates and there is a scientific reason for it. We all know that the sensation of hunger is not a function of having a full stomach or not, but depends upon the concentration of sugar in the blood. So, if we start eating after the day's fasting, normal diet, i.e. the grain or proteins and carbohydrate, vegetables etc., if we start with this kind of food, then we will not be feeling satiated, except after a long period, because all these proteins take a certain time to be changed to sugar, thus, increasing the concentration of the sugar in blood, but if we start by eating a sweet thing like dates, then it will be assimilated in very few moments, after 15 minutes and the percentage of glucose will increase in the blood. Thereby, he will not be feeling very hungry and we know that if we take sweets then we will not be eating much. The second point, that was mentioned by Dr. Hassam, was that fasting was a great opportunity to stop certain harmful habits, for health and he mentioned smoking. Of course, fasting gives an occasion to every one of us to avoid many harmful habits and addictions even the coffee addiction, alcohol & drug addiction. A man who wants repentance and wants to start a new life, can take advantage of Ramadan. That is, what I say to all of my patients, because for example the percentage of nicotine decreases during Ramadan and this is a problem faced by any smoker, because he can not stop smoking because his body, his organs are familiar now with a certain degree of nicotine and if he stops then he will be suffering from withdrawal side effects, but if he follows fasting, he fasts during the month, the percentage of nicotine will be lower by the end of the month of Ramadan and he will be, thereby able to overcome this and other harmful habits. A further point mentioned by Dr. Hassam, regarding the benefits of fasting, is a prevention against glycemia, because as we all know the degree of glucose decreases in the blood during the fasting month, this relaxes the pituitary glands, thereby enabling it to counter the overeating habits, because it can be very tight, I am talking about the glands and there by glycemia may start at this stage. These are some of the benefits of fasting, which I wanted to mention.

Dr. Abdul Muttalib,

I have a few comments about therapeutics as mentioned in the Holy Quran. In the Holy Quran, honey has been mentioned in general as medicine, without indicating disease. Spring water has been mentioned as treatment for skin diseases in connection with Prophet Ayyub. Allah ordered a plant of cucumber family to grow about Prophet Younus, which cured him from injuries inflicted on him by a crocodile or a fish when he was thrown from the ship. Allah swears by fig and olive: والتين والزيتون وطور سنين وهذا البلد الأمين The commentators have mentioned that figs and olives may be a

cure for kidney disease, liver disease and piles. There is a Hadith quoted by Bukhari 'Allah has sent no disease for which he sent no cure'. In the Holy Quran, there is a mention about leprosy in connection with Prophet Issa. He could cure leprosy, but how? It is not mentioned. Blindness is mentioned in connection with Prophet Issa and Prophet Yaquob. How could Prophet Issa cure the blindness, is not mentioned, but Prophet Yaquob was cured of blindness by throwing the shirt of his son, Prophet Yousuf, on his shoulder. Prophet Zakaria became dumb on hearing the news of a son to be born to his wife at a very advanced age, so he could not speak for three days. About deafness,the Holy Quran says, 'Then we drew a veil over their ears for 309 years in the cave, so that they could hear not', in Sura Ashab al-Kahaf (سورة أصحاب الكهف). Prophet Ibrahim and Zakaria and their wives did not bear any children till a very advanced age and then they got the message of having children and which is un-thinkable at our age. Prophet Moosa was stammering and he was cured by only praying. Madness is mentioned in the Holy Quran, on many occasions in connection with un-believers: « والذين في قلوبهم مرض فزادهم الله مرض »Sleeping sickness: The seven sleepers,i.e. Ashab al-Kahaf (أصحاب الكهف) went on sleeping for 800 years. The cause of their sleep and how their nutrition, hydration were maintained, is not mentioned in the Holy Quran.

Dr. A.R. Hijazi

I would like to say that what was said about the effects of honey did not convince me. First of all, I would not like you to believe that I am against these natural medicines or the application of Hadiths and Quran, in this field. But I think some objectivity is necessary to convince the listener. As far as honey is concerned, I would like to express the following points:-

First, Mr. Najam said that when he selected his patients, he looked for the reasons of diarrhoea and he looked for the microbes, i.e. the bacteria and then proceeded, etc. This is excellent but he did not mention anything about the reasons of the diarrhoea for which he used honey as a cure. I think that diarrhoea has several causes, that have not been mentioned by the speaker. And I am not going to speak in detail about this subject and I do not think that the internal medicine practitioners would say anything to the contrary. Fruther he knows that there are two kinds of honey. The flower honey and the tree honey and the two kinds of honey are different in structure (nature) but the honey which is sold in the market is a mixture, though is sold as pure honey. Third, he tried to explain how the honey stopped diarrhoea and what he said it was more of an assumption and not based on scientific basis. Now, I would like to end. The thing is that there is little objectivity in this field and then if you have more objectivity, you will be more convincing to the listeners and we will have better effects on Islamic Medicine. I would also like to refer to the remark made by Prof. Fouad Hifnawi. He said that medicine should have two head-dresses; Islamic turban and the modern hat and this really upset me, because we do not want to have a modern hat and the Islamic turban (العمة), but we want only one Islamic head-dress.

Dr. Zuhair Al-Baba,

As far as treatment with honey is concerned, being a chemist, I look at it from the chemist's point of view and pharmacological point of view. We know that honey changes its structure according to the plant on which the bees feed. We also have the normal honey and the honey of the queen bees. There is no doubt that there is a chemical structure and the chemical components of the honey are known. I wish that the lecturers who talked about treatment with honey had mentioned something about the preparation methods, they resorted to. Whether there was any difference in the sources of the honey and whether there was any difference in the concentration degree of the chemical and physical specification of the honey they used? The 2nd question, in fact, is a linguistic question. I wanted to put forward to the lecturer concerning the word (محيض) for menstruation, because we studied in the University of Damas-

cus and we used the word (طمث), which means menstruation and probably this is in the Arabic language only, because according to the speaker there is a difference between (الحائض) and (الطامث) in Arabic, which means menstruation, because there is a Sura also in this regard: لم يطمثهم انس قبلهم ولا جان May be (الطمث) is the end of the menstruation, (نهاية المحيض).

Dr. Omar Hasan Kasule

Mine is a brief comment. I was very pleased when I listened to the studies by the respected professors, talking about practical studies relating to Islamic Medicine. I would like to suggest, that we should co-ordinate these studies and carry them out in several centers and several Muslim countries. We have collaborative studies, so that several of our professors work on the same problem. Some people in Pakistan, some in Egypt, some in Kuwait. Let us say, for example, about the use of honey in treatment. Each of the investigators may take a small part of it, so that when we come to present it, it is really a complete picture and I think, the Islamic Medicine Organization, here can carry out the necessary co-ordination. I was really pleased. It gives us pride to see that such studies are carried out with such high academic excellence.

Dr. Francisco Guerra

I just want to point out that a book was published about 15 years ago in America dealing with the basic regime to modify the condition of the body by the alternative use of honey in vinegar. This book, written by Dr. Javed, made a revolution and produced, particularly in America, a fight for this type of diet ana there was considerable social interest upon the effects of honey in the development, revolution of certain diseases.

Dr. Omar Shaheen,

I have a number of questions to put: The first question is addressed to Dr. Salem Najam, about the belief of the group who had taken part in research. The object of the question is that each cure or each therapy, has its feasible effects. I do not know the right translation of feasible effects; it might come up to 50% of which is influence. I can not support that honey has that effect, but it might have some psychological effects, particularly if the group is a Muslim group, which believes in the Holy Book and in the traditions and he believes in the faith, which will help with the use of honey. But this does not minimize and belittle the value of the experiment made by Dr. Salem and I would like to thank Dr. Salem for this experience as he had followed the right scientific methodology. He took up a sample, a quality control sample and in the methodological followup and in determining the qualifications of the sample which he used and put before us the conclusions which are determined in it and are clear cut and which are liable for further analysis. Also, there are a number of questions. Another, which occurred to me as a result of the paper of brother, Dr. Hassam Gareeboo, particularly when he talked about the uses and about the advantages of fasting; particularly if it is practised by a faithful, a (مؤمن). We are here to tie up a man's faith to science because faith does not differ with science, though science might differ with faith. I say, he gives a number of theoretical hypotheses that were not substantiated and difficult particularly with regard to what he pre-supposed regarding the effects of fasting on psychosomatic and chronic neurological diseases and even on delirium and depression. If this hypothesis which he advanced was right to a certain degree, then the psychological medicine would be very easy and this is the object, but still an ambition, but to achieve this ambition is something else. I would like to add that this is an out--look which was right in the middle ages, when the psychosomatic patient was tied up and carried and when he was healed and cured, he was released and given food. This out-look is not Islamic at all. Particularly, as Islam is the religion of humanity and compassion and the weak is the prince of the group. In

this respect I would like to give an example: Neuro-genic shock, is the refusal of a patient to take food for a long period, which can end up with starvation. I say this type of psychological disease begins with fasting, in the belief that, it will cure him. Suppose a lady who is over-weight and wants to reduce it by fasting, but this system of cure would only end up with death and for this reason, the question is, "Are there any experimental procedures which establish the relationship between the psychosis and fasting?" I wish he could supply further information.

Dr. Adnan Jaljoli,

I will congratulate my friend, Dr. Mohd. Emarah on the brilliant conclusions he has reached, in using honey in treating and healing many chronic diseases. The first question, I put is what was duration which he advised the patient to use this system of cure after the disappearing of the symptoms. Second question is whether there has been a relapse among some patients, if so then what he advised his patients to do.

Dr. Osama Abdul Aziz

My first comment is on fasting. When God imposed fasting on man, there is no doubt that there has been a wisdom behind it. It was an order, an injunction, which the Muslim should abide by and one of the pillars of Islam is that the Muslims should stick to fasting. It was a good attempt by the lecturer to show the advantages of fasting and he gave us some of the medical advantages; and how we use this information, show the people that fasting is not only a religious ritual, but useful also, medically speaking, but it is not by necessity that fasting is a cure. On the contrary, I see that fasting is a pain, and when God bade fasting, He did want that we may suffer and feel the pains of the poor when we feel the pinch of hunger and this is the basic wisdom (principle) of fasting. I would like to say that we should not pick up all things and interpret God's orders and injunctions as a cure and as necessity, because when fasting was ordered, it was not ordered or imposed for the overweight people or for those who suffer from Gastric diseases, but it was imposed on all the Muslims to feel the pains of hunger. The second point which is relevant to the use of honey in treatment and in healing and curing. I pay tribute to the three papers, which have been submitted regarding the use of honey in treatment, but I would like to raise one point. We say: (فيه شفاء للناس) that, 'There is a cure in it for people'. We know that it has been mentioned in Quran and Prophet (ﷺ) also said, 'There is cure in Quran and with honey'. We do not want to say that it is a cure for a certain physical disease that we give honey and it will be healed It might happen in some diseases and it might be useful for many diseases, but this is not a fast and rigid rule, but that it is a basic rule that I give honey for each disease to heal, otherwise we will be self contradictory and we, as doctors, know that honey is not useful in curing certain diseases, such as those who suffer from cardiac murmur diseases. Honey will not heal this cardiac murmur disease. So, we should not mix the religious values with the medical uses and this will not belittle the papers, submitted by the scientists on the use of honey in dealing with diseases and treating them.

Dr. Ahmed Shawki Ibrahim

God says, 'They secrete from their abdomens a syrup, which is a cure'. Now 'a cure for people', this Verse says, (الشفاء), 'cure'. It has been mentioned at 6 places in the Quran and there is not the word (الشفاء). It is an indefinite noun. We say (شفاء) and it is not a defenite noun. There is a difference. In the absence of a definite article, it means, honey can be a cure for some diseases, but not for all the diseases. And the Prophetic Tradition says, that (شفاء), it means that honey could be used as a cure for some diseases, but not absolutely as a cure and the Quranic Verse: 'In it, there is a sign for people to think over'. أن في ذلك لآية لقوم يتفكرون

Dr. Maher Halawa

First question is addressed to Dr. Salem Najam, on the effect of honey and its use in treatment of positive stool examination of diarrhoea. The second comment, on his interpretation of the concentration of glucose in the honey, might be one of the reasons for the healing of the mucous membrane of gastro intestines, is not acceptable, because when honey comes up to intestines, it becomes diluted as a result of the gastro intestinal secretions, but as to the honey composed of antibiotics, they are non-specific first and then natural proteins which are digested when they come out from intestines. Second question is addressed to Dr. Mohd. Emarah. I thank him for his paper and substantiating it with slides. Did you think of giving some local anaesthesia to the patients before treating them with honey, to reduce the irritation which would increase the blood in conjunctiva.

Dr. Hassan H. Ali

This question is addressed to Dr. Fahim and Dr. Emarah, on the use of honey in treating bladder ulcers and chronic eye irritations. My question might be the result of missing the first part of the two papers. Before using honey as a clinical cure, was this paper preceded by a paper on guinea-pigs and whether the conclusions of the experiments on guinea-pigs give access to the use of honey to be applied to man and to the treatment of man.

Dr. Abdul Monim Abdul Aal

My comment is on the paper presented by Dr. Abdul Latif. Regarding the Quranic Verses: 'Do not approach women during menstruation, until they are purified'. What is meant by purification, means the stop of the flow of blood and then the wash. The second point is that this verse of the prescription on forbidding to approach a woman, is similar to forbidding the pork and bacon, when in the West the foreigners are proud of eating the bacon and pork, without being hit by disease and that the germs, they find in the pork, they could get rid of them, but we do not even talk of ham, because we were ordered by God not to eat it and as bacon and ham in tropical countries will decay or not very soon. This is the same to the Verse of not approaching the women during menstruation. It might be due to psychological reasons. Even the image of blood might be disgusting, might have psychological effects.

Dr. Said Ashour

I thank you my colleagues and particularly the prof. from Al-Azhar University, who has submitted to us a paper which cater between religion and science and which had been of great advantage to us. I want to refer to a remark made by Dr. Ahmed Shawky May God bless him and bless us, to take advantage of the papers. We need not go back to treatment and pretreatment and healing and pre-healing. The second point is that the Almighty God and all the Scriptures and all the Traditions, when they refer to honey, they did not determine the type of honey. They said, 'Bee honey', whether it is derived from the trees or other sources. Though the types of honey might be different, but it must be clean and pure honey and it says, (فيه شفاء). 'In it there is a cure'. That is without a definite article. I am not a doctor; As it is mentioned before there are common factors, though the types and kinds of honey are different, but still there are common elements and ingredients and these ingredients contain the cure in them. The second point, which is relevant to the Turban and the Hat. These are symbolical terms. These are symbols. By turban we mean our Islamic legacy and heritage and by the hat, Western civilization, it means science. I quite agree with my colleague, Dr. Hifnawi. He has already put on the hat and our forefathers put on the hat and accept Islam, when they embarked on the sciences of Greeks and had not they translated these sciences of Greece, they would not have helped to flourish the Islamic Civilization, because the cause of civilization rules that the successors take down from the

pre-decessors, otherwise we would have remained stagnant. If any generation has to make its own start then we would have found ourselves near to the stone age. If I want to set fire, I would have to take two pieces of stone and try to kindle the fire. I would not belittle the greatness of Western civilization, that it has taken from our resources and excelled them. Our forefathers had put on the hats and the Westerners put on the turban, because the Westerners took over the sciences from the Muslims and when one of the Greek religious figures said at the time of Crusades, he said, We lack their sciences and they lack our faith. This is the view of the Christian Westerners. If they have excelled us nowadays there is no objection at all that we put on the hat, side by side with the turban. Since, as our brother, the Prof. who has said with pride that beside the Faculty of Medicine there is a Faculty of Islamic Legacy and some principles of religion and this Prof. gave his lecture in English, because the methodology which he talked about was, the Western methodology and we will excel the Westerners if we stick to our heritage and our faith and we hope that one day we will force them to put on the turban. Now, this is a transitory stage. We put on a turban and we put on a hat, until we gather up our heritage and legacy and their heritage and legacy with which they have anticipated us.

Dr. Fahim Abdul Rahim

As regards the sources of honey, we said that it must be fresh. We did not necessarily get it from the flowers or trees, but usually the honey we get, comes from the flowers of cotton and clover and some other flowers, but it is necessary that it should be fresh, because it contains the basic ingredients, before those ingredients are metabolised. Abdul Rahim asked the question about the psychological effects of honey. All our patients are Muslims. Yes, we work at the Faculty of Medicine at al-Azhar University. We receive a number of Christian patients, but most of our patients are Muslims, and we adopt the Islamic style or the system of the Muslim doctor, who begins with the verse of (« بسم الله الرحمن الرحيم ») then he wins over the trust of the patients. I wish, all of us could begin with the psychological effect and win over the trust and the confidence of the patient, because the trust of the patient speeds up his treatment and his healing by 50%. We dispense the Islamic treatment to the patients who have passed the experiment of the Non-Muslim. The honey which was mentioned in Quran might give a psychological thrust to the treatment and the healing of the patient and we wish that we could adopt the honey in the treatment of many diseases, but strange that many of the Christian patients come to us and visit us and we ask them to continue using honey and many respond .

Dr. Salem Najam

As a matter of fact, Dr. Saeed Ashour has replied to many questions, posed, but I would like to add two simple points. To get the honey was really a problem, because the honey existing in the markets was not well composed and we found difficulties to get and we have tried to get the honey directly from the farms. The composition of honey consisted of: water 17%, sucrose 16%, glucose 56%, minerals and citrones and un-known materials accounted for 4%. It contains vitamin B1, B6, H and C and also calcium, potassium, sodium, phosphorus, iron and iodine and some of the honey contains radium. The last point of Dr. A.R. Hijazi, how to make honey, how do we compose honey? It has hot been well studied so far, but I will tell you the reference, suggesting that after using the honey, it increases the substance of prototheon in the tissues and this substance activates the growth of cells as it plays major role in oxidization process. Dr. Hassan Ali posed a question about the experiment of honey on animals and we have adopted this Quranic Verse:فيه شفاء للناس! In it there is cure for people . This is used for People and not for animals. How does honey affect the animals, I promise you to try it on animals later on.

Dr. M. Amarah

I want to thank the distinguished colleagues who were interested to pose some questions as far as my lecture is concerned and this means that they have been following it up. Dr. Adnan has posed two questions: one is about the period of treatment. It amounted to 3 months, but some times the patient came after 6 months or one year. But when he gets cured, of course I lose interest in following up the patient, because there is an amelioration, though it is very slow, because if it does not happen during the first period then it does not ameliorate. Now what happened to some of the patients who relapsed; it happened to two of them. He had the herpes of cornea and I want to mention one thing to be taken into account, formulating the recommendations. I would like as of today to set forth the co-operation, protocol on the use of honey in treating eyes. I agree with Dr. Osama Abdul Aziz and that is what we should ascertain or confirm. There are some diseases that cannot be healed. Incision of the eye could not be treated with honey, but honey does heal some diseases. Why do not we use some sort of anesthesia in the honey. 50% of the patients were female. They said that the irritability of the honey is not harmful, but I do fear this, because it might harm the eye, though the patient who did not feel it and I do not want to expose the patient to any of these risks. Another proposal was mentioned, the second part, what I intend to do is to use experimental animals when using the honey, the guinea-pigs in laboratories and to give them the honey and to take a sample of their eyes and to see what is going to happen and of course, this can only be accomplished when we have cooperation of other colleagues. Now I think that I have thus replied all the questions which have been posed.

Dr. Mohd. Abdul Latif

I will comment on the question posed by Dr. Abdul Munim, very briefly. Although my answer would not be complete unless he reads my whole paper. The question he raised, has gone through a controversial issue. What is meant by 'harm' whether it is the organic harm and God said, (لا تبطلوا صداقاتكم بالمن والأذى) and before studying this we have thoroughly discussed it and we reached this result. Since the reason precedes the judgement and this has been said by God, who created the soul and the body. This is a literature which we would think thoroughly of and we should think of what is meant by harm. He did not say (كتب عليكم) or He did not say (فرض عليكم). God has clarified that this subject matter which is concerned with instincts of man, this should be avoided and here, scientists and shariah scientists have said, that this harm is an organic harm. What has been included in Judaism, was derived from the pharaos and if you read it a little bit further, you will find out what I meant. Another point, I think because you were not attending the whole lecture. You are differing with basis on which this Quranic Verse is founded, because God has said, « يسألونك عن المحيض قل هو أذى فاعتزلوا النساء في المحيض ولا تقربوهن حتى يطهرن ، فإن تطهرن فأتوهن من حيث أمركم الله » The Prophet's Traditions said,

He explained this question in a very detailed manner.

« توضى ثلاثاً ، ثم خذي فرصة (أي قطعة من الصوف أو القطن) فرصة ممسكة أي مغموسة بالمسك وليست مبللولة بالماء »

We have here scientists and great Shariah Scientists, who can tell us about this. The Prophet (ﷺ) said, (توضى ثلاثاً) which means that you have to wash 3 times a day, the vaginal douche and this is included in all Fiqh Books, and Al-Sayyada Aisha (رضى الله تعالى عنها) has said (تتبعي أثر الدم) you have to follow the traces of blood, from upward to downwards, rubbing vaginal wall with a piece of wool, which has an antiseptic effect. The other point is raised by our colleague from Damascus, and I appreciate what he has said. He does not differ with me and I said that the Arabs have described the woman by(كابر،دارس، فارك ، عارك) so on and so forth. And the Arab linguists, in all the dictionaries مارك means معركة and دارس means درس and فارك means فرك

Dr. Ahmed Shawki Ibrahim

Modern science has proved that what ever is extracted from the bees is not only the honey, there is the poison of bees that is used also in treating some diseases and there is also the honey. So, there are four things which are extracted from the bees. The milk of the honey, the honey, the toxins the poisons of the bees. So, they are extracted as fluids. The Quran says:

« يخرج من بطونها شراب مختلف ألوانه »

Fluids of different colours, but they all have the benefits of healing some diseases and that is why God says,

« يخرج من بطونها شراب مختلف ألوانه فيه شفاء للناس أن في ذلك لآية لقوم يتفكرون » .

And with this comment, there is a reference to the experimental science, which we are dealing with now. There is a Fiqh point which should be dealt with and Dr. Abdul Sattar, who is the reporter of the Fiqh Encyclopedia will deal with this point.

Dr. Abdul Sattar Abu Ghuddah,

While expressing my full appreciation for the information, we listened to with regards our Jurisprudences, I want to mention one thing on the Tradition, mentioned by our Doctor. He said

« خذي فرصة ممسكة فتطهري بها »

And when we take such Traditions, we are following the original Traditions (السنة الأصلية) because as we all know that there have been some alterations and modifications in the Traditions to the extent that when we come to derive a Tradition, we do not derive it from the Fiqh books, but we derive it from the original books of Traditions. What has been included in Bukhari and Al-Muslim (بخارى ، ومسلم), there has been mentioned خذي فرصة ممسكة فتطهري بها what is meant by it (التطهر) is to remove all the traces, which the woman has been in and as has been said; الدوش أو الغسل we have to get rid of the whole trace before being on the التخلي قبل التحلي again, because this we should get rid of what is contradictory to ..... and then he has to..... .... and this is the proof that they should make sure that they have finished with the periods and then they should wash as it has it has been mentioned, and the Quran says

« يسألونك عن المحيض قل هو أذى ، فاعتزلوا النساء في المحيض ولا تقربوهن حتى يطهرن ، فإن تطهرن فأتوهن من حيث أمركم الله »

there is الطهارة and التطهير. Because this is the maximum, which is 15 days and after these 15 days it could be considered as الفقهاء then she is asked to be washed thoroughly and then now if we take this story, we will find that there is no problem aftermath of the whole thing is, to be sure that she is pure and that the place is clean and if the woman is sure that she is pure and she washes herself then there is no problem. Actually I told this story to prove my point.

Prof. Ibrahim Badran (Chairman)

I think this is enough and we have to adjourn the meeting now.

PART EIGHT

CLINICAL- CUM - PHARMACOLOGICAL EVALUATION OF THERAPEUTIC PROCEDURES USED BY MOSLEM PHYSICIANS

Part Eight: *Clinical - Cum - Pharmacological Evaluation of Therapeutic Proce – dures used by Moslem Physicians.*

CHAPTER ONE

(Papers Presented)

REPORT ON THE SECOND SESSION

This session was conducted from 11.30 a.m. to 1.30 p.m., by H.E. Hk Mohammed Said, Advisor (Federal Minister) to the President of Pakistan on Tibb, as chairman, Dr. Isa Al-Naser and Prof. Gunther Stille were co-chairman and moderator respectively. This was a scientific session on applied researches in which the chairman gave first his opening remarks and then six papers were presented on "THE CLINICAL - CUM - PHARMACOLOGICAL EVALUATION OF THERAPEUTIC PROCEDURES USED BY MOSLEM PHYSICIANS". Later on general discussions were allowed.

Editors.

OPENING REMARKS OF THE CHAIRMAN

H.E. HK. Mohammed Said

The subject of this 2nd Session is "Clinical - cum - Pharmacological evaluation of therapeutic procedures used by Moslem Physicians". It is a very important subject forwarded for discussion in this session of this International Conference on Islamic Medicine. I may say without fear of contradiction; as such approach is fundamental one, if at all we earnestly and honestly decide to establish research disciplines for Islamic Medicine. We have received heritage in the form of books as well as manuscripts on Materia Medica and Pharmacopoeia, available in different countries of the world. Tib or Islamic Medicine Materia Medica and Pharmacopoeia, available in different countries of the world. Tib or Islamic Medicine has been involved in the Sub-continent have been practising the Tib and it is still practised in India and Pakistan and it is a recognized system of medicine of both Governments. There is enough material in practice as well as in print for clinical - cum - pharmacological evaluation. I am sure you are well aware of the interest that the World Health Organization is taking in Tib or Traditional Medicine. The W.H.O. has also prescribed certain methods of such evaluation of which. Dr. Atta-ur-Rehman, my colleague and an illustrious scientist of Pakistan, is well aware and I hope he joins us in discussion which will be useful. I remember an example of China, where Chairman Mao-za-Tung had appealed to the Chinese people to report all formulae, so far hidden as secrets of trades. Hundreds and thousands formulae were disclosed and recorded. These were handed over to research workers and laboratories for evaluation. I have closely studied Chinese Medicine and I know that clinical trials and evaluations have resulted in official pharmacopoeia of Chinese Medicine. I have collected a large number of case histories from Hospitals in China. I hope that our deliberations and discussions in this session will be fruitful and supply enough material for future developments.

We have here on our panel six speakers this afternoon and I now invite Hk. M.M. Ali Khan to kindly present his paper. I hope our speakers will take care and limit themselves within 15 minutes time limit and not beyond that.

ILTEHAB TAJAWEEF-E-ANF (SINUSITIS)
(A clinical and Therapeutic Study)

Hk.M.M. Ali Khan and Hk. Mohd. Iqbal Ali

INDIA

INTRODUCTION

Chronic sinusitis is a chronic inflammation of nasal sinuses in which the lining mucous membrane becomes thickened with recurrent purulent exudation. Occasionally chronic sinusitis is due to recurrent acute infections. However, many cases are not caused by chronic bacterial infection but due to other factors such as irritating dust, tobacco, smoke and others. Antibiotics may cause some momentary relief in the first group but not in the other. Vasoconstrictors used locally may cause some transient relief of symptoms. Surgical drainage may be indicated.

Other symptoms are sneezing, headache and tenderness at the site of affected sinus (Logan Turner's[1], Warner[2], Ronald Bodley[3] and Davidson[4]. In Unani classics, all the signs and symptoms which correspond to sinusitis are described under "Nazala-e-barid" (Ibn Sina[5], Azam Khan[6], Kabiruddin[7] and Ghulam Gilani,[8]) .

This study presents a clinical and therapeutic study of 77 cases of Iltehab Tajaweef-e-Anf (Sinusitis) attended this Institute.

The aim of study: To find out effective and curative herbal medicines for chronic sinusitis.

MATERIAL AND METHODS

Material

1) 77 cases of chronic sinusitis
2) Drugs: a) D_3 & b) I_1

Methods

I A special case sheet was designed to record the case history, pathological and biochemical reports.

II *Criteria for the selection of cases:*

i) Repeated sneezing
ii) Nasal discharge
iii) Headache or heaviness of head
iv) Nasal obstruction
v) Radiological confirmation of the disease

III *Dosage and Mode of Administration*

a) D_3:	Gulebanafsha	(Viola ordoratae Linn)
	Asloosoos	(Glycyrrhiza glabra Linn)
	Gauzuban	(Onosma Bracteatum Wall)
	Ustakhudus	(Lavandula stoechas Linn)

(Nadkarni[9], Chopra[10], Najmul Ghani[11], and Azam Khan[12]).

Preparations

5 gms. of each drug is soaked in 240 ml of water, boiled, reduced to half and sieved.

Administration

120 ml. is given twice daily before meals.

b) I_1: contains the following drugs:

Post-e-Haleela Zard	(Terminalia chebula ritz)
— do — kabli	(— do —)
— do — siyah	(— do —)
Baleela	(Terminalia belerica Roxb)
Amla Muqashar	(Emblica officinalis Gartum)
Gule surkh	(Rosa damascena Mill)
Ustakhudus	(Lavandula stoechas Linn)
Bisfaij festaqi	(Polypodium vulgare Linn)
Aftimoon	(Cuscuta reflexa Roxb.)
Khismish	(Vitis vinifera Linn)
Asle Khalis	(Hymenoptera)
Roghan-e-badam	(Prunus amygdalus Baill)
Khande sufaid	(Sugar)

(Nadkarni[9], Chopra[10], Najmul Gani[11], & Azam Khan[12]).

Preparations:

All these drugs pounded and mixed with honey to make a confection.

Administration:

5 gms. twice daily is given with water.

Allocation of Treatment

The simple randomisation method is adopted for the treatment.

FOLLOW-UP

The clinical examination of the case is done every week.

The X-ray of the nasal sinuses was taken after 2 months. After cure the follow-up was done once in a month for six months.

Criteria for Assessment of Results

Cured:	When all the symptoms and signs disappear & x-ray of the nasal sinuses becomes normal.
Relieved:	When all the symptoms and signs disappear but abnormality still remain radiologically.
Partially relieved:	When there is only 40-70% relief in the symptoms but there is no change in previous x-ray findings of the nasal sinuses.
Poor response:	When the relief is below 40% in the signs and symptoms.
Not relieved:	When all the signs and symptoms remain unchanged.

Precautions

Advise to avoid exposure to cold, sour food articles and fruits, freezed articles, ice cream, cold drinks, banana, guava and curd etc..

By simple randomisation method 2 groups of the cases were formed:

Group I (consists 43 cases) was given the drug D_3
Group II (consists 34 cases) was treated with drug I_1

Observations:

Males were more in number than females. The highest number of patients were observed in the age group of 31-40 years followed by the age 20-30 years and 11-20 years respectively.

The chronicity of the disease varied from 1 year to 16 years. 45.5% of the cases had chronicity of 1-4 years, 27.2% cases of 5-10 years, 6.5% cases of 11-15 years and 20.8% cases of more than 15 years.

The highest number of cases observed were of frontal sinusitis, followed by both maxillary and frontal and both maxillary.

The nasal discharge was present in 72 cases, headache in 58, sneezing in 55, nasal obstruction in 52, local tenderness in 53 cases, and nasal polypi in 47 cases.

The urine and faeces analysis did not reveal any abnormality in these cases. Eosinophilia was present in 40 cases (51.9%).

RESULTS

Out of the total 77 patients, 4 were dropouts while there were no patients of nil response. Complete cure was obtained in 42 cases while a good relief was obtained in 21 and partial relief was in 10 patients.

The formula D_3 was given to 43 cases. The general response was 100% excluding the dropouts. 20 cases were completely cured, 11 were relieved and 9 partially relieved. There was no case of Nil response.

The formula I_1 was given to 34 cases. 1 was dropout. The general response was 100%, 22 got complete cure, 10 were relieved and 1 partially relieved.

DISCUSSION

77 cases of chronic sinusitis were divided in 2 groups each under different formula. Simple randomisation method has been adopted, allotting days of the week for admission under different groups. For both the 2 formulae D_3 and I_1 — general response was 100%. The herbal medicines which were used in the treatment of chronic sinusitis had no adverse effects in the prescribed dosage.

In this disease where there are no curative drugs in the conventional system of medicine, the herbal medicines offer the patients of chronic sinusitis the hope of cure.

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INTESTINAL AMOEBIASIS AND ITS TREATMENT WITH METRONIDAZOLE AND A HERBAL COMPOUND

Hk. Mirza Abdul Noor Beg

INDIA

INTRODUCTION

Amoebiasis is an endemic disease with varying intensity in many areas in the world particularly in the tropical and developing countries.

Although various chemical drugs are fairly effective against amoebic dysentery yet none of them is free of side effects. The iatrogenic diseases are increasing gradually all over the world.

Herbal antiamoebic medicines on the other hand, were reported over many centuries ago until now to be fairly effective and free of side effects.

In this work, we tried to do a comparative study between the antiamoebic effect of metronidazole and certain herbal medicines used in the treatment of amoebiasis in Islamic medicine.

MATERIAL AND METHODS

The herbal medicines were prepared from the following herbal ingredients:

Name described in the text of Islamic Medicine	Botanical Name
1. HABB - UL - AS	MYRTUS COMMUNIS
2. AFAS	QUERCUS INFECTORIA
3. MAMIRAN	COPTIS TEETA
4. BAZAR - UL - BUNJ	HYOCYAMUS NIGER

All of the four ingredients taken in equal quantity, were reduced to form a compound powder at Takmeel-uttib Pharmacy.

The present study was carried out at the clinic of Takmeel-ut-Tib Pharmacy, Lucknow. Children brought with gastro intestinal complaints along with other cases attending clinic for some other disease were subjected to normal routine stool examination and only those 50 cases, whose stool examination showed cysts or trophozoites of Entamoeba histolytica were selected for present study and these cases were subjected to detailed investigation and examination. Stool examination was done by direct smear examination and Iodine staining methods.

On the basis of therapy used the cases were classified into two groups.

GROUP	NO. OF CASES	DRUG	DOSE/KG.	DURATION
H	25	Trial drug	T.D. S(50mg)	7 days
M	25	Known drug metronidazole	T.D.. S(50mg)	7 days

Stool examination of both groups 'H' and 'M' was done on 8th, 9th and 10th day. The case who had become negative for Entamoeba histolytica in three consecutive days were again subjected for stool examination on the 17th day to reconfirm the reappearance or disappearance of the cysts and trophozoites.

RESULTS

TABLE I

AGE IN YEARS	TOTAL NO. OF CASES	GROUP 'H'	GROUP 'M'
		NO. OF CASES	NO. OF CASES
1 - 2	3	1	2
3 - 4	5	3	2
5 - 6	10	4	6
7 - 8	8	2	6
9 - 10	6	5	1
11 - 12	4	2	2
13 - 14	14	8	6

TABLE II
SEX INCIDENCE IN 'E' HISTOLYTICA INFESTED CHILDREN

SEX	TOTAL CLASS	GROUP 'H'	GROUP 'M'
	NO. OF CASES	NO. OF CASES	NO. OF CASES
MALE	35	18	17
FEMALE	15	7	8

TABLE III

SHOWING THE PRESENCE OF GIARDIA LAMBLIA IN PATIENTS WITH ENTAMOEBA HISTOLYTICA

ASSOCIATED PARASITES	TOTAL CASES	GROUP 'H'	GROUP 'M'
	NO. OF CASES	NO. OF CASES	NO. OF CASES
E. Histolytica Alone	18	9	9
E. Histolytica with Giardia	14	7	7

TABLE IV

SHOWING NUMBER OF SYMPTOMATIC CASES IN 'E' HISTOLYTICA INFESTED CHILDREN

SYMPTOMS	TOTAL CASES	GROUP 'H'	GROUP 'M'
	NO. OF CASES	NO. OF CASES	NO. OF CASES
Symptomatic	36	16	20
Asymptomatic	14	9	5

SIDE EFFECTS

In group 'H' one case had complaint of loose motion and one reported mild abdominal discomfort, which were considered due to the disease process rather than due to the medicine. No effects were detected on white cells or on platelets.

In group 'M' one case had several complaints like headache, pain in abdomen, nausea, vertigo and bitter taste and the drug was discontinued on 3rd day. Two other cases had nausea and headache and one had marked flatulence.

TABLE V

SHOWING RESULTS OF TREATMENT IN BOTH GROUPS OF 'E HISTOLITICA INFESTED CHILDREN

RESULT	GROUP 'H'	GROUP 'M'
	NO. OF CASES	NO. OF CASES
Cured	21	22
No response	4	3

TABLE VI

SHOWING EFFECT OF BOTH DRUGS ON GIARDIA

WORM	GROUP 'H'		GROUP 'M'	
	INITIAL NO.	DISAPPEARANCE	INITIAL NO.	DISAPPEARANCE
Giardia	7	3	7	5

DISCUSSION

Fifty cases of intestinal amoebiasis were included in the present study and were equally divided in two groups (H) given Herbal medicine and (M) given Metronidazole. The duration of treatment in both groups was the same. The clinical improvement was judged by the recovery from the symptoms as well as disappearance or absence of cysts and trophzoites in stool.

28% of the patients were in the age group of 13 to 14 years and 36% of the patients were under 10 years of age (Table I and II).

Stool examined, demonstrated 36% of cases, E. Histolytica alone. Giardia lamblinia, were detected in 28% of cases (Table III). Asymptomatic cyst passers were also detected (Table IV).

After one week therapy the clinical cure in the cases of group 'M' who received metronidazole, was 88% as compared with the cases of group 'H' who were on the herbal medicine (84%) (Table VI). It was also observed that the 'Herbal medicine' has antigiardial property also (Table VI).

In group 'H' no side effects were noted while in group 'M' who received Metronidazole three patients had side effects such as headache, vertigo, nausea and flatulence and one case discontinued the treament on the third day.

From this study it was concluded that though metronidazole used for intestinal amoebiasis has a better response but the hazards of side effects exist with it. While on the other hand, the herbal medicines have a fairly good response (84%) without any side effects.

Owing to the danger of widespread iatrogenic diseases due to chemical preparations in treatment, we have to search for effective non toxic and potent preparations for various ailments out of the texts of the classics of Islamic Medicine.

ACKNOWLEDGEMENT

I am thankful to Mr. Syed Imtiaz Ali, M. Sc.. Lecturer, Department of Botany, Shia Degree College, Lucknow and Honorary Secretary Takmil-ut-tib Pharmacy for granting permission and providing facilities to carry on this study at the clinic of Takmil-ut-tib Pharmacy, Lucknow, India.

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PRELIMINARY PHARMACOLOGICAL STUDY OF THE FLOWERS OF SPHAERANTHUS HIRTUS L.

Drs. M.Tharwat Ghoneim, Ahmed Rajai El-Gindi, Riad Al-Alami and Rushdi Fattooh

KUWAIT

INTRODUCTION

Sphaeranthus Hirtus L. (globe flower) is a herb that grows in different parts of the world specially in India and Pakistan. The herb was reported to possess different therapeutic uses. The roots of the plant were used as stomachic and anthelmintic. The flowers were used as what is called blood purifier in skin diseases and in jaundice (Nadkarni 1976) [1]. The flowers were reported to produce some beneficial effects when given alone or in combination with other plants such as Fumaria, Chirata and Tephrosia in boils, abscess, itching, skin eruptions. Also the plants have been used in palpitation (Kabiruddin (1929) [2]. The plant was mentioned by Avicenna (1037 A.D.) [3] to be very useful in chronic ulcers, joint diseases, convulsions, jaundice and cough.

It was found of importance to investigate the possible pharmacological effects of the extract obtained from such a plant.

MATERIALS AND METHODS

A — Extract of the plant (AE)

The aqueous extract of the flowers of Sphaeranthus was prepared according to the method adopted by Hakeems [4]. 10gr. of the dried flowers of Sphaeranthus hirtus were kept in 200 ml distilled water for 24 hours, then extraction was completed by boiling the whole mixture to concentrate it to half of its original volume. The extract was freshly prepared and used for the experimental work. (100 gm. of the dry flowers produced 28.67 gm. of the dry aqueous extract).

B — Pharmacological Methods

a) The animals used included rabbits, albino rats, guinea pigs and toads of either sex. The animals were kept under the same conditions, given water *ad libitum.* The animals were kept fasting 12 hours before sacrifice.

b) The investigation of the pharmacological properties of the aqueous extract (AE) of Sphaeranthus was carried out using the following procedures:

1. Isolated perfused rabbit's heart (Burn [5] 1952)[a]. The effect of the aqueous extract of Sphaeranthus (AE) was studied on the force of contraction as well as the rate of contraction. The effect was also examined on the coronary outflow using different doses of the (AE). Doses of vasopressin (O.I U) were also given to investigate the effect of (AE) on the coronary vasoconstriction induced by vasopressin. The results were statistically analysed.

2. Isolated rabbit auricles (Shoepke and Shideman, 1960). The contractile amplitude is recorded. The increase in height of lines on the Kymograph after addition of the drug to the bath was measured and compared with the height before addition, in order to express the inotropic effect of the drug as a percentage of the height or amplitude before the influence of the drug. The chronotropic effect was expressed as the percentage increase in number of lines (heart beats) per unit time.

3. Isolated rabbit aortic strip (Furchgott and Bhadrakom, 1953)[7].

4. Blood pressure fo anaesthetised rabbit (Ghosh 1971)[8].

5. Isolated perfused toad's heart (Burn, 1952)[9b]
6. Isolated rabbit duodenum and jejunum
7. Isolated guinea pig ileum (Turner 1965)[10]
8. Isolated guinea pig tracheal strip (Ghosh, 1971)[11]
9. Isolated rat jejunum (Van Rossum and Ariens, 1959)[12]
10. Isolated rat stomach fundus strip (Vane, 1957)[13]
11. Isolated guinea pig vas deferens (Leach, 1956)[14]
12. Isolated rectus abdominis muscle of the toad (Burn, 1952)[15c]

RESULTS

On the isolated mammalian heart, the AE in a dose of 1.53mg produced a slight and temporary depressant effect on the rate and force of contraction. This was followed by slight stimulation in amplitude of contraction. The effect is dose dependent (Fig 1.). The AE was found to increase the coronary outflow. In a dose of 1.529 mg, the AE produced an increase in coronary outflow equivalent to 14.5% ($P > 0.05$). In a dose of 3.058mg, the AE increased the coronary outflow by 29.8% ($P < 0.01$). Administration of vasopressin (0.1U) reduced the coronary flow by 49.2% ($P < 0.001$). Administration of the AE in a dose of 3.058mg immediately after vasopressin caused a decrease in coronary outflow equivalent to 15.20% from control value ($P > 0.05$) when compared with control). When this was compared to vasopressin, there was highly significant increase in coronary flow equivalent to 66.7% from the vasopressin group ($P < 0.01$ when compared to vasopressin). Administration of vasopressin after the AE, produced only a non significant decrease in coronary outflow equivalent to 14.8% of control ($P > 0.05$) and when compared to vasopressin group, there was still an increase in coronary outflow equivalent to 67.6% of vasopressin group ($P < 0.05$). (Table 1). The effect of the AE (dose of 3.058 mg) on coronary outflow persisted for more than 5 mins. (Fig 2) shows the effect of the (AE) in addition to that of vasopressin.

On the isolated rabbit auricles, the (AE) caused a decrease in the rate when given in concentration of 1.1486 and 2.2936 mg/ml bath solution ($P < 0.01$ and < 0.05 respectively). In a concentration of 2.2936 mg/ml. bath solution, the (AE) produced a statiscally significant increase in contractibility ($P < 0.05$) (Table II, Fig.3 & 4).

On the isolated toad's heart, the (AE) produced a temporary depressant effect that was followed by a slight increase in amplitude of contraction. The effect is dose dependent (Fig.5). The stimulation was not mediated through sympathetic stimulation. On the isolated rabbit aortic strip. the (AE) did not alter the response of the aortic strip to adrenaline. It can decrease the response to angiotensin (Fig.6).

On the anaesthetized rabbit blood pressure, the (AE) produced a very slight effect. In doses up to 17.14mg/kg body weight, the (AE) did not alter the response to adrenaline (Fig.7). The (AE) inhibited the response to histamine.

On the isolated rabbit duodenum and jejunum, the (AE) in a concentration of 0.5734mg/ml. bath solution produced a primary stimulant effect that was followed by a long lasting gradual inhibition in the tone of the muscle. The (AE) can inhibit the response of the muscle to histamine (Fig.8) and Serotonin (Fig.9) and in large concentration it can slightly inhibit the response to acetylcholine (Fig.10).

On the guinea pig ileum, the (AE) in concentration of 1.4335 mg/ml. bath firstly produced a stimulant effect by its own which was gradually abolished. In this concentration, the (AE) can selectively inhibit the response of the muscle to histamine but not to acetylcholine (Fig.11). Only large concentrations that can slightly reduce the response to acetylcholine (Fig.12). The (AE) can reduce the response of the

muscle to serotonin (Fig.13), angiotensin (Fig.14) but not nicotine (Fig.15). The initial stimulation produced by the (AE) was abolished by atropine (Fig.16). On the guinea pig trachea, the (AE) in a concentration of 1.7202mg/ml bath solution produced a potent relaxant effect, in addition, it strongly inhibited the histamine induced contractions (Fig.17). The effect was persistent for a long duration.

The (AE) in a concentration of 0.819 mg/ml bath solution reduced the response of rat fundus strip to serotonin (Fig.18) and only slightly and temporarily to acetylcholine (Fig.19).

On the isolated rat jejunum, the (AE) in a concentration of 1.1468 mg/ml bath solution produced relaxant effect. It strongly reduced the response of the muscle to angiotensin (Fig.20). It slightly reduced the response to acetylcholine (Fig.21).

The (AE) in concentrations of 0.7167-1.4335 mg/ml bath solution and with times of contact of 1-3 minutes, did not affect the response of guinea pig vas deferens to contractions induced by adrenaline (Fig.22). The same concentration reduced the response to histamine and not to acetycholine (Fig.23).

On the rectus abdominis muscle, the (AE) showed only a slight potentiating effect to contraction induced by acetylcholine (Fig.24).

DISCUSSION

The aqueous extract of Sphaeranthus was found to possess a spasmolytic effect on the smooth muscles.

The relaxant effect is suggested to be mediated through a direct action on the smooth muscles. This was shown from the inhibitory effect of the (AE) on the contractions induced by angiotensin on several preparations such as the guinea pig ileum, rat jejunum and isolated rabbit aortic strip. The (AE) was able to decrease the vasoconstrictor effect of the directly acting vasopressin on coronary circulation. The inhibitory effect on smooth muscles induced by the AE is not mediated through a ganglion blocking effect because the (AE) did not alter the response of any of the smooth muscle tested to nicotine. The relaxant effect is also not related to adrenergic stimulation. The (AE) did not affect the response of rabbit aortic strip or guinea pig vas deferens to adrenaline.

In several isolated smooth muscles, it was found that the (AE) produced a primary stimulant effect which was followed by an inhibitory action. The first effect was abolished by atropine suggesting that the (AE) may contain more than one active ingredient, one is a cholinergic stimulant and the second is an inhibitor. The (AE) was found to possess anti-histamine effect as well as antiserotonin effect. The (AE) inhibited the response of several isolated preparations to the contractions induced by histamine. It inhibited the effect of histamine on blood pressure. Preziosi (1958) [16] used the rabbit blood pressure for studies on antihistamines where diminished responses to histamine after administration of a drug indicates antihistaminic activity. Within certain concentrations, the effect of the (AE) was specific for antagonism of histamine and serotonin. In larger concentrations, the (AE) slightly reduced the response of some isolated preparations to acetylcholine suggesting that the (AE) may possess slight anticholinergic effect. The (AE) produced a statistically significant increase in the coronary outflow. This action is mostly due to a direct effect on the coronary circulation. The increase in coronory flow is not believed to be mediated through increase in the force of contraction. Doses of the (AE) that produced increase in the coronary flow did not show significant inotropic effects. Only large doses of the (AE) possess inotropic effect. The (AE) has some negative chronotropic effect. The effect of (AE) on coronary flow was firstly studied on normal circulation. Vasopressin is known to cause acute coronary vasoconstriction (Lindner et al 1953 [17] . The (AE) was able to antagonize the vasoconstrictor effect of vasopressin on the coronary circulation. Vasopressin antagonism was reported repeatedly after administration of coronary dilating drugs in the Langendorrff heart as well as in intact animals (Lindner et al 1953)[17].

TABLE I

EFFECT OF AQUEOUS (AE) OF SPHAERANTHUS HIRTUS FLOWERS & VASOPRESSIN ON CORONARY FLOW

	Control	Effect of 1.529 mg AE Sphaeranthus	Effect of 3.058 mg. AE sphoeranthus	Effect of vasopressin (0.1U)	Effect of 3.058 mg AE sphaeranthus after vaspressin	Effect of vasopressin (0.1U) after 3.058mg. AE sphaeranthus
Mean ± S.E.	10.95 ± 0.454 (22)[a]	11.555 ± 1.250 (6)	13.104 ± 0.823 (16)	5.134 ± 1.085 (8)	8.558 ± 0.626 (10)	8.604 ± 0.992 (9)
p^{b}_{1}	—	> 0.05	< 0.01	< 0.001	> 0.05	> 0.05
% change from control	—	+ 14.50%	+ 29.8%	− 49.2%	− 15.2%	− 14.8%
p^{c}_{2}	—	—	—	—	< 0.01	< 0.05
% change from vasopressin	—	—	—	—	+ 66.7%	+ 67.7%

[d] Figures are the average of coronary flow in (ml) per minute of 3 minutes after administration of drug.

(a) Number of animals
(b) as compared to control group
(c) as compared to vasopressin group

TABLE II

EFFECT OF AQUEOUS EXTRACT (AE) OF SPHAERANTHUS HIRTUS ON THE RATE AND FORCE OF CONTRACTION OF ISOLATED RABBIT'S AURICLES

	RATE[a]				FORCE OF CONTRACTION[b]			
	Control	Effect of (d) 0.5473 mg. AE of sphaeranthus per ml bath	Effect of 1.1486 mg AE of sphaeranthus	Effect of 2.2936 mg AE of sphaeranthus	Control	Effect of 0.5743 mg AE of sphaeranthus	Effect of 1.486 mg. AE of sphaeranthus	Effect of 2.2936 mg AE of sphaeranthus
Mean ± S.E.	102.42 ± 5.95 (12)[c]	97.80 ± 6.97 (10)	79.00 ± 4.79 (12)	81.88 ± 7.42 (8)	2.229 ± 0.223 (12)	2.172 ± 0.206 (10)	2.518 ± 0.339 (12)	3.385 ± 0.417 (8)
p	—	> 0.05	< 0.01	< 0.05	—	> 0.05	> 0.05	< 0.05
% change from control		− 4.50%	− 22.9%	− 20.1%	—	− 2.5%	+ 12.9%	+ 51.9%

(a) The rate is expressed as number of lines (heart beats) per unit time as recorded from the contractile amplitude of auricular contraction
(b) The force of contraction is expressed as the height of lines (in cm) recorded from the contractile amplitude of contraction (Schoepke and Shideman 1960).
(c) Number of animals
(d) The concentration of AE of **sphaeranthus** calculated per ml bath solution.

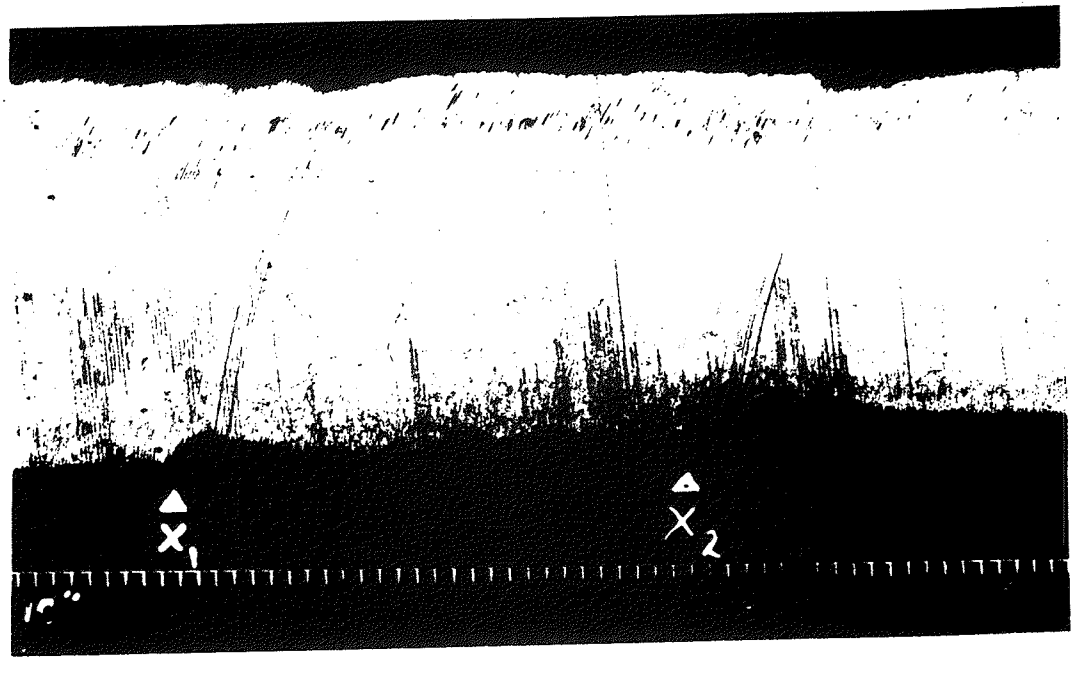
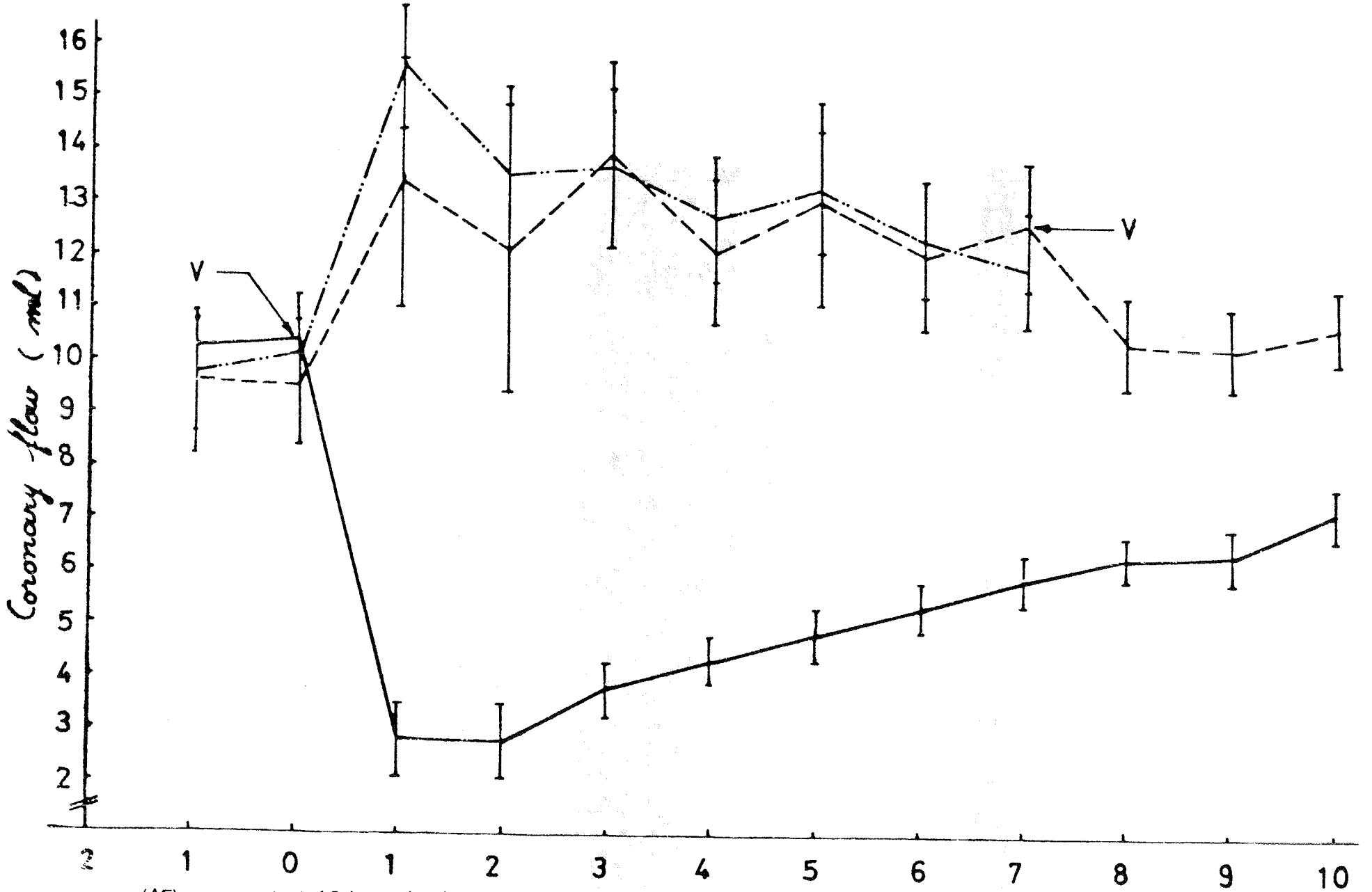


Fig.1: Effect of (AE) of sphaeranthus on the isolated perfused rabbit heart.
x_1: 1.5290 mg (AE)
x_2: 3.0580 mg (AE)



(AE) aqueous extract of Sphaeranthus (3.058mg)
Vasopression (0.1U)
(AE) followed by vasopression

Fig.2: Effect of Aqueous extract of sphaeranthus & vasopression on coronary flow.

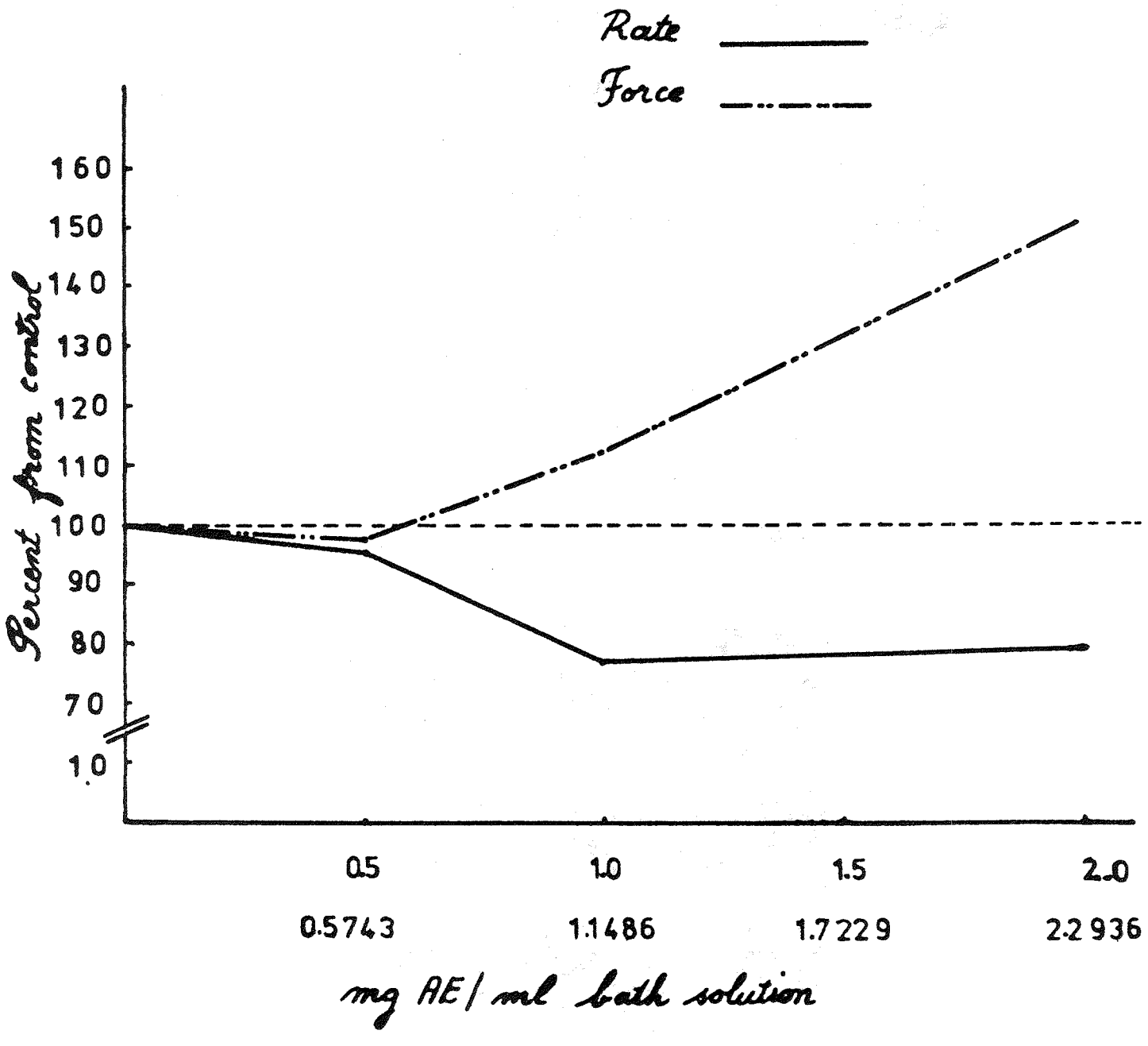


Fig.3: The effect of (AE) aqueous extract of Sphaeranthus on isolated rabbit's auricles. The effect is on the rate and force of contraction.

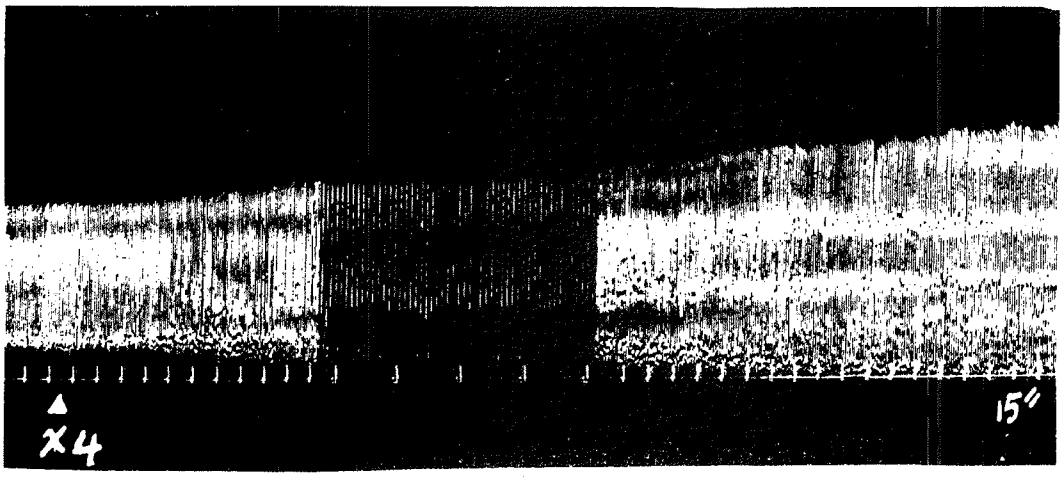


Fig.4: Effect of (AE) of sphaeranthus on isolated rabbit auricles.
x_4: 1.1468 mg AE / ml bath solution

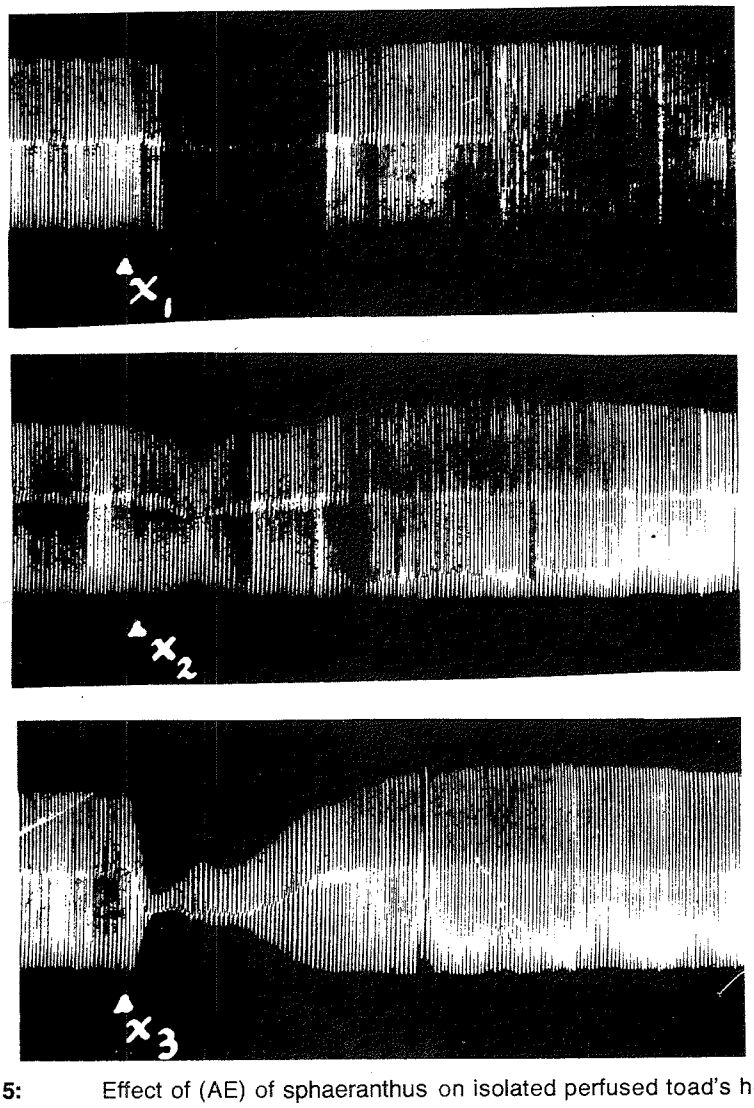


Fig.5: Effect of (AE) of sphaeranthus on isolated perfused toad's heart
x1: 2.867 mg (AE)
x_2: 5.734 mg (AE)
x_3: 8.601 mg (AE)

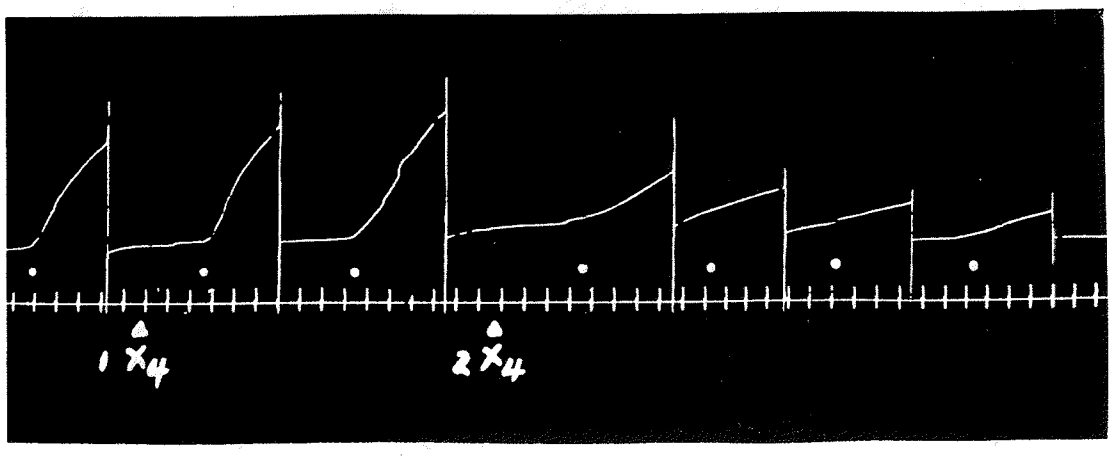


Fig.6: Effect of (AE) of sphaeranthus on isolated rabbit aortic strip.
1 × 4: 0.1433mg (AE) / ml bath solution
2 × 4: 0.2867 mg (AE) / ml bath solution
Unmarked contractions are due to angioten sin.

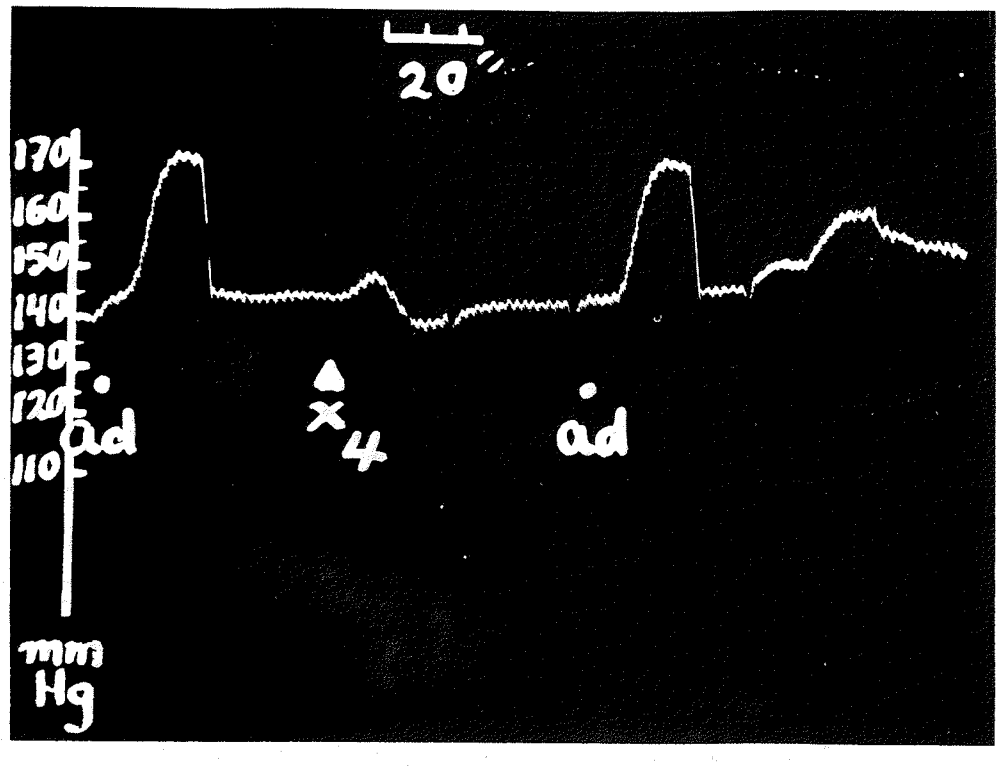


Fig.7: Effect of (AE) of sphaeranthus on anaesthetized rabbit. rabbit, 1.75kg. body weight, anaesthetized with urethane (1gm/kg. body weight)
X_4: 17: 14mg. AE / kg body weight given by i.v.i.
ad: adrenaline

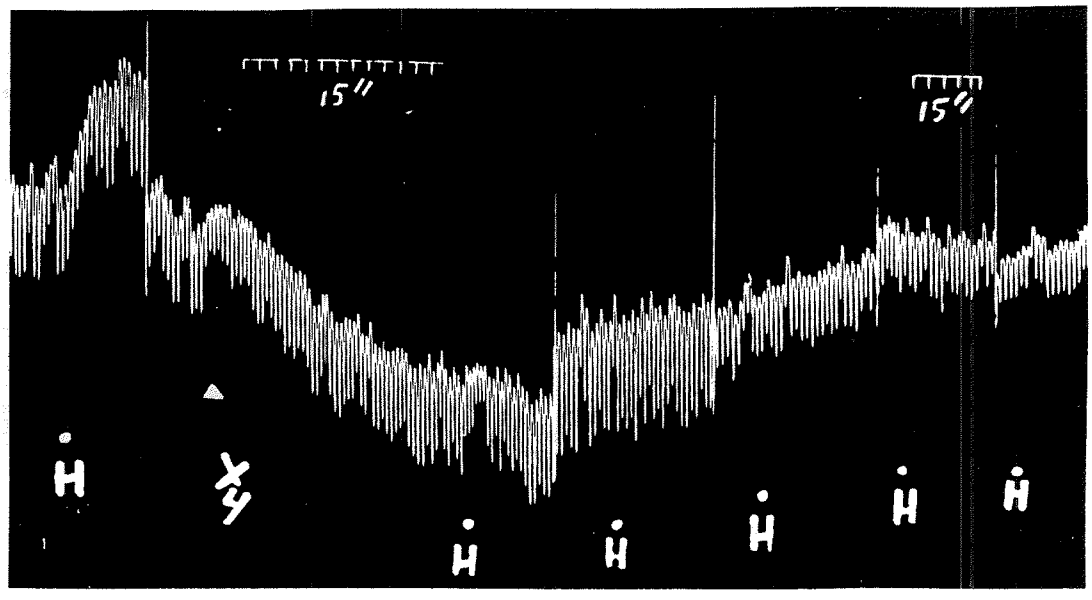


Fig.8: Effect of aqueous extract (AE) of sphaeranthus on isolated rabbit duodenum
H: Histamine
x_4: 0.5734 AE/ml bath solution

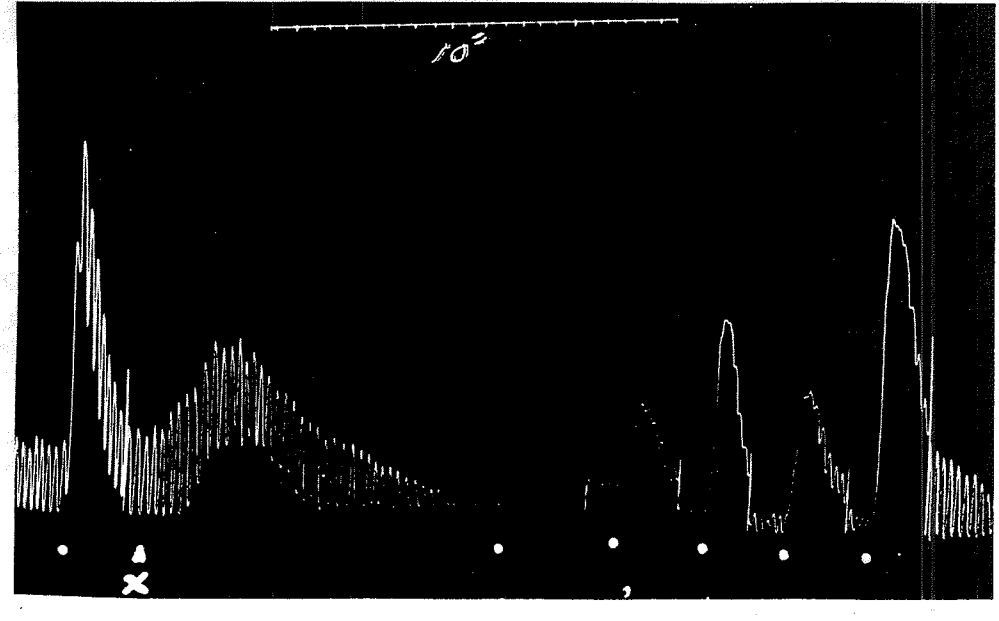


Fig.9: Effect of aqueous extract (AE) of sphaeranthus on isolated rabbit duodenum. Unmarked contractions are due to serotin.
x: 1.1468 mg AE / ml bath solution

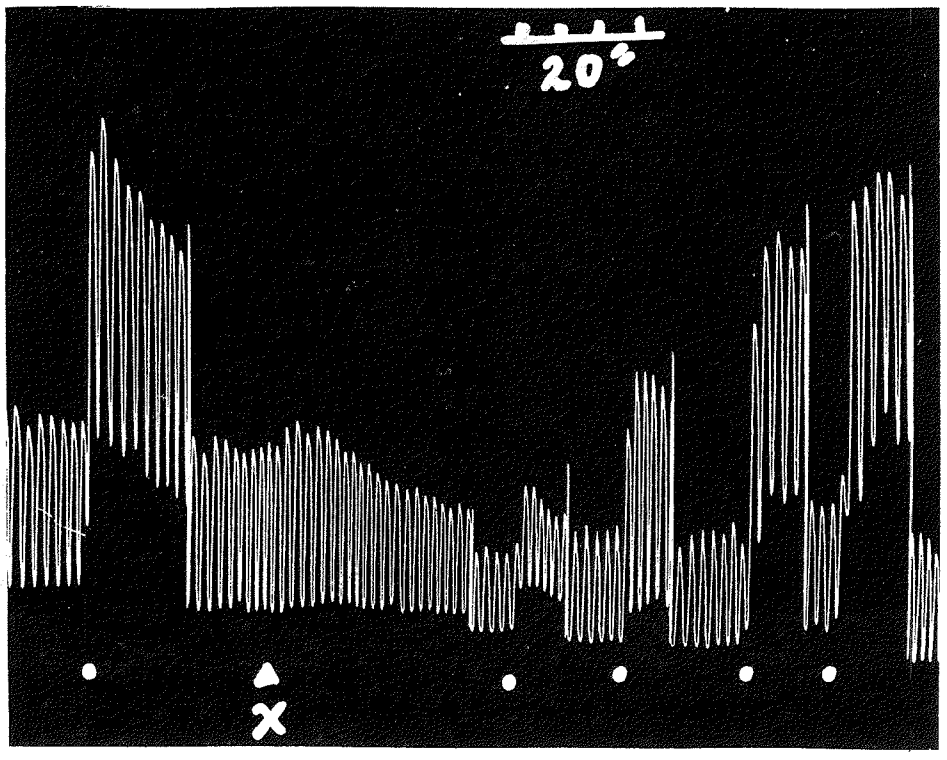


Fig.10: Effect of aqueous extract (AE) of **sphaeranthus** on isolated rabbit duodenum. Unmarked contractions are due to acetylcholine
x: 2.2948mg (AE) / ml bath solution

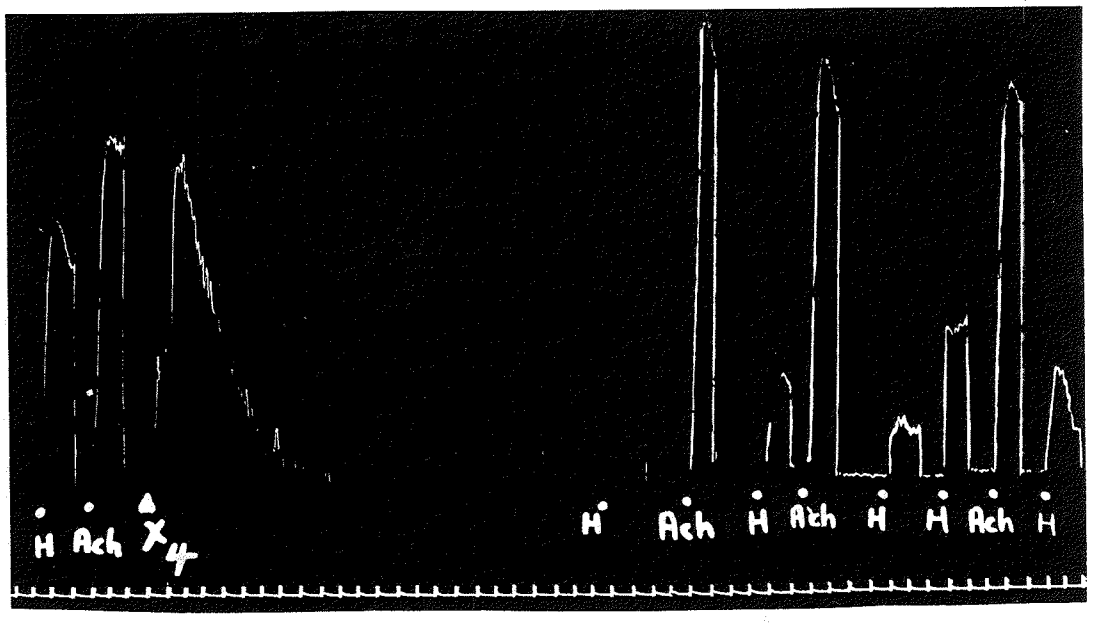


Fig.11: Effect of aqueous extract (AE) of **sphaeranthus** on guinea pig ileum.
H: Histamine
X_4: 1.4335 mg (AE) / ml bath solution
Ach: Acetyl choline

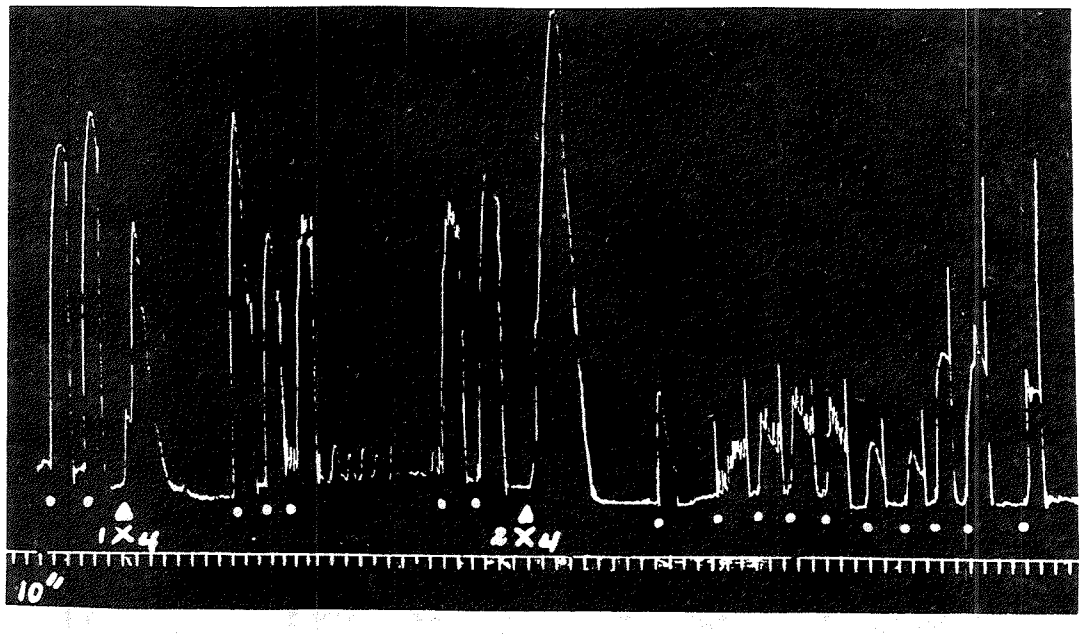


Fig.12: Effect of aqueous extract (AE) of **sphaeranthus** on guinea pig ileum.
Unmarked contractions are due to acetylcholine
1 × 4: 1.1468 mg (AE) / ml bath solution
2 × 4: 2.2936 mg (AE) / ml bath solution

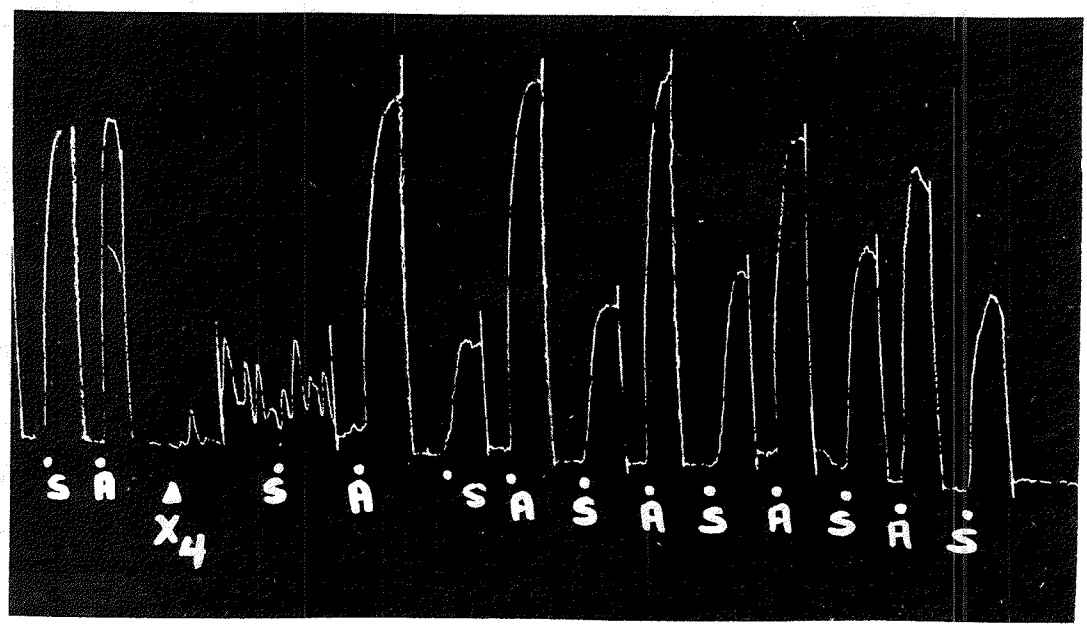


Fig.13: Effect of aqueous extract (AE) of **sphaeranthus** on guinea pig ileum
S: Serotonin A: Acetylcholine
X_4: 0.5734 mg (AE) / ml bath solution

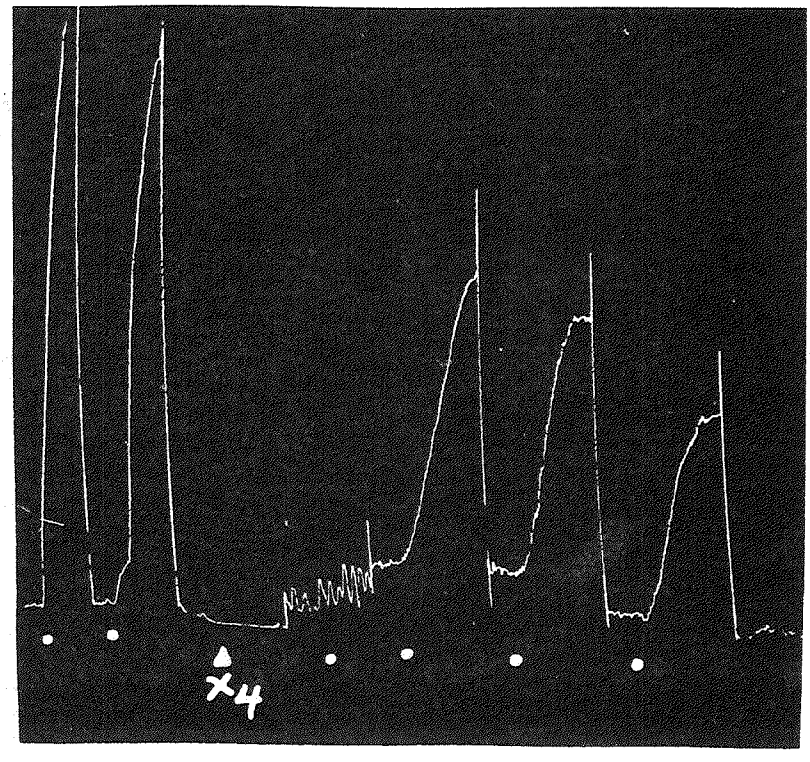


Fig.14: Effect of aqueous extract (AE) of sphaeranthus on guinea pig ileum
Unmarked contractions are due to angiotensin .
X_4: 0.5734 mg (AE) / ml bath solution

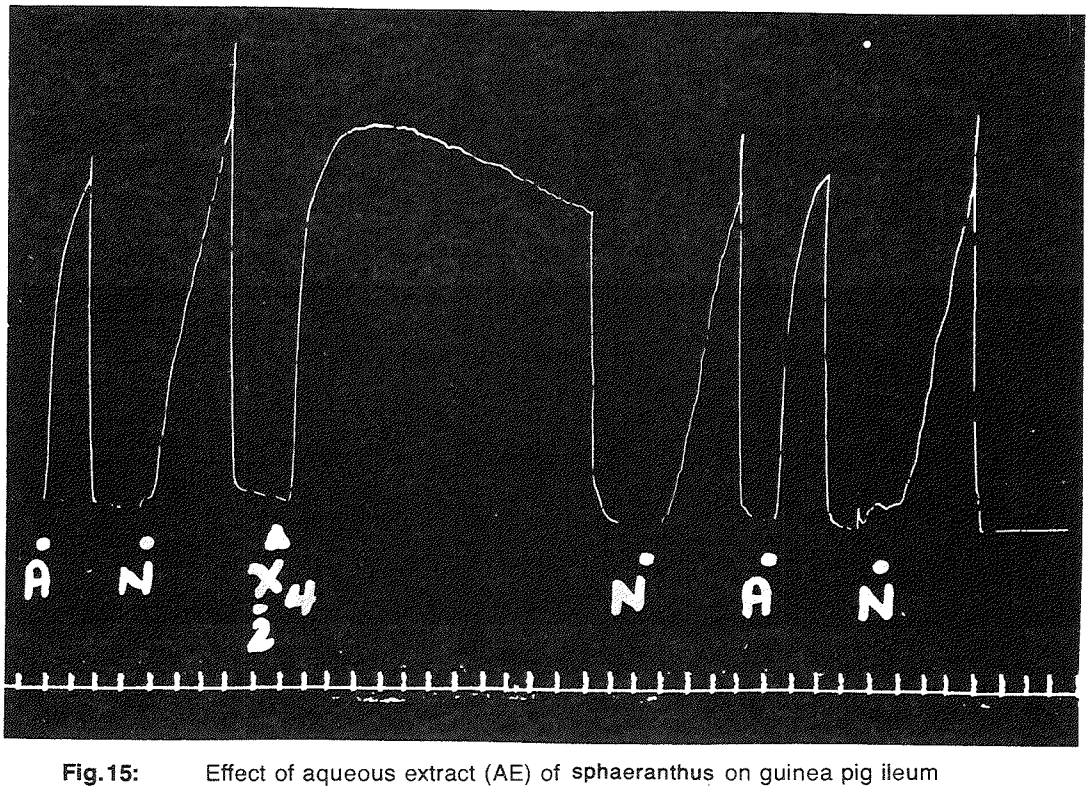


Fig.15: Effect of aqueous extract (AE) of sphaeranthus on guinea pig ileum
N: nicotine A: Acetylcholine
X_4: 0.71675 mg (AE) / ml bath solution

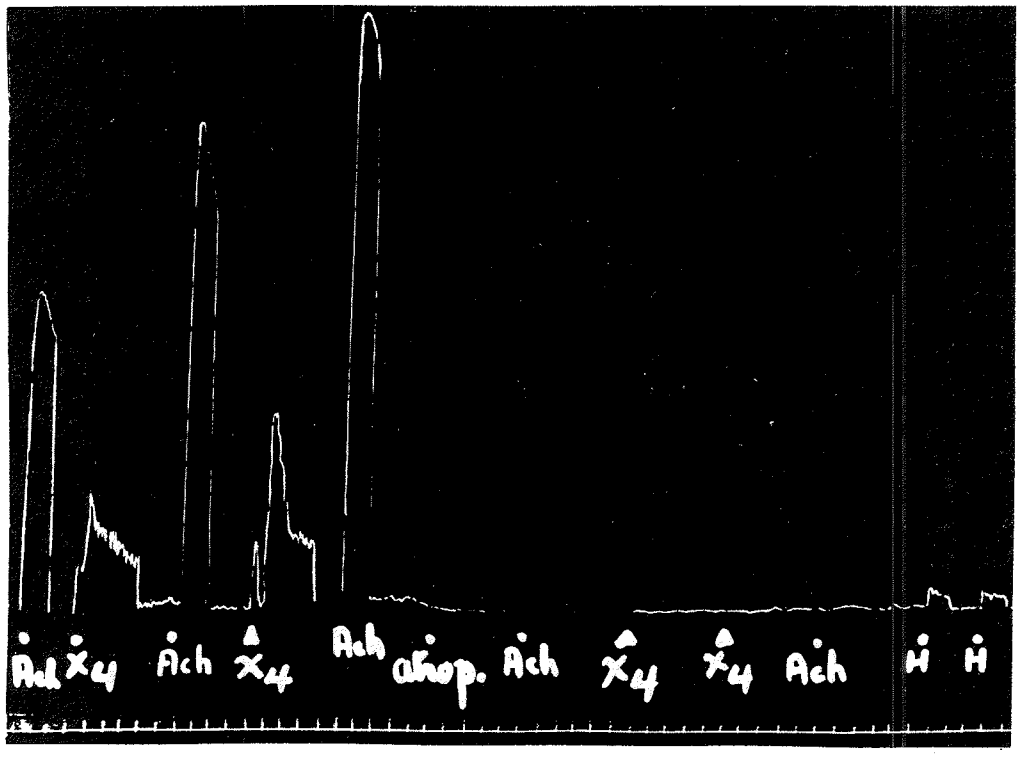


Fig.16: Effect of aqueous extract (AE) of **sphaeranthus** on guinea pig ileum
Ach: acetylcholine Atrop: Atropine
H: Histamine
X_4: 1.4335 mg (AE) / ml bath solution

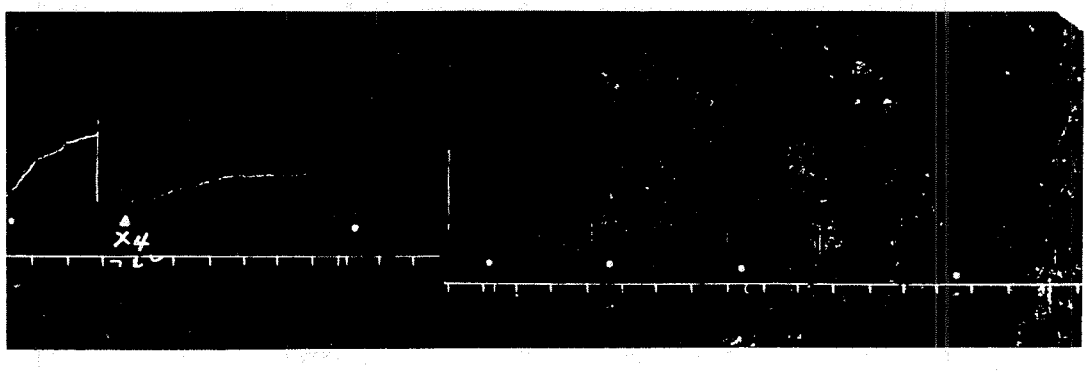


Fig.17: Effect of (AE) aqueous extract of **sphaeranthus** on guinea pig tracheal strip. Unmarked contractions are due to histamine.
X_4: 1.7202mg (AE) / ml bath solution

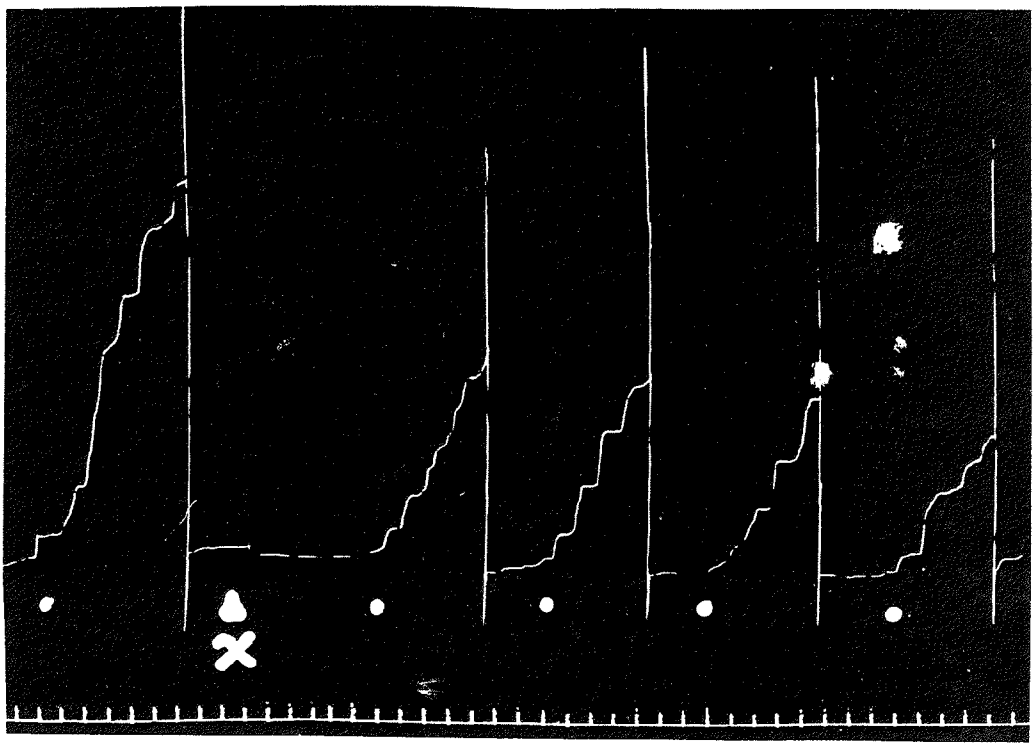


Fig.18: Effect of aqueous extract (AE) of **sphaeranthus** on rat stomach fundus
Unmarked contractions are due to serotonin.
x: 0.819 mg (AE) / ml bath solution

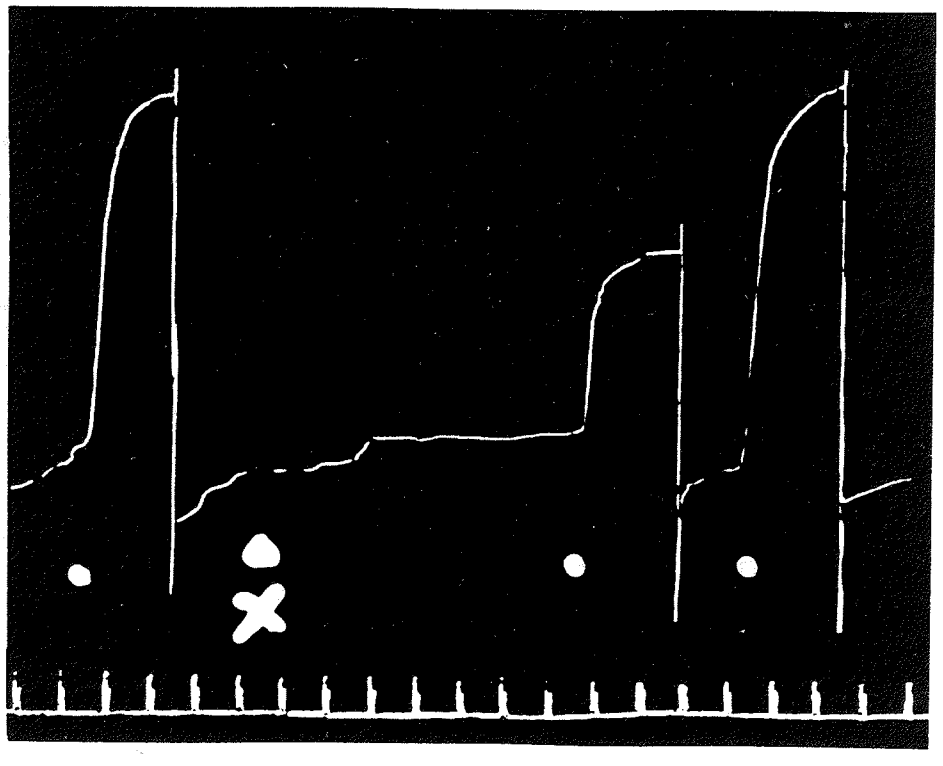


Fig.19: Effect of (AE) aqueous extract of **sphaeranthus** on rat stomach fundus strip.
Unmarked contractions are due to acetylcholine.
x: 0.819mg (AE) / ml bath solution

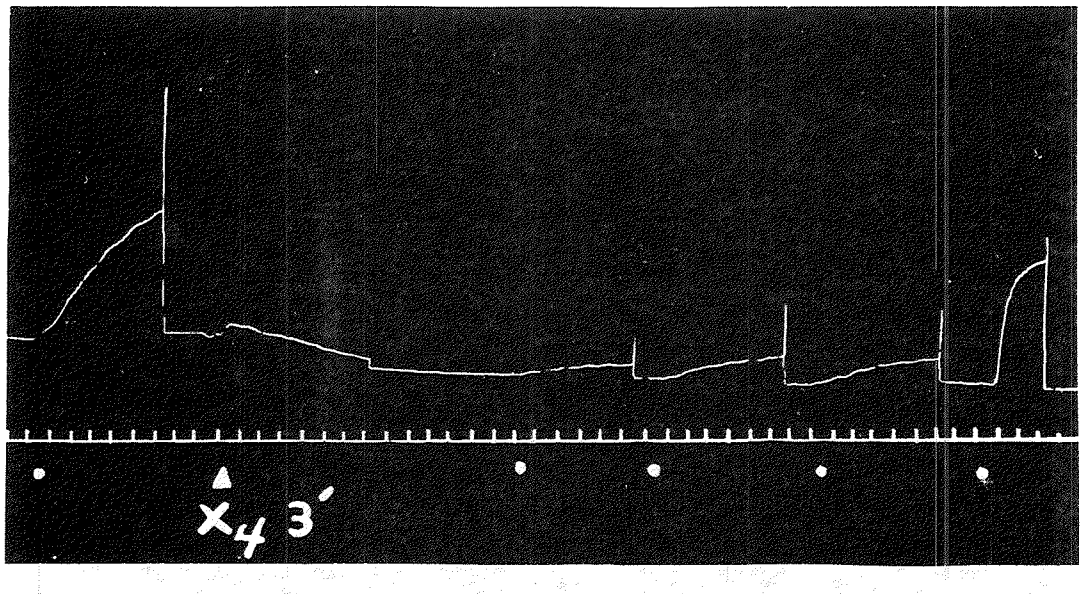


Fig.20: Effect of (AE) aqueous extract of **sphaeranthus** on isolated rat jejunum.
Unmarked contractions are due to angiotensin.
x_4: 1.1468 mg (AE) / ml bath solution

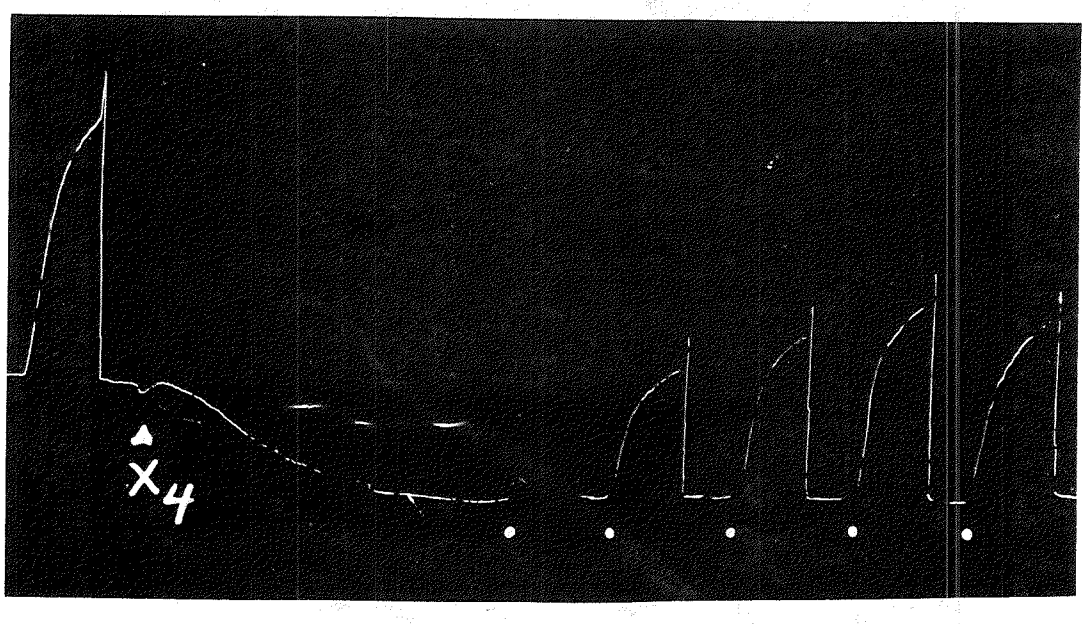


Fig.21: Effect of (AE) aqueous extract of **sphaeranthus** on isolated rat jejunum.
Unmarked contractions are due to acetylcholine.
X: 1.1468mg (AE) / ml bath solution

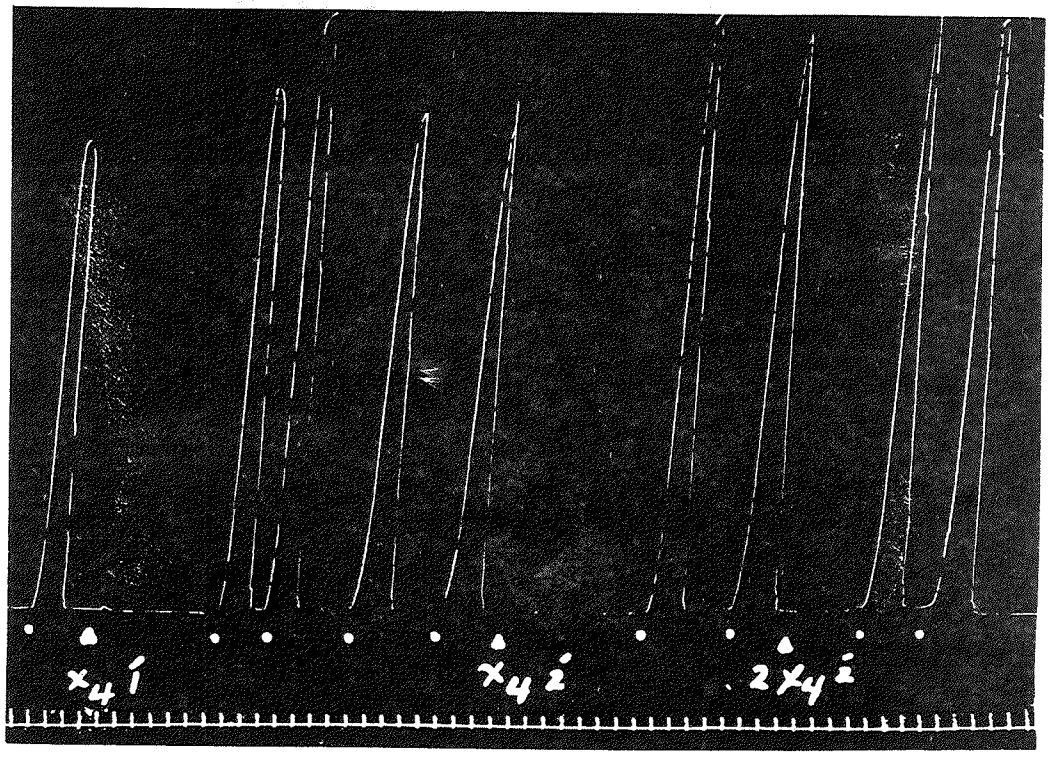


Fig.22: Effect of (AE) aqueous extract of **sphaeranthus** on isolated guinea pig vas deferens.
Unmarked contractions are due to adrenaline
x_4: 0.7168mg (AE / ml bath solution.
2 × 4: 1.4335 mg (AE) / ml bath solution

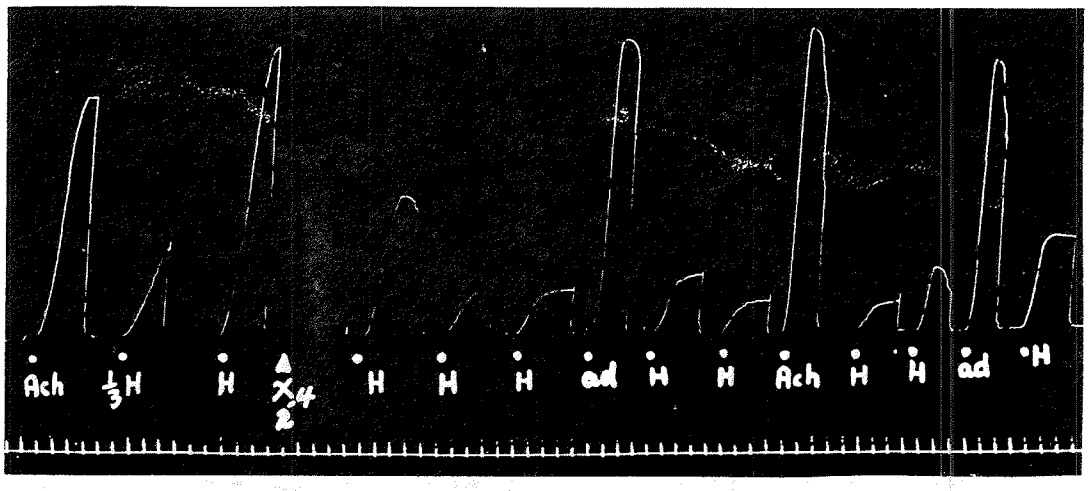


Fig.23: Effect of aqueous extract (AE) of sphaeranthus on isolated guinea pig vas deferens
H: Histamine Ach: Acetylcholine
ad: adrenaline
x_4: 1.4335 mg (AE) / ml bath solution

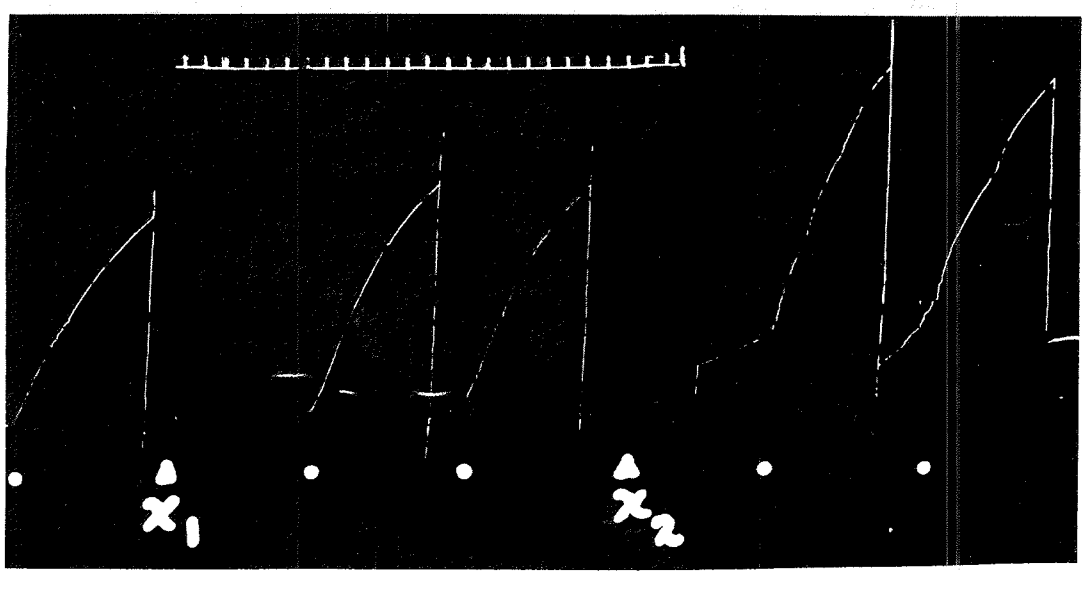


Fig.24: Effect of (AE) aqueous extract of sphaeranthus on toad rectus abdomnis muscle. Unmarked contractions are due to acetylcholine
X_1: 0.7168 mg (AE) / ml bath
x_2: 1.4335 mg(AE) / ml bath

The (AE) produced a slight non-significant effect on blood pressure.

It is concluded that the (AE) contains one or more active ingredient(s) which possess antihistamine and antiserotonin effects in addition to a bronchodilator and smooth muscle relaxant effect. The (AE) also showed a coronary vasodilator effect.

This is only a preliminary report. Further investigations are required to explore the chemical composition of this plant in order to determine the exact pharmacological effect of any possible active ingredient that may be present in this plant. Also toxicity studies for acute and chronic administration of the (AE) or any active ingredient. The preliminary data obtained in this work are encouraging.

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ANTI-MICROBIAL AGENTS IN ISLAMIC MEDICINE

Dr. Inamul Haq

PAKISTAN

INTRODUCTION

Medicinal plants have been used during the ages for the cure and treatment of diseases but it was during the Islamic Era that the concept about antimicrobial agents was born. The Arabian physicians not only described the infections of the body but mentioned several medicinal plants and vegetable substances against rabies and hydrophobia in their pharmacopoeias[1] or medical formularies[2]. The use of medicinal plants against rabies and other infections during Islamic Era show that the same possess some anti-microbial / anti-viral properties.

The Islamic medicine which is mostly based on herbal medicine is known to be catering to more than 80% of the population in the regions comprising the Muslim world. Since the infectious diseases are mostly prevalent in these regions, there is a need to develop some anti-bacterial agents of plant origin - comparable to antibiotics considering the local conditions and resources of these countries. Antibiotics are imported in these countries at the expense of foreign exchange. Research has already confirmed that higher plants possess considerable anti-bacterial activity when compared to modern antibiotics like chloramphenical and streptomycin[3]. Thus the study started in 1973 on 1500 varieties of higher plants available in U.S.S.R., Turkman S.S.R and N. Caucasus showed that plants were rich source of antibiotics[4].

Many plants claiming to possess anti-dysentric , anti-septic, germicidal, fungicidal properties[5] and those considered to be effective against such diseases of microbial etiology like small-pox, tuberculosis, typhoid, diptheria[6] etc. are reported in the literature on traditional medicine. Similarly plants with anti--bacterial and anti-viral activity[7] have also been described in the literature. Considering that Islamic countries where traditional medicine is being practised are rich in medicinal plant resources, research efforts should be intensified to find out useful anti-microbial agents also because such agents are considered to be less toxic as compared to modern antibiotics because of their intimate connection with the nature.

Being prompted to discover some anti-microbial agents of plant origin, we in the National Institute of Health, Islamabad, started a screening programme for monitoring anti-bacterial activity in medicinal plants in collaboration with P.C.S.I.R. Laboratories, Peshawar. The ultimate object of the study is to develop some dosage forms of herbal origin with antimicrobial activity comparable to modern antibiotics.

MATERIALS AND METHOD

Preparation of Extracts

Plants were cleaned, dried at a room temperature, powdered and the powders were extracted in soxhlet with ethanol. Solvent was removed and the extracts after fractionation with chloroform were used for the test.

Test Organisms

In our investigation the following micro-organism were used:

Vibrio cholera, E. Coli, Bacillus subtilis.
Staphylococcus aureus, Shigella dysenteriae and Salmonella typhi.

Preparation of samples for testing

Tween 80 was used as solvent vehicle for the plant extract. All extracts were dissolved in the aforementioned solvent to give a concentration of 10mg/ml.

TABLE 1

ANTIMICROBIAL ACTIVITY OF SOME WILD GROWING PLANTS

S.No.	NOMENCLATURE	Activity against					
		B.Subtilis	E.Coli	Vibrio cholera	Sh.Dysenteriae	Staph.aureus	Styphi
1.	Arenaria leptoclados Guss. St,lf.	- ve	-ve	- ve	- ve	- ve	- ve
2.	Argyrolobium roseum, CAMB, st.	- ve	- ve	+ ve	- ve	- ve	- ve
3.	Dianthus crinitus rim. st. lf.	- ve	+ ve	+ ve	- ve	+ ve	- ve
4.	Polygala hohenacke_riana, Fisch & May,st,lf	- ve	+ ve	+ ve	- ve	- ve	- ve
5.	Saussurea heteromalla. D.Don, st,lf.	++ve	++ve	++ve	++ve	++ve	++ve
6.	Impatiens balfourii Hk. st. lf.	- ve	+ ve	+ ve	+ ve	+ ve	- ve
7.	Dipsacus mitis, st. lf.	- ve	+ ve	- ve	+ ve	+ ve	- ve
8.	Urtica dioca st, lf.	- ve	+ ve	- ve	- ve	- ve	- ve
9.	Tagetes patula L.st, lf, Fr.	- ve	+ ve	- ve	- ve	+ ve	- ve
10.	Kickxia incana Wall st, lf	- ve	+ ve	- ve	- ve	+ ve	- ve
11.	Spiraea vaccini-polia D.Don, st,lf.	- ve	+ ve	+ ve	- ve	+ ve	- ve
12.	Salvia moorcroftiana, st, lf, Rt.	- ve	+ ve	+ ve	- ve	+ ve	+ ve
13.	Hedera nepalensis K.Kock. lf, Rt.	+ ve	+ ve	+ ve	+ ve	- ve	+ ve
14.	Anemone Obtusiloba D.Don. st. lf.	- ve	- ve	- ve	- ve	- ve	- ve
15.	Oxalis pescaprae. st, lf.	- ve	- ve	- ve	- ve	- ve	- ve
16.	Lithospermum qrvense L. St, lf.	- ve	- ve	- ve	- ve	- ve	- ve
17.	Reseda aucheri Boiss. st, lf.	- ve	- ve	- ve	- ve	- ve	- ve
18.	Silene viscosa (L) Pors st, lf.	- ve	- ve	- ve	- ve	- ve	- ve
19.	Silena Conoidea L.st, lf.	- ve	- ve	- ve	- ve	- ve	- ve
20.	Convolvulus glomeratus Clarke st, lf.	- ve	- ve	- ve	- ve	- ve	- ve
21.	Reinwardtia indica Du Most. st.	- ve	- ve	- ve	- ve	- ve	- ve
22.	Potamogeton indicus st.	- ve	- ve	- ve	- ve	- ve	- ve

NOTE:-

i) Tween - 80 was used as solvent.

ii) Abbrevations used: st. (stem), lf (leaf), Rt (root).

Anti-microbial testing

The conventional cup-plate diffusion method was used to test the anti-microbial activity of plant extracts. Molten nutrient agar was poured into petri dishes as a basal layer and when it got solidified, seeded agar was poured over it. The agar was left to set after which 8mm core of agar was removed carefully with the help of a sterilized cork-borer from six peripheral positions and one central. The wells thus formed were aseptically filled up with the samples. The Central hole was filled with tween-80 as a blank. After holding the petri dishes for two hours in the same position they were incubated for 18-24 hours at 37°C and zones of inhibition produced by plant extracts or otherwise were recorded after the incubation period. Those extracts which showed no zones of inhibition were denoted with negative (-) sign while those producing zones of inhibition were denoted with positive (+) sign which were measured in cm by vernier calliper. Extracts were denoted with + or ++ signs depending on the size of zone of inhibition.

RESULTS AND DISCUSSION

Primary screen results of *anti-microbial activity are given in Table I.* As can be seen, out of 22 plants screened, 12 have shown interesting activity. It is evident from the above study and work carried out elsewhere that higher plants could offer a good potential for the development of anti-biotic drugs. In fact many plants like Psoralea corylifolia[8], Myrtus communis[9], Nigella sativa[10], Clycyrrhiza glabra[11], Cannabis sativa[12], Jetropha podagrica[13], and many others used in the Islamic Medicine for different purposes are lately reported to possess antimicrobial properties but they are not used in therapeutic for the above purpose. It was in view of the above consideration that the proposed study was undertaken.

In the first paper published in Fitoterapia in 1980 we described the results of anti-microbial activity of 71 extracts obtained from 26 species of medicinal plants[14]. Subsequently, another paper was published in the same journal reporting the results of anti-microbial activity of 90 extracts obtained from 33 species of wild growing plants[15]. The results of the above screening are reproduced in Table 2 and 3 respectively.

With the above study, anti-microbial screening of 81 plant species have been completed. These studies definitely show that some of the medicinal plants possess good anti-microbial activity when compared against modern anti-biotics. Being encouraged worthwhile to prepare some dosage form out of the plants screened. For this purpose, Myrtus communis, the essential oil of which had exhibited good anti-bacterial activity specially against E. Coli and Shigella dysenteriae in a previous study, was selected. This plant is commonly used as such in traditional medicine for different purposes.

An anti-diarrhoeal oral emulsion and a cream for topical use were prepared from the essential oil. While the stability and toxicological study of the oral emulsion is still in progress, the topical cream in a 5% V/W conc. demonstrated good anti-bacterial activity comparable to Furacin cream of S.K. & F. However, the work is still in progress which will be prescribed in some later publication.

CONCLUSION

Medicinal plants used in the Islamic medicine offer a great reservoir for the discovery of new anti-microbial drugs comparable to anti-biotics used in modern medicine. Since almost all the antimicrobial agents are being imported into the countries comprising the Islamic world and considering the local availability of medicinal plants in these countries, it is imperative that a serious scientific effort should be made to find out new anti-microbial drugs of herbal origin relevant to the disease pattern in these countries.

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ANTI-INFLAMMATORY AND CNS DEPRESSANT ACTIVITIES OF XANTHONES FROM CALOPHYLLUM TRAPEZIFOLIUM TH. W.

Drs. S.K. Nazimuddin, C. Gopalakrishnan, D. Shankar Narayan, Mrs. N. Nazeemunissa Begum and Mr. L. Kameswaran.

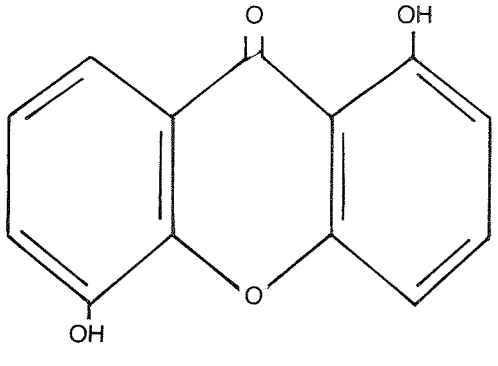
INDIA

INTRODUCTION

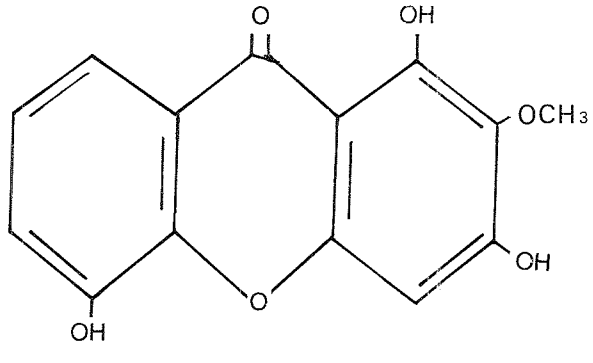
The plant Calophyllum trapezifolium Th.W. belongs to the genus calophyllum (Family Guttiferae). It is a moderate size evergreen ornamental tree. Various parts of these plants are commonly used in the treatment of rheumatism, skin diseases, dysentery and bleeding piles etc. in the traditional systems of medicine, (Nadkarni)[1], (Chopra et al)[2]. More than half a dozen calophyllum species had been so far investigated. Kalyanaraman et al[3] have reported the occurrence of various xanthones from the heartwood of calophyllum trapezifolium Th.W. In a collaborative study (Gopalakrishnan et al)[4], the pharmacology of several xanthones of C. Inophyllum such as Jacareubin, Desoxyjacreubin etc. was investigated and a variety of effects such as CNS depressant, anti-inflammatory, antimicrobial etc. have been reported. According to a review article of Hostemann and Wagner[5], not many investigations have been made on the pharmacology of xanthones and hence it was thought worthwhile investigating the pharmacology of the xanthones obtained from C. Trapezi-folium.

MATERIALS AND METHODS

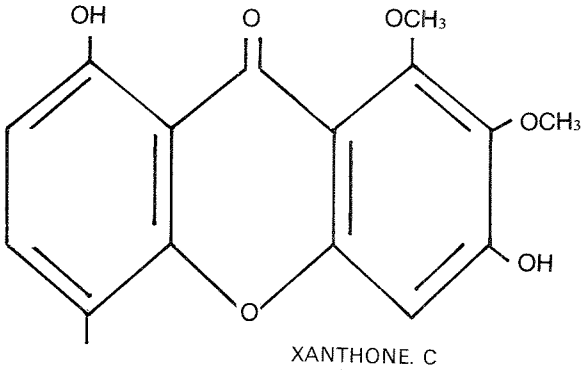
Isolation of the xanthones: Isolation and purification of the xanthones namely Dihydroxy xanthones (DHX), xanthone C(XC) and Xanthone E(XE) from the plant C. Trapezifolium were done essentially according to the procedures of Kalyanaraman[3]. The chemical structures of the xanthones and the abbreviation given in brackets given below, have been used whenever needed through out this paper in describing the pharmacological action of the xanthones.



1-5 DIHYDROXY XANTHONE



XANTHONE E
<X C>



XANTHONE. C
<X E>

Drug Preparation and Administration: The xanthones of C. Trapezifolium (DHE, XC and XE) were not freely soluble in water and hence fine suspensions of the compounds in 2% gum acacia (w/v) were prepared using a "Remi Homogenizer" at 3000 rpm. These were administered to rats and mice intraperitoneally and the volume of the suspension was kept constant at m./kg. The same volume of gum acacia suspension was administered to the control animals intraperitoneally.

Animals: Swiss albino mice (20-30gm) and wistar albino rats (100-200g) of either sex were used. They were fed with the standard pellet diet and housed for a week in laboratory animal.

EFFECTS ON CENTRAL NERVOUS SYSTEM

a) *Gross Behaviour:* This was studied according to the method of Turner[6]. Xanthones of C. Trapezifolium was administered to groups of 5 mice each in doses of 10, 30, 50, 100, 300, 800 mg/kg body weight. Gross behavioural changes were recorded at 15, 30, 60 and 120 mins. after the administration and were compared with the gum acacia treated control animals.

b) *Pentobarbital Sleeping Time:* This was studied in groups of animals (10, in each) of albino rats. The test compounds were administered 30 min. before the injection of Pentobarbitone sodium (Nembutal, 30 mg/kg) intraperitoneally. The duration of sleep was assessed as the time between the loss and the return of the righting reflex. Results were expressed as per cent increase in sleeping time of the drug treated rats versus those of the control group.

c) *Ether Anaesthesia:* This was studied according to the method of Bhide[7] using pairs of rats, of which one animal was administered with gum acacia and served as control, while the other animals were treated with the test compounds at 100 mg/kg i.p. and exposed to 2ml of ether for 2 min. in an inverted large funnel. The animals were removed immediately after 2 min, placed on the table and the time taken, for regaining the righting reflex was recorded and the per cent potentiation of ether anaesthesia was calculated. For each group, 10 pairs were used.

d) *Forced Motor Activity:* This was studied according to the method of Dunham and Miya[8]. 20 Wistar rats of either sex were divided into 4 groups of which three belong to test groups and the remaining one served as control.

ANALGESIC ACTIVITY

This was studied in groups (10 in each) of rats according to the method of Gujral and Khanna[2], using an analgesiometer. Tail flick response to radiant heat was observed in animals treated with gum acacia, xanthones (100 mg/kg) and morphine hydrochloride (15 mg/kg).

Anticonvulsant activity: This was evaluated in rats as per the method of Dikshit, Tiwari and Dikshit[10] using a convulsiometer. Five groups (10 in each) of rats were subjected to Maximal electroshock seizures (MES), by passing a current of 150 in A through a pair of corneal electrodes for 0.2 sec. and the characteristic tonic extensor spasm of the hind limb was noted. Animals showing positive response only were used for the studies. The test, positive control and the negative control animals were administered with the xanthones (100 mg/kg), phenobarbitone sodium (Gardinal, 100 mg/kg) and gum acacia 30 min before the indication of seizures respectively. The ability of the test compounds to abolish the tonic spasm of the hind limb was noted and compared.

Antipyretic Activity: This was studied essentially that of Maren[11] in rats. Pyrexia was produced by administration of Brever's Yeast (20% w/v 1 ml/100 g.s.c.) Peak temperature increase could be obtained only 18hr. after the administration of yeast. The ability of the xanthones (100 mg/kg) to decrease the elevated body temperature was compared with the control (Gum acacia) and the positive control (para cetamol 100 mg/kg) animals by using a clinical thermometer.

EFFECTS ON CARDIOVASCULAR SYSTEM:

Frog's heart in Situ: This was studied as per the method of Burn[12]. The effect of graded doses of the xanthones on the rats and force of myocardial contraction was studied and recorded on a smoked drum.

Dog's blood pressure and myocardiogram: The effect of I.V. administration of graded doses of the xanthones on blood pressure and myocardiogram of anaesthetised dogs (5 animals) was recorded according to the method of Chushney[13].

ANTI INFLAMMATORY EFFECT: The anti inflammatory effect of the xanthones was evaluated using albino rats by the following three different techniques:

1. Carrageenin induced hind paw oedema (Winter et al)[14].
2. Cotton pellet implantation (Winter et al)[15].
3. Granuloma pouch (Selye)[16].

For compounds which showed an anti inflammatory effect by parenteral administration, oral anti inflammatory effect by parenteral administration, oral anti infalmmatory effect was determined by techniques 2 only. In all the experiments the xanthones were administered at a dose level 50 mg/kg, while the positive control animals were administered with phenylbutazone (100 mg/kg) or dexamethasone (1 mg-/kg). The control animals were administered with 2% gum acacia at a volume of 2 ml/kg. Anti inflammatory effect was expressed as per cent inhibition of the oedema volume/weight of granuloma tissue-/volume of the exudate which was calculated by the formula (1-T/C) x100, where T and C are the mean value of the drug treated and control groups respectively.

Effect on Adrenalectomised rats: Test compounds which exhibited an anti inflammatory effect in adrenal intact animals were studied for the effect in bilaterally adrenalectomised rats, in order to find out the involvement of adrenal glands in the mediation of thin anti inflammatory effect. Bilateral adrenalectomy was done according to Zarrow et al[17] and the anti inflammatory effect of the xanthone at a dose level of 50 mg/kg was examined according to the method of winter et al[15].

EFFECT ON PERITONEAL MAST CELLS OF RAT:

Staining and counting of the ruptured intact mast cells were done according to the technique described by Bray and Van Arsdel[18], in order to elucidate the effect of the xanthones on the rupture of mast cells induced by the mast cell degranulators such as compound 48/80, diazoxide and triton-x-100.

EFFECT ON PROTHROMBIN TIME:

To groups (10 in each) of albino rats were administered gum acacia, and xanthones (DHX, XC and XE) daily for 10 days. The plasma was collected from each animal on the 11th day and the prothrombin time was estimated according to the method of Quick[19].

RESULTS:

Effects on CNS:

a) *Gross Behaviour:* Preliminary screening of the xanthones of C. Trapezifolium revealed that the xanthones have a definite modulating effect on the behavioural pattern of mice. All the xanthones were found to produce a mild degree of CNS depression characterised by ptosis, sedation, sleep, ataxia, decrease in muscle tone and decrease in spontaneous motor activity. The CNS depressant effect was predominent at a dose level of 200 mg/kg and this effect was observed within 15min. after the administration of the test compounds and the effect lasted for 60-90 min. All the xanthones up to a dose of 800 mg/kg did not produce any untoward symptoms and there was no mortality up to 24 hrs.

b) *Pentobarbitone sleeping time:* The xanthones exhibited varying degrees of potentiation of the pentobarbital sleepig time as evidenced by the Table I.

c) *Ether anaesthesia:* Here again, the xanthones significantly potentiated ether anaesthesia as depicted in Table 2.

d) *Forced Motor Activity:* The effect of the xanthones on forced motor activity revealed that the compounds have varying degrees of impairment, indicating loss of muscle tone as evidenced by the Table 3.

Analgesic Anticonvulsant and Antipyretic Activities: The xanthones did not produce any of these activities in albino rats.

Effect on cardiovascular system: None of the xanthones employed in the present study had any effect on rate and force of contraction of frog's heart as well as the blood pressure and myocardiogram of dogs.

Anti inflammatory effect: The xanthones of C. Trapezifolium produced significant anti-inflammatory effects in rats as tested by the carrageenin induced hind paw oedema. Cotton pellet granuloma and granuloma pouch techniques. Table 4 summarises these results.

Anti inflammatory effect upon oral administration: Table 5 shows the anti inflammatory effects of the xanthones upon oral administration.

Anti inflammatory effect in adrenalectomised rats: Table 6 shows the results of the anti inflammatory effects of the xanthones in adrenalectomised rats.

Effect on rat peritoneal mast cells in vitro: The xanthones did not show any significant mast cell membrane stabilising effect, as evidenced by their inability to prevent the rupture of mast cell induced by polymyxin B, diazoxide and Triton X-100

Effect on Prothrombin time: While the prothrombin time in the control rats was 12 ± 0.62 secs, the prothrombin times of DHX, XC and XE were in the orders of 12.2 ± 0.66 sec., 12.0 ± 0.28 sec. and 12.4 ± 0.48 respectively, which were not statistically different from the control values.

DISCUSSION

The xanthones of C. Trapezifolium have been found to produce a variety of interesting pharmacological effects in experimental animals. The findings of the authors are in agreement with the findings related to Garcinia mangostana, Calophyllum inophyllum and Mesua ferrae (Shankarnarayan et al)[20] (Gopalakrishnan et al)[4]. While the xanthone -c- glucoside such as mangiferin and xanthone - o - glucoside such as mangostin, 3,6, dio-glucoxide have been reported to produce CNS stimulant, analgesic, anti conculsant (Bhatacharya et al)[21]and cardiotonic effect (Shankarnarayan at al)[22]. No such activities could be observed for the xanthones of C. inophyllum and M. Ferrea (Gopalakrishnan, Shankaranarayan, Nazimuddin)[4] and xanthones of C. Trapezifolium studied at present.

The xanthones used in the present study have been found to produce significant anti inflammatory activity in normal as well as in adrenalectomised rats by both intraperitoneal and oral routes. The slight decrease in the anti inflammatory activity of all the xanthones upon oral administration suggests that there might be some impairment in the rate of absorption of the xanthones from the gastrointestinal tract which requires further study. The exact mechanism by which the xanthones produce anti inflammatory activity is not known. Unlike indomethacin and meclofenamate, xanthones of C. Trapezifolium do not stabilise the mast cell membrane as evidenced by their lack of antagonism activity against various mast cell degranulators. Since the xanthones mangostin has been reported to inhibit prostoglandin synthetase (Shankaranarayan)[20], it would be interesting to elucidate the effect of the xanthones of C. Trapezifolium on the activity of prostaglandin synthetase.

Though the anti inflammatory agents in clinical use exhibit analgesic and antipyretic properties, the xanthones used in the present study do not possess analgesic properties.

Quite interestingly, the xanthones used in the present study do not produce any prolongation of

prothrombin time in rats, which is a common side effect encountered with the anti inflammatory compounds such as acetylesalicylic acid.

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TABLE 1

EFFECT OF XANTHONES OF C. TRAPEZIFOLIUM ON PENTOBARBITONE SLEEPING TIME

Drug	Dose	PBS TIME MEAN ± S.D.	% Increase
G.A.	2 ml/kg	77.30 ± 6.60	—
DHX	100 mg/kg	93.6 ± 6.3	19.8*
XC	100 mg/kg	101.5 ± 8.5	31.3*
XE	100 mg/kg	105.6 ± 9.2	36.3*

* P = < 0.01

TABLE 2

EFFECT OF XANTHONES OF C. TRAPEZIFOLIUM ON ETHER ANAESTHESIA

Drug	Dose	Ether Anaesthesia Mean ± S E M	% Increase
F.A.	2 ml/kg	4.25 ± 1.25	—
DHX	100 mg/kg	6.25 ± 1.28	47.05*
XC	100 mg/kg	7.25 ± 1.48	70.50*
XE	100 mg/kg	8.60 ± 1.65	102. 60*

* P = <0.01

TABLE III

EFFECT OF THE XANTHONES OF C. TRAPEZIFOLIUM ON FORCED MOTOR ACTIVITY

Drug	Dose	Balancing time Mean ± SEM	% Decrease
GA	2 ml/kg	126.80 ± 4.41	—
DHX	100 mg/kg	82.80 ± 6.55	34.7*
XC	100 mg/kg	76.50 ± 5.60	39.7*
XE	100 mg/kg	71.50 ± 6.20	43.6*

* P = 0.01

TABLE IV

ANTI INFLAMMATORY EFFECTS OF XANTHONES ON C. TRAPEZFOLUM

DRUG	HIND PAW OEDEMA VOLUME (ml)			COTTONPELLET GRANULOMA WT. OF COTTON PELLET (MC)			GRANULOMA POUCH VOL. OF EXUDATE (ML)		
	MEAN ± SEM	% Re-duction	P	Mean ±SEM	% RE-duction	P	Mean ± SEM	% Re-duction	P
Gum Acacia	1.57 ± 0.17	—	—	55.3 ± 6.7	—	—	2.76 ± 0.54	—	—
Dexame-thazone	0.49 ± 0.15	68.8	(0.001	26.6 ± 3.8	52.3	<0.001	0.90 ± 0.20	67.4	<0.001
Phenyl Butazone	0.46 ± 0.11	70.7	(0.001	25.3 ± 6.0	54.3	<0.001	0.98 ± 0.34	64.5	<0.001
DHX	0.98 ±0.11	37.6	(0.01	37.5 ± 4.1	32.2	<0.01	1.66 ± 0.52	39.9	<0.01
XC	0.91 ± 0.18	42.0	(0.01	34.1 ± 5.2	38.3	<0.01	1.49 ± 0.24	46.0	<0.01
XE	0.83 ± 0.15	37.1	(0.001	29.5 ± 4.6	46.7	<0.001	1.38 ± 0.25	50.0	<0.001

TABLE V

ANTI INFLAMMATORY EFFECT OF THE XANTHONE OF C. TRAPEZIFOLIUM UPON ORAL ADMINISTRATION IN RATS

Drug	Dose mg/kg.	Carrageenin induced hind paw oedema vol. in ml. Mean ± S.D.	% Potentiation
Gum Acacia	2ml	1.62 ± 0.20	—
Phenyl Butazone	100	0.54 ± 0.16	66.7*
DHX	*50*	*1.22* ± 0.18	24.7*
XC	*50*	*1.16* ± 0.22	28.4*
XE	*50*	*1.11* ± 0.17	31.5*

* P (0.01

TABLE VI

ANTI INFLAMMATORY EFFECT OF THE XANTHONES OF C. TRAPEZIFOLIUM IN ADRENALECTOMISED RATS

Drug	Dose mg/kg	Cotton Pellet Granuloma wt. of cotton pellet in mg. Mean ± S.D.	% Potentiation
Gum acacia	2 ml	56.6 ± 6.4	—
Dexamethazone	1	28.7 ± 7.0	49.3
Phenyl Butazone	100	32.0 ± 6.0	43.5
DHX	50	42.4 ± 5.8	24.9
XC	50	40.2 ± 6.2	29.0
XE	50	34.5 ± 5.6	39.1

PROTECTION OF GASTRIC MUCOSA BY ALOE VERA

Dr. A.Kandil and W. Gobran

EGYPT.

INTRODUCTION

Peptic ulcers are very common. It is estimated to be present in 5.8% of men and in 1.9% of women in the population. The lesions are ulcerations of the mucosa and underlying structures, usually of the lesser curve of the stomach or first part of the duodenum. The ulcers usually start as an acute form when they are small and multiple and surrounded by petechial hemorrhages. They tend to heal readily unless there is gastric stasis and superacidity when they become chronic and erode the wall of the viscus, (Warner, 1964).

The gastric mucosa is remarkably resistant to injury. Two factors normally protect the stomach from autodigestion, namely the gastric mucosa and the epithelial barrier. The application of an irritant to the gastric mucosa is followed by outpouring of large quantities of mucus that owes its protective capacity to its physical characteristics and its ability to absorb pepsin. The epithelial lining has remarkable properties of repair and is able to reproduce itself within 36 to 48 hours, (Silen, 1974).

A peptic ulcer is the result of a continued action of the gastric juice on an area of mucosa which is presumably of lowered resistance. There are three causes for this low resistance namely neurogenic, chemical or infective causes. The neurogenic causes result in abnormal vegal impulses from the hypothalamic region. This leads to vascular spasm and ischemia which may proceed to necrosis.

In addition, the vagal stimulation will lead to hypersecretion of the gastric juice, Chemical agents like cortisone and acetyl salicylic acid can lower the mucosal resistance by producing qualitative changes in the mucus and decreasing its total output, (Boyd, 1961).

On the other hand, Aloe vera is known in folk medicine to possess a satisfactory healing capacity. The legend of this herb started in ancient Egypt thousands of years ago. It was specified in Ebers papyrus which was documented in the first dynasty 2270 years B.C. (Kamal, 1964).

Recently el-Zawahry and Hegazy (1970) demonstrated the therapeutic value of Aloe vera in healing protracted skin ulcerations. This attracted our attention to explore any possible therapeutic or prophylactic effect for this plant against gastric ulcerations.

MATERIAL AND METHODS

Preparation of the Aloe Vera Pulp Extract:

Thirty leaves of the plant were cut with stainless steel knife and washed thoroughly with water. Then they were dried and kept for 24 hours in a vertical position to exclude the drained juice containing aloin. The edges of the leaves were cut, then they were split to curette the pulp which contain the mucopoly - saccharide material. The pulp was mixed in a blender for one hour, sieved by fine gauze and kept in a refrigerator.

Implementation:

Four animal group of 12 male albino rats each (160-180 gm) were chosen to carry out prophylaxis and treatment experiments.

Induction of Gastric Lesions:

This was performed for all the animals by applying a neurogenic and a chemical method simultaneously. Therefore the animals were forcibly immobilised for 24 hours according to our method pub-

lished two years ago (Galal et al.1975). At the same time the animals received 100 mg/kg. body weight of acetyl acid per os.

Prophylaxis Groups:

Each rat in the first group received 2ml of the extract twice daily per os for six days before induction of gastric lesions. The second group received only equimetric saline solution in the same manner. Then both groups were exposed to forcible immobilisation and chemical treatment for induction of gastric lesions.

Treatment Groups:

The third animal group received 2ml of the extract per os twice daily for six successive days after the immobilisation. The fourth group received saline in the same manner for the same period.

Recording the gastric lesions was carried out for all the animals after incising the gastrum along the lesser curvature. The stomach was washed by saline and examined by the naked eye and the lens. Recording of the PH of the gastric juice was measured by PH meter (Beckman).

RESULTS

The results are shown in table I and II.

TABLE I

The Prophylactic Effect of Aloe Vera (A.V.) on Induced Gastric lesions by 24 Hours Fixation and Aspirin 100mg/kg in rats.

	Animal Groups	No. Of Rats	No. Of Lesions	Mean No. Of Leasions/animal	Mean PH
I	Rats receiving A.V. for 7 days before induction of gastric lesions.	12	24	2	4.35
II	Control rats with induced gastric lesions.	12	160	133	4.30

$$\text{Prophylaxis } \% = \frac{136}{160} \times 100 = 85\%$$

TABLE II

The Curative Effect of Aloe Vera (A.V.) on Induced Gastric lesions By 24 Hours Fixation and Aspirin 100 mg/kg in rats.

	Animal Group	No. Of Rats	No. Of Lesions	Mean No. Of Lesions/animals	Mean PH
III	Rat receiving A.V. for 7 days after induction of gastric lesions.	12	42	3.5	5.23
IV	Rats receiving no treatment after induction of gastric lesions.	12	84	7	5.18

$$\text{Curative } \% = \frac{42}{84} \times 100 = 50\%$$

DISCUSSION

The results show that Aloe vera extract possesses a reliable prophylactic potential against this particular model of gastric lesions induced by forcible immobilisation and acetyl salicylic acid administration. If complete prophylaxis against gastric lesions is referred to as 100%, the extract of Aloe vera was able to produce 85% prophylaxis. On the other hand, if complete curative treatment is presented by complete absence of gastric lesions, the Aloe vera extract produced a curative treatment equal to 50%. Gastric lesions induced by this method are probably due to two main etiological factors namely neurogenic and chemical irritation.

The brunt of nervous stress according to many workers may attack the gastric blood vessels. This condition is manifested by increased capillary fragility and permeability leading to petechiae, hematomata and even thrombosis. Consequently the gastric mucosa will be exposed to a degree of ischemia which lowers its resistance, (Bourne, 1953, Coligado and Flesher, 1967).

When the chemical factor in the form of acetyl salicylic acid was added to the nervous stress, the gastric lesions were intense. They took the form of large hemorrhagic spots, ulcers and hemorrhagic streaks, as seen in the results.

It is most likely that the prophylactic and curative effect of Aloe vera is due to its protection of the gastric mucosa and supporting its resistance against the sequelae of chemical and nervous stress, without interfering with the gastric PH.

CONCLUSION

Aloe vera extract was successful as a prophylactic measure against gastric lesions induced by chemical and nervous stress in rats.

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GENERAL DISCUSSION

Dr. Atta-ur-Rehman

I would like to congratulate the speakers for very interesting talks this morning. The point I wish to make is that the conventional study of medicinal plants has involved the pharmacological trials, phyto--chemical trials, toxicological trials and clinical trials have tended to follow all these studies. There has been a recent serious re-thinking on the advisability of this approach, because quite often, either the animal experiments tend to be negative and yet the plant is known to have definite biological activity or the active constituent can often not be isolated, because they are often too unstable to be isolated and so there has been thinking in United Nations Organization as well as by the World Health Organization as to the advisability of undertaking direct clinical trials on those herbal extracts which have been used for long periods in different traditional systems of medicine. A resolution to this effect came out by the W.H.O. in 1977, when they said that one should, in fact, go into direct clinical trials and the phyto--chemistry, toxicology and pharmacology can all follow afterwards. Now the point I wish to make here is, if this approach is adopted in all seriousness and with a due sense of urgency, then this does place the Islamic countries in a position of decided advantage over the West. In the West, there is a highly restrictive legislature which prevents the Western scientific groups to indulge in direct clinical trials and even in some Islamic countries, there have been objections from the medical quarters that, would this not be equivalent to using human beings as guinea pigs? But after a lot of discussions there is now an International consensus of opinions, as illustrated by the W.H.O. resolution, that this would not be so, because these plant materials have been used for centuries, safely and in fact, if one wants to put an additional scientific base to it, one could indulge in preliminary toxicological studies before going into clinical trials, but this does put us into a position of decided advantage and I would plead over here that in different Islamic countries as well as non-Islamic countries, where this type of work is going on, they should launch major programmes of clinical trial trying to, choosing a few specific diseases, specially those diseases which are amenable to quantized analysis, e.g., blood pressure, cholesterol levels and so on, and choosing those plant materials which have been used for a long time and then accumulate statistical data. If a plant is toxicologically safe and if the plant extract is active, then there is no logical reason why it could not be introduced into an integrated pharmacopoiea directly, without having to bother about the chemical constituents, their structure and so on, present in it.

Dr. Tharwat Ghoneim,

The introduction of the plants, directly into clinical use without the previous study, can be very serious. This is very very serious and very dangerous. Even if their toxic effects do not appear in one year or two years or even twenty years, but after one hundred years some toxic effects may appear. Thus, even if there is an International agreement to do this, we are afraid for the new generation. Something may appear iatrogenic or toxicity. So these are very dangerous and thus it is better to have an idea about the drug, experimentally studying the toxicity for few years on animals and then the picture is to be transfered to human beings.

Hk. Mohammed Said,

I think Dr. Atta-ur-Rehman was talking about those medicine or botanical plants, which are already in use for centuries. I think, he meant that.

Dr. Wolfgang Volter

Perhaps I should make a comment on this, because in my opinion, there are two different systems we have right now in the world, e.g. in W.Germany. I will demonstrate this, in the afternoon, in my lecture. If today, we apply a drug, we have to do a tremendous amount of study, we have to investigate the metabolism, we have to isolate the metabolite of the drug, which are formed in the body and even

then we have to investigate the metabolized difference, pharmacological studies. Thus in many companies, right now, they are afraid of creating new drugs, because a lot of work and money is involved in the creation of new drugs. One thing Dr. Atta-ur-Rehman said is that, one gets least (minimum) harm with drugs, which are used since centuries. Of course, perhaps a preliminary toxicity should be made. But on the other side what is right now, advised in our country, to my opinion is too much, because it prevents us from new developments.

Hk. Abdul Razzak,

I would just like to add to what Dr. Atta-ur-Rehman has said. Well, leaving aside the ethical considerations, as he has said about the International agreement, we, in India, have already launched this scheme, since 1964, of having the composite drug trials. First we subject them to clinical trials and then to other Parameters. Well the toxicity and other considerations have been taken note of, because these drugs are in daily use over thousands of patients and no un-toward effects have been reported so far, because to start on what is being contemplated in Germany and other countries, it will take about a million years to complete this study, but you have some data based on clinical practices which can be safely introduced and of course if, you want, you can have rapid clinical screening or rapid toxicity tests done, but to link it with pre-requisites, like pharmacological studies, chemical structure etc., it will be time consuming and we will be denying humanity, what our ancestors have already, debated, experimented and given to us. That is my submission.

Dr. Zuhair Al-Baba

What I want to just mention is that the whole issue has got its philosophical aspect. I mean when some body goes to a time honoured herb or a folk medicine and tries to find what is the active ingredient in it and do some experimental studies, let us say animal experimentation, or pharmacological studies. The matter is not only to secure the safety and efficacy of drugs, but to my mind, there is another dimension. It is man's attempt at knowing what is going on and trying not only to utilize the nature, but to improve it. I mean, let us say, the story of semi-synthetic and synthetic products. He discovers penicilline but then he plays with the molecules. He may add a missile group he may substract hydrogen atom and I think this is quite justified and to my mind, people believing in herbalism, have some times appealed to me as some sort of an anti-science movement. It is not always, back to the natural movement or a green revolution in medicine as they claim. Sometimes it is an attitude analytical to science. To my mind, there is no real clash between herbalism and synthetic chemistry and chemo-therapy etc. I would like to think of them as a continuous spectrum and going back to nature is to try to make use of the time honoured experience of man with the natural sources of the drugs, but then let us not forget that man, all the time has been trying to control his destiny and to improve in nature and it is completely his right to do so.

Dr. Inamul Haq,

Perhaps, I feel that it will be unsafe to jump on directly to clinical trials on human beings, because lately there has been reports in China, that some recipes which have been used for long, have been found to cause lead poisoning. So, I feel that some toxicological studies must be done before we jump on directly to clinical trials on human beings.

Dr. Gunther Stille,

I think we should proceed and see the problem of animal experiments and clinical trials very differentially. The toxicological studies are necessary for special questions. If you use a drug for some hun-

dreds of years, I think chronic toxicological studies are not useful, but you are not able to exclude a contragenity or iatrogenity, because these effects are very secret and it is not possible to show these effects without very clear aged studies in animals or human beings, though I think we must use the animals. On the other side, if you look on the pharmacological effects, you can use animals, but that is for the practical medicine, much more important. If you look on the therapeutical effects, then you must use men. It is impossible to show therapeutic effects on animals and we must always differentiate between the pharmacological effects and therapeutical effects. I think if you have a drug which you have used for so many times, it is more important to see on the therapeutical effects than pharmacological effects, because it can be scientifically interesting to look on the pharmacological side. I say it, as a pharmacologist. I think the main and important one is therapeutic effect. I think we should speak about it very very differentiately.

Hk. Mohd. Said (Chairman)

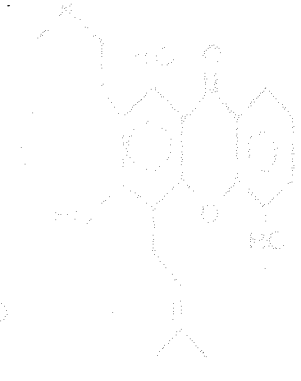
I thank you Dr. Gunther Stille. I think we have no question now. I will not advocate the use of a medicine or a drug without examining the toxicity, but at the same time, I would agree with W.H.O. stand that to save time we should try herbs which have been in use for centuries without any side effects. If you go into details, we have a very glaring example of thaladomides. This drug was perfected by a very very large and perfect organization, but it produced side effects and thousands of children were born without limbs and with crippled bones. So, there is also a danger in the most modern scientific research. Any way, we have to be very careful about the use of the drugs. Now in the end I would like to thank the speakers and also the audience and my thanks to the Organization of this Conference, for giving me the honour to preside over this session. Now the session is over. Thank you very much.

Part Eight: *Clinical - Cum - Pharmacological Evaluation of Therapeutic Proce - dures used by Moslem Physicians.*

CHAPTER TWO

(Some Selected Papers — Not Presented)

1. ANTI-ULCER AND ANTI-MICROBIAL ACTIVITIES OF GARTANIN - XANTHONE FROM GARCINIA MANGOSTANA LINN.
   Mrs. N. Nazeemunisa Begum, et al.
2. ANTI-INFLAMMATORY EFFECT OF GUL-E-TESU. (BUTEA M MONOSPERMA LAM FLOWERS).
   Dr. S.K. Nazimuddin, et al
3. POSSIBLE EFFECT OF SOME EXTRACTS OF NIGELLA SATIVA L. SEEDS ON BLOOD COAGULATION SYSTEM AND FIBRINOLYTIC ACTIVITY.
   Prof. M. Tharwat Ghoneim, et al.
4. CORRELATION BETWEEN ISLAMIC VALUES AND THE INCIDENCE OF CANCER.
   Dr. Ahmed Al-Kadi, et al.



ANTI ULCER AND ANTI MICROBIAL ACTIVITIES OF GARTANINXANTHONE FROM GARCINIA MANGOSTANA LINN

Mrs. Nazeemunissa Begum, Dr. S.K. Nazimuddin,
Mr. C. Gopalakrishnan, Mr. D. Shankaranarayan
and Mr. L. Kameswaran.

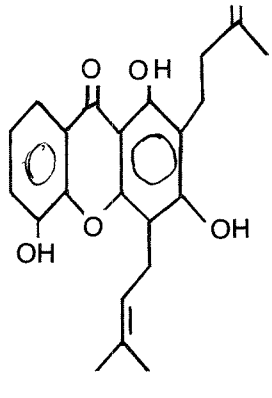
INDIA

INTRODUCTION

The tree garcinia mangostana linn, belongs to the family guttiferae. The rinds of the fruit is an astringent and is useful in the treatment of diarrhoea and dysentry (Chopra).[1] In the recent days, new synthetic agents with specific pharmacological actions like histamine - 2 (H2) Receptors antagonists are widely used in the therapy of gastric ulcers and after realisation of the importance of penicillin as a therapeutic medicine in about 1940, it gave a tremendous stimulus to the search of micro organisms capable of yielding new antibiotics and this search was also extended to cover the higher plants. In view of this and the reports on the anti ulcer activity and antibiotic effects of certain xanthones of garcinia mangostana (Shankaranarayan et al)[2] xanthones of calophyllum inophyllum and mesua ferrea (Gopalakrishnan et al)[3] anti ulcer activity of xanthones of calophyllum Trapezifolium (Nazimuddin et al)[4] and antibiotic effect of a xanthone Morelline from Garcinia morella (Rao and Natarajan)[5], it was thought worthwhile to investigate the anti ulcer, anti bacterial and anti fungal activities of gartanin - a xanthone from garcinia mangostana Linn.

MATERIALS AND METHODS

Isolation of Xanthone Gartanin: The isolation and purification of gartanin was done essentially according to the procedure of Kalayanaraman.[6] The rinds of the fruits of Garcinia mangostana was dried, powdered (10 kg) and extracted with hexane (5 × 10 lit) solvent removal gave a yellow solid with some supernatant oil. The oil was decanted and the residue washed with small quantities of hexane. The remaining yellow powder was dried (12g). This showed two spots in t.l.c (Silica benzene: Methanol - 25: 0.5). The faster moving spot resolved into a two coloured spot when the t.l.c. was repeated in chloroform: hexane (90:10) and the plate exposed to iodine. The crude material (25g) was chromatographed over silica gel (1 kg) and eluted with chloroform: hexane (60: 40). 25 ml fractions were collected. Fractions 10-18 were mixed and evaporated to give xanthone Mangostin (200 mg). Fractions 19-29 gave a mixture of xanthone mangostin and gartanin (3 g). Fractions 30-41 gave pure xanthone gartanin (1 g). The mixture of xanthones mangostin and gartanin (3 gm) was rechromatographed over silica gel (250 g). Elution with chloroform hexane (60 : 40) and collections in 10 ml fractions gave xanthone mangostin (300 mg) and xanthone gartanin (2.5 g). The structure of gartanin is as follows:



GARTANIN

Drug preparation and Administration:

Since the xanthone gartanin was insoluble in water fine suspensions of the above was prepared in 2% gum acacia using a Remi homogeniser at 3000 rpm.

Anti-ulcer Activity:

The preparation developed by Shery et al[7] has been used for the present study. Two groups (six each) of Wistar albino rats were fasted for 48 hrs., and they were allowed to have only water ad libitum. One hour before the pyloric ligation, the group I animals were treated with distilled water which served as controls and to the group II animals was given gartanin (Dose 50 mg/kg) intraperitoneally. The animals were then anaesthetised with ether and under aseptic conditions, a mild incision (1 cm) was made below the xiphoid process and extended downwards. After cutting through the muscle layer, through the linea alba the stomach was exposed and the pylorus was ligated with a cotton thread. The cut ends of the muscle layer and skin were sutured. The animals were sacrificed after 18 hrs. and the stomach was removed. The stomach contents were collected for examination and the stomach was opened along with the greater curvature, mounted on a cork board and the ulcers were examined and visually scored in arbitrary units of 0-4 according to severity (Bonny Castle).[8]

0 = normal, 1 = scattered haemorrhagic spots and hyperemia, 2 = deeper formed haemorrhagic spots and some ulcers. 3 = Haemorrhagic spots and well formed ulcers and 4 = extensive haemorrhage, ulcers and perforation. Histopathological studies were also conducted by taking section of the stomach in both control and treated animals.

Measurement of Volume of Gastric Secretion:

The volume of the gastric contents was recorded. After the measurement of the gastric volume, the contents were centrifuged to get a clear supernatant fluid for determination of total and free acid.

Determination of Free and Total Acids in Gastric Secretion:

This was done by titrating an aliquot of the specimen filtrate with a standard solution of NaoH using 2 indicators in succession such as methyl orange and Phenolpthalein.

INVITRO ANTIBACTERIAL AND ANTIFUNGAL EFFECTS:

Test Organisms: A total of 8 bacteria belonging to various families and 4 species of fungi, both of yeast and filamentous type were used in the present study, such as the following:

BACTERIA: Staph. aureus, pseudomonas aeroginosa, proteus vulgaris, klebscella pneumonia, E. coli, vibro cholera.

FUNGI: Trichopyton mentagrophytes, microsporum canis, epidermophyton floccosum and C. albicans.

METHODS OF ANALYSIS

Three replicates were maintained for each of the tests carried out and each test was repeated to confirm the data obtained therein.

Cup-plate method: To find out the optimum concentration of the drug to be used. S. aureus and T. mentagrophytes were seeded in nutrient agar and Sabouraud's dextrose agar (SDA) respectively and poured in petri dishes. After solidification wells were bored with cork - borer each well was filled with different concentration of the drug prepared by serial dilution from an initial concentration of 1 mg/ml for bacteria and 10 mg/ml for fungi. The plates were incubated at 37°C and 48 hrs., in case of bacteria for one week at room temperature for fungi, and the results were recorded. A concentration of 100 mcg for bacteria and 5 mg/ml for fungi were found to be the optimal levels and these were used in further tests.

Superficial streak or point inoculation method: For evaluating the activity of the xanthone against bacteria and fungi, plates were poured with nutrient agar containing 100 mcg concentration of the respective drug samples for bacteria and sabouraud's dextrose agar 5 mg/ml slants containing the drug were prepared for testing fungi. After getting young cultures of bacteria tested earlier were streaked on the agar and incubated for 48 hrs. at 37°C. The results were recorded and compared. Activity on fungi was car-

ried out in SDA slope cultures. To avoid overgrowth and cross contamination, one slant was used for each fungi tested. The agar slants were incubated at room temperature and the results were recorded after one week and compared.

Mic by Tube Dilution:

Nutrient broth (2 ml) in test tubes were impregnated with the xanthone at the initial concentration of 100 mcg/ml and was serially diluted up to 1.0875 mcg/ml concentration. One loopful of the test bacterium from a young culture was added to each tube and shaken well. The tubes were incubated at 37°C for 48 hrs. and the results were recorded. Uninoculated broth tube and the tube with no drug served as negative and positive controls respectively. The test was repeated thrice and the results compared and confirmed.

RESULTS AND DISCUSSION

Anti-ulcer Activity

Microscopic examination of the incised stomach revealed the fourth degree of ulceration in the control rats characterised by extensive haemorrhage, ulceration and perforation. Animals treated with xanthone exhibited a marked protection against the ulcers induced by pyloric ligation. The ulcer scoring for the gum acacia treated rats was found to be 3.50 ± 0.27 (mean ± S.E.) while the animals treated with the xanthone gartanin was found to be 0.74 ± 0.24. The test animals exhibited only scattered areas of hyperemia and occasional haemorrhagic spots.

There was a significant difference in the total volume, total acid and free acid between the control and drug treated showing effective anti-secretary activity of the drug.

VOLUME		FREE ACID		TOTAL ACID	
Control Test		Cont.: Test		Cont.: Test	
Mean 11.46	5.40	5.66	1.05	11.86	4.40
SD ± 3.10	0.73	0.71	0.74	3.79	1.21
P<0.0.01		0.001		0.01	
S		H.S.		S	

INVITRO ANTI BACTERIAL AND ANTI FUNGAL EFFECTS

The results on the effect of gartanin on the growth of bacteria invitro showed that it had varying degrees of anti bacterial activity, as tested by different assay techniques at an optimal concentration of 100 mcg/ml. Gartanin was able to inhibit. 3 out of 8 bacteria i.e. it inhibited S. aureus, S. typhi and E. coli.

As regards the antifungal activity the xanthone gartanin was active in inhibiting the growth of M. Canis only.

The MIC for gartanin when tested for antibacterial activity was found to be 50 - 100 mcg/ml.

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ANTI-INFLAMMATORY EFFECT OF GUL-E-TESU (BUTEA MONOSPERMA LAM FLOWERS)

Drs. S.K. Nazimuddin and Syed Khaleefathullah

INDIA

INTRODUCTION

Gul-e-teesu (Butea Monosperma, Syn.B.Frondosa flowers (B.M.) belong to the family Leguminacae. The flowers are claimed to be tonic, aphrodiasiac, diuretic and yield yellow dye (Chopra *etal* [1], Nadkarni [2], Satyavate *etal* [3]). It was also claimed to be a blood purifier, anti-inflammatory, corrective of humours namely bile, phlegm and black bile (Mohd. Hussain [4]), anti-helminthic, antipyretic, appetiser and used in spleenomegally (Najmul Ghani Khan) [5]. A crystalline fraction composed of the glycosides butrin and plasitirin isolated from the alcoholic extract of the petals reduced the number of implants in the mated rats, (Kapila *etal)* [6]. A good deal of controversy exist regarding the antioestrogenic effect of the alcoholic extract of the petals of the flowers. An aqueous extract of the flowers was reported to possess a protective effect in experimental liver injury (Nazimuddin *etal*) [7] and effective against viral hepatitis (Shakira *etal*) [8]. But the present study deals with the findings of the Unani drug, Gul-e-Teesu (B.M) on the activity against experimental inflammation.

The anti-inflammatory activity of the drug was evaluated by (I) rat hind paw oedema, (II) cotton pellet granulation tissue formation and (III) Granuloma pouch methods, the first method being an acute inflammatory model (exudative) and the latter two being chronic inflammatory models (Proliferative).

MATERIALS AND METHODS

Acute Inflammation: It was induced by rat hind paw oedema method (winter *etal)* [9], in three groups of rats (5 animals in each). Oedema was induced by injecting 0.1 ml of 1% carrageenin, 30min., after administering the following: Group I, control-distilled water (2ml/150gm) Group II, B.M. (2ml150gm) and Group III Phenylbutazone (100 mg/kg). The volume of each paw was measured plethysmographically before and 4 hours after the injection of carrageenin. The percent inhibition of the oedema was calculated by the formula $(1-T / C) \times 100$, where T and C are the mean paw volumes of drug-treated and control groups respectively.

Chronic Inflammation:

a) Granuloma Pouch: This type of chronic inflammation was induced in 4 groups (5 in each) of rats as per the method described by Selys [10] Granuloma pouch was induced in rats by injecting 20cc of air, followed by 0.5 ml of 2% V / V croton oil in ground nut oil, into the loose connective tissue between the shoulder blades. All the three groups of animals were administered with the following, 24hrs. before induction of granuloma pouch and subsequently continued for 7 days. Group I Control-distilled water 2ml/150gm., Group II Test -B.M. 2ml/150gm., Group III Positive Control - Phenylbutazone - 100mg/kg. All the animals were sacrificed on the 8th day, the pouch was opened and the exudate was collected and measured. The percent inhibition of the volume was calculated by the formula previously mentioned.

b) Cotton Pellet Implantation: This was done according to the method of Winter *etal*[11], in 4 groups (5 in each) of rats by implanting sterile cotton pellets (10mg) subcutaneously in the groin region, after anaesthetising the animals with ether. Administration of drugs was started 24 hrs. before the implantation of the cotton pellets and subsequently continued for seven days. The animals were administered with the following: Group I, distilled water; 2ml/150gm., Group II B.M. 2ml/150gm, Group III Phenylbutazone; 100mg/kg. All the animals were sacrificed on the 8th day and the cotton pellets with the surrounding granulomatous tissue were removed, dried at 55° for 24 hrs. and the percent inhibitions in the

weight of the granuloma formation was calculated by the formula previously given.

Effect on total serum proteins and Albumin: Globulin rats:

Since there is a change in the albumin globulin ratio in experimental animals in chronic phase of inflammation (Werner)[12] (Arrigoni - Martelli, E) (B) blood was collected from the animals, in which inflammation was induced according to the method of winter *etal*[11] and the total protein, albumin and globulin were estimated by the Biuret method[14].

Effect on adrenalectomised rats: Drugs which exhibited an anti-inflammatory effect in adrenal intact animals were studied for their effect in bilaterally adrenalectomised rats, in order to find out the involvement of adrenal glands in the mediation of their anti-inflammatory effect. Bilateral adrenalectomy was done according to Zarron *etal* [15] and the anti inflammatory effect of the test compounds at a dose level of 2ml/150gm. of B.M. was studied according to the method of winter *etal*[11].

Effect on rat peritoneal mast cell, in vitro: Lewis and Whitle [16] have reported that nonsteroidal anti-inflammatory drugs like indomethacin, flufenamate and meclofenamate, stabilise the peritoneal mast cells of rat and prevent the rupture of mast cells and the associated histamine release, induced by pharmacological agents such as compound 48/80, and antigenic challenge. Hence an attempt has been made to elucidate the effect of B.M. on the rupture of mast cells induced by the mast cell degranulators such as comp.48/80, polymyxin-B, diazoxide and Triton X-100. Staining and counting of the ruptured and intact mast cells were done according to the technique described by Bray and Van Ansdel[17].

RESULTS

Anti-inflammatory effect: B.M. produced significant anti-inflammatory effects in rats as tested by the Carrageenin induced by hind paw oedema method. Cotton pellet granuloma and granuloma pouch techniques. Table I summarizes these results.

Estimation of total serum proteins: albumin: Globulin ratio:

The Table II summarizes the estimation of total serum proteins, albumin, globulin ratio. The data clearly show that B.M. has a definite role in preventing the albumin, globulin ratio reversal which occurs during inflammatory conditions.

Anti-inflammatory effect in adrenalectomised rats:

The Table II showed anti-inflammatory effect in bilaterally adrenalectomised rats.

Effect on rat peritoneal mast cell in vitro:

B.M. did not show any significant mast cell membrane stabilising effect, as evidenced by their inability to prevent the rupture of mast cell induced by Polymyxin-B, diazoxide, Triton X-100 and Comp. 48/80.

DISCUSSION

B.M. have been found to produce significant anti-inflammatory effects in adrenal intact and bilaterally adrenalectomised rats. The exact mechanism by which it produces anti-inflammatory activity is not known. However, the present study has shown that there was no involvement of adrenal glands in the mediation of their anti-inflammatory effect and it did not stabilise the mast cell degranulating effect of various pharmacological agents such as compound 48/80 etc.., as a number of non-steroidal anti--inflammatory agents do. Whether the anti-inflammatory activity of B.M. could be attributed to blocking prostaglandin synthetase, needs further study. A number of anti-inflammatory agents such as steroids, aspirin like compounds, gold salts and pharmacological doses of estrogen have been shown to interfere with the immunological events, such as adjuvant — induced arthritis. In view of this, it would be of inter-

est to extend such studies on B.M. as on immunosuppressive agent and elucidate its role in various immunological and inflammatory reactions.

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TABLE I
ANTI-INFLAMMATORY ACTIVITY
O F B M

Group	Hind Paw Oedema Volume (ml)			Cotton Pellet Granuloma wt. of cotton pellet in mg.			Granuloma Pouch Volume of exudate in ml.		
	Mean ± SEM	% Reduction	P	Mean ± SEM	% Reduction	P	Mean ± SEM	% Reduction	P
Control	1.40 ± 0.05	—	—	51.2 ± 1.87	—	—	2.51 ± 0.13	—	—
Phenyl Buta Zone	0.39 ± 0.03	72.20	< 0.001	23.7 ± 1.37	53.70	< 0.001	0.78 ± 0.08	72.20	< 0.001
B.M.	0.60 ± 0.05	57.15	< 0.01	30.2 ± 1.64	41.00	< 0.01	1.19 ± 0.08	52.60	< 0.01

TABLE — II

EFFECT ON TOTAL PROTEIN (SERUM) AND A.G. RATIO

	Total Serum Protein g/100 ml.	Albumin g/100 ml.	Globulin g/100 ml.	A / G Ratio
Gp.I Normal	4.293 ± 0.03	0.805 ± 0.03	3.488 ± 0.04	0.230
II Control	5.644 ± 0.56	1.494 ± 0.222	4.150 ± 0.346	0.360
III Phenyl Butazone	4.270 ± 0.12	0.845 ± 0.045	3.425 ± 0.20	0.246
IV B.M.	4.605 ± 0.06	0.895 ± 0.03	3.610 ± 0.07	0.275

TABLE III

EFFECT ON ADRENALECTOMISED RATS

Cotton Pellet Granuloma wt. of cotton pellet in mg.				
Group	Mean ±	S E M	Y. Red	P
Control	60.1	2.72	—	—
Ph. But	30.1	1.19	49.92	< 0.001
B.M.	36.9	2.95	38.70	< 0.01

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POSSIBLE EFFECT OF SOME EXTRACTS OF NIGELLA SATIVA L. SEEDS ON BLOOD COAGULATION SYSTEM AND FIBRINOLYTIC ACTIVITY

Drs. M. Tharwat Ghoneim, Ahmed Rajai El-Gindy, R. El-Alami E. Shoukry and Sami Yasseen

KUWAIT

INTRODUCTION

Nigella Sativa L. seeds have been reported to possess many pharmacological effects. It has been reported that the Prophet Mohammed (ﷺ) said that the black seed is a remedy for every disease except death (al-Jawzeyah) [1]. Nigellone, an active principle isolated from Nigella Sativa and was shown to possess a protective effect of guinea pigs against histamine induced bronchospasm and was found to be free of toxic effects (Mahfouz and el-Dakhakhny 1060a) [2]. Fractions from Nigella seeds were used therapeutically in the treatment of bronchial asthma in adults (Mahfouz *et al* 1960b) [3]. The Nigella was also found to possess antibacterial effect (Toppozada et al, 1964) [4].

It was claimed, by some people in Kuwait, that in certain cases of epistaxis, a preparation obtained from Nigella seeds was useful in the management of such cases. The people extracted the crushed Nigella seeds with a natural fat, few drops of the product were instilled in the nostrils, few minutes later, bleeding ceased. In addition, they reported that no recurrences of bleeding were observed after several times of application of the drug.

MATERIALS AND METHODS

Male rabbits obtained from local breeding were used throughout this work. The animals were kept under the same conditions, given food and water *ad libitum.* The animals were classified into 2 main groups, the first was used for the *in vitro* study. The second group used for the *in vivo* study. A control group was used with each test group and procedures of both control and test were done simultaneously.

Blood was obtained from the orbital plexus of the rabbit using a capillary tube.

Drugs

1) The fatty extract of Nigella Sativa seeds (Yasseen, 1981) [4]. The Nigella Sativa seeds were crushed. Fresh natural fat (ghee) was used to extract the seeds in a concentration of 1.143kg. for every 100gm. of the crushed seeds. The fatty extraction of the seeds was carried out by heating the fat with the crushed seeds for 20 minutes (on a water bath). The extract was then filtered through a thick muslin, (Fraction I). The fatty extract when melted again was separated into two layers, an upper fatty layer (fraction 11) and a lower aqueous layer (Fraction 111). The natural fat used for extraction (Fraction IV) was tested for any possible effect on coagulation system. All of these fractions are fatty in nature. In order to be mixed with blood or plasma, they were emulsified with tween 80. The effect of the emulsifying agent (fraction V) alone was studied on blood coagulation system.
2) The petroleum ether extract of Nigella Seeds: 250gm. of Nigella Sativa seeds were crushed and extracted with petroleum ether (40/60). Eighty grams of extract were obtained.

PREPARATION OF THE WORKING SOLUTIONS OF THE DRUGS

Fraction I

The whole fatty extract was emulsified with tween 80 in a concentration 5gm of extract emulsified with 2ml tween 80 and completed to 100ml with saline. The working solution was obtained by diluting this fraction with saline. 1:10 V/V.

Fraction II

The whole fatty extract was melted, the upper fatty layer was separated and emulsified with tween 80 in a concentration of 2gm with 1ml tween 80 and completed to 100ml with saline. The working solution was obtained by dluting this solution with saline. 1:10 V/V.

Fraction III

The lower aqueous layer of the fatty extract was separated and diluted with saline. 1:10 V/V.

Fraction IV

The natural fatty extracting agent was emulsified with tween 80 in a concentration of 5gm emulsified with 2ml tween 80 and completed to 100ml with saline. The working solution was diluted with saline. 1:10 V/V.

Fraction V

The emulsifying agent tween 80 was mixed with saline in a concentration of 2ml diluted to 100ml. The working solution was diluted with saline. 1:10 V/V.

Fraction VI

The petroleum ether extract was emulsified with tween 80 in a concentration of 2 gm with 1 ml tween 80 and diluted with saline to 100ml. The working solution was diluted with saline. 1:10 V/V.

The In-Vitro Study

In the *in vitro* study the working solutions were mixed with plasma or blood according to the procedures, in a concentration of 10%V/V. and incubated for 2 minutes.

The in vivo study

The petroleum ether extract was prepared for injection of the animals. Two grams of the petroleum ether extract was emulsified with 1ml tween 80 and completed to 100ml with saline. Male rabbits were slowly injected with this solution in the ear vein in a dose equivalent to 10mg of the petroleum ether extract per kg body weight daily for 7 days. Withdrawal of blood samples for the different tests was carried out 24 hours after the last injection.

Procedures

The preparation of platelet rich plasma (PRP) and platelet poor plasma (PPP) was done according to Owen et al (1975) [5].

Procedures included the following:

1) Whole blood clotting time (Dacie & Lewis, 1975) [6]
2) Plasma clot time (Austen & Rhymes, 1975) [7]
3) Kaolin Cephalin clotting time (Austen & Rhymes, 1975) [8].
4) Prothrombin time (Austen & Rhymes, 1975) [9].
5) Thrombin time (Austen & Rhymes, 1975) [10].
6) Stypven time (Austen & Rhymes, 1975) [11].
7) Euglobulin clot lysis time (Austen & Rhymes, 1975) [12].
8) Partial thromboplastin time (Nye et al 1962) [13].
9) Bleeding time (Thienes et al 1957) [14].

In this test, rats were used. Male white albino rats weighing about 150gm each were used. The rats

were anaesthetized with thiopentone sodium in a dose of 6 mg 100gm body weight intra peritoneally. The abdomen opened by crucial incision, the liver was gently lifted out. A piece of liver was cut from a portion of the edge with sharp scissors, leaving a cut surface of about 10mm long and 3-4mm wide. The drugs were applied to the cut surface, the bleeding time was then determined. The length of bleeding time was determined by gently blotting with pieces of filter paper of 10 seconds intervals. The end point was sharp and indicated by a blood clot clinging to the filter paper, but with little or no liquid blood wetting it. The significance of the difference of the mean from that of the control group and from those treated groups, is determined by calculation of the critical ratio.

$$\text{The critical ratio} \quad \frac{-X_1 - -X_2}{\sqrt{\frac{(SE_1)^2}{N_1} + \frac{(SE_2)^2}{N_2}}}$$

where $\bar{X}_1$ and $\bar{X}_2$ are the mean bleeding times being compared, SE_1 and SE_2 are the standard errors of $\bar{X}_1$ & X_2 and N_1 & N_2 are the number of animals used.

The differences are considered significant if the critical ratio equals 2 or more than 2.

RESULTS

In the *in vitro* study, the petroleum ether extract (Fraction VI) and the upper layer of the fatty extract of Nigella produced statistically significant shortening in the whole blood clotting time. On the plasma clot time, all fraction produced significant shortening when compared to control group but only Fractions I, II and VI produced significant shortening in this parameter when compared to the group of emulsifying agent (Fraction V). Only the petroleum ether of extract (Fraction VI) produced significant shortening in the Kaoling cephalin clotting time when compared to either control group or emulsifying agent group.

On the stypven time, the petroleum ether extract (Fraction VI) and the upper layer of fatty extract (Fraction II) produced a significant shortening when compared to the emulsifying fraction group (Fraction V). It was found that the emulsifying group produced a significant prolongation in the stypven time when compared to the control group. On the euglobulin clob lysis time the petroleum ether extract (Fraction VI), (Fraction I) and (Fraction III) produced significant prolongation in this parameter (Table I).

The petroleum ether extract and the whole fatty extract of Nigella produced a significant shortening in the bleeding time in the rat as indicated by the increase induced in the critical index by both fractions (Table II).

In *in vivo* effect of the petroleum ether extract produced significant shortening in the whole blood clotting time, plasma clot time and Kaolin cephalin clotting time. No significant effect was shown on the prothrombin time or thrombin time. There was significant shortening in the partial thromboplastin time. The euglobulin clot lysis time was significantly prolonged (Table III).

TABLE I

THE IN VITRO EFFECT OF THE DIFFERENT FRACTIONS OF NIGELLA SATIVA ON SOME BLOOD COAGULATION PARAMETERS AND FIBRINOLYTIC ACTIVITY

	Control	Fraction I** (The whole fatty extract)	Fraction II (The upper layer of the fatty extract)	Fraction III (The Aqueous phase of the fatty ext.)	Fraction IV (Theextracting fatty substance alone)	Fraction V (The emulsifying agent)	Fraction VI The petroleum ether extract)
Whole blood* clotting time	416.4 ± 71.6 (7)[c]	337.5 ± 14.7 (8)	220.6 ± 20.5[ab] (9)	360.0 ± 62.5 (9)	183.3 ± 21.7 (9)	491.1 ± 89.1 (9)	141.7 ± 41.9[a,b] (9)
Plasma clot time	124.6 ± 5.9 (19)	79.6 ± 3.9[ab] (12)	82.0 ± 5.3[a,b] (10)	91.0 ± 7.6[a] (6)	86.6 ± 7.6[a] (10)	100.0 ± 5.7[a] (8)	64.4 ± 6.8[a,b] (10)
Kaolin Cephalin clot time	46.7 ± 3.4 (14)	45.3 ± 4.3 (9)	46.5 ± 5.6 (6)	40.7 ± 2.7 (6)	48.3 ± 4.1 (9)	45.0 ± 6.9 (8)	28.4 ± 1.99[a,b] (7)
Stypven time	14.9 ± 2.6 (16)	16.1 ± 1.8[a] (11)	10.7 ± 0.5[a,b] (12)	16.9 ± 1.7 (11)	14.7 ± 1.0 (10)	21.7 ± 2.3[a] (12)	12.8 ± 1.03[b] (11)
Euglobulin clot lysis time	87.4 ± 7.6 (10)	186.3 ± 49.1[a,b] (8)	107.5 ± 12.3 (8)	126.6 ± 12.9[a,b] (9)	96.30 ± 8.7 (8)	82.3 ± 16.8 (8)	227.5 ± 51.6[a,b] (8)

* Figures represent the mean ± S.E.
** Figures are in terms of seconds except the euglobulin clot lysis time in minutes
a. Statistically significant when compared to control group
b. Statistically significant when compared to the emulsifying group
c. Figures represent the number of animals.

TABLE II

EFFECT OF THE FATTY EXTRACT AND PETROLEUM ETHER EXTRACT OF NIGELLA SATIVA ON BLEEDING TIME IN THE RAT

	Control	Fatty extract	Pet. ether extract
Mean ± *	*180.7* ±	95.6 ±**	*151.3* ±**
S.E.	*12.2*	*6.3*	*16.9*
n	*(22)*[a]	(9)	(12)
Critical index	—	25.49	5.32

* time in terms of seconds
** statistically significant according to Thiens equation
a Figure between brackets represent the number of animals used

TABLE III

EFFECT OF ADMINISTRATION OF THE PETROLEUM ETHER EXTRACT TO RABBITS ON SOME BLOOD COAGULATION PARAMETERS AND FIBRINOLYTIC ACTIVITY

	Whole blood clotting time (seconds)	Plasma Clot time (seconds)	Kaolin Cephalin time (seconds)	Prothrom-bin time (seconds)	Thrombin time (seconds)	Partial Thramboplas-tin time (seconds)	Euglobulin time (seconds)
Control	355.3 ± 55.36 (6) a	117.4 ± 7.83 21.	54.6 ± 3.7 27	14.0 ± 0.49 20	18.5 ± 0.97 27	58.3 ± 6	151.2 ± 40.1
Treated	248.3 ± 19.9 (10)	84.30 ± 4.3 (38)	45.8 ± 2.4 (42)	13.0 ± 0.42 (25)	17.2 ± 0.92 (28)	40.1 ± (11)	307.5 ± 42.6 (6)
% change fram control	- 30%	- 28.2	- 16.1	- 7.1	- 7.0	- 31.2	+ 102.1
P	<0.001	<0: 001	<0.05	>0.05	>0.05	<0.05	<0.05

(a) figures between brackets represent the number of animals

DISCUSSION

The fatty extract of Nigella sativa seeds was reported by many people to stop bleeding in some cases of bleeding nose (epistaxis). This work, was suggested to investigate the possible effect of such a preparation on blood coagulation system.

The problem was complicated by the fact that the material consisted of the extract in addition to the fatty solvent. The extract itself contains several components. It was also suggested to study the effect of such fatty extract in comparison to the petroleum ether extract of the Nigella sativa seeds. The petroleum ether extract was reported to contain most of the active ingredients of Nigella seeds (Gad *et al* 1963 [15] , El-Dakhakhny, 1963 [16]). The petroleum ether extract and the upper layer of the fatty extract were shown to shorten the whole blood clotting time. This suggests that the fatty solvent many extract from the Nigella seeds some fatty soluble constituents that affected the blood clotting time. The petroleum ether extract and the fatty extract were emulsified with tween 80, in order to make them miscible with plasma or blood. The effect is not due to the emulsifying agent. The shortening in whole blood clotting time could be due to, at least partially, a coagulant effect. Coagulants accelerate the clotting of normal and some pathological blood both *in vivo* and *in vitro* (Cross, 1964) [17] . The petroleum ether extract (*in vivo* and *in vitro*) and the fatty extracts of Nigella (in vitro) produced significant shortening in the plasma clot time. Again, the effect is not due to the emulsifying agent and not due to the fatty solvents as shown in Table I. The effect is not mediated through the aqueous phase of the fatty extract.

The mechanism of action is non specific, the effect could be through one or more of the clotting factors. This test, involves the whole blood clotting process and thereby measures most coagulation factors (Miale, 1972) [18] . The effect also may indicate that the effect of such extracts may be induced, at least partially, through the intrinsic mechanism of blood coagulation (Owen et al 1975) [19]).

The fatty extract and petroleum ether extracts of Nigella produced a shortening in the bleeding time. The bleeding time depends on a number of factors. Hoemostasis in wounds measuring the bleeding time depends upon the rate at which a stable platelet thrombus is formed and thus measures the efficiency of the vascular and platelet phases (Tocantins, 1936) [20] .

The petroleum ether extract (*in vitro*) produced shortening in the Kaolin cephalin clotting time. This test detects the intrinsic procoagulation activity of plasma except platelet factor 3, factor XIII and factor VII (Owen *et al*, 1975) [21] . The petroleum ether extract can stimulate or enhance the activity of one or more of the factors sensitive by such a test. The petroleum ether extract produced the same effect when given intravenously.

The fatty extract and petroleum ether extract (*in vitro*) produced a significant decrease in the Stypven time. The Russel's viper venom (Stypven) is known to have thromboplastic activity when added to recalcified plasma (Miale, 1972) [22] .

The effect could be due to an action on platelets, or possibly due to the fatty nature of the extracts. It was reported that thrombocytosis and various hyperlipidemic states tend to be associated with an abnormally short stypen time (Owen *et al* 1075) [23] .

The fatty extract and petroleum ether extract inhibited the fibrinolytic activity *in vivo* and *in vitro.* The mechanism of this effect is not known but it may be due to an inhibitory effect on the activation of plasminogen or inhibiting the preformer plasmin activity. The drugs having antifibrinolytic activity such as epsilon amino caproic acid and tranxamic acid were reported to be used successfully in epistaxis (Hardy, 1974) [24] . They also could improve the effectiveness of therapy in haemophilia following dental extraction (Reid et al 1974) [25] , Wzlsh *et zl* 1971) [26] . Inhibition of fibrinolytic activity may be advantageous even though the basic disease may have other causes.

The extracts of Nigella sativa seeds have some effects on the blood coagulation and fibrinolytic

activity. The claim that the fatty extract was used successfully by the public in certain cases of epistaxis has a certain degree of reality. The fatty solvent may play a mechanical role in stopping bleeding. Other possible mechanisms may share in this effect. Chemical investigation of the constituents of Nigella should be carried out and other investigations are needed to complete the picture.

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CORRELATION BETWEEN ISLAMIC VALUES AND THE INCIDENCE OF CANCER

Dr. Ahmed el-Kadi and Dr. M. Ashraf Ghoor

U.S.A.

United States health statistics indicate that the incidence of cancer is increasing in spite of technological advances of modern medicine.[13,56] A previous study by one of the authors (A.E.) [57] has implied that the increased incidence of diseases was directly or indirectly related to the violation of Islamic values. While this idea is easily acceptable in areas such as venereal and some other communicable diseases with social or hygienic connotation, it is difficult to imagine that such a purely physical disorder as cancer could be related to Islamic values which are primarily ethical and social in nature.

Epidemiological cancer studies, however, show that numerous types of cancer develop more frequently in persons who violate one or more of the Islamic injunctions. This applies to cancers of practically all organ systems of the body. The cancer risk factors which eliminated or reduced by following the Islamic teachings include ingested or inhaled materials, personal hygiene matters, social and ethical norms, and altered states of the mind.

The following is a brief review of some of these risk factors, and the Islamic injunctions which would lead to their elimination or reduction. It should be made clear that this review is far from being comprehensive or complete. The review will only list a few of the Islamic injunctions, the violation of which has been documented to increase the risk of cancer.

In the area of ingested or inhaled materials, three examples will be listed. These are the injunctions to avoid excessive consumption of food or drinks to avoid the consumption of alcohol or other intoxicating drugs, and to avoid the consumption of any harmful material.

As to the excessive consumption of food or drink medical research has shown that excessive food intake increases the risk of cancer. In general, the incidence of tumors in mice can be lowered by placing the animals on restricted diets. [2] Reduction of the caloric consumption by one third practically eliminates the appearance of breast cancer. In humans, overweight was found to increase the incidence of breast cancer [19,22,24] as well as cancer of the endometrium. [26,38]

As to the consumption of alcohol there is now ample evidence that alcohol intake, either along or in association with tobacco smoking, increases the risk of cancer. In 1975, 11, 150 cancer deaths in the United States were attributed to alcohol consumption. [17] Alcohol increases the incidence of cancer of the mouth, pharynx, larynx and esophagus. [30] Multi-centric carcinomas of the oral cavity as well as cancer of the hypopharynx and larynx are often found in patients in whom heavy smoking is associated with alcoholism. [10,47,52] The co-carcinogenic properties of Ethanol or alcoholic beverages have been recently outlined. [18]

As to the injunction to avoid the consumption of any harmful material we feel that this injunction applies to tobacco consumption since adequate evidence is now available to document the harmful effects of its use. 30-35% of all cancer deaths among men and 5-10% of all cancer deaths among women may be attributed in part to cigrette smoking. [16] Smoking increases the risk of cancer of the lungs, mouth, pharynx, larynx, esophagus, bladder, and pancreas. [30,26,27,53,54, 55,32,33,34,35,41,42] Chewing tobacco also increases the risk of oral and pharyngeal cancer. [26,11,12]

Under the second category of risk factors related to personal hygiene, three Islamic injunctions are selected which stress and outline proper oral hygiene, proper anal hygiene and proper genital hygiene.

As to oral hygiene, there is evidence that poor oral hygiene increases the risk of oral and pharyngeal cancer.[26,51]

As to anal hygiene, proper anal hygiene is an important factor in the prevention of a variety of anal disorders of inflammatory nature. It has been suggested that chronic ano-rectal disease may increase the risk of cancer of the anal canal.[39,40] We feel, therefore, that the lack of proper anal hygiene may directly or indirectly increase the risk of cancer of the anal canal.

As to genital hygiene, there is now evidence that lack of circumcision in the male increases the incidence of cancer of the penis [30] and possibly cancer of the cervix of the female partner.

Under the third category of risk factors related to social or ethical norms, four Islamic injunctions are selected: one stressing early marriage and active reproduction, another one prohibiting premarital and extramarital sexual relations. The third injuction is the requirement to cover one's body with some difference in details with regard to males and females, and the fourth injunction being the prohibition of homosexual relations.

As to the injunction of early marriage and active reproduction, we find the violation of this teaching leads to increased incidence of certain cancers. Almost 300 years ago Ramazzini noted that there was increased incidence of breast cancers in nuns.[29] Recently, it was found that the incidence of cancer of the breast and cancer of the endometrium increased in unmarried women.[26,28,29,30] Besides, the delay of the first pregnancy also increases the risk of breast cancer.[20,21,24,25,26,30] There is increased risk of breast cancer if the first pregnancy is delayed until after the age of 30 to 35, while there is a substantial protection for women who had their first pregnancy under the age of 20 and some protection below the age of 25. Nulliparity was shown to increase the risk of endometrial cancer.[38]

As to the prohibition of premarital and extramarital sexual relations, we find that having multiple sexual partners increases the risk of cancer of the cervix.[30,37] There is also an increased incidence of cancer of the prostate with the increased number of premarital and extramarital sexual partners, and with an increased history of venereal disease.[13].

With regard to the requirement to cover the body, it was found that chronic exposure to the sun frequently results in the production of cancer of the exposed areas of the skin.[56,7,8,9,30,14,15,50] The incidence of cutaneous malignant melanoma has been increasing by about 5-7% per year in the United State's white population. The striking increases by region of the body have been observed on the lower extremities in women, particularly between the thigh and foot; on the trunk in men, particularly on the back; and on the upper extremities in both sexes..[13]

As to the prohibitions of homosexual relations lead to increased incidence of immune deficiency and to a variety of diseases including cancer.[60,61,62,63,64]

Under the fourth category of risk factors related to altered states of the mind, only a few Islamic injunctions are listed just to make a point. These are the injunctions stressing the faith and unlimited confidence in God and His support to His believers, the balance frame of mind of the believer, and the injunctions which put the believer in a better position to deal and cope with stress.

There is now growing evidence that negatively altered states of the mind, such as anxiety, depression and inability to cope with stress lead to immune deficiency[G-1, 2, 3, 4]. It was also found that social bonding and an emotionally stable environment improve host resistance.[G21] Since it is now known that the incidence of cancer is greatly increased in persons with immune deficiency [49, 30, 31, 36, 13, G-9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20] it is reasonable to conclude that the negatively altered states of the mind increase the risk of cancer. As a matter of fact, several studies have shown an increased incidence of cancer in patients with anxiety, depression, or emotional distress.[G-5, 8, 6, 7].

With all the above evidence, it would seem that persons without religion would have an increased incidence of cancer. This was found to be true in Los Angeles, California. A group of investigators found that the incidence of cancer of the pancreas was significantly higher in persons with no religion when compared with Catholics, Protestants, Mormons and Jews.[23]

To summarize, we have shown that excessive intake of food, and the consumption of alcohol and tobacco increase the risk of cancer. Poor oral hygiene, poor anal hygiene, and poor genital hygiene increase the risk of cancer. Violation of the advice for early marriage and active reproduction increases the risk of cancer. Promiscuity, nudity and homosexuality increase the risk of cancer.

The lack of faith and confidence in God, the lack of a balanced frame of mind, and the lack of ability to cope with stress increase the risk of cancer. In other words, violation of Islamic teachings increases the risk of cancer.

This study and other studies currently under preparation dealing with diseases other than cancer tend to support the earlier claim of one of the authors (A.E.) that the implementation of Islamic teachings will lead to the reduction of disease, and that Islamic Medicine with the wisdom and knowledge of Islamic teachings, will be a superior and more effective brand of the healing arts.

PART NINE

SEMINAR ON ADVANTAGES OF HERBAL TREATMENT

РАЗДЕЛЕНИЕ

Материал для дополнительного чтения

Part Nine: *Seminar on Advantages of Herbal Treatment.*

CHAPTER ONE

(Papers Presented)

1. REPORT ON THE THIRD SESSION.
   Editors.

2. THE ROLE OF HERBAL REMEDIES AS AN ALTERNATIVE TO MODERN DRUG THERAPY.
   Dr. Simon Y. Mills.

3. BIOLOGICAL ACTIVITY OF SOME SAPONOSIDES.
   Prof. Jerzy Lutomski.

4. METHODS OF OBTAINING A NEW HERBAL DRUG USING DATA OF TRADITIONAL MEDICINE.
   Dr. Ovidiu Bojor.

5. SOME APPROACHES TO THE STUDY OF INDIGENOUS MEDICINAL PLANTS.
   Prof. Atta-ur-Rehman.

6. OBSERVATIONS ON THE ROLE OF CLASSICAL METHODOLOGY IN MODERN PHYTOCHEMISTRY.
   Prof. Salimuzzaman Siddiqu

7. MEDICALLY APPLIED FLAVONOIDS, ESPECIALLY RUTOSIDES.
   Prof. Wolfgang Voelter.

8. COMMENTS.
   i. Prof. Gunther Stille.
   ii. Prof. G. Sakait Rama Rao.

9. GENERAL DISCUSSION.

REPORT ON THE THIRD SESSION

This session, which was a seminar on "THE ADVANTAGES OF HERBAL TREATMENT", was conducted from 5.00 p.m. to 8.30 p.m., by Prof. Abdul Wahab Borollosi, Prof. Olav Thulesius and Dr. Ahmed Ragai El-Gindy, as chairman, co-chairman and moderator respectively. In this seminar, first the chairman gare his opening remarks and then five eminent and world famous scientists presented their papers. Later on two other famous scholarly professors gave their comments on the papers. Then the general discussion was allowed. The session ended after the closing remarks of the chairman.

Prof. Ovidiu Bojor could not attend the conference, but as per selection, his paper is published in the concerned chapter.

Editors.

THE ROLE OF HERBAL REMEDIES AS AN ALTERNATIVE TO MODERN DRUG THERAPY

Dr. Simon Y. Mills

ENGLAND

PREAMBLE

The practitioner of herbal medicine in the modern world has few ways in which to present his arguments for the advantages of his chosen therapy to the scientific and medical community. There are several reasons for this. It is inherently difficult to analyse, quantify or predict the exact pharmacological action of an agent that is both chemically extremely complex and highly variable as between samples. There is in fact very little doubt that even the attempt to accomplish this in order to gain complete scientific 'respectability' for herbal medicine is doomed to failure. An equally difficult problem in communication is provided by the insistence of the serious herbal practitioner that the aims of the therapy must be qualitatively distinct from those of modern western medicine. This is a point ignored in most popular accounts of herbalism in the west and deserves a little elaboration here. It is a central abiding principle in the professional practice of herbal therapy that the patient manifests uniquely a will to live, a life force, an unquantifiable and astonishing ability to grow, prosper and thrive, to transform environmental stresses into health in the positive sense of that word. This means that the practitioner accepts that there is already present a will and ability to recover from setbacks and disease, a 'vis medicatrix naturae' as Hippocrates put it, and that it is therefore the practitioner's obligation to aid the natural healing process when this is obstructed. The process of disease is seen, not as something to be arbitrarily removed by direct antogonists to the pathological process as visualized in modern 'allopathic' therapy, but as a manifestation of a thwarted recovery process. The symptom is seen, literally, as a 'signpost', to be read as part of an attempt to locate the nature of the obstruction, to assess the *needs* of the underlying vital functions. Herbal remedies are then seen as essentially *supportive* of these functions, and it is considered that an evaluation of their potential as healing agents must be bound to this fact. The herbal practitioner therefore resists the facile listing of herbal remedies as effective for ameliorating arbitrary pathologies. Much more important to him is to understand something of the physiological activity of a remedy than to be told that it is good for arthritis or asthma or whatever. Each patient is considered as a unique case, to be treated most likely with a unique formulation of remedies independent of the pathology he or she might be labelled with.

All this means that the parameters by which a herbalist finds a remedy valuable are often quite distinct from those current in scientific medical thought. Evidence of validated antipathological activity is genuinely less important to the herbal practitioner than the day-to-day experience of its efficacy in the personal encounter. The value of any scientific findings is seen more as a potential elaboration of a total view of the remedy's activity in the physiological realm than as a binding definition of its actions and limitations. Much more could be said of the implications of this viewpoint, of the different view of the effects of treatment and its course in time, of the new light cast on the concept of the 'side-effect', and of the accommodation that the herbalist finds possible with the pharmacological complexity and variability of the materia medica. However, that is the province of a more philosophical treatise. The purpose of this article is to demonstrate by means of example how the evidence that does exist for a few individual remedies can be assembled to make a case for their vitalistic application in the manner briefly described.

In the presentation of what analytical and experimental evidence does exist information will have been called from a very wide variety of sources. To reduce the opacity of this paper accredition will not be made for absolutely every analytical statement. Rather there will be appended a general literature list

from which the bulk of the detail has been obtained. Specific literature citations will be restricted to the most notable claims in the text. The author will be pleased to provide any reader with detailed sources for any other item that interests him particularly. The restriction in citations will be particularly apparent in the lists of constitutents for each remedy and in the more widely accepted pharmacological acvities.

Crataegus Monogyna (Jacq):

This is one species of a pair that is found widely throughout Europe that is for medicinal purposes taken together (the other more temperate species being C. oxycantha). C. Monogyna is found in Europe and around the Mediterranean regions into north and West Asia. It is a shrubby tree found commonly in hedgerows in cultivated areas with corymbs of small white of pink flowers giving way to red berries in the autumn. The leaves are lobed and stipulate. Throughout Europe Crataegus has earned a reputation as a useful remedy for disorders of the heart and for dropsy; its use for coronary and circulatory difficulties is a more recent phenomenon that other long-established usages but this perhaps reflects the increasing understanding of heart function in the last century. However, it is now one of the prime remedies for treating a variety of cardiac problems in the European materia medica, appearing to have the ability to dilate the coronary vasculature whilst also having a bradycardic effect on heart rate. It finds equal applicability for angina and other coronary difficulties as for the treatment of arrythmias, especially where the latter have arisen from prior coronary disturbance. Beyond this there is apparently a general vasodilatory effect that helps in the overall treatment of some cases of hypertension and in some of the circulatory problems consequent on arteriosclerosis (e.g. intermittent claudication). In brief, the modern herbal practitioner sees Crataegus as a superb heart 'food' and relaxant with a gentle but cumulative general vasodilatory effect as well.

There is a considerable body of experimental evidence to support these impressions. A list of constituents for the leaves, flowers and berries would include the following:

Flavonoid glycosides (incl. rutin, quercitrin)
Triterpenoid saponins ('Crataegus lactone')
Procyanidins
Trimethylamine

Condensed tannins (forming red phlobaphenes, insoluble complexes).

It is well-known, following Szent-Gyorgy, that flavonoids have an observable effect on the vasculature, reducing capillary fragility (providing essential in vivo support for ascorbic acid), dilating coronary blood vessels, slowing the heart rate whilst increasing stroke volume. They would thus provide a fair explanation for the effects of Crataegus if they were not also widely found in many other plants and foodstuffs that do not exhibit these effects to any notable degree. Further support, however, is provided in the report that the phlobaphene fraction (i.e. deposited condensed tannin complexes) showed evidence of a prolonged vasodilatory effect on the coronary vessels, and in addition increased the amplitude of the heart's contraction and potentiated the effects of caffeine, adrenaline, adenosine and papaverine on coronary circulation [1]. Increased vagal tone slowing heart rate is a fair conclusion from the known effects of the procyanidins (yielding cyanides on hydrolysis), and from the suggestion that the whole plant exhibits anticholinesterase activity [2]. Perhaps the most active components may yet prove to be triterpenoid saponins. This class of plant constituents has only recently been investigated and has already been shown to be instrumental in the actions of Panax ginseng and Glycyrrhiza glabra (see below) for example. Most pertinent here is the work that has been done on the saponin fraction of Aesculus hippocastanun that has shown that it is notable in the whole remedy's action in reducing oedema and benefiting varicosed veins [3,4]. Whatever the pharmacological explanation however there are clinical records showing the ability of the berries to reduce hypertension caused by both arteriosclerosis and renal damage [5], and the flowers to improve the health of heart patients troubled with mitral stenosis and

progressive coronary occlusion [6] . Other studies concluded that the remedy had a favourable effect in cardiac arrythmias , especially extrasystoles and paroxysmal tachycardia [7] , and prevented ECG changed due to hypoxial [8] . A reduction in digitalis dosage after treatment with Crataegus is a strong possibility [9] . No side effects have been reported during therapeutic use, toxic problems only arising with massive intravenous dosages or with non-therapeutic doses administered chronically [5] .

Allium sativum (L)

This remedy has generated perhaps more scientific curiosity and research than any other plant not cultivated for supplies of allopathic drugs. It has through the ages accrued an almost phenomenal reputation for helping a wide variety of conditions. It has moreover played a significant part in the diet of many countries. The main limitations to its use in European countries has been a strong social objection to the odour on the expired air of the taker, but there have been areas where this has not been insurmountable and there is also the use of de-odourized preparations that have prospects in some applications. In general, the uses of garlic have fallen into two groups: the antimicrobial action it appears to possess, and the number of interrelated benefits it seems to have on the circulation. Of the two, it is the former that has been concentrated on in traditional herbalism ("a good preservative against infections"): Parkinson (1640 AD) whilst the use of garlic for circulatory problems, unusually, owes much to modern research findings for the plant. We shall look first at some known constituents:

Volatile oil-allin, separated from enzyme alliinase in intact plant; when crushed the two interact and allin is converted to allicin which is further oxidised to diallyl disulphide[10].

Glucokinins
Germanium
Mucilage

From an early stage it was clear that the volatile fraction, notably allicin was responsible for the antibacterial action of Allium [11] , it was found to be active in concentrations as small as 1:85,000 [12] . Clinical evidence for antimicrobial activity has generally supported the traditional usage. Initial controlled trials to check the use since ancient times of Allium for leprosy were sufficiently encouraging for further testing to be recommended [13] . It was found to perform commendably in the treatment of tuberculosis [14] , and achieved a sound reputation in both World Wars in preventing sepsis and controlling suppuration. Some of the most interesting work has been done to investigate the potential of Allium sativum in normalizing bacterial populations in the gut: it has been one of the more common claims for the remedy by practitioners that it could check gut infections without destroying normal healthy flora. Some backing, if not explanation, for this assertion comes from Weiss [15] , who reported a complete change in intestinal flora after Allium treatment, and from Marcovici [16] who reported significant improvements in dysenteric diseases. Other clinical work has demonstrated relief in a number of gastro-intestinal disorders, including flatulence, vomiting, nausea, abdominal distension and dyspepsia [17,18] . Given these findings, supported by herbal practitioners today, it is hard to avoid accepting that the action of Allium on the bacterial population of the gut is selective. Effects on the gut that are possible relevant to this activity include a general stimulation of digestive juices [15] , and an increased absorption of thiamine from the intestine [19] . There has also been observed a direct antimicrobial effect against staphylococci, streptococci, Escherischia typhosa, Bacterium dysenteriae, B. enteritidis, and Vibro cholerae [20,21,12] .

At the early stage of research, the applicability of Allium to the treatment of cardiovascular disease was established. Marcovici was among many who suggested that the elimination of toxin absorption from the gut was central to this function [22] , and this is a theme still taken up today. However, there is also clear evidence for direct effects on the circulation and vasculature; in reducing post-prandial blood cholesterol levels [23] , and blood sugar levels [24] - possibly involving the glucokinin constituents - as well as platelet aggregation, thromboxane synthesis and thus the tendency to thrombosis [25] . Circumstantial

evidence for the beneficial effect of Allium on the circulation comes from an examination of the statistics for heart disease in countries with or without a high consumption of garlic in the diet [26].

The traditional use of garlic for tumours is also supported by recent research. Enough in vitro and in vivo results have been forthcoming for one researcher to conclude that "it may lead to an effective therapeutic attack on the cancer problem" [27,28]. Japanese researchers have suggested that it is the presence of unusually high levels of the mineral germanium that is a vital feature in the antitumour activity [29].

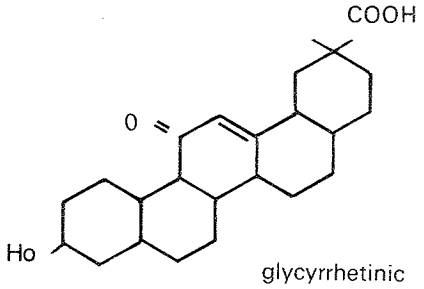
In total, there does seem ample backing for the herbal practitioner's view of Allium as an effective aid to the body in its attempts to come to terms with pathogens in its environment.

Glycyrrhiza glabra (L)

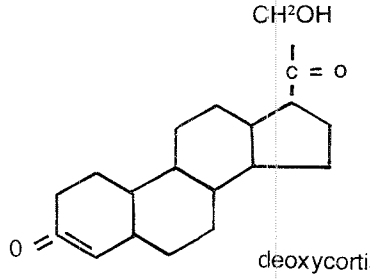
This is another plant whose traditional usage and modern potential have happily overlapped, with the latter being particularly notable. A brilliant survey of the subject has been conducted by Gibson [30] and much of what follows is provided, along with full references, by him, with a minor contribution from other sources. In the past Glycyrrhiza has been used for its soothing and healing actions on the gastro--intestinal tract and the respiratory system principally. There are incidental reputations for fever management and urinary disturbances as well. On examination, its constituents are found to include:

Glycyrrhizin (salts of glycyrrhizic acid)
Triterpenoid saponins
Flavonoids
Bitter principle (glycyramarin)
Asparagin
Oestrogenous substances (including β-sitosterol)

The key feature in the activity of the plant seems to be a steroidal fraction that includes the aglycone of glycyrrhizin, glycyrrhetinic acid, and the near steroidal triternoid saponins. The similarity of these substances to steroidal hormones has helped to explain a number of hormonal effects in many medicinal plants. In Glycyrrhiza



glycyrrhetinic acid



deoxycortisone

these effects are prominent. Thus it has been shown to have anti-inflammatory and anti-arthritic effects similar to hydrocortisone, to resemble the activity of ACTH in causing aldosterone-like retention of water and sodium, and loss of potassium at the kidney, increased blood pressure, and decreases in haemoglobin levels. It enhances the immunosuppressive action of cortisone, but on the other hand, inhibits its antigranulomatous action and its effects in increasing liver glycogen storage. The action of glycrrhetinic acid here is dependent on a functioning adrenal cortex: there appears to be a direct ACTH - like effect increasing adrenal production on the mineralocorticoids and androgens, but there is also an effect on reducing the breakdown of the corticoids at the liver and kidney. The effect can be dramatic: it has been reported [3] that a woman with Addison's disease was maintained completely with an initial dose of 60g liquid extract of Glycyrrhiza per day, this dose being eventually reduced so that a maintenance dose of

3g daily was achieved. Whatever the full explanation of this effect proves to be it will also include the raising of serum levels of glutamicocaloacetic acid transaminase and glutamicpyruvic transaminase and thus the uncoupling of oxidative phosphorylation. The potential local actions of Glycyrrhiza are supported by the anti-inflammatory effects exhibited in treatment of corneal injuries and in cosmetics. There is further support for an inflammatory effect in the widespread allopathic use of Glycyrrhiza constituents for petic ulcers, though this is put largely to the ability of the remedy to promote an adherent film of protective mucus over the gastric wall, and possibly to reducing gastric acid secretions. Glycyrrhizin is found to increase bile secretion and the excretion of bilirubin and to have an antipyretic effect comparable to sodium salicylate.

These varied effect support the notion among modern herbal practitioners that Glycyrrhiza is well suited to providing benefit in any attempt to wean a subject off excessive administration of cortisone or other steroids. It appears to have many of the relative advantages of ACTH with yet easy applicability by mouth. There is postulated the possible danger of hypokalaemia and hypertension due to the mineralocorticoid effect if Glycyrrhiza is taken in large doses for an extensive period. This is no doubt a real risk but apart from glycyrrhizin the whole plant possesses diuretic components, notably asparagin and the flavonoids, that may diminish this effect. The application of Glycyrrhiza to disorders of the respiratory system seems to be backed by its anti-inflammatory (and anti-allergenic) effects, with effects in tuberculosis comparable to deoxycortisons. There is also the reflex effect on the activity of bronchial muscle and the mucociliary escalator of all mucilaginous plants [23] . Its traditional and clinical use for asthmatic conditions and excessive coughing seems well supported here.

Cichorium intybus (L)

This plant is chosen arbitrarily as an example of one of the many 'bitter' remedies used throughout the world for their ability to stimulate the upper digestive system, increasing appetite, promoting the flow of digestive juices, and by increasing bile flow, 'cleansing the liver'. It has generally been accepted that the mechanism involves a reflex response to stimulation of the bitter taste receptors in the mouth (i.e. bitters are quite inactive when given by tube direct into the stomach). What has transformed the understanding of these bitter substances is the finding [33] that the immediate result of stimulation of the bitter taste receptors is the release of the gastro-intestinal hormone gastrin. This in turn is known to increase gastric acid secretion (and thus the sterilizing stomach acid 'barrier' to gastrointestinal infection), increasing intestinal mobility, and increasing the secretion of bile and pancreatic juices. There is also an increase in salivary secretion (but not amylase)[34] . From these effects it is easy to project benefits for liver function especially in its detoxifying and eleminatory functions, and for the pancreas, including the endocrinal secretions linked as these are to the flow of pancreatic juices and thus explain in turn the apparent benefit that bitters have for disturbances in blood sugar levels. Gastrin is also active in increasing appetite and a general sense of well-being; with this and the undoubted benefits on digestion it is not surprising that bitters were for long considered superb general enhancers of vitality.

Silybum marianum (L)

This Mediterranean plant has been used in middle Europe for liver complaints for many years, the seeds being considered the active part. A protective effect on the liver has in fact been recently demonstrated [35] , notably against the common experimental hepatotoxins carbon tetrachloride and phalloidine (from Amanita phalloides) and against chemically-induced cirrhosis. This protection lasted many hours after treatment. The conclusion drawn has been that the cell membranes of the hepatocytes have in fact been stabilized against the destructive effects of toxins. The main activity in the remedy has been conclusively associated with an unusual type of flavanoid-lignoid complex or flavolignan, in this case known as silymarin: this has been shown to enhance the activity of polymerase A produced in the hepatocyte nucleolus so leading to increased ribosomal RNA activity and thus protein synthesis in the cell. It is this,

with the membrane-stabilizing effect that is seen to explain not only the ability of the remedy to help protect toxicity, but to stimulate regeneration and repair as well.

Vitex agnus-castus (L)

It is one of the claims made for medicinal plants that they have an amphoteric or normalizing effect rather than a dynamic unilateral one. The actions of Vitex appear to be a good example of this. Its traditional use has been for disorders of the female reproductive system, with an almost contradictory list of indications (heavy menstruation and amenorrhoea for example) and including a notable effect impromoting lactation. In recent practice its applications have if anything been wider, forming the basis for treatments for all manner of menstrual disorders, particularly premenstrual problems, menopausal symptoms, menorrhagia and dysmenorrhoea. The impression gained in usage has been that the remedy somehow normalizes the balance of sex hormones at different times of the month, with if anything a slightly progesteronal effect. Support for this has been provided by Probst and Roth [36,37] who have shown that Vitex has effects similar to the corpus luteum on human subjects, established by histological investigation of the endometrium by curettage, by cytological examination of vaginal secretions, and by observing changes in basal body temperature. Further work with the oestrus cycle of rats showed the effect in shortening the oestrus only apparent in test animals already having abnormally frequent or lengthy cycles; from this and from clinical therapeutic results with patients it is surmised that the effect of the remedy is to normalize corpus luteum function, along with perhaps ovarian function in general, via the controling centres in the hypothalamus, rather than simply replacing corpus luteum hormone (there are no suitable steroidal components of the plant in any case) [38] . Confirmation of a significant effect on lactation has also been provided [39] .

DISCUSSION

A review of the available evidence for a number of herbal remedies is here presented. The remedies have been selected from a wide field and reflect the average state of affairs that pertains to the investigation of the better known remedies, although it must also be said that there are a great many remedies that have been barely examined experimentally in modern times. From what has been said at the beginning of this paper it will be apparent that the aim of assembling this information is to provide a modicum of independent support for the claims of herbal practioners for their remedies, and incidentally reveal to a few that observable pharmacological activity is a property of herbal remedies (contrary to some allopathic pronouncements). The ultimate purpose of this paper, however, is to present the case for the use of herbal remedies as a valid healing therapy in the modern age. It is thus useful to reiterate the message of the preamble, that the herbal practitioner sees the herbal remedy as essentially supportive of body function, amphoteric rather than unilaterally active, promoting a vital body response to invasion or obstruction rather than aiming simply to remove the superficial characteristics of the latter. We thus find the herbal practitioner using Crataegus equally in cases of high and low blood pressure for its tendency to normalize this parameter. The evidence suggests that by supporting the function of the heart whilst also having vasodilatory action, may be something in this. We also find the practitioner using Vitex as a general normalizing remedy in a variety of gynaecological conditions, and we have the supporting contention that the remedy acts pivotally on the hypothalamic-pituitary axis. Body function can be supported in more direct ways too. The use of the bitter remedies provokes a reflex response on the part of the body that is comprehensively useful in improving a range of functions associated with the body's relationship with food. It is contradicted only when that relationship is already marked by overactivity, for example in hyperacidity or vomiting. Otherwise, the bitter effect is clinically useful for many upper digestive problems, including such diverse conditions as anorexia, diabetes and hypoglycaemic syndrome, hypochlorhydia and tendency to enteric infections, chronic liver disease and liver-centred toxic

problems. A third way to support vital function is by using trophic remedies; these are remedies which have an almost nutritious action on a specific organ or tissue. Silybum marianum, we say, demonstrated such an action on the liver parenchymal cells, and in a sense we can see the same relationship to the adrenal cortex of Glycyrrhiza glabra, with its ACTH action and also yet its corticosteroid - enhancing effect in the periphery. Similarly the total action of Allium sativum on the blood stream can be considered trophic, improving a broad range of functional parameters and we have already witnessed the trophic effect of Crataegus on the heart.

The action of herbal remedies in support of vital body function therefore comes in three categories, 1) the amphoteric regulation of excessive functional oscillations, 2) the direct provocation of a healthy reflex response and 3) the straightforward trophic effect. Central to any of these actions is the intrinsic complexity of each remedy's constitution. One very ofter finds constituents present with apparently contradictory isolated pharmacological actions, as for example in the water-retentive glycyrrhizin and other diuretic constituents in Glycyrrhiza; the impression gained is of a potentiating of individual contributions to the total action so that the whole plant is made up of more than the sum of its parts. Thus even in those remedies with an almost allopathic effect such as Allium with its antimicrobial action and Glycyrrhiza with its anti-inflammatory effect, there is sufficient complexity in both the active constituents of the plants and of other reported pharmacological effects to make it clear that we are not comparing them directly with allopathic counterparts. Evidence of supportive actions as outlined above in particular give each such remedy a much more founded and substantial effect overall, perhaps at the expense of the dramatic effect familiar in allopathic circles.

This is only a fraction of the case that could be prepared for herbal medicine. Many more remedies would have to be discussed to provide the complete story. It is hoped, however, that sufficient has been said to make the point that herbal medicine is worthy of consideration as a valid health care alternative in the modern world. One is mindful of the comments of the World Health Organization on the role of traditional medicine where the facilities of modern medicine are lacking. The author would hope to make a plea that herbal remedies be considered in an even more positive light. Those with scientific training will perhaps contend that the use of scientific data to support a case for using techniques that cannot be completely validated or even explained by the rigours of the experimental method is a case of having the best of both worlds. To this the author must answer that if it came to a conflict then the herbalist would turn his back on the experimental method rather than to the evidence of his own eyes and ears and that of his patients; however, there is no need for a conflict to occur, the scientific method does contribute to man's understanding of the world when used with enlightenment and true humility. It is to everyone's best interests to work together towards improving the quality of life and health.

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BIOLOGICAL ACTIVITY OF SOME SAPONOSIDES

Prof. Jerzy Lutomski

POLAND

Besides Panax ginseng, which was supplied in oriental familiar medicine for centuries, Aralia mandshurica and Eleutherococus senticosus have gained some meaning in modern medicine recently. Although pharmacological studies are constantly continued the adaptogenic, tonic, stimulant, anabolic and general strengthening effects of Panax ginseng, Aralia mandshurica and Eleutherococcus senticosus are now well known[3, 7, 16, 17, 18]. The most effective components of Araliaceae species have been recently considered to be a saponin fraction. The compositions of these fractions differ much. Panax ginseng saponins consist mainly of 20-S-protopanaxadiol and 20-S-propanaxatriol glucosides[15]. Aralia mandshurica saponins were found to be exclusively oleanolic acid derivatives[13]. Meanwhile, we, in the Polish Institute of Medicinal Plants, in search of plant with approached biological properties to Panax ginseng, have limited our research entirely to some plants containing triterpenoid glucosides - exactly the derivatives of oleanolic acid. The triterpenoid glucosides are widespread in plants which belong to various families, and among the animals which belong to sea urchins/ Echinodermata/. The substances take place in vital organs and tissues. The triterpenoid glucosides demonstrate -same as exogenetic provenance material - a physiological activity in warmblooded animals. They influence metabolism, the state function of organs and of the whole organisms. That is why they are included into metabolism in biological systems and they demonstrate- as low molecular regulators- some polyfunctional properties.

1. CHEMICAL CHARACTERISTICS OF TRITERPENOID GLUCOSIDES:

The triterpenoid glucosides belong - according to the character of aglykon - to the following series: α- (fig.1) or β - Amyrin (fig.2), Lupan (fig.3), Hopan (fig.4), Dammaran (fig.5), Lenostan (fig.6), Holostantyp (fig.7).

There can be the following monosaccharides in carbohydrate part: D-glucose, 3-0 methyl-D-glucose, D-galactose, D-xylose, D-chinovose, L-arabinose, L-ribose, D-fucosa, α - rhamnose, Lyxose and D-glucuronic acid. They form one or two carbohydrate chains of linear or branched structure. Now, I will present some variants of classification of triterpenoid glucosides which consider several curiosities of carbohydrates.

After many investigations, one can accept that the appearance of triterpenoid glucosides in several plant families makes a chemitaxonomic stigma. The following families are especially rich in these substances: Caryophylaceae, Compositae, Chenopodiaceae and others. The representatives of these last three mentioned families are:

Aralia mandshurica from Araliaceae,
Calendula officinalis from (Compositae), Astraceae.
Beta vulgaris from Chenopodiaceae.

They have been examined in our Institute.

a) Aralia mandshurica: Aralia mandshurica is one of more important Astraceae plants. The saponosides from Aralia mandshurica possess aproximal inhibitory and stimulatory properties; as the root of Panax ginseng, for example. As the result of phytochemical investigations in the Institute of Medicinal Plants in Poznan, nine saponosides were isolated [13] (with six unknown ones among them). All these compounds possess the same aglycone - cleanolic acid and therefore they were called cleanosides. There were five monosaccharides found in the carbohydrate part of the substances mentioned above: L-arabinose, D-glucose, D-galactose and glucuronis acid.

Further procedural details of identification and isolation were presented in Polish Journal Herba Polonica in 1977 [13] .

b) Calendula officinalis L: Marygold (Calendula officinalis L.) from Astraceae was another saponin plant which we were interested in. The plant contains a rich fraction of oleanolic acid derivatives. The extract obtained from dried herb contained about 65% saponin compounds. Chromatographic analysis showed the presence of over 10 saponin compounds which aglycon was identified as oleanolic acid, after acid and alkaline hydrolysis. There were glucose, galactose and glucuronic acid found in the carbohydrate part [8,9,10] .

We have also found some differences in the structure of carbohydrate parts of saponins from Calendula officinalis L. flowers and from its roots. There was glucuronic acid taking place at C-3 atom of oleanolic acid in flowers, whereas there was glucose in the same place of the compound in the plant's roots. Actually known saponosides are presented on fig.8 for the flower extract and on fig.9 for the root extract separately.

c) Beta vulgaris L: White beet (Beta Vulgaris L.) from Chenopodiaceae, apart from a great number of organic nitric connections (i.e.12 aminoacids), contains also betaine and pyrolidonocarboxylic acid. They are saponosides with oleanolic acid as aglycon. Three saponins have been isolated by Krecu [12] (Soviet Union), and she defined them as saponosides A,B and C (fig.10).

We also found a number of these compounds in the root of white beet, during our Institute research. After their saccharose purification they were developed on column chromatograph with the use of polar extract agents. There were 11 compounds obtained, all of them having oleanolic acid as aglycon and glucuronic acid, glucose, arabinose and galactose in carbohydrate part, in different quantity ratio. Apart that, free oleanolic acid and its sodium were also found.

2. BIOLOGICAL CHARACTERISTICS

The isolated Aralia mandshurica, Calendula officinalis and Beta vulgaris fractions went under some pharmacological experiments [19] carried out on animals. The goal of the experiments was to define the substance's influence on the lipid content in blood serum and homogenized liver in experimental hyperlipidemia in (Wistar) rats. Hyperlipidemia was evoked by a fatty diet. The studied substances were applied to stomach. All studied animals went under the following experiments:

a) Lipid determination in blood serum containing:
   (a) total lipids by the method of Postma and stroes [14] ,
   (b) triglycerides according to Eggstein and Kreutz [5] ,
   (c) total cholesterol by the method of Blaszczyszyn [14] ,
   (d) free fatty acids by the method of Duncombe [4] ,
   (e) β-lipoproteins after Koller and Bellaj [11] ;
b) Lipid determination in the homogenised liver (total lipids, cholesterol, triglycerides), by the same methods as for blood serum;
c) the determination of glucose level in blood serum by the o-toluidine method;
d) liver weight determination.

The rats fatty diet containing coconut butter and cholesterol resulted in the increase of lipid level in blood serum and the homogenized liver. The increase was more distinct in liver, as far as total lipids, triglycerides and total cholesterol go.

All of them, oleanolic acid derivatives from Aralia mandshurica and the same group of saponins from

Merigold herb and those from White beet (50mg/kg / dose) were observed to decrease the total lipid level (21-37%), the triglyceride level (20-30%) and the cholesterol level (17-25%) in blood serum and homogenised liver. The most active were saponine fractions from Aralia, then from Marigold and White beet.

Separate studies on the influence of oleanoside fractions on central nervous system depended on the measurement of rats spontaneous motility and their hexabarbital sleeping time period.

The experiments showed some distinct antistress activity, catacholamines regulation inducing role in brain structures, and inhibitory influence on the animals motor activity plus on the hexabarbital sleeping period, and therefore, on central nervous system.

Taking the mentioned pharmacological properties of the studied saponoside fractions into account, we may assume that, after some continued clinical experiments, oleanosides of Aralia and Marigold will especially be of some basis leading to their introduction to the market in the form of geron-phitotherapeutics.

In recent years, the cause of senescen has been more often considered with the aspect of immunological reactions. Observations concerning aged people give much evidence for the immunological changeableness resulting in i.e. progressing infectional and cancer disease morbidity[6]. Therefore, there was our goal to define the influence of the isolated oleanosides on some immunological aspects, in our further studies. We have observed that Marigold and and White beet saponosides do not stimulate cellular response.

Examinations of immunological properties of plant originating substances are conducted according to the III-stage scheme. In the first stage experiments possible influence of the substance on the humoral response is tested as well as cell mediated response, phagocytic system and regeneration abilities of cells after x-radiation.

The second stage experiments are the repetition of the positive change if parts already made, but they are considerably widened.

In the third stage there are conducted detailed directed experiments dealing with the influence of the plant originating substances on to the type of immunological response selected in the previous stages.

Oleanoside complex of Aralia mandshurica was tested on the basis of the above mentioned scheme with the reservation that the third stage has not been carried out up to now.

Oleanosides from Aralia mandshurica were obtained in the shape of yellow powder containing 40% of pure component. Experiments were made on mice, guinea pigs and rabbits adimistrated this substance in water solution, orally, through the stomach wash in doses of 10mg. and 50mg. per 1kg. of weight.

Practically it was possible to define the toxic dose of oleanosides from Aralia mandshurica (OMA). The toxic influence either on to the organisms, or cells was not observed in the course of in vivo or in vitro experiments.

In cooperation with the scientists [7] from the Immunological Department of the Medicine Academy in Szczecin, we made a series of immunological experiments:

1. Influence of OMA onto the dynamics of the phagocytosis process in animals. Examinations were conducted in vitro by means of isotopic method using as antigen sheep red blood cells (SRBC) labelled with chrome 51 as antigen, and by means of Wright method in the modification of Dolezal with the use of staphylococcal antigen.

Leucocytes and Schilling percentage formula were also counted. Six groups of rabbits were experimented on. They obtained OMA in doses of 10mg and 50mg. per 1kg. of weight and staphylococal vaccine in one dose of 1mg and repeated doses of 0.1ml. The most optimal results, it is the highest

increase of ingestion and digestion of antigen by granulocytes were observed in the groups obtaining OMA repeatedly every day for 7 to 10 days in doses of 50mg per 1kg. of weight and also for 7 to 10 days in little doses of staphylococal vaccine. The further parameters of phagocytosis process we were interested in, were levels of leucocytes and particularly granulocytes. It was observed that application of OMA only for 10 following days in 50mg per 1kg of rabbit weight caused statistically considerable decrease of the amount of leucocytes and particularly granulocytes 10 days after the completion application of this substance. Such a decrease was not observed when OMA was applied for 10 following days simultaneously with staphylococal vaccine in little doses.

2. Next, influence of OMA onto the humoral response was evaluated by defining the number of cytoplasmatic cells in the spleen producing 19S antibodies by means of Jerne method in the modification of Sterzl and Mandel, and antibodies levels in blood: antistaphylococal, anti-E. coli. agglutinins and hemolisins by Adler method.

Examinations were made by applying OMA to mice and rabbits.

There was ascertained that OMA cause different organism humoral response depended on the animal species.

3. Testing of OMA influence onto the cell-mediated immune response was conducted by obtaining blastic transformation test using phytohemagglutinin, capillary migration test using phytohemagglutinine and tuberculin and skin test using 2,4,2 DNCB.

Influence of OMA onto the cell-mediated response within the range of blastic transformation process and production migration inhibitory factor were examined in 2 sets of tests namely by applying OMA in vivo or in vitro. It was found that OMA applied in vivo do not behave as mitogenic substances or do not stimulate production of lymphokine which inhibits migration of leucocytes. Those results were confirmed by examination of the delayed hypersensitivity reactions with the use of DNCB. There was not observed increase of reactions in the groups obtaining OMA when compared with the control group.

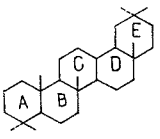
4. There were made further evaluation of OMA influence onto the regeneration of spleen cells after x-irradiation of mice with sublethal doses of x-rays on total body. Examinations were made by giving OMA to mice before x-irradiation, or first mice were irradiated and next they obtained OMA. As far as regenerating spleen foci, spleen weight, spleen index and time of mice survival were considered. It was observed that the best results were obtained by applying to mice OMA in doses of 50mg. per 1kg. of weight and irradiating them next.

5. There was examined the medium time survival of mice with implanted Ehrlich carcinoma, in the same experiment. The highest value was obtained in the animal group, administered 10 OMA doses before implantation of Ehrlich carcinoma.

6. Examination of OMA influence on the phagocytosis parameters in the animals given cyclophosphamid in one dose of 200 mg per rabbit seemed to be an interesting experiment which proved protective influence of OMA on the phagocytosis process. These were observed the increased values of ingestion and digestion of antigen by granulocytes under the influence to OMA doses of 50mg 1 kg. of weight for 10 following days. Protective influence of OMA on the phagocytosis process in rabbits obtaining hydrocortison was not observed.

It may be possible that Aralia mandshurica, because of low toxity (210 mg/kg) and distinct influence on immunological mechanismus, will in future become the source of immunoregulating medicaments.

However, further examinations are necessary.



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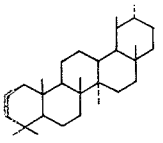

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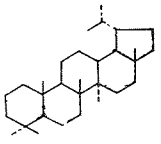

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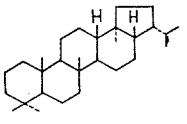

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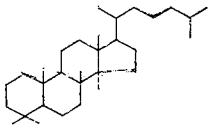

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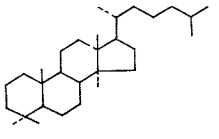

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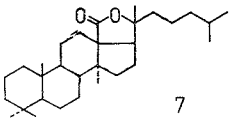

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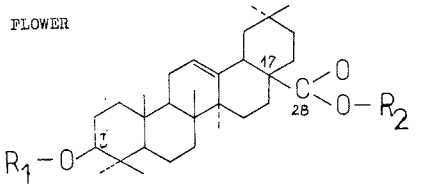
Fig. 8 FLOWER



A: R_1 = glu/1-4/ gal/1-3/ > gluc$_5$ R_2 = glu

B: R_1 = glu/1-4/ gal//1-3/ > gluc$_5$ R_2 = H

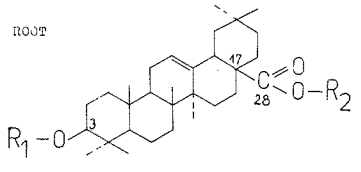
C: R_1 = gal/1-3/gluc$_5$ R_2 = glu

D: R_1 = gal/1-4/gluc$_5$ R_2 = H

E: R_1 = glu/1-4/gluc$_5$ R_2 = H

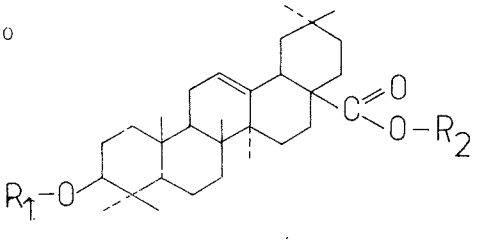
F: R_1 = gluc$_5$ R_2 = H

Fig. 9 ROOT



1. R_1 = gluc R_2 = H
2. R_1 = gal/1-4/gluc R_2 = H
3. R_1 = gal-gal/1-4/gluc R_2 = H
4. R_1 = gal/1-4/ gluc/1-3/ > gluc R_2 = H
5. R_1 = gal/1-4/ gluc-gluc/1-3/ > gluc R_2 = H
6. R_1 = gal-gal/1-4/ gluc-gluc-/1-3/ > gluc R_2 = H
7. R_1 = gal/1-4/ gluc-gluc-gluc/1-3/ > gluc R_2 = H
8. R_1 = gal/1-4/ gluc-gluc/1-3/ > gluc R_2 = gluc
9. R_1 = 6'-O-methyl-gluc$_5$ R_2 = H
10. R_1 = H R_2 = Na

Fig. 10



A: R_1 = O-β-D-Gluc R_2 = CH_3

B: R_1 = O-β-D-Gluc R_2 = H

C: R_1 = Gluc$_5$ R_2 = H

METHODS OF OBTAINING A NEW HERBAL DRUG USING DATA OF TRADITIONAL MEDICINE

Dr. Ovidiu Bojor

ROMANIA

There is no doubt that the herbal drugs are and will still be one of the three main resources of raw materials for obtaining medicines during the next millenium, i.e.:

— substances produced by the animal and human cells;

— substances produced by the vegetable cells;

— substances obtained by synthesis (either in imitation of some structures already existent or created by the human intellect).

As a secondary source minerals, especially trace elements, should not be overlooked.

Herbal drugs are used at present all over the world no matter how developed the countries are, only the extent and manner of use being different. If in the developed countries 30-50 percent of the drugs contain natural active substances, in the developing countries more than 80% of their drugs are natural. There is also another difference: the modern medicine, European or classical, called "scientific", prefers pure active substances called also active principles whereas the traditional medicines prefer vegetal extracts, that is a total of active substances. This difference is also a consequence of the medical systems that are based on theoretical or philosophic arguments. We want to stress from the very beginning a fact we consider a very important one: a medical or a therapeutic system cannot be validated or cancelled by the investigating means of another system. If we try to do so, we make a fundamental mistake. In other words, if we do not know the theoretical basis of a medical system we cannot declare it efficient or not. We have stressed this because the researchers in the drug field in the industrialized countries try to demonstrate in a subjective, unilateral way and to characterize a drug or a traditional cure by means of investigating methods belonging to their system.

What we want to present in this paper is the methodology required to obtain a Herbal Drug on the basis of the traditional medicine data, by using modern techniques and by taking the basic principles of the concerned system into account. That is why we have selected those phases or stages as well as the fundamental conceptions which are common for all medical systems.

If I am wrong, please correct me; any suggestion in this respect must be directed to the success of this Congress which is to get assistance to the sick people.

1. Preparing or formulating a drug

We think that irrespective of the medical system, everybody agrees that a new drug should be more efficient, less harmful when given at normal therapeutical doses, but at the same time more active than former one.

The drug should also be reproducible and easy to be administered (to children, old people or to those with very severe diseases), less expensive and accesible thus to the greatest possible number of patients.

We hope that you will agree with our statement that in preparing or formulating a drug and especially in administering it, in combining drugs or other therapeutical techniques we must find upon the axiom: there are not diseases but sick people. We do not want by this to offend the drug manufacturers, the drug businessmen, but to call the physicians' attention to the fact that each person, each suffering

individual should be considered in the first person singular, in all his or her functions, physiological and spiritual complexity.

The main stages which are the basis of obtaining a "Herbal Drug" are presented in the diagram annexed to my paper. I shall not present chronologically the stages, as they can be examined by all the participants in the volume containing the proceedings of this Congress . Allow me however to point out the "key" aspects, necessary for obtaining a "Herbal Drug" of a good quality.

The first stage is to formulate a new drug. Being a drug presented on a traditional basis, the team of specialists should know thoroughly the principles of the concerned medical system, be it Islamic, Arabian, Ayurvedic, Hellenistic, Chinese, Siddha or whatever it may be.

As sources of the information old or new treatise, manuscripts, data gathered from people using currently herbal drugs, or — what is more difficult from some families or healers, data transmitted and kept secretly from generation to generation as a family heritage should all be used.

All these data may be compared with those provided by classic medicine, but only as general information without exerting any negative influence.

From the point of view of scientific research, this first stage has the character of a basic research, implying creativity, philosophy, logic analysis, connections, inspiration.

2. Raw Material

The raw material necessary to obtain a herbal drug comes from the spontaneous flora or cultures at present, but in the future tissue or cell cultures obtained in laboratory are envisaged as well.

As far as the raw material — that is the medicinal plants — are concerned, I should like to call your attention to two important aspects:

1. *The Stock of the spontaneous flora is limited* precisely to the species which are widely used. The merchants of medicinal plants wishing to obtain large profits after having bought them at very low prices, would not give their attention to the protection of the country-side and would exploit to a maximum the existent stocks in different geographical areas. There are too few those thinking of protecting the species, too few those thinking of the future generations. The medicinal plants belong to an ecosystem and if the biological balance is impaired by an irrational exploitation, that will have disastrous repercussions on the other factors of the ecosystem.

In Romania, we have drawn up and developed a methodology of evaluating from a qualitative and quantitative standpoint the resources of medicinal plants during the last 30 years. The methodology — known as the "Economic mapping of the spontaneous medicinal flora" aimed at inventoring the available quantities of the raw material taking into account the Nature conservancey.

The spontaneous medicinal flora is exploited in a controlled manner at present, the collection d is carried out in the same district (s) after a number of years, thus permitting the vegetation to be restored. Besides, it is compulsory to sow the field again with a specific species if the entire plants or their roots or rhizomes have been collected. I have already applied and recommended this system in some developing countries.

2. *The cultures* represent the second source of raw material. The cultures of medicinal plants represent important advantages over the spontaneous flora. They permit the cultures to be programmed, preferably in the neighbourhood of some industrial units which process and use a propagation material superior from a genetic and phytochemical point of view.

The character of the scientific research in this field is fundamental and applied.

We think that especially in the developing countries the cultivation of medicinal and aromatic plants represent a starting line in assuring a source of raw materials.

Irrespective of a small, medium or large scale industry, the sources of raw materials must be assured for a period of ten years at least.

3. Standardization of Raw Material

Another factor required to obtain a Herbal Drug is to assure a controlled supply of high quality raw material as constant, as possible from a phytochemical standpoint.

The quality of a drug depends on the time of collection, on the drying and storage conditions, the duration of its activity (expiring date), purity, content of active constituents, etc. This kind of research is less theoretical and has a more practical character.

The quality conditions vary from one plant to another, from one country to another. They should be stipulated by teams of specialists keeping in mind the economic aspects as well.

Standardization of the raw material is essential in assuring a reproducible drug with constant properties.

4. Pharmaceutical Technology necessary to obtain a new Herbal Drug

Extracts, infusions and ointments are the traditional dosage forms of vegetal drugs. They all contain complexes of active principles and not pure substances.

A great number of vegetable drugs may be administered as such. To this group the plants containing alkaloids, cardiac glycosides, saponins, tannins, anthocyanins, vitamines, essential oils and other active constituents belong, which given in amounts of 1-4g assure the daily therapeutical requirements.

Our investigations as well as those of other teams of research workers have demonstrated that the above mentioned plants administered as such after powdering them, yield their active substances directly to the gastric juice, the gastro-intestinal resorption being superior to an infusion or a docoction because of the wide surface of contact. On the other hand a series of active substances are not deteriorated by heat or organic solvents.

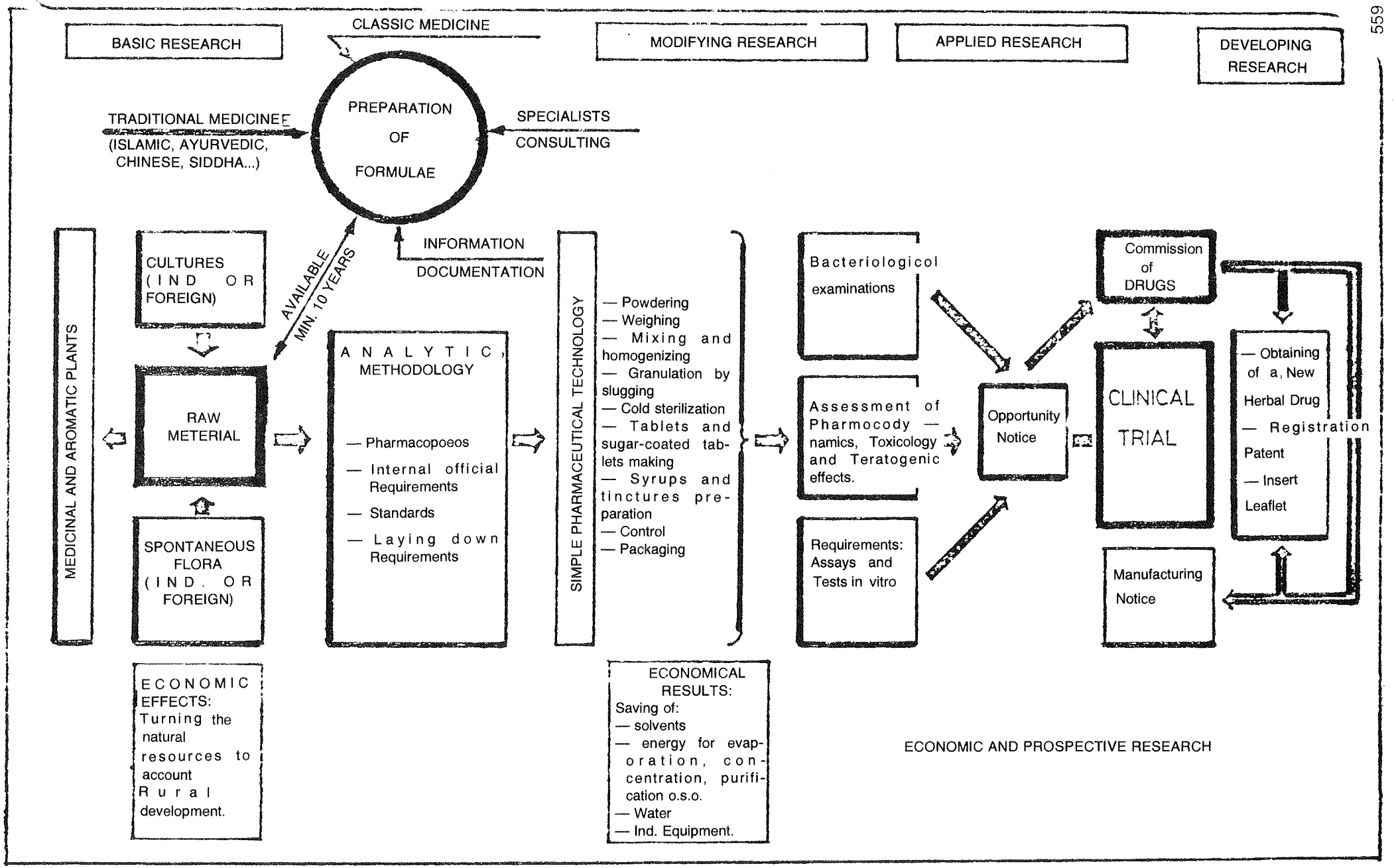
For all drugs belonging to that group we recommend to manufacture tablets or coated tablets directly from the raw material. The whole technology consists in finely powdering the plants, weighing the components, adding some trace elements or other ingredients if necessary, homogenizing, granulating by "slugging", sterilizing in the cold and tableting. This simple methodology may replace the hydro-alcoholic or alcoholic extract in the countries where alcohol is prohibited for religious reasons (which one must take into account too).

This is but only one example of how a new Herbal Drug can be obtained in a small-scale industry requiring 10-50 people, simple equipment and technology and a minimum investment.

The control and investigations of this phase have a character of modifying and applied research.

If the assesment of pharmacodynamics differs from one medical system to another, there common items are however essential for any system: the toxicological study, the teratogenic effects and the bacteriological examination. The first two items imply a more complex methodology and should be carried out by a specialist (a micro-biologist). We insist on the microbiological control especially for Herbal Drugs obtained directly from the raw material which, owing to less hygienic conditions of collecting and preservation, may contain pathogen germs: bacteria, fungi, parasites.

Medicinal plants should be never allowed to be treated with herbicides, fungicides and insecticides,


BASIC RESEARCH
CLASSIC MEDICINE
MODIFYING RESEARCH
APPLIED RESEARCH
DEVELOPING RESEARCH
TRADITIONAL MEDICINEE (ISLAMIC, AYURVEDIC, CHINESE, SIDDHA...)
PREPARATION OF FORMULAE
SPECIALISTS CONSULTING
INFORMATION DOCUMENTATION
AVAILABLE MIN. 10 YEARS
MEDICINAL AND AROMATIC PLANTS
CULTURES (IND OR FOREIGN)
RAW METERIAL
SPONTANEOUS FLORA (IND. OR FOREIGN)
ANALYTIC METHODOLOGY
— Pharmacopoeos
— Internal official Requirements
— Standards
— Laying down Requirements
SIMPLE PHARMACEUTICAL TECHNOLOGY
— Powdering
— Weighing
— Mixing and homogenizing
— Granulation by slugging
— Cold sterilization
— Tablets and sugar-coated tablets making
— Syrups and tinctures preparation
— Control
— Packaging
Bacteriologicol examinations
Assessment of Pharmocody — namics, Toxicology and Teratogenic effects.
Requirements: Assays and Tests in vitro
Opportunity Notice
Commission of DRUGS
CLINICAL TRIAL
Manufacturing Notice
— Obtaining of a, New Herbal Drug
— Registration Patent
— Insert Leaflet
ECONOMIC EFFECTS: Turning the natural resources to account Rural development.
ECONOMICAL RESULTS: Saving of:
— solvents
— energy for evaporation, concentration, purification o.s.o.
— Water
— Ind. Equipment.
ECONOMIC AND PROSPECTIVE RESEARCH

very harmful substances for man.

The few examples, I have given so far, show how a new Herbal Drug can be obtained on the basis of traditional medicine data. What is new in this is only the technology and the dosage form. This aspect is perfectly illustrated by the words of Mr. R.H. Bannerman, programme Manager, Traditional Medicine, WHO: "We must therefore combine local genius with modern scientific technology".

5. **Organizational Aspects**

In most countries there are "Commissions of Drugs" or similar bodies belonging to the Ministry of Health. In Romania, for instance, that Commission includes pharmacists and physicians in all medical specialities who discuss the proposals of a new drug, give an Opportunity Notice, send the first batch of the drug in clinics for clinical trials and finally give an Approval for Manufacture, which enables the manufacturer to start producing the new product. Finally, the new drug is registered and then sent to the market after the insert leaflet and the design on the package have been prepared and settled. Launching a new drug is not the final stage. Public should be informed of the new product, but the advertising and marketing activities should be decent, convincing ane not trying to sell it at any price. We consider the drug is not a trade object, a business, but a help given to a suffering person.

6. **Economic Aspects**

More than 14 years ago on the basis of the "Expert Group Meeting of Small-Scale Industries in Arab Countries of the Middle East" (Beyrouth, Nov.1968), the recommendations on policies and programmes for the development of small-scale industries and the transition from artisan, handicraft activities to modern small-scale industries, regional and international co-operation was taken under consideration. But in the field of manufacturing medicinal plants and obtaining new Herbal Drugs no important progress has been made.

It was also generally recognized that the traditional sector in the Arab countries of the Near and Middle East is the dominant sector and accounts for an overwhelming majority of all manufacturing establishments.

In developing countries the small-scale industry sector coincides very largely with the group of establishments employing more than 5 and fewer than 50 persons per establishment. The small-scale industry should be defined to include those industries using modern technology but in which employment and investment in fixed capital are modest. It also shows that small-scale industry is almost exclusively a private enterprise activity in most of the developing countries. These general aspects are also applied partly to obtain new drugs from plants on the basis of data provided by the traditional medicine.

Bringing now my speech to a conclusion, I want to emphasize that when we prepare a new drug on the basis of the millenary experience of an ethnical or social group or of a medical system, I think that such a drug should be easily accessible to a great number of individuals.

In my opinion the drug as well as the medical assistance must not have frontiers or become a monopoly or object of unjustified incomes. The drug should not be a business. If I could impose my conditions, I would forbid the drugs to be licensed. The drug and all that science has attained so far in this field must be in my opinion the common weal of all the mankind so much the better as more than 75% of the world population has still a poor médical assistance not very different from what it was thousands of years ago.

I also consider that the more developed nations, the international organizations and bodies should endeavour to promote the traditional medicine on a new scientific, sincere and unbiased basis. Healing physical or psychological suffering, liquidating malnutrition and the extreme poverty of people must be considered as charities.

All the countries, irrespective of their size, power or degree of development have an equal right to life, to freedom, to health. When all these desiderata become true the "Health for all by the year 2000" will no more be a simple noble ideal but pure reality.

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SOME APPROACHES TO THE STUDY OF INDIGENOUS MEDICINAL PLANTS

Prof. Atta-ur-Rahman

PAKISTAN

The bulk of the populations of the Afro-Asian countries, particularly those living in villages, rely on the indigenous medical systems to provide relief from disease. Systematic scientific investigations, particularly during the current century, have resulted in the identification of a growing number of active constituents many of which are now routinely used in modern medicine. These include reserpine for the treatment of cardiac arrhythmias, vincamine as a vasodilator, and vinblastine and vincristine as anti-tumor agents etc. Isolation and structural studies have accordingly been directed in many laboratories around the world aimed at isolating new natural products which could prove to be valuable chemotherapeutic agents.

In order to derive a logical appreciation of the role that traditional medicines, particuarly herbal prescriptions, play in alleviating disease, it is important to attempt to understand the mechanism by which life functions at the molecular level. Living organisms exhibit a highly complex panorama of remarkably intricate and beautifully organised chemical reactions which can be studied in unambiguous quantized terms. While philosophers may ponder and argue over the correctness of considering man as a summation of his molecular components, the study of life is made more amenable to an analytical study if it is considered in terms of its interacting components, at atomic, molecular or higher levels of organisation.

When one examines life at the molecular level one finds that literally millions of different chemical reactions are occurring in the human body. Most of these reversible reactions are under strict enzymic control, and the point of equilibrium in each of these reactions is determined by a large number of variable factors such as pH of the surrounding medium, concentration of interacting molecules etc. Thus in each person, the point of equilibrium of these reaction will vary. The overall summation of these equilibria will therefore result in a differing biological spectrum and hence make each individual uniquely different from any other although certain broad categorisations may be made. The concept to temperament or "Mezaj" can thus be rationalised.

It is apparent that the enormous complexity of the biological system does not lend itself readily to a scientific analysis of all that occurs within it. This is one reason why modern medicine has concentrated attention on the use of individual chemotherapeutic principles rather than complex mixtures. The precise metabolic pathways of individual substances administered to living systems can be monitored with greater ease by radio-isotope tracer techniques, allowing a degree of rationalisation of the mechanisms by which the drugs interact.

In the case of herbal preparations, literally thousands of different chemical substances may be present and it is impossible even with the highly sophisticated scientific tools available today, to determine how each component in the herbal mixture is acting on the body. Herbal preparations, even with demonstrated biological activity, have therefore generally been ignored in western medicine.

Furthermore, inspite of the fact that herbal remedies have been used safely since centuries for obtaining relief from various ailments, the prevailing laws in the west do not allow clinical trials of such plants preparations on human beings. This means that even where towicological and pharmacological studies have demonstrated that a particular herbal preparation is safe and active, it usually cannot be legally incorporated into the existing pharmacoepia.

This state of affairs does not exist in most Afro-Asian countries, which places them in a position of

great advantage. As herbal preparations have been used safely over the centuries, the risk involved in undertaking direct clinical trials is minimal and this can be further reduced by preliminary toxicological studies. The advisability of undertaking direct clinical trials of herbal prescriptions has been a matter of some considerable discussion in international forums in recent years, and the concensus of opinion by the World Health Organisation and other international bodies such as U.N.I.D.O. has been that *animal experiments should follow and not precede* clinical trials with those herbal remedies whose safety and efficacy has been established in the traditional system of medicine. Thus the World Health Organisation, at a meeting on the "Promotion and Development of Traditional Medicine" held in Geneva from 23rd November to 2nd December 1977 has resolved that: *Clinical research is necessary for drug trials and validation; it is better organised in association with hospital or treatment centres. Drug trials on animals should be an extension of these studies. It needs to be emphasised that the biological properties of certain medicinal plants should first be tested with the preparations used by traditional healers. The effectiveness of some drugs could be lost when chemical principles are extracted from the crude drugs and then tested. This procedure is mandatory for the screening and verification of drugs derived from traditional medicinal plants".* A similar resolution, advocating direct clinical trials, was adopted at the U.N.I.D.O. Tedhnical Consultants Meeting held in Lucknow, India in March 1978.

For a scientific approach to the study of established herbal remedies it is imperative to establish research institutes of an international level of excellence with all the necessary facilities by way of sophisticated instrumentation, books and journals and highly qualified man-power. These institutes would necessarily have to be multi-disciplinary in character incorporating departments of clinical pharmacological, toxicology, microbiology, virology, biochemistry and phytochemistry. The researches should begin by clinical trials with those herbal prescriptions which are reputed to be effective in diseases which are amenable to quantized analysis. The body of statistical data which would accumulate would then speak for itself regarding the efficacy or otherwise of the drug being tested. In cases where definite biological activity is observed, detailed toxicological evaluations would need to be carried out to establish the safety of the drug in various classes of patients e.g. children, pregnant women etc. Drugs passing these toxicological trials can then be incorporated in an integrated pharmacoepia, and detailed studies regarding the mode of action of the drug, nature of active constituents etc. can follow.

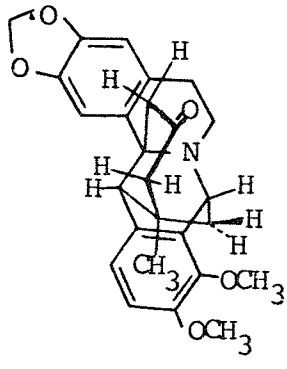
It is vitally important to appreciate that the development of new drugs for different disease is a formidable and expensive proposition even to the huge research organisations of the multi-billion dollar pharmaceutical companies. Several thousand compounds have to be synthesised before one promising candidate suitable for clinical trials can be made available, and this also usually falls by the wayside once the detailed clinical and toxicological data are collected.

According to a report published by the U.S. drug industry, a sum of 722.4 million U.S. dollars were spent in 1974 alone on company financed research and development, and only 19 new drugs were introduced in the market during that year in the United States. This would imply that an expenditure of some 38 million U.S. dollars is involved in the form of research and development costs before a single new drug is introduced into the international market! The legacy of the indigenous medical systems thus offers an extremely cheap and viable alternative for treatment in the Islamic countries. The search for "active single ingredients" on the other hand is a very expensive proposition and requires a very high order of scientific expertise and basic institutional infra-structure such as high level institutes of chemistry, biochemistry, general and clinical pharmacology etc. If the efficacy of individual herbal preparations in specific diseases can be scientifically established by means of comprehensive pharmacological and clinical trials, and toxicological data is satisfactory, then there is no reason why herbal extracts should not be incorporated into an integrated pharmacoepia.

It would be appropriate to mention some of the researches being carried out by our group on the isolation and structure elucidation of the chemical constituents of plants which find use in the indigenous

medical system. One plant chosen for such a study is *Berberis aristata.*

Berberis aristata DC (Berberidaceae) is shrub found in the northern mountainous regions of Pakistan and in the Nilgiri Hills of Southern India. The extracts, made from the root bark, are known as "rasaut" and are used in the traditional system of medicine for the treatment of jaundice and skin diseases. As a result of careful isolation studies, two new alkaloids, "Karachine" [1] and "Taxilamine" [2] have recently been isolated. [2,3] Karachine is the first naturally occurring berbinoid of this skeletal system and is the most complex of more than 50 protoberberine alkaloids presently known. Its structure has been elucidated largely on the basis of its high resolution mass and 360 MHz (FT) NMR spectra, and the positioning of groups confirmed by Nuclear Overhauser Effect studies.



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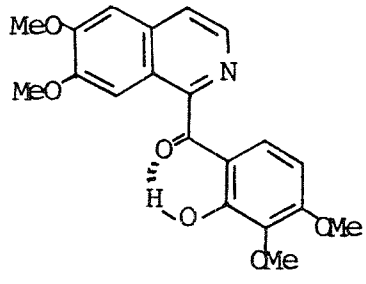
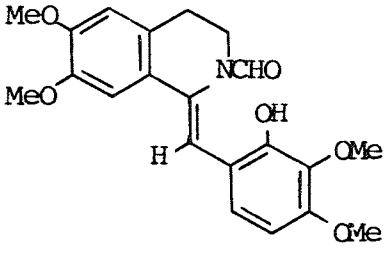


(2)

Texilamine [2] is the fourth member of a class of pseudobenzyliso - quinoline alkaloids. The other three members of this class are polycarpine [3] found in *Enantia polycarpa* Engl. and Diels (Annonaceae), rugosinone [4] obtained from *Thalictrum rugosum* Ait (Ranunculaceae) and (—) — ledecorine [5] present in *Corydyalis ledebouriana* K.et.K. (Fumariaceae). Its structure has been elucidated on the basis of a 360 MHz NMR and high resolution mass spectral studies.



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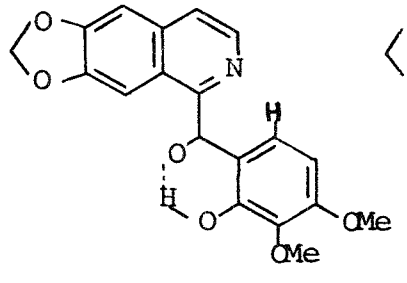

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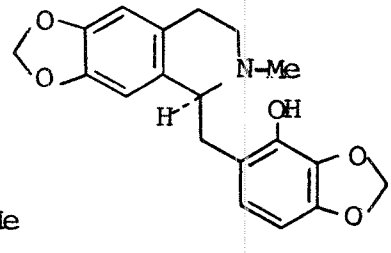
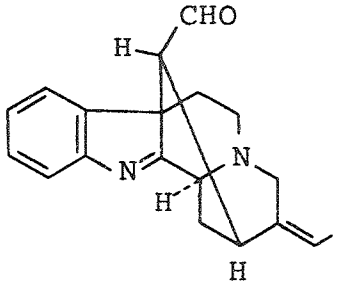


(5)

Another plant under study is *Rhazya stricta* Decaisne (Apocyanaceae). This is a small glabrous erect shrub which grows profusely in the North-Western region of Indo-Pakistan sub-continent. The leaves of this plant are used by the traditional practitioners as a bitter tonic for sore throat, in fever, in general debility and as a curative for chronic rheumatism. The fruits and leaves are considered efficaci-

ous in cases of boils and eruptions. As a result of isolation and structural studies carried out by us a number of new alkaloids have been isolated from its leaves and their structures elucidated.[4,5] These are strictalamine[6], rhazimal[7], rhazinol[8] and rhazimol[9]. Pharmacological studies are underway



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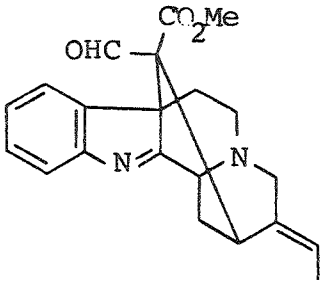

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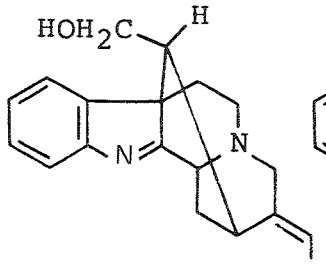

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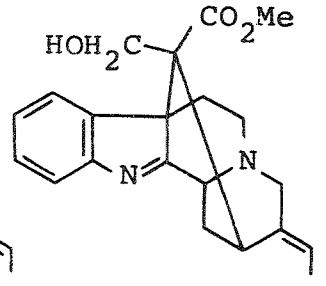
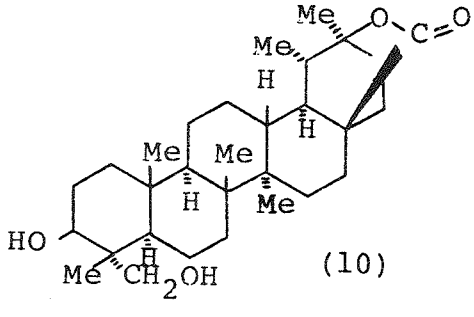


(9)

to determine the biological activity of these new alkaloids.

Another interesting plant chosen for a detailed phytochemical study is *Fagonia indica* linn. This is a small spiny undershrub which is widely distributed in Pakistan. Locally known as "sachi booti" or "dhamasa", an aqueous decoction of the leaves and young twigs is a popular remedy for the treatment of various skin lesions. The plant is claimed to be a remedy for cancer in its early stages. A new sapogenin[10] "Nahagenin" has been isolated from the hydrolysed extracts of the aerial parts of the plant, and its structure has been elucidated on the basis of a 400 MHz PMR spectrum, a 100 MHz CMR spectrum, and high resolution mass spectrum.[6] The structure [10] has been confirmed by an X-ray crystal structure determination.

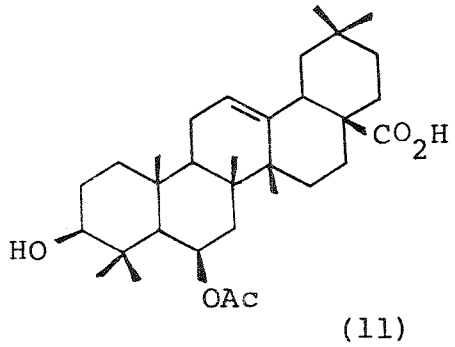


(10)

Betula utilis, locally known as "Bhojpatter" is a tree commonly found at high altitudes in the temperate Himalayas extending from Chitral eastwards to Azad Kashmir, and in Sikkim and Bhutan. The infusion of its bark has found wide use in indigenous medicine as an antiseptic, carminative and in hysteria. Our interest in the systematic investigation of the chemical constituents of Pakistani medicinal plants has led us to a chemical investigation of the bark of *Betula utilis.* This has resulted in the isolation of a new triterpenoid, "Karachic acid [11] ", the structure of which has been solved on the basis of chemical and spectroscopic studies.

The isolation of a number of cucurbitacins with cytotoxic properties promoted us to investigate the active principles present in the fruits of *Cucumis prophetarum* (Cucurbitaceae), a plant locally known as "Choti indrayan" or "Khar indrayan". It is a perennial trailing herb with ellipsoidal echinate fruits. The

plant grows wild in various regions of Pakistan, Rajputana (India), Saudi Arabia and tropical Africa. The fruit is used in indigenous medicine as an emetic and purgative. It is known to contain cucurbitacine B and D and traces of cucurbitacins G and H.



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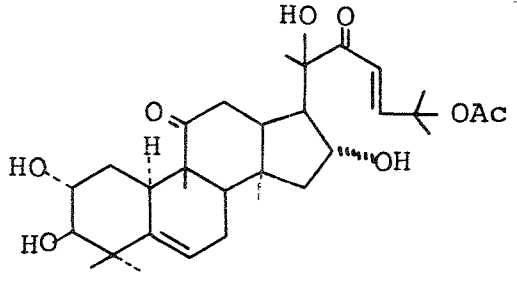
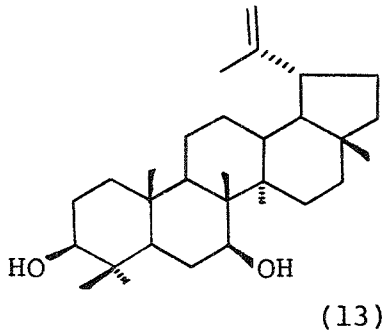
As a result of isolation studies carried out on the fruits of this plant, we have isolated a new cucubitacin, Cucurbitacin Q-1 [12] which closely resembles Cucurbitacins O and P in its structure [8]. The cytotoxicity of these cucurbitacins against Eagles KB strain of human carcinoma of the nasopharynx has been demonstrated, and it has been shown that the side chain double bond and tertiary acetate are essential for cytotoxic activity. The activity of cucurbitacin Q-1 would therefore be of interest, and it is being studied by the National Institute of Health, Bethesda, U.S.A.



(12)

Siddiqui and co-workers had previously reported a new triterpenoid, "Loranthol" from the berries of *Loranthus grewinkii,* a parasite found widely distributed on pear, apricot and almond trees. The gum from these berries is widely used in the indigenous system of medicine as a general tonic, relaxant and laxative. This triterpenoid has been re-isolated and its structure has been elucidated on the basis of chemical and spectroscopic studies to be (13) [9].



(13)

Lastly mention may be made of our work on the anti-tumor alkaloids of Catharanthus roseus. This plant is locally known as "Sada bahar", and has been used in various indigenous medical systems for the treatment of diabetes. As a result of isolation studies, two highly active anti-cancer alkaloids have been isolated by Canadian and American workers. Known as vinblastine and vincristine, these drugs are used in medicine for the treatment of Hodgkins disease, choriocarcinoma, acute leukaemia in children and other solid tumors. Their trace occurrence in the leaves of C. roseus however raises their price to several thousand dollars per gram, and poses a serious problem to the pharmaceutical industry.

As a result of efforts exerted over the last 15 years, we have succeeded in developing two different synthesis of these drugs which have been published[10-16] and internationally patented. Efforts are now underway to scale up the laboratory work to a pilot plant level. A farm has been grown in the Karachi University Campus, and a pilot plant for concentration of plant extracts has been installed in the Institute. The synthetic approaches are expected to make these drugs very cheaply available, and have opened the way to a whole series of new anti-tumor drugs.

The work carried out by us on the 7 indigenous medicinal plants cited above is illustrative of many other similar systematic phytochemical studies underway in our laboratories. The necessity of establishing regional centres of general and clinical pdharmacology, to study the biological activity of such plants and the natural products isolated therefrom, cannot be over-emphasied.

In summary, traditional medications offer an area of research activities which places the Afro-Asian countries in a position of decided advantage over the West on account of the restrictive legislature in America and Europe, and the obsession of Western medicine to look for single active ingredients. Medications in which there is no single active substance but the biological activity is due to the synergistic and detoxifying action of a large number of compounds, cannot be easily adopted by "modern medicine"for the treatment of various disease. The future and prospects of "Islamic Medicine" depend on the speed and efficiency with which research programmes on the lines indicated above can be launched.

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OBSERVATIONS ON THE ROLE OF CLASSICAL METHODOLOGY IN MODERN PHYTOCHEMISTRY

Prof. Salimuzzaman Siddiqui

PAKISTAN

At the first Kuwait International Conference on Islamic Tibb, held in January 1981, I had offered some observations on the progress of medicine in its historical context, and imperatives of the regeneration of Tibb in modern times. In the course of my presentation, I had in the light of Avicenna's analytical approach to the theoretical and practical aspects of Tibb, pointed out its basic commitment to an expressly scientific attitude. With reference to this position, I further stated that in the different fields of exact and semi-exact sciences there can be one and only one systematised body of knowledge at any given time, and that in the progress of Tibb it is essential to aim at its integration with the new knowledge provided by these scientific disciplines.

Leading on from there, my paper on the present occasion deals with the role of classical methodology in modern phytochemistry. In this connection, we first of all, have to take into account the fact, that medicinal plants had formed the main base for the treatment and prevention of various human ailments in the eastern as well as western system of medicine, till about the turn of the century. However, the subsequent phenomenal successes with the development of chemo-therapy, the role and study of drugs of plant origin suffered a great setback and it is only during the last few decades that there has been a gradual recovery of interest in the medicinal flora.

This recovery of interest in the field of medicinal plants was particularly stimulated by the acceptance in the medical world of the therapeutic virtues of the alkaloids of Rauwolfia Serpentina in the treatment of hypertension, mental ailments and cardiac arrhythmias of various origins. In more recent years the discovery of the alkaloids of Vinca rosea, namely vinblastine and vincristine, in the treatment of certain forms of cancer, has provided further support to the importance of multi-disciplinary studies in the therapeutic constituents of medicinal plants.

An important factor in the promotion of this sphere of studies relates to the emergence of new techniques like paper and column chromatography, electrophoresis, counter-current distribution and vapour phase chromatography, as a result of which the isolation of uniform substances from the usually intractable complex of closely allied physiologically active constituents, has become relatively a simple matter, compared with the old orthodox procedures employed during the earlier days of my work on medicinal plants. On the other hand, the advent of electronic appliances like U.V., computerized mass spectrometers and N.M.R. have revolutionized the scope and pattern of structural studies in chemical constituents.

However, without in any way wanting to minimise the importance of these techniques and facilities, particularly in the field of studies relating to correlation of structure and activity, I find that the classical procedures continue to have an important place in the isolation of plant constituents and the experimental management of chemical reactions.

In illustration of the points I have made out, I would first of all refer to the vital importance of handling fresh undried plant material for studies in their constituents, in order to avoid structural changes which are likely to occur in them through aerial oxidation and enzymatic action in the process of drying and storage. Little attention has been given to this factor, apparently due to the fact that most of the phytochemical studies have been carried out in the western countries where fresh drug materials of tropical and humid tropical regions were not available.

By way of an outstanding example on the basis of my own earlier work, I would cite the case of the

young sprouts of Cicer arietinum Linn. (Benal gram; chana). On working up the fresh undried, uncrushed material, it was possible to isolate from its alcoholic extract two isoflavones and an amino acid, named as Biochanins A, B and C. While one of the isoflavones was later identified with formonenetin, Biochanin A was established as a new product through degradative studies followed by synthesis. In contrast to this, not even a trace of the crystalline constituents could be obtained from the sprouts after drying them in shade. Much the same, though not quite such a drastic situation could be recorded in respect of work on Rauwolfia and Holarrhena alkaloids. More recently the validity of this approach has been exemplified in our studies in the fresh fruits of Melia azadirachta and Garlic cloves. I have specifically referred to these observations, because a reinvestigation of many plant materials, observing this procedure, holds out both an opportunity and a challenge for the scientists working in our region.

The second aspect of the subject matter presented here is concerned with the general neglect of classical procedures prior to the application of modern analytical devices to which I have referred for the isolation of uniform constituents. The former methods are primarily based on exploiting the varying of character of the basic, acidic and neutral components of plant extracts in respect of their solubilities, basic or acidic strength, and often widely varying solubilities of the salts of organic bases and acids. It may perhaps surprise many of my colleagues here that right from my earlier work in the '30 's on alkaloids, triterpenoids and flavonoids and other plant constituents, down to the present day, a host of new substances have been isolated without recourse to chromatographic and other mechanical operations. One of the greatest advantages of the classical method of isolation and reaction management consists in the fact that once a method has been ultimately worked out large quantities of products can be obtained with comparative ease, affording the possibility of comprehensive pharmacological studies, and also investigations of structure and activity relationship, based on their derivatives. It is true that with the modern facilities for structure elucidation substances in milligram quantities are suffice for it, but they are by far not enough to undertake the work to which I have referred.

The rationale of the views presented in the paper is further provided in the appendix, with reference to relevant publications and citations of certain specific illustrations.

MEDICALLY APPLIED FLAVONOIDS, ESPECIALLY RUTOSIDES

Dr. Wolfgang Voelter

WEST GERMANY

INTRODUCTION

Already more than forty years ago Szent-Gyorgi and his co-workers [1] suggested that deficiency in flavonoids cause the disease scurvy. The substance, isolated from lemons or red peppers influences the capillary permeability and was therefore designated as Vitamin P. However, it could be proven later that the compounds isolated by Szent-Gyorgi and co-workers [2] (citrin, a mixture of hesperidin and eriodictyol) have no vitamin character.

CHEMICAL STRUCTURES

The flavones (2-phenylbenzo-8-pyrone), isoflavones (3-phenylbenzo-8-pyrone), flavonols (3 hydroxy-flavone), flavanones (2,3-dyhydroflavone) and flavonols (3-hydroxyflavone) are sub-groups of the naturally occuring flavonoids.

OCCURENCE AND PHYSIOLOGICAL EFFECTS

The 8-pyrones occur in tissues of plants as *glycosides* & as free aglycones. Rich sources are leaves and blossoms, the concentration in roots, fruits and green wood is much lower.

The physiological importance of flavonoids is still a matter of discussion. Effects on enzyme activity, metabolism, liberation of histamine, capillary permeability, redox reactions and growth are discussed. [3 - 11]

BIOSYNTHESIS

Investigations on ^{14}C-labelled compounds demonstrated that ring A of the benzopyrane is formed by three acetate units, ring B and three carbon atoms of the heterocyclic system have their origin from cinnamic acid, hydroxycinnamic acid (coumaric acid) respectively caffeic acid. [12-14]

FLAVONOID DRUGS

Betuale Folium: The leaves of the birch-tree have a relatively large content in hyperoside and myricetin galactoside. The drug is used for treatment of rheumatism and arthritis.

Crataegi Flos and Folium: The dried blossoms and leaves of the all over Europe growing hawthorn have a two to three percent content of a whole series of flavonoids like quercetin, hyperoside, rutin, vitexin or rhamnosyl vitexin. The drug is successfully applied for treatment of heart diseases and arterio-sclerosis.

Ginkgo bilobal: The leaves of the gingko-tree are rich in kaempherol, quercetin, luteolin and corresponding glycosides. Extracts are used to improve the blood supply.

Arnicae Flos.: The blossoms of Arnica montana L. contain several biologically active flavonoids like isoquercitrin, astragalin and luteolin-7-0 glucoside. Extracts are used for curing injuries and heart's diseases.

Tiliae Flos: Lime-blossom-tea is rich in quercitrin, isoquercitrin, astragalin. The tea is used for the treatment of colds and rheumatism.

Sophorae Flos and Fagopyri-Herba: Both plants are used as raw materials for the isolation of rutin as they contain this flavonoid in a percentage of up to 25. Because of the oedema-preventing action of rutin and especially its hydroxyethylated derivatives [15] large amounts of this flavonoid are needed.

METHODS FOR DETECTION AND STRUCTURE ELUCIDATION

In the past two decades, the methods for structure elucidation of natural products changed drastically by a series of different commercially available spectrometers. The parameters of proton nuclear magnetic resonance, [16-21] carbon nuclear magnetic resonance, [22-25] infrared spectroscopy,[26] absorption spectroscopy, [27] optical rotatory dispersion, [28] circular dichroism, [29-31] mass spectrometry and computer analysis [32-39] of a natural product nowadays often allow rapid unequivocal structure elucidation of an unknown compound.

As circular dichroism (CD) spectra can be measured from optically active compounds only, the method is mainly applied to natural organic compounds like terpenes, steroids, carbohydrates, amino acids, nucleosides etc. Since 1960, many stereochemical and conformational problems have been solved by means of the parameters of the CD spectra of these natural products.

Already a great deal of experience exists in the field of ^1H NMR and mass spectroscopy of flavonoids. [8,40] Most aglycones show intense molecular ion peaks. Interpretable mass spectra of flavone glycosides are received only from their trimethylsilyl, permethyl and trifluoroacetyl derivatives. [10,41]

With commercially available circular dichroism apparatus for pyranose solutions no cotton effects can be measured even at wavelengths around 200 nm because the sugar chromophores absorb 30-50 nm below 200 nm. However, if a sugar with different asymmetric carbon atoms is attached to an optically inactive chromophore absorbing at wavelengths $>$ 200 nm an inherently symmetric, but asymmetrically perturbed, chromophore is received. According to the theory of circular dichroism cotton effects are expected in the wavelength range of the absorption band of a compound. Flavone glycosides usually show two major absorption bands in the region of 240 to 400 nm. Band I is expected between 280 and 380 nm and band II occurs in the spectroscopic range of 230 to 280 nm. The band located at higher wavelength is due to the absorption of the cinnamoyl system (ring B). The benzoyl system (ring A) causes absorption band II. As closely spaced cotton effects may have different signs and the rotational strength is related to the induced electric and magnetic dipole moments, often different electronic transitions of a chromophore are detectable by circular dichroism only and not by absorption spectroscopy.

According to our investigations the following conclusions can be drawn from CD spectra of flavone glycosides: 1) 3-0-glycosides show a characteristic strong positive cotton effect around 250 nm (band II range) if the bond is B-glycosidic. A neighbouring negative cotton effect is located around 230 nm and shows also strong intensity. 2) Flavone glycosides with sugars attached to ring B show much less characteristic patterns. 3) Flavone C-glycosides have characteristic dichroic properties as the asymmetric atoms of the carbohydrates are closer located to the flavone chromophore than in O-glycosides. Carbohydrates attached C-B-glycosidically to ring A show a chracteristic strong negative cotton effect around 270 nm.

Valuable information is received from the comparison of the CD spectra of flavone glycosides measured in alcohol with those received in alcohol/$ALCl_3$ solution. To demonstrate these effects the absorption and CD spectra of myricitrin, 7, 4'-di-O-(B-hydroxyethyl) rutoside and 3', 4', 5, 7--tetra-O- (B-hydroxyethyl) rutoside are compared with each other. Flavones with hydroxyl groups at C-3 or C-5 or with an orthodihydroxyl system form complexes with aluminium chloride. [40] No complex formation with aluminium chloride is therefore possible in the case of 3', 4, 4, 7-tetra-O-(B-hydroxyethyl) rutoside; the absorption and circular dichroism spectra of this compound are therefore almost identical if recorded in ethanol or ethanol in the presence of $AlCl_3$. Flavones which contain hydroxyl groups at C-5 (e.g. 7, 4'-di-O- (B-hydroxyethyl) rutoside, robinin, myricitrin) show in the presence of aluminium chloride a strong negative cotton effect around 280 nm followed by a strong positive CB-band around 258 nm. These data demonstrate clearly the utility of circular dichroism to characterise flavone glycosides and to receive valuable information about the configuration and conformation of this class of natural products. [42-45]

PHARMACOKINETICS OF HYDROXYETHYLRUTOSIDES

The pharmacokinetics of flavonoids in man are of fundamental interest with respect to their wide clinical application.[46-49] However, a clearcut and direct proof of the intestinal resorption of flavonoids remains still a difficult experimental task. There are several problems in the applicability and the detection limits of the classical chromatographic and spectroscopic methods. And the use of suitable labelled radioactive compounds depends on the success of complicated chemical synthesis and on the maximum doses allowed for clinical studies. Therefore, most of the in vivo experiments had to be done on animals. A recent paper on the metabolism of hydroxyethylrutosides reports compatible results on excretion after oral administration in man and in animals.[50] In these experiments ^{14}C-labelled hydroxyethyl groups were used.

In the following a new method for the quantitative spectroscopic detection of hydroxyethylated flavone glycosides in human blood and urine after intravenous and oral administration is reported.

Hydroxyethylrutosides exhibit a pronounced negative cotton effect around 340 nm. This characteristic CD band corresponds to the wellknown UV absorption at that wavelength and its circular dichroic absorption can be taken as quantitative measure for the detection of hydroxyethylrutosides in solution. Human serum shows also a CD band at 340 nm. In contrast to the cotton effect of hydroxyethylrutosides this protein band is positive. Because of the opposite cotton effects of hydroxyethylrutosides and serum very small changes in the relative concentrations can be detected. Calibration curves revealed that one is able to detect amounts down to 0.1 mg hydroxyethylrutoside per 100 ml serum by direct measurements. There is no need for a chromatographic procedure, extraction, isolation or enrichment before the CD measurements. In order to make sure that there are no disturbing time-dependent phenomena like degradation the stability of hydroxyethylrutosides in serum was tested and no change of the wavelength or intensity of the 340 nm band was found up to 48h at 4°C. The CD will register only the intact flavone glycoside e.g. as soon as the sugar part is lost chirality is lost and the chromophore in the aglycone is no more detectable by CD. Therefore, this detection method is not only sensitive but also very specific. Simple numeric addition of the intensities of the CD band of pure hydroxyethylrutoside and serum solution and comparison to experimental values of solutions of the same concentration revealed that association effects of rutosides with serum proteins will lead to intensified chiroptical properties.

After injection of 1500 mg rutosides to male volunteers CD spectra of the serum and urine were taken. A strong decrease in the CD band with time is observed. With decreasing level of rutosides in serum an increase of their concentration in urine is observed. Pure urine has usually no cotton effects, and only few minutes after injection the CD spectrum of the drug can be recorded directly from urine probes. From various measurements can be concluded that after i.v. administration a relatively large quantity of HR will be excreted unchanged in urine within 1-2 hours. After oral administration of 4g hydroxyethylrutosides, a maximum in the concentration level is found several hours after application, and the drug can be detected by circular dichroism up to 24 hours in blood. It should be mentioned that in the CD measurements also protein bound rutosides will be found. The cotton effect typical for hydroxylethylrutosides was not detected in urine during experiments with oral administration. From CD measurements of rutoside solutions in stomach juice it appears that the drug remains stable for several hours in this medium.

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COMMENTATOR'S SPEECH

Prof. Gunther Stille

W. GERMANY.

It is impossible to comment upon all the details of the pharmacotherapeutic presentations of today. I will pick out some important points in respect to clinical evaluation of herbal drugs of the Islamic heritage.

Under "Applied Research" the organizers of this meeting invited contributions to modern methodology and results of double-blind, well planned trials with sound statistical analysis.

There is no doubt that these modern methodology of drug evaluation in humans is very useful in clinical pharmacology to record the pharmacodynamic effects of drugs in men. But we have to differentiate between the pharmacodynamic effect and the clinical effectiveness or efficacy of drugs in men. To record the pharmacodynamic effect is one and to seize the therapeutic usefulness is another thing. Just the later question is crucial for the clinician.

Now there are some doubts as to whether the methods of modern Western natural science are suited to the verification of therapeutic efficacy and usefulness of all type of remedies from the heritage of classical Arabian medicine. The differences between modern drug therapy and the herbal therapy of the classical doctors are founded upon differences in the basic understanding of disease.

For modern natural science, the cause of disease is a molecular or cellular defect. In classical medicine a disharmonia of humors and functions are the reasons for the diseased state of a patient. This concept reminds of the concept of modern cybernetics.

Now let us look at some contradictions.

1. The controlled trial is based on randomization. A representative sample of patients is deivided arbitrarily into treated and untreated groups. This is based on the premise that all patients with a specific disease react in a comparable way within the limits of statistical deviations. However, according to Ibn Sina and other ancient sages the patient is an individual, characterised by his personal temperament. Ibn Sina said, "One must realize that every individual person has a temperament entirely peculiar to himself, and it is impossible for any other person to have an identical temperament, or even to approximate thereto". Thus the premise for randomization is not fulfilled. The problems of randomization is discussed by Western clinicians and clinical pharmacologist too. The question is, how to build up a control group without randomization. One possibility is, for example, to work with "matched pairs".
2. The controlled trial uses only one or a very limited number of symptoms as criteria for evaluation. We speak of a reductionistic approach in which we strip the image of the diseased man of all personal attributes. This is in contrast to classical Arabian medicine which describes the patient by a great number of general attributes and which tries to complete the picture of the patient not only by numerous somatic data, but also by his environment — the climate, the season, cosmic influences etc. We know this problem in the Western medicine very well, and there is an uneasiness about this situation.
3. There is one very important and essential difference between Western natural science and classical medicine. Since Galileo, scientists produce artificial conditions for their scientific observations. This is the basis of the experiment and, therefore, of the controlled clinical trial. Medical doctors become scientists, when they include and exclude patients by arbitrary criteria and so manipulate the conditions of observation. Ancient doctors, in contrast observe the patients in their natural environments and natural conditions.
4. A very important condition, especially for the doubleblind study, is that the doctor is excluded as far

as possible. This means that not the therapeutic ability of the doctor with the drug is tested, but rather the intrinsic curing activity of the drug. This is a very important point. There must be some doubt that the herb or the chemical have any curing efficacy at all. In my opinion there is a pharmacodynamic effect of a drug, but efficient or inefficient in a definite patient is the therapy of a certain doctor, who uses the drug as an instrument. In good modern practice and in classical medicine the doctor is essential for therapeutic success. Herbs, purgation and blood-letting are instruments in his hand. It is difficult to imagine a "blind doctor" in the sense of double blind study in classical medicine.

The controlled study is well-suited to study certain pharmacological effects. I stress here the word, pharmacological effects. For instance to study instrumental functions of a drug; as decrease of blood pressure, inhibition of stomach secretion, diuresis, etc. But disease is more than one of its symptoms. The famous doctors of the past thought that there is no disease, but only diseased patients. But until now, there have been no alternative approaches to clinical evaluation of drugs. The statisticians stopped their efforts with the elabortion of controlled studies. But I would like to encourage you to look for new scientific methods and directions, and not to move into the inappropriate track of controlled, double-blind studies for the therapeutic effectiveness of the remedies of your heritage. This is not a criticism, but a stimulation. Please remember, there is a danger, for isntance, in my country, that the herbal therapy would be killed by the official requirements of controlled studies.

COMMENTATOR'S SPEECH

Prof. G. Sakait Rama Rao

INDIA.

The use of herbal medicine in Islamic medicine was based occasionally on the existing experimental methodology and mostly on practical experiences of ancient physicians. They are used as crude, single or compound preparations.

Prof. Atta-ur-Rehman correctly pointed out that a sizable population of rural area of Afro-Asian countries have faith in indigenous drugs. Some of the herbal preparations are still being used in modern medicine, such as extracts, tinctures, to a limited extent, but the purified alkaloids, glycosides etc. are widely employed.

Prof. Symon Y. Mills emphasizes that the effect of herbal preparation should be qualitatively distinct from modern drug therapy. Sometimes we see the patient preferring treatment with crude herbal preparation especially when they experience drug toxicity, drug refractoriness and drug interactions. In my opinion the Islamic system of medicine should be given a fair trial keeping in view of traditional approach. Prof. Mills also agrees with it. Prof. Atta-ur-Rehman explained temperament (مزاج) scientifically as an enormous complexity of biological System. Of course, it is very difficult to analyse it scientifically. He explains it as a reversible reaction, influenced by enzymatic control influencing pH variability and interacting molecules etc. of animals and human system. The concept of four humours and temperament is not easily understandable to the modern physician. However, careful study of classical medicine may reveal a surprising knowledge, out of which many ideas for productive research can be drawn. Integration of modern system with Islamic system of medicine must be emotionally achieved by the co-ordinating efforts of a modern scientist to study Islamic Medicine and vice versa, which will help in fact finding, such as confirmation or condemnation. Prof. Salimuzzaman Siddiqui and Prof. S.Y. Mills agree to this.

It is proposed that crude drug preparations carry with them centuries long experiences of ancient physicians regarding their efficacy and toxicity. Hence, they can be used directly on human beings for research purposes, after obtaining hints from the ancient literature. This may save time, money and men. Of course, this is not accepted by the Western scientists.

Research on Crude Drugs: Prof. Atta-ur-Rehman's suggestion is correct in asking for joint efforts in the research programme on crude drug preparations. That is, expert Hakeem as well as an expert Doctor should work together with the aid of modern methods of investigations.

Here I would like to add that our aims should be:

1. The properties mentioned in the ancient literature can be confirmed after scientific study.
2. A new property can be discovered. e.g., just this morning you might have listened to the paper of Mr. Nazimuddin. Butea frondosa is known to the ancient physician and it is anthelmintic. It also adds to the anti-fertility agent. He has discovered anti-inflammatory property also. Similarly R.L. Kashmir has discovered the oxytocic propety of Adhatoda Vasaka, which was only mentioned in the ancient literature as expectorant, bronchodilator and also helps in liquifaction of sputum.
3. By using these drugs in combination with modern drugs, the toxicity can either be reduced or prevented.
4. This is to be scientifically studied. The toxicity produced by modern medicine can be treated.
5. Real mechanism can also be discovered.

Prof. S.Y. Mills says that it may serve as a model for independent support for the claims of herbal practitioner for their remedies.

Research of Isolated Active Ingredients: One has to admit that the active substances of vegetable kingdom after determination of their chemical structure have served as the model to inspire the organic chemist as to make various molecular modifications in original structure of the drug, so that more effective and less toxic drugs may be obtained. There are certain examples.

Now Dr. Mills has described certain points. It is Crataegus monogyna manopena. This is helpful in the disorder of the heart and also in dropsy and he explains that it is a coronary vasodilator and also general vasodilator and therefore it is useful in bradycardia , angina and also blood pressure. This is to be tried or rather to be compared with standard drug like, Digitalis. He has also analysed flavonoid, glycosides and triterpenoids saponins. He has mentioned about Allium Sativum. This is an old preparation and it is also used as a dietary element and anti-infective and anti-inflammatory properties were already described by ancient physicians. Glycyrrhiza is another herb and it is well known to the ancient physicians. The steroidal effects, which they have discovered and that is having Hydro-cortisone like action and also ACTH like action and the mechanism have also been discovered and this is really worth appreciating.

Prof. Jerzy Lutomysky studied several plants e.g. Aralia mandshurica, Marygold and White beet.He has described hypolipoidemic actions and hypocholesteremic actions and anti-stress actions, immunological actions and he also described toxicity out of which he has obtained Aralia manshurica is found to be very effective. And this is again to be compared with a standard drug.

Prof. Salimuzzaman Siddiqui also agrees to the integration of new knowldege and this is only responsible for the progress of the Tib and he describes the classical methodology is more beneficial. The classical methodology here is no hard and fast rule. The classical methodology according to the ancient physicians (that is Unani or Islamic medicine) is different from the classical methodology adopted by the doctor of the 19th century or the beginning of the 20th century. Now, he described one more point, that is, plants' aqueous extracts, cold water extract, hot water extract may differ in their properties and contents. It is true and secondly the fresh plant will give rise to some active ingredients and after drying, the aerial dried preparations may not give the same. He has given the example of Bengal gram and it is correct.

The next speaker, Dr. Wolf Gang Volter has described many things about flavonoids and their utility, effects on gastro-intestinal system, binding with the plasma protein , chromotographic study, pharmacokinetic study, isolation and determination of structure. These all are very worthy and I do not know whether this has come to N.N.D. (New Non-official Drug) or not but still under trial, we can not say. Dr, Atta-ur-Rehman studied Berberis Aristata (Rasout). According to the old literature it is helpful in jaundice and skin diseases.He has extracted several active ingredients and also he has studied other herbs e.g. Rhazya Stricta, "Sachi Booti" Fagonia indica and "Bhojpatter" Betula utilis. He has described certain important properties like antimalignant property from "Sachi Booti" and some properties like emetic and purgative, which were also noticed by ancient physicians in Cucumis prophotarum.

If I am prermitted, my suggestions will be as follows:-

1. A compound preparation may contain many ingredients and sometimes if few ingredients may not be available and they also may be costly; research to be conducted to discover a drug to replace it.
2. It is to be noticed, whether by deleting single drug or a few other drugs (herbs) from the compound preparation, the efficacy may be maintained or not.
3. The value of Munzij (منضج) and Mushil (مسهل) to be established.

4. Restricted diet or special diet prescribed by the Islamic doctor is to be studied scientifically. Its benefits to be established scientifically.
5. Then dietetics (علاج بالغذاء), now the ancient physicians, specially Avicenna has described several substances of nutritional value, e.g. honey, vinegar, fruit juices and whey etc. They were commonly used by the ancient physicians for implementing in the nutrition, especially for chronic diseases. Now this is to be kept in mind by the modern physician and the blood chemistry should also be studied.
6. The calcinated Iron, copper and other Kushtajat (کشتجات) etc. are sometimes prepared with the help of herbs. The modern concept of the essential trace-elements in the diet for maintenance of health and their effects; their toxic effects and therapeutic effects must be studied.

Any medicine, whether it is modern or ancient, is a science enriched by years of sacrifice. However, it is intended to convey, that the research on herbal preparations need careful thinking and re-organization. In the beginning it may look more difficult but on continuation, it may be less expensive, less time consuming and more rewarding, if properly planned. And the quality of research depends upon able guidance and proper supervision, honest and intellectual approach and adequate financial aid.

GENERAL DISCUSSION

Dr. Francisco Guerra

This is a seminar on the Advantages of Herbal Treatment and it is very important to establish general principles, on why Islam is basing therapeutic treatment on traditional medicine or Herbal Treatment?

I was very much stimulated by the approach of Dr. Stille and I wish to remind Prof. Atta-ur-Rehman that I was the one who prepared the report of the experts of World Health Organization, about the Herbal Treatment in 1977, with one expert from Moscow and the other from United States. I was Prof. of Pharmacology for many years and I disagree with what Dr. Stille has pointed out, because the pharmacological approach of the basis of Herbal Treatment is futile now-a-days. There are many words from Akernaks, that disease is not just a disfunction or dishealth, is not a destruction or effect of research. Disease is what the society or the individuals live with. Not necessarily that a cell is sick or strong. This is one point.

To tell you more, over 60% of the modern society, can not be approached pharmacologically. Why Islam bases treatment on herbal treatment? Primitive man has always relied on the environments to get material for food and then he learned that there were several drugs, botanical drugs or plants that produce certain effects and this is why he discovered drugs, with medical actions, with stimulating actions and with all sorts of actions. Then Islamic medicine was based mostly on Galen, but was expanded considerably after the 8th century. This is why, Islam today , relies on natural drugs, because Galen established that the drugs obtained from animals had a similar nature or temperament, as you would like to say, as the human body in the lack of activity. Galen, like the Islamic writers disliked, the use of minerals, because minerals have different effects on human body and it could be dangerous. Indeed they are dangerous for the human body. So, that is why, Islam today, like many centuries before is relying on natural drugs from the botanical origin. Now, in a drug of natural origin (botanical thing), there are two ingredients. One is of mystical nature, that has effect upon the mind and there is pharmacological action. To say that the drug that only produces diarrhoea is active, is wrong.

Most people, who work in the South of Asia, are relying mostly on the work of a colleague, Dr. Chopra's work, who was the man to point out what Canther already established very many years ago. When Canther published his book on 'Travels in the East', he was the first who mentioned Rauwolfia and which started all the revolution in research of American and European companies in the research of natural drugs, in the botanical use in the South East Asia. I was the one who established this research for these countries. I discovered five plants in Mexico with anti-diabetic actions which I reported in the pharmacological meeting in Brussels and that led to the Vinca, for the treatment of Cancer, leukemia in children. Prof. Volter has been working on the flavonoids. I was the one, after Barbera, who discovered in the peel of the orange, the rooting, I established the anti-rheumatic action. But I envy the work of Atta-ur-Rehman and Volter or Siddiqui, because there is nothing more complicated and more difficult in Chemistry than Phyto-chemistry. Nothing can be more tedious, more laborious than to carry on the work you are doing. But the thing we have to learn here, this is why, this is a Conference on Islamic Medicine. The Islam has a responsibility, a tradition, and anthropological roots and we have to understand that there is Islamic Medicine, because there is Islamic tradition and the Islamic traditions are based on these types of drugs we are describing now.

Prof. Thulesius

What I have learned today is, that we can start with an animal model. We can use the effects of herbal preparation and then can find out some of the ingredients and can test them seperately. I think this was very nicely brought out by Prof. Atta-ur-Rehman from Pakistan. And I think the scientific approach is the important one, if we want to have a scientific conference, I disagree with Prof. Stille, if

he thinks that we cannot do any control study on Herbal medicines. I think this should be possible and I do not know if you have any alternative to offer us than a double blind or a control clinical study. What are you fearing and I disagree with people who say that control studies on herbal medicine are not allowed in Western countries. In Sweden, we have done such studies and for example pollen on Prostatitis and I am always very suspicious of drugs which have no side effects, then they are not active drugs. Now the active drugs, which are mentioned in Rauwolfia, they have side effects, which were pointed out and they have been tested by scientific methods and the Vinca alkaloids, they are also plant products, but they are effective in the treatment of cancer and this can be shown scientifically. And Rutosides, which are mentioned, you can show that they are anti-oedematous, that they have an anti--oedematous actions. Ergot alkaloids, Belladona alkaloids, glysric, acid products, which can induce hypertension. So, I do not know what we are talking about. Are you afraid of critical scientific methods. Now, I think scientific methods do not exclude the doctor and do not exclude the wholestic view of the doctor which is a very important factor, which should be added to this. The one should not exclude the other or otherwise you can only say it is a placebo medicine.

Prof. Abdul Wahab Boroliossey (Chairman)

Thank you very much for a short and very indicative and really true comment. If I had time I would have asked him about the various types of drug researches in Germany. Are they controlled or not? This problem is between him and myself, to get that answer from our colleague.

Dr. Mohd. Aslam

I thought it would be important here to give you a brief outline what is happening in United Kingdom, regarding the traditional medicines, because for the last four or five years the Department of Health in London has been basicaly in a problem because of the two million immigrants living in U.K. and they are using the medicines. In fact we have four or five Hakims in every large city in the U.K., which has resulted in large amounts of the herbal medicines or Unani and Ayurvedic medicines about which the group has been talking today, being imported into the Western countries. How did the study start? The study really started, when I asked the Department of Health, if they had any data on the number of Hakims, operating in the United Kingdom , and if they knew the type of medicines that they were selling and if they knew how many they were in each city? After four or five weeks a reply came and the reply was, "What is a Hakim?" That is the amount of ignorance which exists in the Western countries, about a system which has many traditions as you have outlined today. The recommendations on the problems which resulted in U.K. and the dilemma which has been faced by the Government is that there are Hakims in U.K. They are all practising this particular system of medicine and then the herbal material, because of the poly-pharmaceutical nature of them, it is very very difficult to carry out quality control. As all the speakers have outlined the analytical and the standardization of this, but in the Western countries the problem arises that the same patients are also consulting the allopathy i.e. the Western system of medicine and I say to you that in fact, perhaps a group like this Islamic Conference today should be pointing out to the Western countries, show them the active ingredients and show the herbal materials and perhaps show the drug inter-actions which may occur in these particular preparations and indeed many drug interactions have occured and have been outlined in the University Hospital of Nottingham and in fact, several deaths have occurred and it is the result of this, which have in fact, given the wrong impression of the whole system of the Islamic Medicine and the herbal medicines. What we require is that we need to filter out the good things which exist in the system but we must not be frightened to say what are the ill effects of medicines, which we are using within this system and in particular I would like to point out to you that the continuous use of the heavy metals in these medicines is a major problem. Because of our advanced technology and the clinical data, which we now have been collecting, it is

quite obvious that many abnormalities of the fetus and physiological functioning is effected by these heavy metals and I urge you very very strongly to reconsider and point out to the physicians and this particular group here today, to take action in filtering out those heavy metals and those herbal materials which are causing the problem.* So that the system could in fact be accepted by the Western countries as much as in the South East Asia. I also urge you that a conference like this would be the most invaluable public relation exercise, if in the near future it would be held in one of the Western countries, to give it more impact of what we are really trying to achieve.

Prof. Abdul Wahab Borollossey (Chairman)

You did not tell us how the department of Health solved the problem.

Dr. Mohd. Aslam

The Department of Health is still in dilemma today, because in U.K., in order to sell any medicine to be sold it must have a product licence and in order to have product licences, it must go through various procedures of clinical trials and the analytical work. And at this very moment, none of the Hakims, who have actually submitted their medicines, have their particular products accepted and this rejection will continue, because the Department of Health has certain boxes and these boxes can only function if they have a system, which allow this to go on. But at the moment, we must change our rules and regulations, so that these herbal medicines could be accepted.

Dr. Muttalib

I have a small comment about the Reserpine, about which Prof. Salimuzzaman Siddiqui has mentioned concerning the side effects of the depression and diarrhoea and nasal blocking. It is written in the book. We have read it and we teach this to the students. But as a physician working for the last 20 years in medical colleges and coming in contact with many persons we did not really encounter these symptoms very much in the Islamic part of the world. So, as an example of side effects, I can cite pulmonary infarction. When we were working as junior doctors in the Western countries, we have been warned to look for this disease. The last 20 years, and working for the last five years in the college, only one case of pulmonary infarction was referred to me; in a girl following a child birth. So, similarly, these reactions are very rare in patients using this drug.

About Prof. Atta-ur-Rehman, I had the opportunity to work at the Diabetic Association in Pakistan for about 10 years with Prof. Ibrahim. During that period, we have worked on two herbs; one is Black berry seeds and the other is Tala Kacha Patta, Prof. Salimuzzaman will be knowing about it and the third one was, (it was in 1966-67), some sort of a leaf was identified to be cure for diabetes, from Peshawar Forest Institute. That was sent to me in Dacca on which I was working. Working for 10 years on these three (3) plants, we found that they have got some reducing actions on sugar, but they are no good to be introduced as a new treatment on the existing drugs. Well, I will finish my talk by giving an example about Semitidine. The millions of Takkas and Dollars have been earned by giving semitidines, which is supposed to be curing peptic ulcer, but it has not done a bit at all on this thing. So, what Prof. Atta-ur-Rehman has mentioned is a very difficult job, to be working on these herbs and to identify the drug which would really bring relief to the suffering people.

* Nothing is mentioned in the Islamic Medicine about the use of heavy metals in the treatment, but heavy metals are being used very frequently in the other systems like, Siddah and Ayurvedic.

Editors.

Dr. Yousuf Ahmed

Dr. Aslam has pointed out that lots of herbs contain heavy metals and that is the major source of contamination in drugs and foods. One question, I have to ask him, is this, that in Western countries like Europe and America, major source of lead is the gasoline and automobiles and nothing is being done or very little has been done. And if at all any thing has been done, it has been phased out. If it is such a dangerous thing it should be attended to first there.

Dr. Islam

You pointed out something, which in fact, the Americans have already tried to reduce by having lead free petrol. The British, because of their financial resources are limited, have tried to reduce it form 0.4 to 0.15 grams per hundred. But, what we in fact are talking about is, actually the amount of heavy metals in medicine, which is a different sort of problem.

Prof. Abdul Wahab Borollossey (Chairman)

I understand, but what Dr. Yousuf wants to put forward to you is that there are already toxic materials existing in the air and which are not prevented. It is not the herbal medicine only. Well, this is another interesting point.

Dr. Osama Abdul Aziz

I would just like to say that I do not know why in our discussions we look neurotic and nervous and why should not we behave in just a smoother way. We can critixize. Yes, and we can say that there are some points that we differ with, either with ourselves or with others. But the point is that I just object to the word that 'The Westerners are ignorant'. This is not a fact. It should not have been said on such a panel here. Whether they know the meanings of Hakim or not, I think this is a very minimal point, that should not come to such a very serious conclusion. In fact, we all learn from the West. We should learn from them and we should co-operate for the benefits of science and for the benefit of progress of man and the world. So, this is a very short comment. I think I took one minute just for the Herbal medicines and their use. I believe that, usually we should not be extremists again and we could say there are some medicines that could be used in a chemical form and there are some others that could be used in the herbal form. And again there is no contradiction between both. We can help each other, our patients either with herbal medicine if it benefits or else if they can not benefit them, we can use the traditional medicines.

Prof. Abdul Wahaf Borollossey (Chairman)

I like to thank you all, but before I close the session, I must ask the members of the panel if they want to respond to any of the comments or are they satisfied. Dr. Atta-ur-Rehman tok note of your suggestion of requesting to initiate a Research Center which should look into the details of such matters.

Dr. Atta-ur-Rehman

This is just a short comment. I mentioned the amount of investment the Western Pharmaceutical industry has to make before discovering new drugs. I think it would be fair to say that even if the majority of the plants that are being used, even if the majority is inactive plant, even if we can find. 1 per cent of active plants, it would be a great service to humanity. I think all that is required is a systematic approach to be launched, to the clinical study of these plants.

Prof. Abdul Wahab Borollossey (Chairman)

Your point is well noticed and I have made a note. I hope in our recommendations, we may ask the newly formed Islamic Medical Center to give due attention to the necessity of establishing or encouraging research in these fields and giving sufficient financial support, as you say for proper, systematic, scientific research on high calibre in the field of medicinal plants. I thank you all, panelists, commentators, my friends on my right and my friends on my left and all participants for your patience and for this interesting discussion.

Part Nine: *Seminar on Advantages of Herbal Treatment.*

CHAPTER TWO

(Some Selected Papers — not Presented)

1. ADVANTAGES OF HERBAL PRODUCTS IN THE TREATMENT OF CERTAIN DISEASES.
   Prof. G. Sakait Rama Rao.
2. CONTINUED USE OF IRRITANT AND CO-CARCINOGENIC EUPHORBIACEAE PLANTS IN ISLAMIC MEDICINE.
   Dr. Ghulam Abbas Miana.
3. POTENTIAL OF HERBAL MEDICINE IN MODERN MEDICAL THERAPY.
   H.E. Hk. Mohammed Said.

ADVANTAGES OF HERBAL MEDICINES

Dr. Hakim G. Sakait Rama Rao

INDIA

It is a happy occasion that today both Hakims and doctors are engaged in the research programme of indigenous drugs. The use of medicinal herbs for amelioration of human suffering dates back to prehistoric times. The old Egyptians, Greeks, Romans, Arabs, Chinese and Indians, all developed their own local materia medica, dedicating themselves in their own spheres. There were considerable variations in the spectrum of prevalent diseases as well as flora in different countries, so much so that a strong belief was grown up that where there is a particular disease, the remedy may also be found in the neighbourhood.

The use of crude drugs including plants is traditional in Unani and Ayurvedic systems of medicines which were based occasionally on the then existing experimental methodology and mostly, on practical experiences of ancient physicians. Even today these traditional systems of medicine are very much in practice in India and they are given equal status as Modern Medicine and are recognised by the Government of India.

Some of the herbal preparations are still being used in Modern Medicine such as extracts, tinctures, to a limited extent, but, purified alkaloids and glycosides are widely employed.

In comparison, herbal drugs in Islamic medicine are generally used as crude single or compound drug preparations in the form of decoction, pills, powders etc...

According to Modern Physician it is often difficult to determine the pharmacological therepeutic and toxic effects of an individual component, present in such Unani herbal preparations, because the extracts of even a single plant may contain different active chemical compounds with either synergistic or antagonistic actions. Their observations clearly suggest the necessity of isolating the individual chemical constituent of a plant extract and further separating main active ingredient existing in it, prior to experimental screening in animals and human beings.

But a Hakim feels that crude herbal preparations have been in use for centuries and have proved to be less harmful inspite of prolonged medicines and the drug interactions are extremely rare when thorough diagnosis is made and drugs are used in proper formulation. The formulations are so made as to minimise the untoward effects and enhance synergism, thereby increasing the efficacy of the preparation as a whole. The idea was perhaps based on the logic of humoral concept and study of temperaments and allied factors in the patient, for e.g., the basic pathological changes in the constitution of the body has been identified by the Hakim as hot and damp, hot and dry, cold and dampt and cold and dry etc.., according to predominance of abnormal humour and the treatment is directed to set right this abnormality. The concept of constitution of human being is well recognised by the modern physician including the genetic variations and drug therapy.

Most of the indigenous drugs were locally available for therapy as well as research and some which were not available, but necessary, were imported from abroad by Hakims. Herbal preparations were preserved by using honey, syrup, vinegar, etc. Some of these items are still being used by the modern pharmacist. In addition, many more chemical preservatives have been developed recently. Alcohol was mostly used as an antiseptic.

Prescriptions according to Hakim essentially consist of a solid preparation (pills, tabs.) or a semisolid one (majoon etc.) along with an excipient such as decoction, infusion, etc. The latter may help in rapid absorption of the main drug or act as an adjuvent therapy influencing the pharmacokinetics and probably increasing the bio-availability.

Ralatability is one of the important criteria for the use of medicine.

Certain drugs like calcinated iron, copper etc. require the aid of herbs and special processing techniques to prepare a final product for medicinal use. Their use in Islamic medicine can be correlated with modern concept of essential trace elements in the diet for maintenance of health.

Munzij and Musshil

These are special kind of medicines practised by a Hakim. They vary according to the defect on the humor (خلط ردی) which is responsible for the disease state. These are especially useful in chronic and resistant conditions. Munzij is decoction prepared out of special class of individual herbs, meant for administration for a specific period, which is to be followed by a Musshil (laxative) a compound drug preparation, to make the body free from the defective humor. Such preparations require scientific study to establish their validity in chronic inflammatory, degenerative, metabolic and malignant disorders.

Toxicity

Severe toxicity to vital organs such as liver, heart, kidney and damage to bone-marrow are rarely heard of, in Islamic medicine. Herbal medicines though less potent are less toxic also (Ref) in spite of their prolonged medication. Hence, it is suggested that combination of modern drugs (which are comparatively more potent and more toxic) with herbal medicines is worth trying, to prevent or treat their toxicity, if there are no interactions. The work is in progress with some of the Indian manufacturers with their indigenous drug preparations and it proved to be successful to a considerable extent. The old herbal drugs need scientific screening in patients whose constitution does not permit more potent and more toxic modern drug therapy and in those where they failed, to produce favourable results.

No specific antidotes were available to the Hakim in olden days to treat poisoning, although several types of poisoning were said to have been treated by physicians. They treated poisoning with non specific antidote (*tiryak*), the value of which was conflicting (according to Maiminoides) but simultaneously demulsents and absorbants, were also used which were indirectly helpful in the elimination of poison from the body.

Diet and Nutrition

The Hakim believes in the treatment of a disease with both drugs and diet together (علاج بالدواء ـ علاج بالغذاء) Diet may be either restricted or special diet advised according to the ailment.

The condition of Hakim behind dietary control is to maintain nutrition and to increase the defence mechanism of the patient specially in chronic conditions. Several substances with nutritive value such as different fruit juices, vinegar, alcohol, honey, whey, barley-water and special proteinous preparations (ماء اللحم) are included as adjuvents, correctives, excipients.

In the light of modern science they would help the patient by providing with carbohydrates, fats, proteins, minerals and vitamins and maintain fluid and electrolyte balance especially in conditions where dehydration is present for e.g. gastrointestinal and other wasting diseases. Restrictions were made to minimise food-drug interactions and to aid drug action (This is to be investigated scientifically).

Value of fruits in health and diseases

Regular intake of citrus fruits such as sweetlimes, oranges etc.. in the form of juice may be helpful in preventing diseases like hypertension, obesity, hypercholestremia or occurance of their complications.

Role of vitamin C in prevention of atherosclerosis has already been studied scientifically with favour-

able results (Dr. Constance Spittle of Ebgland refer British information service release (1974) by Dr. Roger Diwin.

According to Islamic Medicine easily digestible food item (like citrus fruit or juice is better taken first)

Bedridden patient is given light diet.

The role of fruit juices and restricted diet or special diet in altering the blood chemistry and their use in therapeutics, need further study.

Diseases Discussed

Therapeutic usefulness of herbal preparations in chronic conditions such as rheumatic disorders, sinusitis, skin diseases, etc., has been amply experimented with satisfactory results. In addition acute conditions like infective hepatitis, a few types of skin allergy, urolithisis etc., are also treated successfully, the response being equal to or better than with modern medicine.

CONCLUSION

We are adopting many things from ancient medical literature gradually one after the other, of course with necessary modifications e.g. 1) Massage 2) Sun bath, 3) diet etc., but with the advanced technology available to use now, we are made to think that we are better off than our forefathers. No doubt, there is an element of truth, but there is no harm in further exploiting ancient literature and benefitting ourselves by collaborating with Hakims well versed with the subject. Joint effect in keen observations may help in understanding several unsolved problems.

Research work has not picked up the momentum required, for indepth study of indigenous drugs mainly due to:

1) Lack of common forum for communication between a Hakim and a doctor, and
2) Absence of generalised awareness of the benefits of herbal medicines.

Modern medicine is enjoying a superior status because it is supported by advanced technology. If the same technology is made available for research in herbal medicine, it will also attain its rightful place in alleviation of sufferings of humanity.

Failure of modern drugs therapy in chronic diseases and their sequels is well known. If the herbal drug therapy is found successful in prevention of complications of any chronic disease it will be a very valuable achievement for humanity.

It is proposed that crude drug preparations which carry with them centuries long experience of Hakims about their utility and safety can be put directly on clinical trials under the supervision of both Hakims and Doctors in various hospitals accompanied by Modern investigations and a list of promising drugs should be prepared for further study, including animal experimentation, and screening of active ingredients by chemical analysis. This can save time, men and money, spent on herbs of doubtful efficacy. If it is not desired on behalf of the doctors, who would prefer clinical trials preceded by pharmacological and toxicological studies as a routine, it is suggested that they can obtain available herbal preparations in the existing form from the standard manufacturers in India or elsewhere and further study for their physical, chemical and biological properties before using them on human beings.

Shortcomings of modern medicine in general are:

1) Drug toxicity
2) Drug refractoriness
3) Necessity of Laboratory investigations,

4) Drug resistance and interactions,
5) Increased cost of medicines etc.

In spite of the available several wonder drugs with their selective activity, the modern physician is sometimes confronted with the above mentioned difficulties. Hence, he is still in search of safe and ideal drugs.

Shortcomings of herbal medicines such as:

1) Difficulty in standardisation
2) Lack of selectivity
3) Slow onset of action
4) Lack of availability due to want of knowledge of pharmacognosy.

NOTE: Several old valuable recipes might have disappeared unnoticed.

The present day available information regarding fundamental and applied research on drug action is scattered and somewhat conflicting. The work done already in the past was again repeated by some scientists unknowingly and by others either to confirm or to condemn the past results. However, it is advisable to have a common platform to chalk out a programme to collect relevant information and to conduct advanced research in collaboration with Hakims and Doctors and disseminate the information thus gathered to different institutions as and when required.

Even now a sizable population of the world lives in the rural areas of the countries like India, Africa, China and Middle East. They feel that the native drug therapy is more beneficial for them. Hence, collaboration of Hakims as well as Doctors is more desirable to achieve the goal of World Health Organisation (i.e. betterment of humanity). This can only be achieved by emotional integrity, mutual frankness and team spirit.

LET EVERY BODY BE HAPPY
LET EVERY BODY BE HEALTHY
LET ALL SEE ONLY PLEASANT THINGS IN LIFE
NO ONE SHOULD EVER SUFFER

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CONTINUED USE OF IRRITANT AND CO-CARCINOGENIC EUPHORBIACEAE PLANTS IN ISLAMIC MEDICINE

Dr. Gulam Abbas Miana
PAKISTAN

Many plants belonging to the family *Euphorbiaceae* are being used in the indigenous health care system of most of the Islamic countries of the world. Glossary of Indian Medicinal Plants[1] lists at least 50 such species (Table I). Prominent among these plants are the following:

1. *Croton tiglium*
2. *Mallotus philippinensis*
3. *Euphorbia resinifera*
4. *Emblica officinalis*

Seeds of Croton tiglium and its oil have been used [1] as purgative and as counter-irritant. Glands and hairs on the fruit of *Mallotus philippinensis* are used as bitter, anthelmintic, cathartic and styptic. [1] Resin of *Euphorbia resinifera,* a native of Morocco, is used as purgative, abortif and as sciatica. [1] The fruits of *Emblica officinalis* is used as acrid, cooling, refrigerant, diuretic and laxative. [1] Fruit is a rich source of Vitamin C and is used in the treatment of human scurvy. Such purgative and irritant activity [1] has been ascribed to almost all of the plants given in Table I.

In 1941, the irritant properties of Croton oil led Berenblum[2] to detect the augmentational and co-carcinogenic effect of the oil in tumorgenesis of mouse skin induced by carcinogenic aromatic hydrocarbons. Berenblum and shubik[3] applied to the skin of mice one single subcarcinogenic dose of 7, 12-dimethyl-benz a-anthracene (a carcinogenic aromatic hydrocarbon), which did not elicit any tumors (Fig. I). Also repeated application of such doses of croton oil had no tumorgenic effect. However, a large number of skin tumor is produced by sequential application of the same doses of these compounds if the carcinogen is administered first and the cocarcinogen subsequently, or if the carcinogen dose is administered throughout (see Fig. I). In this way, co-carcinogenic activity of croton oil was established.

EXPERIMENT	EXPOSURE OF ORGANISM					TUMORS PRODUCED
1	AR	AR	AR	AR	AR	+
2	AR	—	—	—	—	—
3	CO	CO	CO	CO	CO	—
4	AR	CO	CO	CO	CO	+

AR = Carcinogenic Aromatic Hydrocarbon

CO = Co-carcinogenic activity of Croton oil

FIGURE I

Hecker and co-workers[4] at the German Cancer Research Centre, Heidelberg, West Germany, undertook a systematic fractionation of croton oil, according to the procedure given in Table II and followed by measurement of irritant and co-carcinogenic activity and succeeded in isolating 11 compounds from the hydrophilic portion of the oil. These compounds are diesters of a diterpene known as phorbol.

Similar diterpene esters were isolated from *Euphorbia resinifera* [5], which were also found to be irritant and co-carcinogenic. Such compounds have now been found in many plants belonging to the family *Euphorbiaceae*. [6] Some of the diterpene esters have also shown anti-tumor activity. [7] Recently, related diterpene esters have been isolated from a number of plants belonging to the family *Thymeleaceae.* [8]

We have investigated the irritant activity of the following plants, which are abundantly available in Pakistan:

1. *Euphorbia caducifolia*
2. *Euphorbia cornigera*
3. *Euphorbia wallichii*
4. *Mallotus philippinensis*
5. *Daphne oleoides*

Except for *Mallotus philippinensis,* all of the plants have shown a high irritant activity. [9] It may be interesting to point out here that whereas in most of the plants studied thus far the irritant activity is located in the hydrophilic fraction, [4] but the hydrophobic fraction of *Daphne oleoides* has been found to be more irritant. Chemical investigations are in progress to isolate these compounds in pure form.

The demonstration of irritant and co-carcinogenic activity by most of the plants belonging to the family *Euphorbiaceae* suggests that these plants may add to the total carcinogen load of the environment of human beings and provoke certain measures in preventive medicine: that the human beings should be prevented not only from contact with carcinogens, but also from contact with what may be called co--carcinogens such as croton oil.

In view of the above, it is suggested that to begin with, the use of such *Euphorbiaceae* plants which have shown irritant and co-carcinogenic activity, such as *Croton tiglium* and *Euphorbia resinifera,* should be banned in Islamic medicine. Further investigations should be undertaken on the other plants to assess their suitability for their continued use as drugs.

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TABLE I: LIST OF EUPHORBIACEAE PLANTS

1. *Acalypha indica*
2. *Aleurites moluccana*
3. *Andrachne cordifolia*
4. *Antidesma bunius*
5. *Baliospermum montanum*
6. *Bischofia javanica*
7. *Breynia patens*
8. *Bridelia montana*
9. *Chrozophora prostrata*
10. *Cicca acida*
11. *Claoxylon indicum*
12. *Cleistanthus colinus*
13. *Codiaeum variegatum*
14. *Croton tiglium*
15. *Drypetes confertiflora*
16. *Emblica officinalis*
17. *Euphorbia species*
18. *Excoecaria acerifolia*
19. *Flueggea leucopyrus*
20. *Hippomane mancinella*
21. *Homonoia riparia*
22. *Hura crepitans*
23. *Jatropha curcas*
24. *Macaranga indica*
25. *Mallotus philippinensis*
26. *Manihot esculenta*
27. *Phyllanthus niruri*
28. *Putranjiva roxburghii*
29. *Ricinus communis*
30. *Sapium indicum*
31. *Sauropus quadrangularis*
32. *Sebastinia chamaelea*
33. *Tragia involucrata*
34. *Trewia nudiflora*

Table II: FRACTIONATION OF CROTON OIL

Croton Oil (IU: 2.4 ug/ear)

O'Keeffe-distribution → *Hydrophobic Portion* (IU: 38 ug/ear)

↓

Hydrophilic Portion (IU: 0.15 ug/ear)

Na_2CO_3 → *Acid Fraction* (IU: 5ug/ear)

↓

Neutral Fraction (IU: 0.15 ug/ear)

POTENTIAL OF HERBAL MEDICINES IN MODERN MEDICAL THERAPY

Hakim Mohammed Said

PAKISTAN

One of the important aspects of the Second Conference on Islamic Medicine is concerned with the beneficent nature of natural drugs in therapeutics. The importance of this aspect is hardly in need of being underscored. When we say that treatment by natural drugs is closer to Nature, we actually do not state something vague or metaphysical but something that is concrete and observable. A balanced diet ensures wholesome corporal resistance and generation of antibodies. Secondly, treatment is effected through the administration of concentrated active principles in herbs which we eat or which are allied to them. They thus bring about cure without generating the side-effects which have become the bane of modern medicine, mostly based upon synthetics.

Plants and man are inseparable. On no other commodity has man lavished such tenderness and the way the wild plants have been genetically tamed is a separate story. Certain plants like *nehar (Calotropis gigantea* or gigantic *swallowwort)* and *yabrinj (Mandragora officinalis* or mandrake) have certain superstitions attached to them. This is no doubt because of the dual properties of many plants. Thus the root and leaves of *bazr el-fujl (Raphanus sativus* Linn. or radish) are likely to cause heaviness in the stomach, but the seeds and the decoction of the plant are likely to act as diuretic, laxative, and lithontriptic agents. And reports, through screening, upon even as familiar a plant as the carrot have established what untold good it is likely to do to man and to the smokers in particular. The very fact that plants like broccoli, spinach, and tomato, supply so much of vitamins to man should serve as an indemnity against disease and help bring about natural cure.

I should like to quote a few examples of how plants have led to the growth of synthetics. During the late thirties it was observed that the cattle fed upon spoilt sweet-clover died of haemorrhage. On further study it was found that this haemorrhagic effect was due to a chemical, dicoumarol, which in the US Pharmacopoeia is known as bishydroxycoumarin. The synthesis of this haemorrhagic agent was finally accomplished by Link, Stahmann, and Huebner in the laboratory in 1941. It was thought that the haemorrhagic property of this chemical could be turned to advantage, and, in fact, Townsend and Mills in 1942 reported that in six patients repeated doses of 200 to 300 mg. every day prolonged prothrombin and clotting time. Vitamin K, about which we will speak later, counteracted this effect. If therefore man makes the sweet clover a part of his diet or takes an allied species like the fenugreek, some indemnity against thrombosis and embolism is expected. And from this particular mishap in the Prairies has cropped up a series of drugs allied in structure to dicoumarol, e.g. Cumopyran, Tromexan Ethyl Acetate, Marcoumar, Dindivan, Warfarin (which was again synthesized by Link and Cowrle in 1947), and so on.

Vitamin K, the antihaemorrhagic factor, was reported by the Danish scientist, Dam, for the first time in 1929. It was found that the haemorrhagic tendency in chicks was overcome by adding alfalfa, spinach, kale, or fish meal to the diet. Dam and his associates, as well as Doisy and his associates, isolated the pure vitamin from alfalfa, calling it K, to distinguish it from the vitamin called K2 which Doisy, McCoquordale, and their co-workers isolated from putrefied sardine. Both K and K2 were shown to be naphthoquinones. And thus medicine was on way to having even more potent synthetic counterparts which apparently acted by counteracting the effects of dicoumarol by lessening, according to Martius and Nitz-Litzow (1953), the rate of aerobic posphorylation. The structural resemblance of dicoumarol to Vitamin K has led to the view that dicoumarol competes with Vitamin K and displaces it from an enzyme system which is required in the synthesis of factor VII and prothrombin.

We thus find how an isolated case of the incidence of haemorrhage in cattle in the Prairies led to a series of drugs having reverse effects.

Griffith and co-workers (1944) also have a ketone group, although it is a flavone compound, and is, in fact, the rhamnoglycoside of quercetin. It is of particular use against recurrent haemorrhages caused by or related to capillary fragility. It occurs in several plants; the stem of the tomato has sizeable amounts of this antihaemorrhagic agent and was first tried clinically in 1944.

It is certainly true that synthetic chemistry has come out with more potent antihistamines than are to be found in Nature. But we should not forget that for a long, long time ephedrine served as the drug of choice against asthma and hay-fever and that its preparations, the base, hydrochloride, and sulphate are still official.

It has been observed that patients with asthma are more sensitive to histamine than normal subjects and these attacks may be prevented by means of ephedrine, a plant drug (although now also synthetically prepared) and adrenaline, a body-product.

Work on chemotaxonomy has not yet started properly. Erdtmann and Darnley Gibbs have already shown that startling discoveries of both fundamental and applied nature could be expected if the work is pursued methodically. It is quite tricky also. An example of this trickiness was cited by Dr. S. Siddiqui 18 years ago when he reported that three crystalline solids had been isolated by himself and co-workers from the Bengal gram (*Cicer arietinum* Linn.) viz. Biochanin A (5:7- dihydroxy, 4-methoxy is a flavone), Biochanin B (identical with the isoflavone for menonatin occurring in soy-bean), and Biochanin C (identical with asparagin which occurs in *Asparagus* spp. and in *Abutilon indicum* Linn., a plant belonging to Malvaceae). It was found that these solids could not be isolated when the gram sprouts were dried in the shade and extracted with solvents. Suh observations bear out the Islamic concept of medicine which claims that drugs are liable to lose their potency if not given in their proper form. Some drugs gain in potency on ageing; others lose. We have seen how even a harmless plant like the clover can become lethal to animals.

Nor is it true to hold that natural drugs, apart from antibiotics, do not counter microbial attacks. Garlic has been used for time immemorial as a carminative, expectorant, febrifuge, and in the treatment of intermittent fevers. Carallito and Bailey (1944) had already isolated allicin from it. Parry isolated two sulphur compounds from it in 1946, having antiseptic and hypotensive properties. Two more principles, having anti-bacterial properties, viz., allisatin I and allisatin II, were isolated from it in 1948.

Another interesting approach was opened with regard to *Peganum harmala* Linn. The isolation of the harmine series of alkaloids was reported as early as 1843, and studies on their constitution by Otto Firchu and Perkin, Robinson, and Manske form a classic in the annals of organic chemistry. As a result of studies by S. Siddiqui, et al., following the mildest chemical procedures, an alkaloid melting 180° higher than harmaline and yielding a phenolic base which melts about 50°C higher than harmalol, the corresponding phenolic base prepared from harmalin, a new base, harmadine, proved to be the principal alkaloid of the seed of *P. harmala* with an overall yield of 1.75% while no trace of phenolic base was found by S. Siddiqui and co-workers from three lots of the materials in the Punjab in Pakistan. This would suggest the possibility that harmalin and harmalol, according to Siddiqui, et al., reported in the literature are entectic mixtures of bases, if it were not for the fact that the former were synthesized by Parkin, Robinson and Manske, and found to be identical with the natural product. Siddiqui further observes:

> It may well be that harmidine is an isomer of harmalin, the absence of which in the seeds may be due to varieties in soil and climatic conditions, but the study of *Peganum harmala* seeds from Iraq seems to exclude this possibility.

The seeds of *P. harmala* in Islamic medicine are prescribed for the expulsion of the tapeworm. It has now been definitely established *(Biochemical Journal,* 264; 1934) that the alkaloids of the plant are

toxic to helminths and protozoa. The highly vesicant principle, bhilawanol (a catachol derivative with a C 15 H25 unsaturated straight-chain side in position 3), is effective in rheumatic pains.

Much work remains to be undertaken upon natural anti-diabetic drugs. Onion has been known to reduce the blood-sugar level. It is also likely that *Syzygium cumini* Linn. is effective against diabetes. Further studies are required upon the bitter gourd to establish whether the anti-diabetic principle in it acts independently of endogenous insulin. Some interesting development on hypoglycemic drugs is taking place in Central America.

One of the weaknesses of natural drugs from the higher plants, it is argued, is the poor microbial activity of such drugs. However, Lin Keng- Tao of the Institute of Materia Medica, Chinese Academy of Medical Sciences, has shown in a recent report that *Fructus schizandrae* which is commonly used as an astringent in traditional medicine, exercises therapeutic effect on certain types of viral or chemicai hepatitis, particularly in lowering the elevated serum glutamic transaminase (SGPT) level and improving some of the symptoms in 68.2% cases. The accumulation of lipids in the liver is impeded, while the deposition of glycogen is increased.

The birth-control steroid, diosgenin, is dependent for its extraction upon *Dioscorea deltoides* Wall. Some important saponins like amelonin, digitonin, sarsaponin, tigorin, and trillium are also obtained from *Chlorogalum pomeridianum, Digitalis purpurea* and *D. lanta, Radix sarsaparilla,* and *Trillium erectum* respectively.

We now come to folklore and the present-day screening of drugs. G. A. Cordell makes the observation with regard to anticancer drugs of herbal origin: "... in almost every instance where a plant has a reputed folklore reputation in the treatment of cancer, a compound displaying either in *vivo* or *in vitro* activity has been obtained". Cordell et al., have studied the following plants and have isolated their active principles as regards anti-cancer properties.

Quinoids	*Jacaranda caucana*
Sesquiterpenes	*Acanthospermum glabratum*
	Michelia compressa
	Capsicodendron dinissi
	Centratherum punctatum
Diterpenes	*Rondeletia panamensis*
	Micrandra elata
	Baliospermun montanum
	Dioca occidentalis
	Aquilaria malaccensis
Simaronbolides	*Ailanthus excelsa*
	Ailanthus integrifolia
Steroids	*Asclepias albicans*
Miscellaneous compounds	*Amyris bipinnata*
	Linum album
	Cassia quinquangulata
Alkaloids	*Fagara zanthoxyloides*
	Zanthoxylum rhetsea
	Ervatamia heyneana

Two alkaloids isolated from *Catharanthus roseus* Linn., vincristine (VCR) and vinblastine (VLB), have yielded favourable results with regard to Hodgkin's disease and choriocarcinoma and acute leukemia in children respectively. Partial synthesis of both has been achieved by Dr. Atta-ur Rahman et al.

Another group of active principles against cancer has its origin in a plant growing in East Africa, *Maytenus oratus* Loes. This group is that of maytansinoids which includes some four maytanside esters attached to C^3 of the macrocycle as well as the free maytansides, maysine, normaysine and maysenine. Maysenine exhibits significant L 1210 and P 388 anti-leukaemic activity and powerful tumour-inhibitory properties against KB cells, mouse sarcoma 180, Lewis lung carcinoma, and Walker 256 intramuscular carcinoma.

The therapeutic aspects of herbal medicines have many facets. Hiroshi Saito, in his study of the pharmacological properties of *Panax ginseng* root, for example, has reported that the different fractions of its extracts exercise different actions, e.g., slight CNS stimulant action, CNS depressant action, histamine-like action, tranquillizing action, blood-pressure depression, blood-pressure elevation, etc. Once such a total study is extended to other plants, we may well check up why certain parts of a plant have been prescribed for certain ailments and which parts are rich in which active principles.

It has been estimated that roughly only 5% of the plant wealth has been studied. But perhaps this figure is on the larger side. The knowledge afforded by plants is almost infinite. The World Health Organization in 1977 realized this as is borne out by its report upon *The promotion and development of traditional medicine.* Among the reasons that it gave for the promotion of traditional medicine one was that of the intrinsic qualities of medicine.

> Since traditional medicine has been shown to have intrinsic utility, it should be promoted and its potential developed for the wider use and benefit of mankind. It needs to be evaluated, given due recognition and developed so as to improve its efficacy, safety, availability, and wider application at low cost. It is already the people's own health care system and is well accepted by them. It has certain advantages over imported systems of medicine in any setting because, as an integral part of the people's culture, it is particularly effective in solving certain cultural health problems... (p. 13).
>
> This document's case-study of Egypt is rather interesting:
>
> *Ammi majus*- a common plant in the fields and waste lands of Egypt - has been shown to contain ammoidin (xanthotoxin), ammidine (imperatorin), and majudin (bugaptene). The extracts of this plant have been shown to induce pigmentation in idiopathic leukoderma (vitiligo).
>
> *Ammi visnaga* — another perennial plant, used in traditional medicine by the ancient Egyptians in the form of a decoction and as a diuretic to treat renal colic — was recently analyzed and found to contain the two principles, khellin and visnagin. Khellin is useful in the treatment of angina pectoris and whooping cough and in the relief of ureteric and gallbladder spasms. It has been found to contain anthelmintic, antianaphylactic, antiatherosclerotic, antidiabetic, and antiulcerogenic properties. (p. 11).

The report discusses herbs like *Nigella sativa* Linn. *(habbet el barakah)* and other plants which are under investigation in Egypt. Among these plants *Solanum laciniatum* is of special interest in that it contains alkamines which are steroidal in nature and which can be converted into steroidal hormones. This plant is the main source of solasodine which is being isolated industrially for the preparation of pre*gnadienone* and used for the synthesis of various hormones.

It ought to be appreciated that the same herb may be used for specific treatment in one country, while in other countries the emphasis may be different. In the Philippines, for example, onion is employed in high blood pressure. Similarly, in the Sub-continent, the rind of the pomegranate fruit is used, in conjunction with aromatics like cloves, as an antidiarrhoeic and antidysenteric agent, while in Sumatra it is employed as an abortifacient. In Cuba the bitter gourd is used for the treatment of diabetes and chronic ulcers of the stomach, whereas in the Sub-continent the value of bitter gourd as a hypog-

lycemic agent has come up for appreciation recently. Expanded vision with regard to the therapy of herbal medicines is one of the likely contributions when the folklores of different countries are collected. It is also possible that an ingredient may be present in much higher quantities in the species in a specific region and hence emphasis is placed upon therapy deriving from that ingredient. Thus, of the different species of mint, the Japanese mint, *Mentha arvensis var. piperascens* contains the highest percentage of menthol (70 — 90%). This variety, known as *Ryokubi,* has begun to be cultivated in Thailand, where by 1977 the yield of crude oil from it had reached 60 tons/year. This variety has been successfully introduced by the PCSIR Laboratories, Lahore, into the Punjab.

In an illuminating paper presented at the 4th Asian Symposium on Medicinal Plants and Spices (Bangkok, 1980) Finn Sandberg discussed the results likely to be expected from an inventory of traditional medicines within a restricted area. He gives the illustration of *Oldenlandia affinis* (family Rubiaceae) which is indigenous to Zaire and Central African Republic at a distance of 20,000 metres. The herb of course bears different native names and is known in the local folklores for facilitating child-birth. Work on the herb by Lorens Gran in Norway has established that the herb contains the so-called Kalata-peptide, comprising 31 amino acids. This peptide is effective orally, and has potent oxytocic activity; and thus in this case the folklore medicine has been scientifically verified. Sandberg has also noticed that some plants cannot be cultivated outside their local ecological zones. An example is that of *Strychnos lianas.* But a herb like *O. affinis* can be easily cultivated.

An interesting example in this context is that of *Acorus calamus* (family Araceae) which in the Sub-continent has not been prescribed for rheumatism. But in China the genera, *Acorus* and *Arisaema,* are reputed to be anti-rheumatic. Asaron and related compounds have been isolated from these species and have shown carminative, sedative, and analgesic effects. Triterpines from the corms of *Arisaema* have anti-convulsive, sedative, and analgesic properties. *Abutilon indicum* Linn. is put to different uses in the Sub-continent and Viet-Nam. Its leaves in the Sub-continent are considered demulcent, its bark astringent and diuretic, infusion of its roots febrifuge, and its seeds aphrodisiac, laxative, and demulcent. In Viet-Nam, on the other hand, the leaves are used as an emollient, stomachic, and antiperiodic. Decoction of its root is considered to be of use as febrifuge and also for the treatment of leukorrhoea. The leaves are also considered diuretic and the seeds are used against dysentery, carbuncles, and sore eyes. Work has been conducted upon *Rauwolfia serpentina* Benth and other species of the genus in Viet-Nam, where, interestingly enough, rutin has been extracted from a leguminous plant indigenous to that country, *Sophora Japonica* Linn. Research is being undertaken in Viet-Nam on herbal drugs for affording relief against fatigue — a disorder inherent in the present civilization.

One of the most promising fields of natural drugs is that of activity. Shoji Shibata reported in 1980 that the intravenous administration of a medical preparation of glycyrrhizin, a saponin of the liquorice root, in conjunction with cysteine and glycine, was proved by a double blind controlled trial to be effective against chronic hepatitis. Hemisuccinate of glycyrrhetic acid *(Carbenoxylone)* is orally administered in stomach ulcer. More recently, however, an antiviral activity of glycyrrhetic acid was reported and Interferon-inducing activity of a glycyrrhizin preparation were observed. Shibata believes that glycyrrhizin and glycyrrhetic are among the most promising natural products. Side-effects like oedema and hypertension have been overcome through chemical modifications. The results so far obtained show that olean-12-en-3β, 30-diol chemically derived from glycyrrhetic acid by elimination of its 11-keto group and the replacement of 20- carboxyl with carbinol is one of the most promising compounds of this series showing separation of pseudo-aldosteronism from therapeutic such as anti-ulcer and anti-allergic effects.

Much of modern research on plant products has hinged upon folklore. Thus the Mexican cactus, *Opentia streptacantha* Linn. and herbs like *Tecoma stans* Juss. are being subjected to clinical trials in Mexico for diabetes mellitus. In the field of cardiovascular research, studies are being made on the

seeds of *Casimiroa edulis* La Llave, popularly known as a hypotensor, and flowers from *Talauma mexicana* Don and *Magnolia grandiflora* L. are considered to be cardiotonics.

Passing from the general to the specific, on the occasion of this Conference, I thought that it might be worthwhile to write upon a theme of *overriding* importance in Islamic medicine, viz. upon the different sidelights of Islamic medicine from different aspects. I have also decided to present my personal experiences and impressions upon a drug which has gained considerable importance in the materiae medicae of the Sub-continent. This drug is based upon tamarisk. This drug has been specially selected as we have been able to prosecute the R & D effort required in its development on the basis of the knowledge bequeathed by the ancient and mediaeval masters of medicine and the conventional methods employed by the practitioners of Islamic medicine. This drug is being marketed under the trade name of *Icterene* and it is meant to minister to cases of jaundice.

2. Having briefly discussed the importance of herbal medicines in the treatment of diseases, I should now like to discuss my impressions about tamarisk. As I have said at the outset, I have chosen tamarisk because I have, by the grace of Almighty, been able to manufacture a drug for the cure of jaundice from a self-growing and wild plant of the province of Sind in Pakistan. I am giving as much information as I can without any reservations and without withholding any information.

3. Tamarisk:

1. *Its Names in Islamic Materiae Medicae*

The taxonomic name of tamarisk is *Tamarix gallica* Linn. syn. *T. troupii* syn. *T. gallica* Anct. Dyer. In Persian it is known as *ghazanjabin, gaz mazaj, ghadbar, ghazmazu, gazan-gaban, galaz, shur gaz, gaz* and *ma'in kalan.* Its Arabic synonyms are: di *manna, thamrat al-turfa, turfa, janz al-turfa,* and *thamrat al-turfa.*

The greater and lesser tamarisk varieties are denoted by the common designation of *gaz mazaj* or *gaz mazu.*

2. History of the Uses of the Drug

Tamarisk which occurs in the form of a shrub or small tree is indigenous to Asia, Africa, and Europe. Known as tamarisk in English, its French name is *tamarise de France.* Dioscorides (Book 1, 101) says that the plant which he designates as *murike* bears a seed like a gallnut.It is used as an astringent in Egypt and Syria, he states. Pliny calls the same tree *tamarika* (24,41). It is the tamarix of Columella. Nicander named the tamarisk tree as *mantie* (prophetic). The Apollo of Lesbos has been represented with a bough of the tamarisk tree in his hand, and the Iranian Magi also prophesied with a spray of the tree in their hands. Herodotus and Pliny describe the plant in the light of similar use.

Coming to the synonyms of the tree in the Sub-continent, it was known as *jhavuka* in Sanskrit. In Hindi and Urdu it is known as *Jhau* and *bari mayn.* It is known as *pilchi* in Punjabi, as *jhavnu-jhadu* in Gujerat, as *jhavukam* in Malabar, as *siru savukku* in Tamilnadu, and as *sirasura* in Telegu.

It is probable that the galls of the tree have been in use in the Sub-continent since long, and the galls of the tamarisk tree were regarded as substitutes for oak-galls. The manna which drops from the tree is collected in the month of June in Arabia and Iran. It is known as *gazangabin* or *gazanjabin* in Persian. The manna is not produced in the Sub-continent.

4. In Iranian works on medicine, the galls of the tamarisk tree are called the fruit, and the manna is described as a dew which falls upon this and other trees, notably the willow and oak, and becomes solid. The practitioners of Islamic medicine consider gazanjabin or the tamarisk manna to be detergent, aperient, and expectorant. According to Dymock et *al. (Pharmacographia Indica,* i, 160) it is the

drosomeli of Galen. They further state:

> In modern medicine manna is still used as a laxative; it slightly increases the action of the bowels, causing more frequent and softer stools without irritation. Its sweet taste makes it acceptable to children. The galls like those of the oak, contain tannic and gallic acids, and may be used as an astringent in the same manner as true galls.

The tamarisk tree has been included in the Islamic materiae medicae of the Sub-continent, from Ayurveda, although it has been known since Classical Antiquity.

3. Habitat and Identification

Tamarisk belongs to the family, Tamaraceae. It grows throughout the Sub-continent as its names in different dialects should amply show. It occurs on riverine banks and near the sea-coast on sandy soils and in swampy areas. It is propagated by means of transplanting or sowing. Its tree, when small, grows rapidly and reaches maturity rapidly, and on maturity dies. It may attain a height of thirty feet. The diameter of its trunk is about three feet, and its boughs are curved. The bark of the fresh branches are slightly reddish and smooth, and bears small white marks. The bark of its foliage and the larger sprays is thin, greenish brown, and rough. Its flowers appear in the form of bunches and these are often white. The leaves are small. Its flowers do not appear separately as male and female. It is a hermaphrodite.

The taste of the tamarisk is bitter and astringent. One species of tamarisk is also prickly, and is prolific in South India and Rajputana. Since it bears many spines, it is called *Kanti Jhau* and *Kanti sharni* (i.e. the prickly tamarisk).

The tamarisk tree is of general occurrence in Iran and Afghanistan and is found in sandy areas in the Sub-continent, especially in the littoral areas and on the sea-coast.

5. Greek physicians have ascribed the occurrence of the tamarisk to river banks and have attributed four kinds to it.

1. The first kind is long, with its foliage like that of the cypress. It is called *athl* in Arabic. Its fruit is called *'adhba* in Arabic, and *nanhi main* and *choti ma'in* in Urdu.
2. The second kind is similar to the first, but does not bear any flowers.
3. This kind has scanty foliage and bears white flowers with a slightly reddish tinge. Its flowers are in branches and present an appearance of oak flowers. It is called *gaz mazaj* and *bari ma'in.* The taste of the flower is pungent and the blossoms possess a little scent. It is greatly favoured by the honey-bee.
4. This variety bears blossoms the size of *Buchanania latifolia* Roxb. and black pepper. The colour is greenish. No flowers appear upon it. It is used for dyeing purposes. This kind is not to be found in Iraq and Iran.

Some writers, on the other hand, say that it comprises only two kinds.

i) This kind is large and cultivated. Known as *athl* in Arabic, it is known in the Sub-continent as *frash.* Its fruit is called *'adhba.* The people of the Sub-continent designate it as *choti ma'in.* In Urdu and Hindi it is *lal jhau* (red tamarisk).

ii) This variety is smaller and wild. Its flower is reddish-white. It is knwon as *turfa'* in Arabic, *gaz* in persian, and *jhau* in Hindi.

4. Tamarisk Constituents

6. The galls of *Tamarix gallica* contain as much as 40% tannic acid (Kirtikar and Basu, *Indian Medicinal*

Plants (Allahabad 1933, vol. 1, p. 248). *Tamarix aphylla* Karst. syn. *T. articulata* Vahl galls contain 36.8 — 43.9% tannin; its bark contains 10% tannin and the *wood* of the tree 1% tannin. The galls contain levulose and glucose, dextrin, and moisture.

As should be evident from the foregoing, the Sub-continent tamarisk galls are very rich in tannin. British Pharmacopoeia recommends the use of the galls in a poxdery form. They are equally rich in tannic acid. *Gazangabin* or tamarisk manna contains sucrose, invert sugar, levulose, glucose, dextrin, and water.

5. *Description*

Gaz mazu, i.e. the tamarisk galls, is much smaller than the true gall; it is three-angled, knotted, and ugly in shape. It has a cavity in the centre which is sometimes filled by mosquitoes or flies, but generally the cavity contains excrementitious matter only. The manna occurs in the form of small grains. When fresh, it is white, but it has the tendency to become viscous and form a thick liquidlike honey. Material like this is produced upon willow and oak in consequence of the puncture by an insect. According to Ehrenberg, the insect which attacks the tamarisk is *Coccus manniparus.* The Persian word, *Gazangabin,* means tamarisk-honey. According to Knecht, in the nineteenth century it was applied to the manna which was collected in the mountainous districts of Chahar Mahal and Faridan from two species of *Astragalus* which is a leguminous plant.

7. Tamarisk manna is collected towards the end of June. According to Aitchison, it is cultivated in Khurasan, where it is designated as *siah chub.* Manna-bearing tamarisk trees are abundantly found in Siah Kuh and Sufayd Kuh and in the Ardiwan Pass they form thickets. Elsewhere the tree is found to grow in saline soils and by the banks of rivers. It is cultivated occasionally as an ornamental in gardens (A.K. Nadkarni, *Indian Materia Medica* (Bombay 1976), vol. 1, p. 1194). Tamarix galls are moderately emollient, expectorant, and detersive with regard to blood. It is therefore incorporated into anti-tussive and cough medicines as well as in drugs promoting aperience. Its chief advantage is that it promotes the passage of stools without any attendant irritation or burning sensation. Not being repulsive in taste, it is regarded particularly useful for administration to children, and can be administered in conjunction with milk. It is also employed as a substitute for oak-galls. *(Idem, Ibid.).* Being revulsive, the leaves of the tree which are soft, resolve inflammations and in dyspepsia they promote the expulsion of stools from the mesentery and the liver. It abates the hardness of the spleen. It is a stomachic and liver tonic *(Khaza' in al-Adwiyah,* vol. III, pp. 313 — 15). All of its constituents are tranquillizing. Drinking of water in a tamarisk bowl has been held to be useful in the inflammation of the spleen. But it is also suggested that this practice should be continued till the termination of the convalescent period.

Ibn-Sina believes that tamarisk acts as a detersive, astringent, and resolvent without exhibiting any intense desiccation. Its aqua, according to him, acts as detergent and desiccative, and it is this desiccative property which promotes constipation which, however, is slight, because it is cold. Its power to resolve is not excessive. Insofar as its desiccative power is concerned, it is not possible for desiccation to be promoted without any capacity being possessed to act as a resolvent. It is only after the removal of humidity that resolution helps promote desiccation.

8. Tamarisk is also used in the cure of jaundice. When bile is retained in the gall-bladder and acts as an obstruction, a decoction of tamarisk-root with vinegar is useful. The juice of its leaves and flowers is also advantageous in jaundice.

6. *Temperament*

Tamarisk is cold and dry in the first degree. Some physicians hold it to be dry in the second degree. Shaykh Ibn-Sina has said that it is cold and dry in the second degree. Being bitter, it should be

hot and this hotness is due to its bitterness. Some investigators have openly said that it is hot and dry.

7. Use and Therapeutic Action

Tamarix has been in use in the Sub-continent since ancient times. Physicians have employed it in the treatment of pseudodysentery in which case a decoction of its leaves and soft branches is useful. *(Khaza 'in al-Adwiyah,* vol. III, pp. 314 — 15).

Dioscorides regards its fruit to be useful in the ailments of the eye and the mouth. Ibn Biklarish al--Isra'ili believes that it is useful as a corrective for irregular periods. (Ibn al-Baytar, *Jami'li Mufradat al-Adwiyah w-al Aghdhiyah).* All these aspects pertain to the use of its leaves, root, branches, fruits, and flowers.

9. It has been recommended for external use also, e.g. in the cure of the ailments of the spleen, oedema, and hot inflammations. Some of its other uses are:

i) Cicatrization of wounds due to small pox by sprinkling a powder of its dried leaves upon the wounds.

ii) Its fumigation brings about the drying of wounds. It also dries haemorrhoids in piles.

iii) An infusion of its root and leaves is of utility in prolapsus ani and leukorrhoea.

iv) Being astringent, a decoction of the herb is used as a gargle in the irritation of the throat, boils and itch in the mouth.

v) It has been recommended in the cure of decomposed and putrified flesh and as a gargle in pyorrhoea and toothache. The ash of the gall removes the yellowness of the teeth.

vi) It acts as a styptic if the flow of blood from an organ cannot be controlled. It stanches the flow, if sprinkled upon the organ.

vii) It destroys the lice, if the head is bathed with a decoction of its leaves.

viii) Fumigation with its smoke dries the humid pox and other humid wounds. Tamarisk leaves, after drying and powdering, will expel malflesh. In this case they are applied externally.

ix) A powder of tamarisk leaves soothes wounds due to burns.

x) Physicians have recommended the chewing of its leaves for curing spongy gums.

xi) For external use a poultice is made from its resin and applied to boils which have become chronic, according to the practitioners of Islamic medicine.

xii) It is used as a tonic for the hair. The preparation used as hair tonic is prepared as follows: Fresh tamarisk root is heated with an equivalent weight of sesame oil and twice its weight of water. When all the water has evaporated, the remaining liquid is strained.

xiii) Decoction of tamarisk root is recommended in colds.

xiv) Poultice prepared from the tamarisk bark and pomegranate peel, if ground finely, is effective in abating the flaccidity of breasts in women. It should be applied twice in 24 hours.

xv) Women suffering from leukorrhoea are advised to sit in a bath containing its decoction *(Khaza' in al-Adwiyah* vol. III, 314 — 15).

8. Chemical Composition

Berthelot submitted to chemical examination the manna obtained from sina'i. It was a thick syrup and was found to comprise cane-sugar, inverted sugar (levulose and glucose), dextrin, and water. The *gazangabin* sample obtained from Iran and chemically analyzed by Ludwig was found to contain dextrin,

uncrystallizable sugar.

The galls of tamarisk have as much tannic acid as those of oak.

9. Prescription and Administration

The drug has an adverse action upon the stomach, but this action is made wholesome and corrected by honey and oil. Its substitute is *athl* which is also known as *frash.* The physicians of Lucknow recommend a weight of 4 *mashas* in decoctions of the herb. Some have recommended a dose of 5 to 7 *mashas.*

10. Drug Preparation

11. I am not in a position to discuss the Muslim contribution to the art of drug-making except to state here that they continually searched for new sources which could be brought to bear upon therapy, making the drugs progressively more efficacious, and providing all kinds of facilities to patients. They not only used their imagination but also at every step took full advantage of the treasure-house of experience which was left to them by their predecessors.

12. Among the achievements of Muslim physicians is their discovery of salts in herbs. They obtained salts by heating the plant or its particular part and scouring them from the ash. Such salts are obtained from barley, *Lycium barbarum* Linn., radish, etc. The salts have been therapeutically shown to be very effective. The procedure followed for the extraction of the minerals is as follows:

13. The plant or the part of the plant containing minerals is incinerated and the ash stirred in water is kept standing for 2—3 days. This liquid is then strained with a muslin cloth. A basin is placed below, so that the water containing the minerals may keep on dripping and collecting in the basin. This filtrate is again poured on the ash and the process is repeated twice or thrice. Almost all the minerals are thus extracted. The water containing the minerals is then evaporated and the salts are then dried and stored.

Another procedure is to put the ash into a basin and to pour water upon it, agitating it by hand or mechanically. The ashy water is then left undisturbed for some time and then filtered. The water is boiled, leaving the salts which are then dried.

Both procedures are virtually the same but for small differences. Salts from *Lycium barbarum* Linn., barley, and radish are obtained in this way.

Hamdard have modified the process according to modern bulk methods employed for filtration, boiling, etc.

14. The process is now known as the Hamdard process. Salts obtained by this process are effective against jaundice.

These minerals have been analyzed in the laboratories of Hamdard and the results are as follows:

15. *Icterene* is an inorganic chemical compound which Hamdard obtained from *Tamarix dioica.* Years of chemical research and therapeutic evolution have proved *Icterene* to be clinically a scientific cure for jaundice. This it probably achieves by expelling the obstruction of the bile.

Icterene has also been successfully employed in oliguria or wherever diuresis is required. In mild infective and febrile states it acts as a diaphoretic and lowers the body temperature.

Clinical experiments of Hamdard have led to the same result, i.e. the disappearance of yellow colour within 3 — 4 days and it is hardly ever necessary to continue the treatment for another three days.

The chemical analysis of *Icterene* carried out by Prof. Dr. Georg Hahn in the PCSIR Laboratories at Karachi has shown the composition of the compound to be as follows:

1. Moisture, 79%
2. Organic matter, 2%
3. Cations:
   Iron, 8.07%
   Cobalt, 1.50%
   Calcium, 1.50%
   Magnesium, 0.17%
   Sodium, 1.70%
4. Anions:
   Chloride, 28.9%
   Sulphate, 31.7%

12. Icterene Dosage

A course of two tablets three times a day for adults in between meals for three days is usually enough to bring about clinical cure, but in many cases 8 tablets in 24 hours can be given vithout causing any harm. In the event of a satisfactory response not being obtained, the period of treatment may be enhanced by another 3 days.

The patient should, while under treatment, drink plenty of liquid material, e.g. fruit (particularly citrus) juices, glucose water, etc. Meat and fats are to be totally avoided.

The drug has not given to known toxic or adverse side-effects.

16. The presentation of the compound is in tablet form. Islamic medicine undoubtedly possesses efficacious treatment against jaundice, while allopathy has yet to find a therapeutic agent for its cure. We are all too well aware of the fact that the jaundice patient, whether treated by allopathy or Islamic medicine, has to be stashed up in a hospital or private clinic for weeks and, in certain cases, for months. The patient is given saline dextrose drips which at times affects the pancreas adversely.

The tamarix fruit (particularly that of *Tamarix indica* Linn.) is considered a refrigerant, digestive, carminative, laxative, and useful in diseases caused by deranged bile. Infusions of the fruits are also given as draughts in febrile diseases.

From what therefore has gone about tamarisk we are led to arrive at the following conclusions:
(i) Nature has provided cure for diseases, and plants specific to certain regions offer therapy in particular regions against diseases that are prevalent in those regions. Thus the inhabitants of cold regions are prone to suffer from gout and rheumatism, and we have thus *Colchicum autumnale (Surinjan)* growing throughout the temperate regions, e.g. Central Asia and Western Europe. The climate of south and western India is hot and humid, and the wood of the sandalwood tree allays heat and pruritus, acting as a diaphoretic. Likewise, medicinal folklore has antidotes for scorpion and, snake-bites and alexipharmics. And this is what the practitioners of Islamic medicine have also said.
ii) Treatment by means of natural drugs enshrines thousands of years of experience and rather than refuting them scientific studies have confirmed their efficacy. We have the example of tamarisk.
iii) It has not been possible for us so far to investigate how the practitioners of Islamic medicine arrived at the idea of extracting salts from the ashes of certain plants. No doubt, one of the chief merits of wheat lies in the fact that, besides being a protein and vitamin source, it has magnesium, manganese, zinc, iron, and copper besides arsenic oxide present to the extent of 0.03 mg./ one kg. grains. *Sha'ir (Hordeum vulgare* Linn.) has 55 mg. of arsenic per 100 g. dry plant; these instances show that the presence of minerals is essential for proper metabilic functioning.

The extraction of mineral salts from plants may appear strange to Western science, but so mysterious are the workings of the human body that these salts inexplicably possess great therapeutic value.

Dr. Georg Hahn, who was head of the Organic Chemicals Division at the Karachi Laboratories of the Pakistan Council of Scientific and Industrial Research, carried out work under the guidance of Dr. Salimuzzaman Siddiqui, F.R.S., and submitted a report upon the composition of salts from *Tamarix* spp. which we have summarized in the foregoing paragraphs.

The minerals which we have obtained from *Tamarix* spp. and which may be regarded as a patent, has been obtained according to the traditional methods, but for the fact that for mass production we have had to introduce unit operations calling for large-scale design. We have yet to see whether these minerals act (a) by effecting some change in blood and curing jaundice; (b) by the enlargement of the bile duct, thereby removing or evacuating the bile; or (c) whether it acts as a bacteriostatic agent. We need to carry out pharmacological studies upon this point, and these studies we have not been able yet to carry out.

All that I can say here is that I have so far tried *Icterene* on about 5,000 jaundice patients and in not one patient have I been able to trace side toxic effects. It has no toxic effects, and I know for certain that allopathic practitioners have prescribed *Icterene* to patients in Karachi and elsewhere.

(iv) It is well-known that in control experiments upon animals, especially dogs, jaundice cannot be induced. When we therefore conduct *in vivo* experiments, we shall have to experiment upon human beings.

(v) The work on tamarisk gives rise to ta series of questions: How much work has been done on other plants in the manner of the work done upon *Tamarix* spp.? Where has such work been done or is being done? Who has done it? Not only are these questions important, but a far more important question is as to how many plants there are on the earth on which such work ought to be done for the well-being of the humankind. We have not even taken the trouble of identifying the plants described by the Masters comprehensively.

This point demands the full attention of scientists and chemists.

I would deem it a privilege if the scientists, chemists, and doctors, present at this representative gathering make this extremely effective and efficacious drug which is a product of ancient wisdom and modern research, an object of their deliberations.

I feel that, if the participants of this Conference, express their views about the possible mechanism through which this drug acts, we should be in a position to stimulate interest in Islamic medicine and the venues it opens for further research. We know, for example, that in modern Western therapy, mineral salts are gaining in importance and the objective is to administer mineral salts with vitamins in an absorbable form; we have the examples of ferrous fumarate and ferrous sulphate. Many salts like zinc sulphate act as potent antifungal agents; the same is true of certain sulphur compounds. Homeopathy, to a considerable extent and Biochemic almost, depend upon the administration of mineral salts. Perhaps *Icterene* through a biochemical process permits the evacuation of bile and promotes diuresis. Many other plants rich in minerals like radish also act as diuretic agents. Modern medicine employs citric acid compounds for diuresis in jaundice. Once the mechanism has been worked out, it might be possible to work upon other diuretic agents like water-melon and *Ribes nigrum* Linn., the latter being used as a diuretic and detergent in Germany. These are only two cross-examples. There are other plants which require investigations upon their diuretic properties and use in jaundice. I feel it sure that, if work is continued upon plant drugs, we should be able to come across many patent therapeutic agents from the Vegetable Kingdom.

There are thus infinite possibilities for drug research, which, so to say, has the sky as its limit.