SATELLITE SYMPOSIUM ON TRADITIONAL MEDICINE AS ADJUNCT TO ASIAN CONGRESS OF PHARMACOLOCY, 1985

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Thanjavur.

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EDITOR'S NOTE

It was a matter of great pride when Indian Pharmacologist Society selected Tamil University, Thanjavur to organise Satellite Symposium on Traditional Medicine as adjunct to Asian Congress of pharmacology that was held in New Delhi during January 1985. Prof. V. I. Subramoniam, Hon. Vice-Chancellor of Tamil University should be thanked for his immediate consent to host this Symposium at Tamil University and for the liberal financial support. Similarly Department of Science and Technology had agreed to support financially this Symposium and publication of the proceeding of the symposium. I am highly thankful to DST, New Delhi for its liberal financial support. I owe to a number of local companies (M/s Pharm Products, M/s. National Pharma. M/s Kamali Chemicals Thanjavur M/s. R & D Laboratories, Yercaud) and a number of other companies who willingly hosted lunch or dinner during this symposium. Tamil University is again thanked for arranging a nice Cultural programme of Bharathanattiyam by State Artist Miss. Swarnamugi. This programme was enjoyed by one and all. I must also thank scientists who showed overwhelming response to this Symposium and contributed a lot to this

symposium by presenting good papers. I will fail in my duty if I don't thank my colleagues and students who played a major role for the success of the symposium. I wish to thank individually my students Dr. S Somasundarm, Miss T.Chandra and Miss V.Thenmozhi. Mrs. S. Hazeena Begum, Mr. M. Jagadeesan and Mr. P. Surendrakumar are kindly remembered for their help in Proof reading Thiru Kovai Meykandasivam, Deputy Director of publication is also thanked for his sincere co-operation. Tamil University and DST, New Delhi are also thanked for their support in bringing out this publication I wish to thank M/s. Sarma's Sanatorium Press, Pudukkottai for their meticulous work. I wish that the papers found in the proceedings will be of use to the scholars who are working in the area of Traditional Medicine research.

(Sd)

J. Sadique

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ADDRESS TO THE SATELLITE SEMINAR

V. I. Subramoniam
Vice Chancellor, Tamil University, Thanjavur.

Delegates to the Satellite Seminar
Dean of Science Dr. Sadique,
and other friends,

It is my prime duty to welcome you all to the Seminar. Though our resources are limited, our earnestness in welcoming you to create an envoirnment for a fruitful dialogue, I assure will be impeccable. I welcome also the two Swedish delegates who have come from a long distance to attend this Seminar.

Many of you who are science-watchers should have noticed that India, especially Tamil Nadu, is re-discovering its past not only in literature, philosophy and the fine arts but also in the sciences. A vast country with glorious kingdoms in the past should have made a considerable contribution to the history of science.

Since all activities of human life are God-centred and later king-centred and since the king himself was conceived of as an incarnation of God, in all medieval kingdoms, medicine, to begin with, was temple-centred. And the mendicants, chiefly the Siddhars in Tamil Nadu, were the founders of a medicinal system called Siddha Medicine. They are eighteen in number, of which one is said to have been a Chinese in origin, and

another was an Egyptian by birth. The Dhanwantri the founder of Ayurvedha was also a Siddhar. Agastya, Bogar and others were noteworthy Siddhars of Tamil Nadu. Some of them were connected with the religious history of Tibet. Nagarjuna of the Madhyamika fame was considered to be a great healer of diseases in Tibet. Siddhars, by and large, livedi n the forest and mountainous regions, performed marvels of cure, enjoyed repute and later attained divinity. One of the few temples in India for Dhanwantry is in Kerala. Siddhars are worshipped in Tamil Nadu. Tanjore itself has the image of Karur-Siddhar. Palani, the famous Pilgrim centre has Bogar. The temples were repositories of the great medicinal secrets and gave curative medicine to the patients along with divine grace. Though diseases were less, I cannot say that all diseases were cured. Atleast some did have complete cures.

The Siddha mendicants had anatomical observation of dead bodies both human and non-human. When millions die in the battlefield, the bodies of the wounded and the slain were specimens for observation; and medicinal cure was determined by observing these bodies and administering to those who were alive.

Instead of statistics, the modern tool of measuring the effectiveness of medicine, observation played the decisive role. Operations were few, though instruments of operation are found here and there with descriptions. By modern standards, they were crude but served the purpose because treatment more than operation—except bonesetting—was resorted to. Body building, beautification, fertility etc. were looked into. Food restriction, exercise and massage were insisted upon. Selective food and eating after digestion were prescribed by Tiruvalluvar, the author of *Tirukkural*. Vegetarian food was his main theme which he insisted on because of religious proclivities. While general health of the subject was the main theme, the constant wars of kings and the use of animal power especially elephants, horses etc., for fighting, brought with it the need for cure of animals. Draught

animals used for ploughing and carrying load, also demanded medicinal cures. A body of knowledge arose for animal cures which were not the same as for man. Thus, man and animals were treated for their well-being. A vast body of knowledge had accumulated as family secrets and later as folk tradition.

The preservation of medicinal cures as famiiy secrets was the 'old patent' system and this primitive patent of secrets ensured continuity, to a large measure. The medicinal cures and later, with the dissolution of the family, some of the secrets also died down. We have the great task of reconstructing those medicines now.

This Seminar, I hope, will attempt this reconstruction so that the world of Medicine may know the great contribution of the Tamils which is less known.

SATELLITE SYMPOSIUM ON TRADITIONAL MEDICINE AS ADJUNCT TO ASIAN CONGRESS OF PHARMACOLOGY JANUARY 22 & 23 - 1985 AT TAMIL UNIVERSITY, THANJAVUR

REPORT

The Satellite Symposium on Traditional Medicine was conducted at the Guest House, New Campus, Tamil University during January 22 - 23, 1985 under the Chairmanship of Hon'ble Vice-Chancellor Prof. V. I Subramoniam, Tamil University. In his Presidential Address, Vice-Chancellor mentioned that Siddha system of medicine, even though it has an ancient past, has not been given due recognition by the British Regime. Siddha system of medicine is popular even among Singalese because it has a deep root with Buddhism. Unani Medicine has been initiated by Muslims and is also popular in India. Ayurvedic medicine is popular in Kerala. Even Allopathic doctors in Kerala, when they suffer from fever and other ailments, resort to Ayurvedic treatments. Both Ayurveda and Siddha have a common approach in the beautification processes. These systems have developed methods for promoting long hair growth and sweet scenting of the body. He further stressed that it is necessary to popularise the traditional medicine because of the cheap cost. Further, he emphasised that research on traditional medicine should be promoted with a view to promote health care of the common man. The inaugural lecture was delivered by Prof.

S. A. Vasawada, Gujarat Ayurved University, Jamnagar. In his address he suggested that health is important to lead a purposeful life. In India, the longevity is increased. So the problems concerned with ageing such as diabetes mellitus, cardiovascular diseases etc , have shown an increase and these problems should be tackled by promoting research on indigenous drugs. Both the Ayurveda and Siddha have discovered Kayakalpa rasayanas which promote longevity. This aspect should be also taken up for active research. The effect of the indigenous drugs on the diseases caused by environmental pollution and modern stresses should be also studied. He appreciated the experimental work being carried out in the Department of Siddha Medicine, Tamil University, Thanjavur. Prof. J. Sadique, Dean, Faculty of Sciences gave a welcome address and Dr. C. Srinivasan, Department of Ancient Sciences, proposed the vote of thanks.

There were one hundred participants from all over India and abroad. The Guest Lectures were delivered by Mrs. Qudsiya Gandhi. I. A S., Director of Indian Medicine and Homeopathy on "Health care delivery methods in Siddha Medicine" followed by other Guest Lectures. Prof. J. Sadique presented a lecture on "Review of research work on Siddha Medicine" carried out at Tamil University. Prof. S. N. Tripathi Banaras Hindu University, Varanasi, spoke on "An Introduction to Ayurvedic system of Medicine" Another lecture was delivered by Dr J. Joseph Thas. Government Siddha Medical College, Palayamkottai on "Oral antidotes for Cobra bite in Siddha medicine". There were altogether Nine Guest Lectures followed by presentation of scientific papers. These lectures were followed by interesting discussions. A Cultural Programme, Bharathanatyam was performed in the evening by Selvi B. Swarnamuki, State Artist, Government of Tamil Nadu. The first day dinner was hosted by Hon'ble Vice-Chancellor, Tamil University.

On 23rd Jan. 1985, 5 Guest Lectures and scientific papers were presented. Dr. S. A Vasawada, Gujarat Ayurved University, delivered a speech on "The Biochemical investigations in Ayurvedic preparations." The Guest Lecture of Thiru

M. K. Gomedhagavelu, I. A. S., Secretary and Commissioner, Department of Indian Medicine and Homeopathy, Tamil Nadu Government on "Development of Siddha Medicine Research" was read by Dr. V. Subramonian, Assistant Director of Indian Medicine. Dr. S. Rajamoni, Government College of Siddha Medicine, Palayamkottai gave a lecture and demonstration on "Varmam" in Siddha Medicine. Dr. Mohamed Abdullah, Sweden, presented a scintillating lecture on "Status of trace elements in health and diseases". The valedictory function was presided over by Prof. V. I. Subramoniam, Vice-Chancellor, Tamil University. He underlined the importance of the interaction of the Siddha doctors and Allopathy doctors to develop or improve Siddha system of medicine. The modern technology should be utilized in research activities. He stressed further that it is of utmost necessity to develop the mother tongue and that research should be oriented towards the improvement of the Nation. Prof. J. Sadique proposed the vote of thanks emphasising the need for multi-disciplinary research in the development of traditional medicine This symposium was jointly organised by Tamil University, Indian Pharmacological Society, Department of Science and Technology, International Union of Pharmacology and Indian National Science Academy.

EVOLUTION OF THE SIDDHA SYSTEM OF MEDICINE

Mrs. Qudsiya Gandhi

Medical Science was born since the day man was born. Through experience, he has learnt about the mysteries of his own body, the inter-relationship between his body and mind and the various sources which would keep his body and mind fit. It was through experimentation that man has enlightened himself about the various cures, methods and modes of treatments for the various ailments that mankind has been subjected to. His experimentation and testing were not confined to the four walls of a sophisticated laboratory room but the vast expanse of the Universe provided him the much needed objects and material for test and experimentation. Whatever truths he stumbled upon accidentally, he tested and retested them. Once the results were confirmed and verified he developed them into systems and theories. The Calcutta University Commission truly observes in its report "the ancient system of Medicine possessed an imposing treasure of empirical knowledge and technical achievements, which cannot be safely ignored even in these days of rapid progress".

The Indian Systems of Medicine also constitute one such ancient system of medicine based on ancient scientific knowledge of anatomy and chemistry and other biological sciences. Among the Indian Systems of Medicine, Siddha is the most ancient system which can be traced back to the pre-Vedic period. It was also born out of the great quest for knowledge of longevity. Through introspection and experimenta-

tion, the ancient Tamils evolved two ways by which man could achieve Mastery over Nature; one is the Yogic way and the other through Medicines.

Those who dedicated themselves to this task were themselves great Yogis known as *Siddhars*. Hence the system of medicine propounded and elucidated by them came to be known as the *Siddha Sytem of Medicine*.

" Siddhar is a Tamil word that is derived from its root " Chit " which means perfection in life or heavenly bliss. It generally refers to eight kinds of supernatural powers attainable by man. The persons who have attained such miraculous powers in life are known as Siddhars. Dawson's classical Dictionary of Hindu Mythology refers to them as ' belonging to a class of semidivine beings of great purity and holiness, dwelling in the regions of the sky between the earth and the sun".

"The earliest Medical treatise in Tamil was propounded by Sivanar (Siddhanar) who was the first to preside over the ancient first Tamil Academy. It was followed by a number of works of immortal Siddhars. According to tradition, Thirumular was the Head of the Siddhars.

The Ancient Siddha Medical Works

The earliest mention of the use of the Medicinal Plants is to be found in Thirumular *Thirumanthiram, Ennayiram, Tholkappiam* and the ancient Tamil works of *Sangam* Literature which are believed to have been written thousands of years before the dawn of the Christian era.

There are now more than 500 works in Tamil dealing with various subjects such as science of life, nature of universe, astronomical data, cosmic dance, atomic theory, space travel, alchemy, Kaya Kalpa, medicine etc., *Tholkappiam* (means 'ancient classic': 3000 BC) declares that amongst the Tamils, the class of people most honoured were the *Arivars* (Sages) who led a secluded and religious life outside the hustle and bustle of

urban life. As usual in those days they retired to the sylvan surroundings of the forests. We also learn from the records of the 12th century A.D., that *Sadhus* (Ascetics) travelled to Cape Comorin (Southern most tip of India) to bathe in the holy sea.

The Tamil system of medicine flourished while the Tamil Rajas were ruling the country. During the *Sangam* age, it was at its peak. According to the Tamil works on medicine, a physician can say at the mere sight of a man whether he was suffering from *bile, vayu or Silethumum.*

With the advent of foreign civilisation and language and their adoption by the people of the Country and the neglect of civilisation of this land, began an era of aversion and abhorrence for all that is native. This resulted in a great set back to the development of the language of the Country, thus rendering the love of study of the Science of the land and the enjoyment of its fruits a thing of the past. The scholarship in Tamil Medicine suffered as a result of insufficient recognition and reward. This led to the secrecy by the good scholars and practitioners in order to keep their income intact and stable. Moreover, forgetting that in Siddha and other Indian Systems of Medicine, medicines are prepared mainly from the products of the Country in which we are born and bred, and that these medicines wolud largely suit the temperament of the people of this Country, the people took to modern medicine which, along with quick and immediate relief, gave them side effects also which are detrimental to their very existence.

Gradually people are learning that this blind aping of Western culture is leading them nowhere. They are now again reclining back to Siddha and other systems of Indian Medicine. Meanwhile, Siddha is not dead. In spite of the availability of modern medical facilities, Siddha system is still

serving and healing millions of the rural population. Now it is gaining popularity even among the elite and the urban population.

I would not like to go into great details about the revival of the Siddha system, but wish to throw much needed light upon the efforts of the Government of Tamil Nadu to popularise Siddha.

As early as the year 1920, the Sir Usman Committee was formed to recommend appropriate steps by means of which the whole Indian Systems of Medicine could be given a new life. Accepting the recommendations contained in the report of the Usman Committee, the Government of Tamil Nadu started a Central College of Indian Medicine to impart formal eduction in Indian Systems of Medicine. Those who graduated from this College were awarded Licence in Integrated Medicine.

In 1964, this College was shifted to Palayamkottai, Tirunelveli District, where a 5½ year Bachelor's Degree course in Siddha Medicine was started. The course which started with an intake of 20 students is now admitting 100 students. So far about 500 students have graduated from this College.

In order to further develop this system, a 3 year post-graduate course in *Maruthuvam* and *Gunapadam* was started in this College itself, and at present we have about 50 post-graduates in Siddha. Government have further plans to extend graduation to other specialities like *Udalkoorugal* and *Noi-nadal, Udal Maruthuvam* etc.

Employment opportunities are promptly provided to the graduates and post-graduates in Siddha system. Similar is the case of the students of Diploma in Pharmacy, who undergo a 2 year course in Pharmacy to enable them to assist the doctors, in identification of raw materials, and preparation of medicines.

The Government have not confined themselves only to the provision of formal education in Siddha and other Indian Systems of Medicine. They have schemes for the hereditary practitioners of Siddha too. These hereditary practitioners are being registered as Rural Medical Practitioners, after they fulfil certain requirements. The Government are also running an Orientation Course for a select batch of RMP's in Siddha and giving them appointments in the rural dispensaries. An apex Board of Siddha Medicine has been formed with many of the members being RMP's. This Board is advisory in nature and gives the Government advice from time to time regarding various aspects of Siddha education and propagation.

As far as propagation and administration of Siddha System of Medicine are concerned, the Government in the year 1970 have formed a separate Directorate with the intention of promoting the speedy revival of the Siddha System of Medicine.

In the year 1984, in consonance with the Sir Usman Committee report, and on the advice of the Siddha Medical Board, the Government were pleased to segregate the Indian Medicine Department from the Health and Family Welfare Department to form a separate Department of Indian Medicine and Homoeopathy at the Secretariat level and have posted a separate Commissioner and Secretary for Indian Medicine. For this, the proponents and well-wishers of the Siddha system are indebted to the Hon'ble Chief Minister, Thiru. M. G. R., our Hon'ble Minister for Health Dr. H. V. Hande, and the Chairman of the Tamil Nadu Siddha Medical Board Thiru. K. A. P. Viswanatham.

Due to the efforts of the Tamil Nadu Government, now this State has Siddha wings in 220 PHC's and 103 Dispensaries in District and Taluk Headquarters and non-Taluk Hospitals. In 8 District Headquarters Hospitals, 25 bedded separate

buildings with Out-patient and In-patient facilities are available. In the rural areas, 21 Rural Dispensaries have been opened. The opening of Dispensaries and Siddha wings would continue till all the General Hospitals and Primary Health Centers have been covered and thus medicare for all is achieved.

As an incentive to students to take up Siddha Medicine Course, Government are awarding stipends to economically backward students. Very high stipends are being paid to post-graduate students also. Everything that is possible to attract students to study and practise this system of Medicine is being done.

To create an awareness among the public regarding the richness of Siddha Medicine, books are being published by translating *cudgeon leaves* and other ancient literature etc. The Siddha Medical Board has taken up the responsibility of printing, publishing and selling of Siddha Books. Government are also taking all steps to make available to the general public, medicines through shops which are now available through General Hospitals and Dispensaries.

But all said and done, two hands are needed to clap. The Siddha practitioners themselves and those who take up the study and practice of Siddha should take up all efforts to popularise this System. This can be attained only when the shroud of secrecy, cloak of jealousy and unhealthy competition are torn apart. I request them to be sincere to their studies and profession and show it to the world that they can also achieve what their forefathers had achieved.

My humble thanks are due to the Vice-Chancellor of the Tamil University, Thanjavur, Dr. V. I. Subramoniam and to Dr. J. Sadique for providing me this opportunity to share my thoughts with all of you.

REVIEW OF RESEARCH WORK ON SIDDHA MEDICINE CARRIED OUT AT THE TAMIL UNIVERSITY, THANJAVUR.

J. Sadique

The Department of Siddha Medicine was started two years ago. One year was spent in the establishment of the laboratory. I wish to present three different programmes of research that are being carried out in this Deparment. Being the first Department of Siddha Medicine that has been established for the first time in the University, we have undertaken research work on the basic aspects of Siddha drug preparations. The Siddha System of Medicine is an ancient system that utilizes various mineral preparations. For preparing a single *parpam* or *chenduram,* different methods are suggested in Siddha Literature. No one has so far established the superiority of one method over the other method, even though the same biological effect is exerted by a particular Siddha preparation prepared by different methods. So we have selected the *'chank parpam'* with a view to establish a suitable method in obtaining a therapeutically active preparation.

Methodology

Chanks of small variety were purified by immersing in lime juice for three days. The purified chank was immersed in (a) *Aloe vera* juice, (b) *Phyllanthus niruri* juice, (C) Lotus

leaf juice. The chank thus treated with herbal juice was calcinated using 10, 15, and 20 cowdung cakes. (1). The calcinated products were ground to a fine powder. The chemical parameters such as total calcium, soluble calcium and total alkalinity were estimated (2). These preparations were added to the plasma and mixed thoroughly so as to evaluate the biological activity of these preparations in the conversion of plasma fibrinogen to fibrin (3). Anti-ulcer activity ofthese preparations was tested in fasting albino rats using pyloric ligation method. The particle size of these preparations was also evaluated using stereo microscopic measurement.

Results and Discussions

From Table 1, it can be noted that the calcium content in chank increases nearly 2 fold after purification of chank with lime juice. Then the purified chank was calcinated using different numbers of cowdung cakes. This did not have any effect on the calcium content of the purified chank. When purified chank was calcinated along with different herbal juices, there was a small reduction in the content of total calcium. This might be due to combination of herbal juice with chank. The weight contributed by the ashes of herbal juice might reduce the value of the calcium content per unit weight of calcinated product. In all these cases, the increased heat treatment did not improve the total calcium content. From the Table. 2, it may be observed that the percentage of soluble calcium improves after increased heat treatment in case of purified chank. The highest value was found after calcination with 20 cowdung cakes. *Aloe vera* juice treatment also improves the contents of the soluble calcium after the increased heat treatment, but a remarkable increase has been noted in the case of *Phyllanthus niruri* and Lotus leaf juice treated preparations, when they were calcinated using 20 cowdung cakes. From these observations, it can be inferred that soluble calcium in *chank parpam* shows an increase after augmented heat treatment. Similarly, the total alkalinity

also improves after calcination with 20 cowdung cakes. This was noticed in all the chank preparations (Table 3). From Table 4, it can be noted that only the chank that was calcinated along with the lotus leaf juice caused the conversion of fibrinogen to fibrin in plasma. It has been suggested that the ionic calcium plays a key role in the process of coagulation (4). Such a change was not noticed in the case of the other chank preparations. Table. 5, indicates that chank preparation prepared with *Phyllanthus niruri* juice exerts maximal protection against ulcer formation produced by pyloric ligation. It is also able to reduce free and total acid levels. Gastric volume is also considerably reduced in comparison to other preparations treated groups. Further, the particle size of various preparations was studied using optical Michel stereo microscope (W. Germany model Ultra phot III BM). It can be noted that the particle size goes down after purification with lime juice (Table 6). When purified chank was calcinated using different herbal juices, there was an improvement in the particle size in the chank preparations. The maximal increase in size was noted in the lotus leaf juice treatment. Moreover in Siddha literature, it is cited that chank parpam is *styptic* (1). The styptic action is due to free ionic calcium. From all these observations the following may be concluded.

1. The lotus leaf juice treatment in the preparation of chank parpam confers bio-potentiality for chank, for styptic action.

2. *Phyllanthus niruri* juice treatment confers anti-ulcer activity for chank preparation.

3. The increased heat treatment did not confer increased potency to chank parpam. So, it may be recommended that the chank parpam with therapeutical potentials can be prepared using the heat out of 10 cowdung cakes.

Screening of anti-inflammatory activity of Siddha drugs

Latiff *et al.* (5) have observed that it is no exaggeration to say that traditional medicine is currently the only means of giving health care to about three quarters of the population of the world, and plants are by far the most important therapeutic agents. Eventhough synthetic steroidal and non-steroidal anti-inflammatory agents are available, the toxic effects of these drugs are grave and they are also not able to prevent the damage in connective tissues in human rheumatoid arthritis. Long acting anti-inflammatory agents that will cure human rheumatoid arthritis are not yet discovered. So it has become imperative to screen Siddha herbal and compound preparations for anti-inflammatory activity, with the hope that one of them may prove to be useful in ameliorating the syndromes of rheumatoid arthritis permanently. In addition, such a search may provide valuable models for new classes of anti-inflammatory activity in both acute and chronic phases of inflammation.

Methodology

Carrageenin inflammation was produced by injecting 0.1 ml of 2% carrageenin per 100 gm. body weight into the subplantar region of hind paw (6). The swelling was measured at different intervals of time by the mercury displacement method (7). The different drugs were suspended in 2% gum acacia solution and they were administered orally 24 hrs and 1 hr before the injection of carrageenin. The percentage of A. I. activity of the drugs was calculated from the volume of edematous legs of control and drugs treated carrageenin induced inflamed rats. The A. I. activity was also compared with standard drug phenylbutazone.

Results and Discussion

From Table 7–11, it can be noted that a number of drugs were able to inhibit edema at different periods of time.

Carrageenin inflammation is an acute inflammation having 3 phases connected with the release of different mediators (8). The first phase (1hr. after carrageenin inflammation) is said to be promoted by histamine. The second phase is associated with the kinin (2½ hr. phase). The last phase (5½hr) is associated with the release of prostaglandins (8). So the swelling measurements have been made in all the three phases with a view to understand which phase of inflammation is being suppressed by the drug. It can be noted from Table 7, that *Enicostemma littorale*. Blume at a dose of 300mg/100gm b. wt. is able to suppress edema to more than 50%, the kinin and prostaglandin phases of inflammation. It has got a weaker activity in the histamine phase. Similarly *Gynandropsis gynandra* is able to suppress all the three phases of inflammation effectively at a dose of 200 mg/100gm b. wt. The leaves of *Cassia tora* exhibit maximum A. I. activity in prostaglandin phase at a dose of 200 mg/100 gm b. wt. like *Aloe vera* juice.

Phenylbutazone at a dose of 10 mg/100 gm b. wt. is able to control effectively all the three phases of inflammation upto 70%. *Phyllanthus niruri* and Nagaparpam showed less than 20%. A. I. activity. Ayaveeram, root bark of *Cassia tora* and *Convolvulus tridentatus* did not show any activity. From these results it is understandable that *Gynandropsis gynandra*, *Enicostemma littorale* are promising herbal drugs with significant A. I. activity.

The long time anti-arthritic activity of *Withania somnifera*

The increasing incidence of arthritis and inadequacy of the present day drug therapy underline the need to improve the technical feasibility of discovering safe and effective anti-arthritic drugs. Although there is no ideal animal model to rheumatoid arthritis, the similarities of the human rheumatoid arthritis (9) and the sensitivity of adjuvant arthritis in rats to anti-arthritic agents make it the best availabl e n c c c l

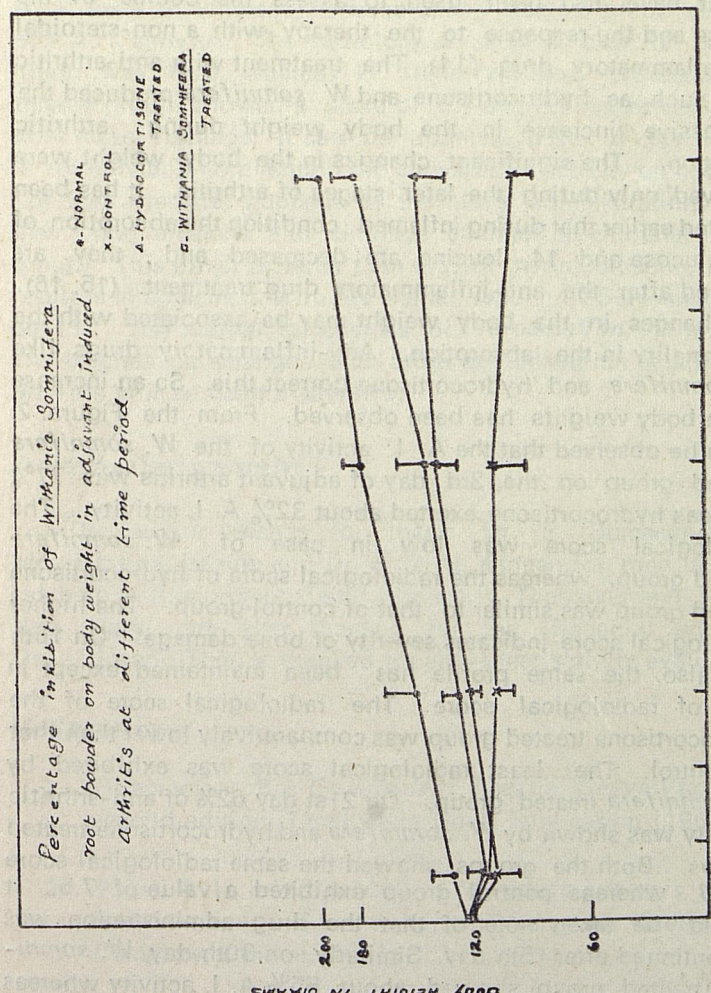
rheumatoid arthritis and the nearest approximation to rheumatoid arthritis (10). *Withania somnifera* which belongs to Solanecea family is being used for human rheumatoid arthritis in the Siddha system of medicine (11). So this drug was chosen for studying anti-inflammatory activity as well as the long term effect in adjuvant induced arthritis.

Methodology

The anti-inflammatory activity was assessed using carregeenin edema (6). The optimal dose was also determined using the above method. Adjuvant induced arthritis was induced by injecting 0.1 ml complete Freund's adjuvan containing the suspension of 10mg heat killed *Mycobacterium tuberculii* per ml of sterile liquid paraffin. The volume of edema was measured on 3rd, 15th, 21st, 30th and 49th day of adjuvant induced arthritis. The secondary lesions appeared on about 14th day after the injection of Freund's complete adjuvant. The *W. Somnifera* was administered orally to a group of rats from one day before the induction of adjuvant arthritis. A standard drug hydrocortisone at a dose of 1.5 mg/ 100 gm. b. wt. was also administered orally. Control group received 2% gum acacia solution. All the drugs were administered orally and continued up to 15 days from the day of Freund's adjuvant injection. Then the drug administration was discontinued. The weights of the rats were checked at different intervals up to 49th day. The anti-inflammatory activity was assessed periodically using arthritic score method (12). The radiological score was also measured periodically using different degrees of bone degenerative changes (13).

Results and Discussions

From the Table (12) it can be understood that the maximal A I. activity was found to be exerted at a dose of 100 mg/100gm body weight of *W. Somnifera*. So this dose was selected for treating adjuvant arthritis. From Fig. 1. it can be observed that the changes in body weights of rats in which the incidence


Percentage inhibition of Withania Somnifera root powder on body weight in adjuvant induced arthritis at different time period.
●-NORMAL
×-CONTROL
▲-HYDROCORTISONE TREATED
□-WITHANIA SOMNIFERA TREATED
BODY WEIGHT IN GRAMS
TIME IN DAYS
200
180
120
60
5
10
15
20
25
30
35
40
45
50

and severity of arthritis were greater during the course of the experimental period, were maximal. The changes in the body weight have also been used to assess the course of the disease and the response to the therapy with a non-steroidal anti-inflammatory drug (14). The treatment with anti-arthritic drugs such as hydrocortisone and *W. somnifera* produced the progressive increase in the body weight during arthritic condition. The significant changes in the body weight were observed only during the later stages of arthritis. It has been reported earlier that during inflamed condition the absorption of 14_C-glucose and 14_C-leucine are decreased and they are restored after the anti-inflammatory drug treatment. (15, 16). So changes in the body weight may be associated with the abnormality in the absorption. Anti-inflammatory drugs like *W. somnifera* and hydrocortisone correct this. So an increase in the body weights has been observed. From the Figure. 2. it can be observed that the A. I. activity of the *W. somnifera* treated group on the 3rd day of adjuvant arthritis was 77% whereas hydrocortisone exerted about 32% A. I. activity. The radiological score was low in case of *W. somnifera* treated group, whereas the radiological score of hydrocortisone treated group was similar to that of control group. The higher radiological score indicates severity of bone damage. On 15th day also, the same profile has been maintained except in case of radiological score. The radiological score of the hydrocortisone treated group was comparatively lower than that of control. The least radiological score was exhibited by *W. somnifera* treated group. On 21st day 62% of anti-arthritic activity was shown by *W. somnifera* and hydrocortisone treated groups. Both the groups showed the same radiological score of 2.7 whereas control group exhibited a value of 7.5. It should be taken note of that the drug administration was discontinued after 15th day. Similarly, on 30th day, *W. somnifera* treated group showed about 85% A. I. activity whereas hydrocortisone treated group showed an A. I. activity of 54%. The radiological score of *W. somnifera* was only 2.8 whereas the radiological score of hydrocortisone treated group was 8.7. Control group showed a value of 18.5. On 49th day after

Freund's injection, *W. somnifera* treated group showed 70% A. I. activity whereas hydrocortisone treated group showed 55% A. I. activity. The radiological score in case of control group was 17.5, whereas *W. somnifera* and hydrocortisone treated group showed a score of 5.7 and 8.8 respectively. So from these findings, it can be understood that *W. somnifera* is not only able to maintain the anti-arthtric activity on 49th day (29 days after the stoppage of the drug administration) but also bone erosions and cartilage changes are minimal in this group. This effect is better than that of hydrocortisone. This result is in agreemenr with the earlier report of Somasundaram on the flavonoidal glycosides of *Clerodendron inerme* (17). The biochemical changes with drugs administration in adjuvant arthritis will be dealt elsewhere.

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TABLE: 1. PERCENTAGE OF CALCIUM CONTENT IN CHANK

S. No.	Description	No. of Cowdung cakes		
		10	15	20
1	Plain Chank	65.8	67.2	66.9
2	Aloe juice treated	57.7	56.8	58.5
3	*Phyllanthus niruri* juice treated	59.9	57.1	58.4
4	Lotus leaf juice treated	56.6	57.4	55.9

Calcium content in raw chank = 37.3%

TABLE: 2. PERCENTAGE OF SOLUBLE CALCIUM

S. No.	Description	No. of Cowdung cakes		
		10	15	20
1	Plain Chank	31.2	41.7	47.0
2	Aloe juice treated	27.9	36.8	47.2
3	*Phyllanthus niruri* juice treated	11.0	32.8	43.0
4	Lotus leaf juice treated	7.39	13.1	30.9

TABLE : 3. PERCENTAGE OF TOTAL ALKALINITY

S. No.	Description	No. of Cowdung cakes		
		10	15	20
1	Plain Chank	9.9	17.1	31.8
2	Aloe juice treated	9.9	15.9	28.9
3	*Phyllanthus niruri* juice treated	2.9	17.1	24.9
4	Lotus leaf juice treated	2.9	4.1	11.8

TABLE : 4. THE BIOLOGICAL ACTIVITY OF CHANK PREPARATION IN THE CONVERSION OF FIBRINOGEN TO FIBRIN

S. No.	Description	The fibrin precipitated		
		10	15	20
1	Plain Chank	—	—	—
2	Aloe juice treated	—	—	—
3	*Phyllanthus niruri* juice treated	—	—	—
4	Lotus leaf juice treated	++	++	++

TABLE : 5. **ANTI–ULCER STUDIES (CHANKU PARPAM)**

S.No.	Drug	Dose/ animal	% Degree of ulceration	pH	Volume of gastric juice (in ml)	Free Acid (in clinical units	Total Acid
1.	Water (pH 7.1)	0.5 ml	100	7.88	3.0	3	6
2.	Chanku parpam (pH 10.33) (Crude chank)	50 mg in 0.5 ml water	120	7.9	6.75	2	4
3.	Chanku parpam (purified) (pH 8.94)	–do–	70	5.6	5.0	2	5
4.	Chanku parpam (*Aloe vera* juice) (ph 8.94)	–do–	110	6.2	5.75	2	6
5.	Chanku parpam (*Phyllanthus niruri*) (pH 9.18)	–do–	56	7.5	3.75	0	2
6.	Chanku parpam (Lotus leaf juice) (pH 8.48)	–do–	84	7.62	5.0	3	8

The purified chanks were treated with juices as indicated in brackets. They were calcinated using 20 cowdung cakes.

TABLE: 6. DETERMINATION OF PARTICLE SIZE OF CHANK AND ITS PARPAMS

S. No.	Description	Particle size in μm
1	Raw Chank	6.3
2	Purified Chank	3.6
3	*Aloe vera* juice treated chank parpam	4.8
4	*Phyllanthus niruri* treated chank parpam	7.0
5	Lotus leaf juice treated chank parpam	8.9

TABLE: 7. THE ANTI—INFLAMMATORY ACTIVITY OF ENICOSTEMMA LITTORALE BLUME IN RATS' CARRAGEENIN PAW EDEMA

Dose in mg/100 g.b.w.	% Anti-inflammatory activity		
	1 hour	$2\frac{1}{2}$ hour	$5\frac{1}{2}$ hour
50	29.3	36	53
100	21.3	42	54
200	10.5	27	46
300	17.3	54	51

TABLE : 8. THE ANTI-INFLAMMATORY ACTIVITY OF GYNANDROPSIS GYNANDRA IN RATS' CARRAGEENIN PAW EDEMA

Dose in mg/100 g.b.w.	% Anti-inflammatory activity		
	1 hour	2½ hour	5½ hour
50	—	—	—
100	61	33.5	30
200	44	50	49

TABLE: 9. THE ANTI-INFLAMMATORY ACTIVITY OF THE LEAVES OF CASSIA TORA IN RATS' CARRAGEENIN PAW EDEMA

Dose in mg/100 g.b.w.	% Anti-inflammatory activity		
	1 hour	$2\frac{1}{2}$ hour	$5\frac{1}{2}$ hour
50	15.4	23	42
100	23	5	33
200	15	23	42

TABLE: 10. THE ANTI—INFLAMMATORY ACTIVITY OF ALOE VERA JUICE AND PHENYLBUTAZONE IN RATS' CARRAGEENIN PAW EDEMA

	Drug	Dose	% Anri—inflammatory activity		
			1 hour	$2\frac{1}{2}$ hour	$5\frac{1}{2}$ hour
1	*Aloe vera* juice	1 ml/100 g.b.w.	29.7	22.4	31.5
2	Phenylbutazone	10 mg/100 g.b.w.	69.3	70.0	75.0

TABLE: 11. OTHER SIDDHA DRUGS THAT HAVE BEEN SCREENED FOR ANTI-INFLAMMATORY ACTIVITY IN RATS' CARRAGEENIN PAW EDEMA

Drugs that show less than 20% anti-inflammatory activity	No anti-inflammatory activity
1. *Phyllanthus niruri*	3. Aya veeram
2. Naga parpam	4. Root bark of *Cassia-tora*
	5. *Convolvulus tridentatus*

TABLE : 12. EFFECT OF WITHANIA SOMNIFERA ROOT POWDER ON CARRAGEENIN INDUCED RAT PAW EDEMA AT DIFFERENT TIME INTERVALS (PERCENTAGE INHIBITION)

Subject	Drug dose mg/100 g.b.w.	1 hr	2 hr	$5\frac{1}{2}$ hr
Withania somnifera treated (crude powder)	100	14.2	26.6	34.0
	150	42.5	7.0	3.0
	200	35.0	15.0	16.0
Hydrocortisone	1.5	42.0	39.0	33.3

TABLE: 13 ANTI-ARTHRITIC ACTIVITY OF W. SOMNIFERA

Days	Group	Dose mg/100 g.b.w	Radiological score	Percentage of anti-arthritic activity Based on Radiological score	Arthritic score
				%	
3rd day	Arthritic group		3.0 ± 0.25	—	
	Hydrocortisone	1.5 mg	2.0 ± 0.21	33.0	
	W. somnifera	100.0 mg	0.7 ± 0.06	76.6	
15th day	Arthritic group		4.2 ± 0.55	—	—
	Hydrocortisone	1.5 mg	2.5 ± 0.32	40.5	48.5
	W. somnifera	100.0 mg	0.92 ± 0.05	78.1	72.0
21st day	Arthritic group		6.5 ± 0.61	—	—
	Hydrocortisone	1.5 mg	2.5 ± 0.28	62.0	
	W. somnifera	100.0 mg	2.5 ± 0.21	62.0	
30th day	Arthritic group		18.8 ± 2.02	—	—
	Hydrocortisone	1.5 mg	8.6 ± 0.62	54.3	32.0
	W. somnifera	100.0 mg	2.25 ± 0.15	88.0	66.0
49th day	Arthritic group		17.5 ± 1.46	—	—
	Hydrocortisone	1.5 mg	8.2 ± 0.75	53.0	51.0
	W. somnifera	100.0 mg	5.3 ± 0.56	70.0	88.0

BIOCHEMICAL INVESTIGATIONS ON AYURVEDIC PREPARATIONS

S. A. Vasavada*

Ayurveda is one of the oldest medical sciences in vogue in our country and this system of medicine utilises indigenous drugs of either plant, animal or mineral origin for the treatment of diseases. An extensive pioneering research work on several indigenous drugs has been carried out during the last 50 years in our country by eminent scientists like Dr. Chopra and others, possibly with a view to obtain therapeutically effective compounds. It would be relevant to remember that quite a few compounds like Digitalis Glycosides, Morphine, Atropin etc. obtained from indigenous medicinal plants are still used effectively in the allopathic system of medicine. Hence the wealth of the indigenous medicinal plants is still being explored all over the world for getting effective drugs.

At the same time, the life sciences have witnessed tremendous progress during the last 30 years and considerable knowledge about the life processes in the living organisms has been acquired. It has also revealed important information about the normal human physiology as well as the pathophysiology of several diseases. Biochemistry has apparently played an important role in these developments.

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One of the remarkable features of these developments is the evolution of new research techniques as well as the reliable and specific methods of investigations like enzyme assays, immuno-electrophoresis radio-immunoassay techniques etc. Such techniques are now advantageously utilised for the evaluation of the efficacy and mode of action of drugs. The indigenous drugs can also take advantage of such developments for gathering the necessary knowledge for a similar purpose.

A review of the previous work indicates that most of the research on indigenous drugs was undertaken to investigate their pharmacognosy, phytochemistry or pharmacology. Similarly the clinical evaluation of some wellknown drugs has also been carried out in the past. It therefore appears that most of the investigations were undertaken with a view to obtain pharmacologically effective compounds from the indigenous medicinal plants or to establish their therapeutic efficacy. Such efforts have however met with a limited success, since only a few compounds obtained from the indigenous medicinal plants viz. Reserpine, Carbenoloxone, Berberine etc. could find use as therapeutic agents in recent times.

Inspite of these limitations, the previous studies have been found to be very useful as considerable information about a number of indigenous drugs has been collected. At the same time, it has been realised that a collaborative research involving several disciplines of biomedical sciences, instead of isolated or individual attempts, will prove to be benificial for research on the indigenous drugs.

The research work at the the Institute of Post-Graduate Teaching & Research, Gujarat Ayurved University, Jamnagar, is preferably carried out on similar lines. The data of some such studies carried out at the Institute are presented in this paper.

1. Panchamritaparpati Kalpa :

This preparation contains mercury and sulphur (as sulphides), Lauha bhasma, Tamrabhasma and Abhrakabhasma. It

is used for the treatment of patients suffering from Grahani (Diarrhoea). It is administered in an increasing dose of 400 mg. each per day for 11 days and the dose is similarly decreased upto 21 days. One of the main objections to the use of such preparation is the toxicity of mercury compounds, and hence various biochemical as well as pathological investigation were undertaken on patients treated with this preparation. The results are tabulated in Table no. I.

Table no. I indicates that the various liver function tests viz. serum bilirubin, alkaline phosphatase, total proteins, S. G. O. T., S. G. P. T. as well as the blood urea levels do not show any significant changes during the course of the treatment. Similarly, it was noticed that the urine and blood samples did not show any abnormal findings during the pathological examination. Thus it appears that the drug does not seem to produce any undesirable toxic effects on the liver or kidney. Later followup studies also did not reveal any toxic effects.

II. Studies on Haridra *(Curcuma longa Linn)* :

Haridra *(C. longa)* is commonly used in Ayurvedic practice as an anti-inflammatory agent. The drug, its petroleum ether extract and curcumin, a phenolic derivative isolated from the drug-has been found to possess anti-inflammatory, anti-allergic, anti-histaminic and anti-serotonin activities during the pharmacological screening. (1, 2, 3,) The present study was undertaken to find out whether the drug possesses any of the side effects, like gastric discomfort, peptic ulceration, disturbance of electrolyte pattern or alteration of metabolism of carbohydrates, proteins or fats similar to those reported for the present day anti-inflammatory drugs of either steroidal or nonsteroidal origin(4).

The effect of the administration of 16 gms. Ghritabhrishta Haridra to the patients during clinical trials is presented in Table no. II. It is seen that the levels of most of the serum electrolytes, except those of sodium, are not affected even after a treatment

period of 30 days. Similarly, the 24 hours urinary 17-ketosteroids levels do not show any significant change. This estimation was undertaken to find out the mode of action viz. stimulation of adrenal-cortical secretions. Such a possibility is ruled out in the present study.

The drug, however, showed a mild hypoglycaemic action in the patients.

III. Role of Mandookaparni (*Hydrocotyle asiatica Linn.*) as Rasayana Dravya ;

This drug is one of the well known Rasayana Dravyas in Ayurveda. Such drugs are used for the rejuvenation therapy to retard aging processes. A study was, therefore, conducted on healthy volunteers and the drug was administered at the dose level of 1 gm. T. D. S. for 30 days. The effect of the drug on clinical, pathological and biochemical parameters was assessed.

The pulse rate, blood pressure, breath holding time, immediate memory score and mental fatigue score showed significant improvement. The haemoglobin and E. S. R. levels were also similarly affected.

The biochemical investigations are presented in Table no. III. It can be observed that serum proteins and cholesterol levels as well as 24 hours urinary nitrogen excretion values do not show any significant change after drug treatment. The immunoglobulins, viz. Ig G and Ig M levels have shown a significant increase, while Ig A levels are not affected by the drug treatment. The results seem to indicate that the property "Vyadhikshamatva" (resistance to a disease), as ascribed to Rasayana drugs could be due to increased levels of immunoglobulins, which are responsible for the natural immunity.

IV. Antiulcer activity of Udumbar (*Ficus racemosa Roxb*) :

Udumbar is recommended for the treament of woudns and ulcers in Ayurveda, since it is considered to promote the healing

process ([5]). It is also used internally as one of the ingredients of a compound preparation for the treatment of diabetes mellitus. Hence the drug was screened for antiulcer activity in experimentally induced acute gastric ulcers in laboratory animals.

The effect of the drug treatment evaluated on acute gastric ulcers induced either by aspirin (6), pyloricligation (7) or stress (8) in rats or by injection of histamine in guinea pigs (9). The drug was found to possess a remarkable anti-ulcer activity in all the experiments.

The effect of the drug on the gastric juice could however be assessed only in pyloric-ligated or histamine induced ulcers on account of the availability of sufficient quantity of gastric juice. The drug was administered to the animals at the dose level of 20 mg/100 gms, 1/1-2 hours before pyloric-ligation or histamine injection to allow sufficient time for its aborption and also to prevent local action.

The results of drug treatment on gastric juice collected from pyloric-ligated rats are given in Table no. IV-A. It can be seen that the ulcer index is considerably reduced, but the gastric juice volume is not affected by the drug treatment. Similarly, the peptic activity is also not affected in drug treated animals. However, the drug decreases the secretion of hydrochloric acid, as can be seen from the significant lowering of the free as well as total acidity of the gastric juice of treated animals. At the same time the hexosamine levels, indicative of the mucopolysaccharide content, are significantly elevated in the treated group of animals.

Almost similar observations are available in case of histamine induced ulcers in guinea pigs, as can be seen from Table no. IV-B.

Thus the antiulcer activity of the drug appears to be associated with an increased secretion of mucopolysaccharide for their protective action against ulcers and also with the decreased

secretion of hydrochloric acid. An increased secretion of hydrochloric acid may be responsible for the aggravation of ulcers.

The results presented in Tables IV-A and IV-B also indicate that the drug has a systemic action, since the administration by both oral as well as subcutaneous route has been found to be effective.

The antisecretory effect of the drug on the gastric juice is presented in Table no. V. Here also the drug has shown a similar action i.e., a significant decrease in the hydrochloric acid secretion of the gastric juice, without significantly affecting the gastric juice volume.

V. Role of Tapyadi Lauha in Pregnancy anaemia:

Tapyadi Lauha contains Swarnamakshik, Roupya, Lauha and Mandoor bhasmas along with Shuddha shilajit and 14 powdered drugs of plant origin. In a previous study carried out in this Institute, it was found that Lauha bhasma is not effective in improving the haemoglobin levels of the patients suffering from Pandu (anaemia). Hence the drug was administered in the form of 2 pills (500 mgs. each) T. D. S. to pregnancy anaemia patients in the present investigation to study its effect. Various haematological investigation, as well as the total serum iron binding capacity, were estimated in the patients after 30 days of treatment.

The various pathological investigations indicated that the different haematological investigations, haemoglobin %, R.B.C. and W.B.C. count, PCV, ESR, etc. did not show any change after the treatment with the drug. The serum total proteins as well as albumin and globulin levels were also not affected.

The total serum iron binding capacity, given in Table no. VI, on the other hand, shows a significant increase. These findings indicate a possibility of increased transferrin levels. However, the results also indicate that the absorption of iorn

from Tapyadi Lauha is negligible, since the total iron binding capacity of the serum has increased, while the haemoglobin levels of the blood have not increased simultaneously.

V. Studies on hypoglycaemic drugs:

The indigenous medicinal plants, used in Ayurvedic practice for the treatment of Diabetis mellitus, have received considerable attention from a large number of scientists in our Institute for their hypoglycaemic action.

The data on two drugs viz. Udumbar (*F. racemosa*) and Dravyadi Quath are presented here.

The hypoglycaemic action of Udumbar was evaluated in rats according to the method described by Maha et al ([10]) The results are presented in Table no. VII. The purpose of these data is to show the application of Friedman's Test for the statistical evaluation of results, wherein the blood sugar values are given numerical ranks. The advantage of this test is a quicker evaluation of data. The aqueous extract of udumbar has obviously shown a hypoglycaemic action, which is significant at 5 % level.

The results of the treatment of the diabetic patients with Dravyadi Quath, prepared from a mixture of Daruharidra *(Berberis aristata DC)*, Devdaru *(Cedrus deodara Loud)*, Haritaki *(Terminalia chebula Ritz)*, Amalaki *(Emblica officinalis Gaetrn)* Bibhitak *(Terminalia belerica Roxb)* Musta *(Cyperus rotundus Linn.)* and Vishala *(Cucumis trigonus Roxb.)* along with Sheelajitvadivadi are given in Table no. VIII. It can be seen that glucose tolerence test was carried out on patients before and after 30 days of drug treatment. The results appear to confirm the hypoglycaemic action of the drug, but the blood sugar values remain at higher levels indicating that the dose of the drug is insufficient and there is a potential danger.

The main purpose of presenting these data is however quite different i. e., to point out a fallacy in the approach to the

present study, since the investigation of G. T. T. during the drug treatment in the diabetic patients may not indicate the correct position regarding the control of blood sugar levels because a heavy dose of glucose is administered to the patients during this test. Obviously, the fasting and post-prandial levels will always be a better guide for the assessment of the efficacy of hypoglycaemic drugs during clinical trials.

As stated in the earlier part of this paper, a collaborate research work by the different scientific disciplines of the bio-medical science will be useful in the enhancement of the knowledge on the indigenous system of medicine, since even the WHO feels that the developing and under developed countries could get benifit of their services for the promotion of positive health. at the same time any research on the indigenous systems of medicine will have to take into consideration the basic difference in the fundamental principles of the practice of allopathic and indigenous systems of medicine.

One of the basic difference relates to the use of either crude drugs or crude preparations for the treatment of a disease. It is necessary therefore to evaluate the efficacy or the mode of these drugs in the form in which they are prescribed. This approach is based on the theory that a crude drug or preparation contains a number of compounds which act jointly rather than singly and thus become effective. A possibility also exists that a compound may retard or suppress the toxic side effects of the other when used in combination.

As far as the role of biochemistry in the investigations on the indigenous drugs is concerned, it may be stated that this science is continuosly developing. The newer developments are bound to have a profound effect on the future evaluation of the indigenous systems of medicine, since all the scientists engaged in such endeavours have one goal i.e., the evolution of a global medicine for the attainment of "Health for all by 2000 A.D.".

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TABLE: I BIOCHEMICAL INVESTIGATIONS IN PATIENTS TREATED WITH PANCHAMRITAPARPATI KALPA

	Initial	12th day	21st day
Serum Bilirubin	0.41 ± 0.22	0.53 ± 0.20	0.49 ± 0.26
Serum Alkaline phosphates	8.08 ± 2.39	10.60 ± 3.44	8.54 ± 2.46
Serum Total proteins	7.45 ± 0.95	7.42 ± 1.21	7.71 ± 0.64
Serum Albumin	4.51 ± 0.48	4.43 ± 0.55	4.73 ± 0.34
S G O T	17.4 ± 8.72	16.3 ± 5.31	13.4 ± 9.02
S G P T	18.5 ± 14.3	24.3 ± 7.0	15.6 ± 8.5
Blood Urea	39.6 ± 8.99	38.6 ± 11.4	32.7 ± 18.7

TABLE II: EFFECT OF GHRITABHRISTA HARIDRA ON SERUM ELECTROLYTES & URINARY 17-KETOSTEROID LEVELS

	Before treatment	After treatment	t	p
Sodium (m.eq./litre)	132.3 ±2.98	124.8±2.66	4.44	<0.05
Potassium (m.eq./litre)	4.85±0.77	4.49±0.69	1	Insignificant
Calcium (mg/100ml)	10.42±0.73	10.21±0.70	1	"
Chloride (m.eq./litre)	100.7 ±3.05	99.16±2.49	1	"
Phosphate (mg/100 ml)	3.65±0.59	3.65±0.36	1	"
17-ketosteroid	12.78±9.5	11.36±6.82	1	"

TABLE III: EFFECT OF MANDOOKPARNI (*HYDROCOTYLE ASIATICA*) ON SOME BIOCHEMICAL PARAMETERS

	Before treatment	After treatment	t	p
Serum Cholesterol (mgs/100 ml)	222.0	212.2	1.16	Insignificant
Serum Proteins (gm %)	7.79	7.74	<1	,,
Urinary Nitrogen (gm/24 hrs)	3.14	3.39	<1	,,
Serum Immuno globulins(Iu/ml)				
Ig A	152.0	170.7	1.94	,,
Ig G	200.0	211.0	2.68	<0.05
Ig M	193.8	226.2	3.63	<0.01

Only mean values are given.

TABLE IV - A EFFECT OF AQUEOUS EXTRACT OF FICUS RACEMOSA ON GASTRIC JUICE. *(PYLORIC - LIGATED ULCERS)*

	Control	Treated	
		Oral	Subcutaneous
Ulcer Index	17.86	1.98	4.33
Volume (ml/100 g)	3.94 ± 0.64	3.84 ± 0.60	2.86 ± 0.42
Acidity (m.eq / litre)			
Free	47.7 ± 4.8	24.0 ± 8.3*	20.8 ± 7.7**
Total	109.2 ± 8.6	91.4 ± 20.7	65.0 ± 7.1**
Peptic Activity (u./ml./15 min.)	12.9 ± 2.6	16.3 ± 3.7	14.2 ± 0.6
Hexosamine (mg/100 ml)	18.18 ± 1.08	95.2 ± 29**	54.85 ± 6.1**

(Dose = 20 mg/100 g)

* = $P < 0.05$; ** = $P < 0.01$

TABLE IV - B EFFECT OF AQUEOUS EXTRACT OF *FICUS RACEMOSA* ON GASTRIC JUICE. (*HISTAMINE-INDUCED ULCERS*)

	Control	Treated (Oral)
Ulcer Index	19.0	8.2
Volume (ml/100 g)	0.84 ± 0.18	0.53 ± 0.12
Acidity (m.eq./litre)		
Free	63.0 ± 7.4	35.7 ± 5.8*
Total	101.6 ± 14.6	73.8 ± 10.7
Peptic Activity (u./ml/15 min)	4.3 ± 0.6	3.08 ± 0.3
Hexosamine (mg/100 ml)	27.2 ± 5.7	44.9 ± 8.6*

* = $P < 0.05$

TABLE V: ANTISECRETORY ACTIVITY OF THE AQUEOUS EXTRACT OF *FICUS RACEMOSA*

Treatment	Volume of Gastric juice (ml/100 g)	*Acidity = (m.eq./litre)*	
		Free	Total
Control	1.05 ± 0.42	19.1 ± 2.36	70.0 ± 8.6
Treated (20mg/S.C.)	0.6 ± 0.16	5.6 ± 2.3**	43.6 ± 6.8*

(* = P <0.05; ** = P <0.01)

TABLE VI: EFFECT OF TAPYADI LAUHA ON THE SERUM TOTAL IRON BINDING CAPACITY IN PREGNANCY ANAEMIA PATIENTS.

	Serum Iron Binding Capacity (mg/100 ml)
Before Treatment	309.4
After Treatment	464.6
*Mean Difference	±155.2
S. D.	±200.0
S. E.	±52.0
t	2.98

(*=P <0.01)

TABLE VII: EFFECT OF AQUEOUS EXTRACT OF *FICUS RACEMOSA* ON THE BLOOD SUGAR LEVELS (FRIEDMAN'S TEST)

Interval	Blood Sugar level (mg/100 ml) Mean values
0 hr	90.07
1 hr	82.20
2 hr	77.12
5 hr	65.66

K = 5; m = 6; M = 187.5; G = 12,5

Significant at 5% level.

TABLE VIII: EFFECT OF DARVYADI QUATH ON BLOOD GLUCOSE LEVELS IN DIABETIC PATIENTS (mg/100 ml)

	Fasting sample	After glucose	
		1 hour sample	2 hours sample
Before Treatment	237.7	385.3	392.6
After Treatment	203.1	323.7	322.2
SD	±73.3	±57.2	±50.4
SE	±24.4	±19.0	±16.8
t	±2.54	±2.48	± 4.5
p	<0.05	<0.05	<0.01

THE SCIENCE OF SIDDHA—AN INTRODUCTION

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Siddha System is one among the several indigenous systems now in vogue. The word Siddha comes from the word 'Siddhi' which means "Perfection" or "heavenly bliss". There are 8 types of Siddhis. They are Anima (the faculty of reducing oneself to the size of an atom), Mahima (the power of expanding onself without limit), Karima (the power of increasing one's weight or disintegrating the atoms of the body and enabling it to pass through more solid matter), Lahima (Becoming very light like feather), Prapthi (the power of attaining everything desired), Prakamiyam (the power to overcome natural obstructions and go anywhere), Esathuvam (Supreme power over animate and inanimate), and Vasithuvam (power of changing the course of nature or assuming any form in creation). Those who have attained these 8 super natural powers or Siddhis are called Siddhars. The Siddhars were of a Tamil sect which maintained Siva as the Supreme God. They were persons holding tremendous powers in themselves. They had investigated and studied fully all kinds of drugs, minerals and poisons and their physical, chemical and psychological properties. They know what was beneficial and what was not, for their existence. They held that the body was the one and only instrument with which one could attain success in spiritual evolution and growth and that if the body could only be made strong and perfect, they could get rid of birth and death eventually through spiritual awakening by rousing the Kundalini (serpent power) lying dormant at the base

of the spinal column in the region of sacral plexus and thereby attain all Siddhis. They were the masters of their bodies and could change the very materials in them by re-arranging the molecules in such a fashion that they had no more sickness or death. There were 18 great Siddhars. They were:

1. Nandi
2. Agathiyar
3. Thirumoolar
4. Punnakkisar
5. Pulasthiyar
6. Poonaikannan
7. Idaikadar
8. Bogar
9. Pulikkaisan
10. Karuvoorar
11. Konganavar
12. Kalangi
13. Azhugini
14. Agappeyar
15. Theraiyar
16. Pambatti
17. Kutambi
18. Sattainathar

The basic principles of Siddha System of Medicine

The Pancha Boodhic theory is the main basis for the Siddha System of Medicine: Prithvi (Earth), Appu (Water), Theyu (Fire), Vayu (Air), and Akash (Sky) are the five elements according to this theory. All the living beings and non-living materials are all formed only by these elements and hence human body also consists of these five elements.

They constitute the original basis of all corporeal things which, when die and are destroyed, resolve themselves again into elements. There is a very close and intimate connection between the external world and the internal man. The human body, composed of these five elements, is a small world in itself and so the five elements, lie at the root of the external world and the internal man. They are found in all bodies in the following forms.

Earth –Bone, Flesh, Nerves, Skin and Hair.

Water –Bile, Blood, Semen, Secretion and Sweat.

Fire –Hunger, Thirst, Sleep, Beauty and Indolence.

Air –Contraction, Expansion and Motion.

Sky –Interspaces of the stomach, heart, and neck.

Every element will be found mixed up with other four elements. One element cannot be viewed disassociated from the other elements. Where there is one element there the other elements also are present. This is explained as follows: Elements are themselves divided into two halves or parts viz., physical and subtle and this subtle is again divided into two equal parts of which one is retained as such and the other part is sub-divided into four equal parts. The process of combination of each of these parts with the retained half in the others is known as five fold combination or Pancheekaranam.

What are present in the cosmos are all present in the human body also. This is another theory of Siddha Science. All the planets in the cosmos have influence over the human body. It also says that the condition of the body is closely associated with nature.

The five elements of the body form three life factors which are called as *Vuyir Thathu.* They are Vatha. Pitha and Kapha. Vatha consists of Akash and Vayu; Pitha consists of Theyu; and Kapha consists of Pirthivi and Appu.

In scientific parlance, vatha comprises all the phenomina which come under the function of the central and the sympathetic nervous systems. Pitha do the functions of thermogenesis or heat production, metabolism within its limits, the process of digestion, colouration of blood, excretion and secretion etc. Kapha performs the function of regulation of heart and the formation of various glands and structures.

If all these three life factors work in a good condition, the body will be in a healthy condition. Diseases occur only on the derangements of these three life factors. The derangements of these factors may occur due to food factors and seasonal variations.

According to Siddhars, there are about 4,448 diseases. There is another classification of diseases viz., 80 Vatha diseases, 40 Pitha diseases and 20 Kapha diseases.

Diseases are diagnosed with the help of 8 factors called as *"Envagai Thervugal"*. They are Naadi (Pulse), Sparisam (Touch), Naa (Tongue), Niram (Colour), Mozhi (Speech), Vizhi (Eyes), Malam (Faeces) and Moothiram (Urine). These 8 investigative materials are widely described by the Siddhars. Naadi (Pulse) is an unique feature of the Siddha system. The condition of the three life factors—vatha, pitha and kapha—in the body can be clearly perceived through the Naadi. All the 18 Siddhars have dealt with the Naadi Science.

Siddhars have explained the various medical subjects viz, Anatomy, Physiology, Embryology, Pathology, Pharmacology, Toxicology, Paediatrics, Gynaecology and Medicine. Diseases of the Eye, Ear, Nose, Throat and Head are also dealt with separately. A list of surgical instruments which are used by the Siddhars are also given in Siddha Texts. 64 types of preparation are being used in Siddha System of Medicine. 32 are internal and the other 32 are external. Among the 32 internal preparations Kattu, Kozhangu, Urukku are very important and these preparations reveal to what extent the Siddhars had advanced in their knowledge of chemistry and metallurgy. Siddhars utilise 11 metals, 64 pashanas and 132 uparasas for their medicines, in addition to the herbs.

Medicines are prescribed to set right the deranged life factors either by addition, reduction or neutralisation, since all matter contains the 5 elements and hence the three life factors. Presence of a particular factor in a particular substance is found

out by the Suvai (Taste) of the substance. The five elements in different combinations form the six tastes.

The anupanam (adjuant) and Pathiya, Apathiyam (Dietary procedures) also play an important role in the administration of medicine.

The physiology in Siddha System consists of 96 basic factors or thathuvas. They are as follows:

1. Bootham	5–Elements – 5
2. Porigal	5–Sense organs – 5
3. Pulankal	5–Object of senses – 5
4. Kanmenthirium	5–Organs of action – 5
5. Kanmavidayam	5–Object of actions – 5
6. Karanam	4–Intellectual faculties – 4
7. Arivu	1–Intelligence – 1
8. Naadi	10–Vital nerves – 10
9. Vayu	10–Vital functions – 10
10. Asayangal	5–Systematic organs – 5
11. Atharam	6–Nerve plexes or stations of soul – 6
12. Kosam	5–Systems – 5
13. Mandalam	3–Vital regions – 3
14. Malam	3–Principles of moral evil – 3
15. Thodam	3–Life factors – 3
16. Edanai	3–Factors of attachements – 3
17. Gunam	3–Cosmic qualities – 3
18. Ragam	8–Predominant passions – 8
19. Vinai	2–Factors of individual action or behaviour – 2
20. Avathai	5–States of soul – 5

Science of Pulse

The Science of pulse forms a very important branch of Indian System of Medicine. It is a science peculiar to the Siddha System of Medicine. Many Siddhars like Agathiyar, Thirumoolar, Siva Vakkiyar, Ugimuni, Theraiyar, Punnakkisar, Machamuni, Pulippani, Sattamuni, Bogar, Ramadevar, Idaikadar, Konganavar and others have dealt with the Naadi system.

The word pulse means the beating of an artery felt with the tip of the finger or fingers at the wrist. The rate and character indicate a person's condition of health. The science of pulse is based on three life factors or *VUYIR THATHU* (i.e.) Vatha, Pitha and Kapha. It cannot be easily understood unless one has a thorough knowledge of the working of these three life factors in the human system. According to Thirumoolar's work on pulse, the following constituent parts forming the fundamental principles in the human body seem to play an important role in the variation of pulse on account of their interpenetrating nature. They are Dasa Vayu (Ten Vital Airs), three Naadi (Idakala, Pinkala and Suzhumuna), six Atharam (six nerve plexes), three mandalums (the three regions of the body Sun, Moon and Fire).

The pulse according to Siddhars is divided into 5 kinds.

1. Vatha Naadi —Pulse indicating the life factor, Vatha.
2. Pitha Naadi —Pulse indicating the life factor, Pitha.
3. Kapha Naadi —Pulse indicating the life factor, Kapha.
4. Bootha Naadi —Pulse felt between the thumb and the forefinger.
5. Guru Naadi —An intermediary pulse felt between all the four fingers.

According to the most commonly accepted view, the natural order in which the forces of the three life factors are indicated and are to be observed, is as follows: The pulse showing vatha

in the first place above the wrist is felt underneath the forefinger; that of pitha below the middle finger; and that of Kapha, the third under the ring finger. The movements of the three pulses will be in the ratio of 4 : 2 : 1. There are variations in the above ratio in a diseased condition of the body.

Siddha Chemistry

In Siddha System, Chemistry had developed into a science, auxiliary to medicine and alchemy. It was found useful in the preparation of medicines ior alleviating all sorts of sufferings, spiritual and as well as corporeal, and also in transmuting baser metals into gold. The knowledge of plants and minerals was of a very high order. Siddha Physicians were also well acquainted with the process of obtaining metals from their ores. It is surprising to know that they had developed such remarkable processes like calcination of metals; preparation of quintessences, extracts and essences from minerals and other natural bodies or substances; preparations of mercury such as oxide and chunnam possessing the marvellous property of transmuting metals; preparation of caustic alkali from the ashes of plants and several other preparations of medicine with high potency and power. Some of them were capable of rejuvenating the human system. One who has made a special study of the Siddha Science will naturally come to the conclusion that it is the precusor of all our knowledge and science. The process of preparing Jayaneer and of distilling several kinds of acids was not unknown to them, since the distilled products had been of much help to them in acting as solvents. Their knowledge of poisons also was considerable.

The process of 'killing' the metals was well known to the Siddhars. It means depriving a metal of its characteristic physical properties, such as its colour and lustre. For instance, 'killed' mercury would mean the variety which is white and non-volatile, when stirred over fire. 'Killing' is usually accompanied by the formation of oxides, chlorides or oxychlorides for the most part (Dr. Rays Chemistry).

Siddha Alchemy

Many of the Siddhars have dealt with this subject. Siddhars have written profoundly and with critical accuracy, yet absenely but they all described the thing sought for indirectly.

Some say they are forbidden to reveal the process; while others have declared it plainly and intelligibly leaving out some points which they have kept for themselves. The different parts of a *magnam opus* in Siddha medicine have to be found out by a comparison of the works of several authors. One of them may describe the materials; another, their preparations; a third their calcination; a fourth, the rules etc., for regulating heat application and so on. The following are a few of the several works on Alchemy written by Siddhars: Agathiyar, Vatha Kaviyam; Sattamuni Vatha Kaviyam; Konganavar Vatha Kaviyam; Yoogimuni Vatha Nool, Yoogimuni Vathanga Theetchai; Konganavar Vatha Kalpa Soothiram; Athiyantha Soothiram; Karuvoorar Gurunool; Karuvoorar Vatha Karpam; Sundaranandar Vatha Soothiram; Romarishi Vatha Soothiram.

Siddha Science of Yoga

Siddha medicine included not only medicine and alchemy but also yoga and philosophy in its fold. Yoga literally means union. Yoga is the means by which are obtained omniscience and the power of achieving and controlling mighty things. It is a regular science and not a vogue dreamy drifting or imagining. It is an applied science, a systamatised collection of laws applied to bring about a definite end. Siddhars science declares 64 kinds of Yoga. There are 8 elements in Yoga. They are: Yama, Niyama, Asana, Pranayama, Prathyahara, Tharanai, Thiyanam aud Samadhi. It is said by the Siddhars that there is no Yoga without concentration or fixedness of mind; there are no miraculas powers without rousing knndalini; there is no wisdom, without mind; there Is no body without repression of respiration.

Siddha Science of Breath is known as Vasi (the practice of correct breathing). There are different phases in the science of breath. They are the physical, the mental and the spiritual. The kind of controlled breathing is the scientific method of charging oneself with vitality and personal magnetism and it is known to the ancients as Pranayamam. Poorakam (Inspiration) Rechagam (Expiration) and Kumbakam (Suppression) are the three inevitable processes in pranayamam.

Siddha science also tells us that a man generally takes 15 breaths a minute and thus makes 21,600 breaths a day and at that rate he can live for a period of atleast 120 years.

Siddhars have also explained the Kaya kalpa treatment (Ways and Means for the rejuvenation of the body). Many plants have been indicated for the purpose of rejuvenation.

Muppu is also a substance used by the Siddhars for rejuvenation It is also used for the effective treatment of diseases. There are many schools of thought about the preparation of the Muppu which basically consists of three salts.

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Principles of Skin Diseases in Siddha system of Medicine

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In the Siddha system of medicine, skin diseases are generally classified into 18 varieties and they are called Pathinen kuttam. All the major skin diseases like leprosy, leucoderma etc., come within this 18 kuttams. Apart from these 18 kuttams seven varieties of karappan (Eczema) and four varieties of ven–kuttam (Leucoderma) are described in Siddha literatures. All these diseases are classified according to the Mukkuttra or thiri dhosic theory, psoriasis is described as Kalanjaka padai in siddha and a complication of this disease is mentioned as Kalanjaka vatham (Psoriatic arthritis). The skin diseases which occur in head are dealt with separately. They are about 46 diseases. In Bala vahadam or kuzhanthai maruthuva nool, 18 varieties of karappan are mentioned.

18 குட்டம்: According to "Yoogi vaidya chinthamani, kuttams are classified into 18 varieties. They are:

1. Padar thamarai perunoi
2. Koppula perunoi
3. Sirangu perunoi
4. Yanai kal perunoi
5. Sevi perunoi (Kathu perunoi)
6. Thol perunoi
7. Karu perunoi
8. Atthikai perunoi
9. Valaiya perunoi
10. Vali perunoi
11. Sori perunoi
12. Sembadai perunoi
13. Pann thol perunoi

14. Tholvedi perunoi
15. Thadippu perunoi
16 Naa perunoi
17. Purai perunoi
18. Ven padal or Ven perunoi

Causes or aetiology of the kuttanoi

Close contact with the diseased persons (i.e.) having sexual contact with the diseased persons and using the utensils etc., of the affected persons may cause the diseases. Intake of rotten foods especially rotten fish, snails may also produce the diseases. It is also mentioned as a karma disease.

In Yoogi 800 it is said that intake of substances of excessive heat or excessive cold, flatulance with indigestion (Mantham) excessive vomiting, excessive sexual habits, deep sorrowfulness, excessive sleep, intake of impure food which is mixed with hairs and mud will produce all type of skin diseases.

According to Thirumoolar the disease is caused by mega noi (gonorrhoea, syphilis etc.) and by some insects.

Thirumoolar classifies the 18 kuttams into three main groups according to the aetiology

''வியாதியுள் மூவாறு விளங்கிய குட்டங்கேள்
சுயாதிகிரந்தி சுழல் மேகத்தால் ஆறும்
பயாதி மண்ணுளப் பலவண்டினால் எட்டும்
நியாதி புழு நாலாய் நின்றது இக்குட்டமே''

He says that mega noi produces six varieties of kuttam; some insects produce six varieties of kuttam and some worms produce the other six varieties of kuttam.

There are some other references also to substantiate the theory of Thirumoolar that the skin diseases are caused by germs and worms In Guru Naddi the following stanzas are seen:

1. பயில் பொழியீர் திரேகத்தில் கிருமி தானே
பறந்து திரிகுட்டம் போல் புள்ளிகாணும்
மயிலதுவும் கிருமியுந்தான் நடந்து புக்கில்

2. மேனியரது சரசரென வெடித்துப் புண்ணாம்
புழுக்கடி போல் காணும்மது கிருமியாலே

3. திரேகமதில் சொறி குட்டம் கிருமியாலே

4. குட்டமுடன் திரேக மெல்லாம் பார்க்கும் போது
குழிகுழியாய் கிருமியினால் கொல்லும் புள்ளி

Signs and symptoms of 18 kuttam

1 Padar thamarai perunoi (pundareeka kuttam)

''கூடுமே தாமரையின் பூவிதழ் போல்
குவிந்துமே கறுப்போடு வெளுப்புமாகுந்த
தேடுமே சிவப்பு வண்ணமாகுந்த
தினவுமிக வாகியே சொறியும் செந்நீர்,
வாடுமே ஐயத்தினுள் பத்தியாகி
வருத்த மிகவுண்டாகி நோவுமாகும்
போடுமே சரீரங்கள் முகங்கள் கால்கள்
புண்டரீகக் குஷ்டத்தின் புதுமை தானே''

There will be eruptions in the skin in the shape of petals of lotus. The colour of the skin may change to black white or reddish in colour. There will be itching sensation. When the patient scratches over the itching area, blood may ooze out of the skin. Kapha becomes predominant in the disease. The body, legs and face are the main places in which the disease starts.

2. Koppula Perunoi (Virpodaga Kuttam)

''புதுமையாய் சரீரமெங்கும் தினவுண்டாகும்
பெருவெடியாய் திக்கெனத் தீ கொழுந்துபோல்
மெதுமையாய் விட்டெரியும் நல்லபாம்பின்
விஷப்படம் போல தடித்து வெளுப்புமாகுந்த

சுதுமயாய் மிகச் சொறியுஞ் சிவப்புமாகுந்த
துக்கமொடு சஞ்சலமு மிகவுண்டாகும்
கதுமையாய் தோலெல்லாம் தடிப்புண்டாகுங்
கணத்தவிப் போடகமான குட்டந்தானே''

There will be itching and acute burning sensation all over the body. Fissures will also be present in the skin. Some times swelling in the shape of hood of vipers occur in the skin. The swelling will be white in colour. Severe itching will be present in those areas and soon the swellings become reddish in colour. Thickening of skin all over the body is another important symptom of the disease. This will produce lot of pain and sorrow to the patient.

3. Sirangu perunoi (Pama kuttam)

''தானான தினவுண்டாய் வெளுத்திருக்கும்
தங்கியே சீப்பாய்ந்த தேகங்குன்றுங்
கானான சரிசமெலா மெரிவுண்டாகுங்
கனமான தாமரையின் குடைபோலுண்டாம்
பானான சொறியோடு தினவுண்டாகும்
பாம்பிடைத் தோல் போல வுரிந்து வீங்கும்
கானான கால்கையுங் குறைந்து காணுங்
கனமான பாமா குட்டமாகுந்தானே''

Paleness of the skin with itching will be seen. Pus may form and so general weakness occurs. Burning sensation all over the body is present. Swelling of the skin in the shape of lotus umbrella, forms over the skin and severe itching will be present. Soon they burst open and skin peels off like the snake peels off its skin and again the skin becomes swollen.

4. Yanai thol perunoi (Kaja kuttam)

''தானாக சடந்தானு மிகக் கறுக்குங்
சடமெங்குந்த தோலுரியஞ் சிவப்புமாகும்
வேனான வறவறெனத் தானிழக்கும்
வெடிக்குமே சொறிதலாய்த் தினவுண்டாகும்

கானாகச் சர்மகுஷ்ட மிதிலுண்டாகும்
கடினமாய் கால்விரல்கள் கனபுண்டாகுங்
கூனாகத் தேகமெங்கும் வலியெடுக்கும்
ஏக சர்ம குட்டந்தானே''

The skin becomes black in colour all over the body. Then the skin peels off and becomes reddened. The skin is very rough and fissured and itching will be present. The toes will be swollen. Pain all over the body is present.

5. Kathu perunoi (Karna kuttam)

''சர்மந்தான் மிகவெடிக்கும் பொரிபோற்றானுஞ்
சடமெல்லாம் வேதனை பச்சென்றுருக்குந்த
தெர்மந்தான் திரிதோட குணமுண்டாகுங்
தேகமெங்கும் பாரிக்குந் திமிறுண்டாகும்
கர்ணந்தான் காக்கணம்பூ நிறமதாகுங்
கண்டிப்பு வீக்கமாய் தானிருக்கும்
வர்மந்தான் மனக்கிலேச மிகவுண்டாகு
மாகான குட்டத்தின் மார்க்கந்தானே''

The skin will be fissured; a rash of small eruptions will be present all over the body with severe pain. The thiri dhosas get affected and swelling all over the body is present. The colour of the ears changes to the colour of kakkanampoo (flowers of kakkanam plant) i. e. Blackish blue in colour and they become swollen.

6. Thol perunoi (sarma kuttam)

''மார்க்கந்தான் பசுமையாய் வெளுப்பண்டா
மாசிவப்பு கருப்புமாய் தினவுண்டாகுந்
தார்க்கமாய் தடிப்பு சீப்பாய்சலாகுந்த
தடைவியிறு கடிதடித்திற் சொறியுமாகுந்
தேர்க்கமாய் திமிரொடு தசையம்பாயும்
தேகான் எரிச்சலாய்ட்ணமாகுஞ்
சீர்த்தமாய் வயிறுதனிற் கண்டிப்பாகுஞ்
சர்ம குட்டம் தன்னுடைய சேதி கேளே''

The skin changes into different colours like green, white, red and black with acute itching. Swelling with pus will occur in the skin. Itching will be present in the upper and lower abdominal areas. Loss of sensation will also be seen. Burning sensation in the abdominal area is noted.

7. Karu perunoi (Krishna kuttam)

''சேதியாய் தேகமெங்குந்தான் குறுக்கு
சிவப்புடனே சிலேத்திமத்திலுற்ப வித்துக்
காதியாய் தோல்திமிர்த்தே கதித்துநாறுங்
கனமான தாதுவிது முட்ணந்தாக்கும்
நூரியாய்யுடம்பெங்குங் நோவுண்டாகும்
நுட்பமாய் புறங்காலி லரையிற்காணும்
தாதியாய் தலை தண்யில் மிகுதியாகுஞ்
சஞ்சலிக்குங் சிருஷ்ண குட்டத்தாண்மை தானே''

The skin becomes blackened and then becomes red in colour. Loss of sensation and numbness with bad odour are present in the skin. Pain all over the body is also present. Acute pain will be present in back of the legs and in hip. The skin in the scalp is usually affected by this disease.

8. Atthikai perunoi (Avuthumbara kuttam)

''ஆண்மையாய் அத்திக்காய் போலரும்பி
யடுக்கடுக்காய் முளைத்ததுமே பெருத்து மெத்தக்க
காண்மையாய் காய்ந்துமே உடம்பெங்குந் தான்
கறுகியே உடம்பு தோல் திரைந்து தொங்குந்
தோண்மையாய் தேகமெங்குந் திமிருண் டாகுந்த
சொறியுமே சரீரத்திற்கு செந்நீர் பாயும்
வாய்மையாய் மயக்கந்தான் மிகவுண்டாகும்
வகுத்த தோரவு துமபுரவு குட்டந்தானே''

Ficus fruit-like swelling are seen densely all over the body. The skin becomes shrunken and loose and descends. Numbness will be present all over the body. Itching is present and blood will ooze out when scratched. Giddiness and unconsciousness may also occur.

9. Valaiya perunoi (Mandala kuttam)

''வருத்ததோர் பச்சைவண்ண மிரத்த வண்ட
மாயிருக்கு முடம்பெல்லாஞ் சிர செல் லாந்தான்
விகுத்ததோர் தலையிலே வெளுப்பமாகும்
மேனியெல்லா மிக தடித்து குறுப் புண்டாகுந்
திகுத்ததோர் தினவாகுஞ் சொரியுமாகுஞ்
சிகப்பான சலம் வீழும் சடம் எங்குந் தான்
வகுத்ததோர் மண்டல குட்டத்தின் செய்தி
மார்க்கமெல்லாம் பார்த்துணர்ந்து மருவுவரே''

The skin will become greenish and reddish in colour while the scalp turns whitish in colour. Swelling will be present all over the body and becomes blackened. There will be severe itching. Pus and blood may come out on scratching.

1 . Vali perunoi (Aperisa kuttam)

''மருவவே தேகமெலா மிகவே நொந்து
மாசற்ற ரத்தமெல்லா மிகக்கறுக்குங்
செருவவே சிந்தையெலா நோவுண்டாகுந்
தேகமெங்குந்த துடிபடா நோவுண்டாகும்
அருவவே வாயு மிஞ்சி யதிக நோவாம்
அதிரல் வேதனையாகுமிகநீர் கொட்டல்
பருவவே வீங்கியே வெடிப்புண்டாகும்
பரந்த வபரிச குட்டப்பண்புமாமே''

Pain all over the body and mental agony are present. The vayu factor in the body becomes excessive and it produces severe pain in the body. Giddiness and increased output of urine are also present. The body gets swollen and fissured.

11. Sori perunoi (Visarchika Kuttam)

''பரிசமாய் வாத பித்தத் துற்பவித்துப்
பரிந்து தொட்டா லெண்ணெய் போல் வெளுப்பமாகும்
விரிசமாய்த் தினவெரிப்பு வேதனையுமாம்
மிகச் சிவப்புத் தடிப்பஞ் தேலுறப்பு மாகும்

மரிசமாய் காலெரிப்பஞ் சலிப்புமாகு
மகத்தான வெட்கிப்பு வயிலிரைப்பு
துரிசமாய் கோபிப்புச் சுறுசுறுப்பு
துரிசான விசர்ச்சிகாகக் குட்டமாமே''

Sori perunoi occurs due to derangement of vatha and pitha. The skin in this condition is oily and pale. There will be pain, itching and burning sensation in the body. Soon the skin becomes thickened and reddish in colour. Gastritis and indigestion will also be present. The patient feels shy of this disease. Some times he will be in an angry mood

12. Senkuttam (Vipathika kuttam)

''சுரப்பாக சிலேட்டுமப் பித்தந்தன்னிற்றான்
துனித துடம்பிலே வெடித்ததுயங்காற்ற வொண்ணா
அறுப்பாக அண்டவொண்ணாத் தணலதாகி
அழன்று னக கால் கண் காது கண்டந்தானும்
வெறுப்பாக வெடித்ததுமே வீங்கிப்புண்ணும்
மேனியெல்லா நற்பாம்பு மின்னலாகும்
சுறுப்பாக சந்தெல்லாம் பரவிநி றகும்
காரணமாம் விபாதிகா குட்டமாமே''

Senkuttam occurs due to the derangements of pitham and kapam. The skin will be fissured and the fissures are not repairable and they become like incisions. There will be severe burning sensation in those areas. The disease mainly affects the upper and lower limbs, eyes, ears and neck. In these areas the skin becomes fissured and ulcerate. A type of shining which is present in snakes is seen in the affected patients. The disease will affect the joints also.

13. Panri thol perunoi (Kideepa kuttam)

''காரணமாய் சரீசரமெங்கும் பச்சையாகுங்
கலத்து யானைத் தொலின் தடிப்புமாகும்
மாரணமாய் மகாதினவு சொறியுமாகு
மகத்தான மூத்திரந்தானடிக் கடிக்கு

நாரணமாய் செந்நீரதாகுமேனி
நலமாய் நாற்றத்தான் மிகவுண்டாகுங்
சிரமான்ச் சிவப்பட்ச வாதமாகுஞ்
சடந்தானு முதுமே கிடப குட்டம்''

The skin all over the body will be greenish in colour and they are thickened like elephant's skin. There will be intense itching all over the body. Frequent micturition is present and the urine is reddish in colour. Unbearable smell is emanated from the body. Paralysis of one side of the body may also result due to this disease.

14. Thol vedi perunoi (sarma thala kuttam)

''கிடபமா யுடம்புவலி யதிகமாகுங்
கிற்றுக வெடித்து வேதனையுமாகும்
தடபமாய் தடிப்பாகி செய்மையாகுந்த
தனை தொட்டால் நோக்காடாய்திண வெழுப்பும்
வடபமாய் மய க்கோடு அசதிகாணும்
மாறுத நோக்கோடு மிகவேயுண்டாம்
திடபதமாய் யுரத்தில்வலியுமாகுஞ்
செப்புகின்ற சர்மதன குட்டமாமே''

Pain in the body is felt. Fissures, thickening and reddishness of the skin are present. There will be severe pain and itching when the affected part of the skin is touched. There will be lassitude and sometimes syncope is also present. Pain in abdomen is also another important symptom of this disease.

15. Thadippu perunoi (Thathuru kuttam)

''சர்மந்தான் சிவப்பாக வட்டனித்து
சலவை போல் வெளுக்குமே தினவுண்டாகுந்
வர்மந்தான் ரோகமிது மிகவுண்டாகுந்த
மயிரெல்லாம் சுருண்டுமே உண்டாகும்
கர்மந்தான் பித்த சிலேட்டும் மிகுக்குங்
காயந்தான் னின் கதித்துமே திமிருண்டாகும்

தர்மந்தான் சடமெல்லா முதலாகுந்த
தாக்கான தத்துரு குஷ்டத்தானே''

Round reddish patches will be seen in the skin. They will then become white and have severe itching. The body is swollen and numbness will be present. The disease occurs due to derangement of pitha and kaba.

16. Naa perunoi (Sithuma kuttam)

''தாக்கான வாதபித்த துற்பலித்து
தளிரான சரைப்பூவின் வண்ணமாகி
வாக்கான வடிவமெலாந் திமிருண்டாகி
வட்டனித்து பசுமஞ்சள் வண்ணமாகுந்த
தேக்கான் திமிரோடு செந்நீருண்டாய்த்
தேகமெங்குந்த மசைக்கொணு செருமையாகும்
நீக்கான் நினைவோடு மறதியாகும்
நிலவர மாகுசித்மா வெணுங் குட்டந்தானே''

Vatha and Pitha dhosa derangement causes this disease. The skin is paler like the colour of surai flower. There will be numbness all over the body. Round greenish yellow patches form all over the body with loss of sensation. Unconsciousness may also occur.

17. Purai perunoi (Satharu kuttam)

''சிததான கண்டிப்பாய் ரத்த வண்ணம்
செழும் பச்சை வெள்ளையாய் சிவப்புமாகுந்
எததான வெரிப்போடு தினவுமாகுந்த
மெளிதான சிலேட்டும் வாதத் துற்பத்தி
பத்தான கரடு கட்டி புண்ணுமாகும்
பாம்பு தோல் போல் திரைந்து பருத்து காணும்
வித்தான முக்கோடு காது கண்ணம்
மிகத்துடிப்பாஞ் சதாரு குட்டந்தானே''

18. Ven perunoi (Suvetha kuttam)

"தடிப்பாக தவள நிறம்போல் வெளுத்து
சர்வாங்கமும் வெளுத்தாற்றான் திரும்பும்
மடிப்பாக மயிர் வெளுத்தா லசாத்தியமாகும்
விரிவுதடு உள்ளங்கை குதங்குய்யந்தான்
நெடிப்பாக நெருப்பு பட்டது போல் புண்ணுய்
நிறமிருந்த லசாத்திய மென்றுரைக்கலாகும
வெடிப்பாக மேனியெல்லாம் வெளுத்து வீங்கில்
வெண் சுவேத குட்டமென்றே விளம்பலாமே"

Whitish colouration of skin occurs. Even if the whole body is whitened it can be cured except in the following conditions. If the hairs are whitened or if there is whitening in palm, anus and vulva or if the colour is like healed burns, the cure is little difficult.

Prognosis of the 18 kuttams: Only 8 varieties can be cured The other 10 are unable to cure as per Yoogi Chinthamani. The 10 kuttams which are not able to be cured are as follows:

1. Koppula peru noi
2. Karu Peru noi
3. Yanai thol perunoi
4. Atthikai perunoi
5. Thadippu perunoi
6. Naa perunoi
7. Pantrithol perunoi
8. Purai perunoi
9. Thol perunoi
10. Thol vedippu perunoi

வாதமலாது மேனி கெடாது தேரையா

Theraiyar quotes that without the affections of vatha the skin or body will not get affected. So in skin disease vatha is mainly affected. It will be in increased or in decreased position. Due to its affection the rasa (body fluid) and the raktha (blood) are first affected and in due course the other 'udal thathus' are also affected.

When Iyam or kabam join with vatha in later stage the ulcers become incurable and also ansarka in the body, syncope and unconsciousness may also develop.

The skin produces various changes according to the stages of affection of seven 'udal thathus'. When rasa or body fluid gets affected, dryness and colour changes of the skin occur. When Raktha or blood gets affected excessive perspiration and oedema of the body will occur. When mamisa or muscle involved boils, ulcers, and water oozing will be seen. If fat or kozhuppu gets affected, obesity of the body, bad odour and fissures in the body are produced. When bone (Enbu) and Bone marrow (Majjai) are affected the deformities of the fingers and limbs occur.

ORAL ANTIDOTES FOR COBRA BITE IN SIDDHA MEDICINE

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Practitioners of traditional systems of medicine claim different drugs of plant, mineral and animal origin to possess oral antidotal activity against poisonous snake bites. However such claims are brushed aside as unscientific by modern scientific and medical communities, as these drugs have the possibility of being ineffective also. In view of the potential dangers associated with these drugs of questionable merit in conditions such as poisonous snake bites and the advantage of having orally active antidotes the study was conducted. Most of the drugs tried in the present study are indicated for snake bites by different Siddha literature. In the process a plant drug from Siddha Medicine with oral antidotal activity was discovered Perhaps this is the first time such a drug activity is established.

Findings

1. Cobra venom used in the present study was obtained from Irula Snake Catchers Industrial Co-operative Society Limited, Madras-603 104, India. LD 50 of this vacuum dried venom was found to be 0.82 mg/Kg, in albino rats, subcutaneously.

2. The fresh juice of *Indigofera tinctoria* Linn is known in Siddha as Neeli (1). This drug was found to be orally effective against the LD 50 of Cobra venom injected subcutaneously. The dose of the drug was 2ml/100g. When given orally the

drug protected the life of 30–40% of albino rats from the lethal dose of cobra venom.

3. In rest of the animals that received the drug, the death was delayed by nearly 135 minutes. The results were statistically significant.

4. Another preparation of the same drug, when injected subcutaneously along with lethal amount of poison a 100% protection was observed. From this it was inferred that the drug has got some direct inactivating action over the venom.

5. Two Polygala sp. plants, studied also revealed potential activity against cobra venom Among this one Polygala sp. was found to be orally effective against the lethal dose of cobra venom. Extensive *in vivo* tests could not be conducted due to want of enough drug.

How the findings were confirmed ?

1. Cobra poison is primarily a neurotoxin. Enzymes, cardiotoxin and other principles present in the crude venom are relatively non toxic or toxic only at very high doses.

2. The neuro toxin present in the cobra venom produces death through peripheral respiratory failure, as a result of neuromuscular blockade (3,2). The mechanism of action of neurotoxin is comparable to that of curare, a South American arrow poison, whose activity is fast and reversible while that of neurotoxin is slow and less reversible (4).

I. tinctoria L. was found to inhibit the action of cobra venom at the neuro muscular junction. Thus it satisfied the prerequisite for any drug to be an effective cobra antidote. In some experiments the drug was also able to reverse the neuromuscular blockade already induced by the poison. In the presence of the drug the venom could not block the neuromuscular junction. The neuromuscular experiments including rat phrenic nerve hemidiaphram (6) and frog rectus preparations, standard

methods, widely used by international scientific community were employed to confirm such activities. The cardiotoxic activity of the venom was also inhibited in the presence of *I. tinctoria* L. as observed from *in vivo* frog heart studies.

Acorus calamus Linn. and two *Polygala* spp. plants were also found to inhibit the action of cobra venom at the neuro-muscular junction.

Previous to the present finding, there is a report about a drug, namely, *Curcuma sp.* (Zingiberaceae) from Thailand. This drug inhibits the activity of cobra neurotoxin at the neuro-muscular junction. But this drug was not active orally (5).

Application of the Present findings in the human context

Perhaps it is the first time that the Medical world comes across a potential oral drug (*I. tinctoria* L.) for cobra envenomation. The following discussion applies mainly to this drug. In India major population lives in rural areas. Hospitals well equipped to tackle emergencies of snake bites are rare in these parts. Hence the interval between the time of attack and the time when the victim is brought to such hospitals, spells the difference between life and death (7). As the drug is found to delay death by 2 hours and 15 minutes it gives a long and safe chance to bring the patient to a hospital.

It is well established that only 30–40% of poisonous snake bites result in death (8, 9). That is only in 30–40% of bites (if all were attributed to cobra alone, which is not actually so), the cobra injects more than 15 mg of poison which is the death producing dose. As the drug affords 30–40% of protection according to the present studies and mortality rate in man is also said to be same, the drug may even give 100% protection in the human context. So by taking the plant juice or the dry drug mentioned, soon after a poisonous snake bite, there is possibility of decreasing the chances of death. Anyhow at this stage it

is advised to take the snake victim, whether he takes the drug reported or not, immediately to a nearby hospital with all usual first aids and precautions. Because findings with other snake poisons are yet to be confirmed, more so when common man still finds it difficult to differentiate between the types of poisonous and non-poisonous snakes.

Acalypha indica Linn. (Kuppaimeni), *Mollugo oppositifolia* Linn. (Katchan thazai), *Tylophora asthmatica* W & A. (Nanjaruppan), *Calotropis gigantea* R. Br. (Erukku), *Enicostemma littorale* Bl. (Vellaruku), *Andrographis paniculata* Nees. (Nila vembu, Sirianangai), *Musa paradisiaca* Linn. (Vaazhai thandu), *Phyllanthus niruri* Linn. (Keelai nelli), *Azima tetracantha* Lam. *Curcuma longa* Linn. (Manjal) *Pergularia extensa* N.E. Br. (Uthamani) are some of the single drugs mentioned in Siddha literature for snake bite. These drugs did not show any encouraging results. Some compound drug preparations of siddha were tried and they also did not give any encouraging results. *Echinatus angustifolia* drops of homeopathy was also found to be of no use.

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VARMAM IN SIDDHA MEDICINE

S. Rajamony

Tamil culture is very ancient. Among our ancestors, there were philosophers, siddhars and medical men, who were all experts in their own particular fields. The wealth of knowledge they possessed is available for us in the palmleaf manuscripts they have left for us. Through these manuscripts, we have come to know many of the secrets of the Siddha medicine, Astrology, 'Vasium', Hypnotism etc. These sciences are now-a-days being utilised to treat many of the ills of modern society. Certain other arts and sciences like the art of Varmam have been kept as closely guarded secrets, because of the fear that these arts may be misused by unscrupulous persons. Gurus familiar in the art of Varmam were very careful in selecting their students and even these students were not taught all the secrets of the art; and they were made to take vows that they will not use these arts either for their personal gain or to seek revenge upon others. These arts were learnt through several years of sincere service to the Gurus. It is said that a minimum of twelve years is needed for a person to acquire a *basic* knowledge in the art of Varmam.

In these days of hurry and fast living, we cannot expect students to have the time and the patience to spend such a long time in mastering this art.

But the art of Varmam, if learnt properly, will be or a valuable asset to Indian Medicine. It may possibly show the way to cure many of the so-called incurable diseases like poliomyelitis hemiplegia, rheumatoid-arthritis, chronic-arthritis, migraine,

bronchial-asthma, cataract of the eye, etc. The art of Varmam indicates that certain diseases like pulmonary tuberculosis, hydrocele, bronchial asthma, paralysis etc., may be due to injuries in certain sites of Varmam.

For example :

1. It is said that if one gets Varmam at Kaipootu Varmam (the medial end of the spine of the scapula), one will get an attack of tuberculosis in about four hundred days time.

2. A Varmam in Thummi Kalam (the supra sternal notch) will result in hydrocele in about a year.

3. Similarly, hydrocele will occur in Varmam in Ananda Vasu Kalam (the region of 9th Costal Cartilage).

4. A Varmam over Adappak Kalam (the 10th rib in the mid-axillary line) in women during pregnancy will lead to hydrocele in the male child or sterility in the female child.

Varmam and Points of Varmam

Varmam means sites where life exists. It also means sites of vitality, mystery, secret, fracture etc. Sites of Varmam are the points in the body where nerves, blood vessels, bones and muscles meet. So, no wonder Gurus in *may* Varmam, believe that the sites of Varmam are the points where life exists.

Types of Varmam :

1.	Padu Varmam (Varmam due to violent injury)	– 12
2.	Thodu Varmam (Varmam due to touch)	– 96
3.	Thattu Varmam (Varmam due to blow)	– 8
4.	Thadavu Varmam (Varmam due to massage)	– 4
5.	Nakku Varmam (Varmam due to licking)	– 1
6.	Nookku Varmam (Varmam due to sight)	– 1

At present we have 108 Varmam for males and 107 for females (excepting the scrotum). There are about 150 important sites of Varmam in our body.

Given below are examples of some important sites of Varmam and their significance:

1. Thilartha Varmam

(Nasion): It is the middle of the bridge of the nose. It is the meeting point of the frontal bone and the two nasal bones. If one gets Asathya Varmam (incurable Varmam) at this site he may die within one and a half hours. If it is Sathya Varmam (Curable Varmam) he may live—but will become unconscious with the mouth open. He may be brought back to normal, by tapping over the vertex; massaging over the site of Varmam; massage over back of the chest and neck. Blowing dry ginger into the nose; rice–kanji as a diet, and Kaya Thirumeni Thailam are other treatments to be adopted.

2. Orakka Kalam

(Below the angle of the mandible): In Varmam at this site, one will sleep for thirtysix hours. His mouth will be open, with the tongue protruding. There will be fever and general weakness. This can be cured by tapping the vertex with clasped hands; pressure over the occipital region; and blowing dry ginger into the nose and ears; and the whole body has to be massaged.

3. Asthi Surukki Varmam

(It is on the side of the trunk, two inches below the 12th rib): Varmam in this site may result in immediate death. If the person lives, his body may bend to the affected side within 40 days and he will die on the 41st day. The whole body will remain cool throughout.

This may be cured by a blow to the opposite side of the body with the back of the foot; tapping the vertex with clasped hands. At last, a kick with the back of the foot to the region of lumbar vertebrae may cure the person. Blowing dry ginger into the nose and ear, rice–kanji and general body massage may also help.

A knowledge about this wonderful scientific art of Varmam may help in curing and preventing many of the diseases which endanger human life. This important branch of Siddha Medicine, if properly studied and advocated can help to enrich even Modern Medicine. This scientific art will have a very bright future, if proper facilities are given for those who are experts (Gurus) in this field and to those who are interested in studying and practising it.

1. THILARTHA VARMAM

It is the region of the nasion of the skull; at the middle of the bridge of the nose at the junction of frontal and nasal bones. The supra–trochlear and infra–trochlear nerves are situated close to this area.

2. KANNADI KALAM

It is at the middle of the body of the nose at the junction of the bony and the cartilaginous parts of the nose. External–nasal nerve is close to this area.

3. MOORTHY KALAM

It is situated in three locations—tip of the nose and the incisive fossae of the upper jaw. Labial branch of the infra-orbital nerve is in this area.

4. ANTHAM VARMAM

It is the superior vestibule of the mouth; close to the II nd upper molar tooth. The parotid duct opens into this region.

5. THUMMI KALAM

It is the supra–sternal notch. The trachea lies deep in this region.

6. PIN SWATHI VARMAM

It is in the region of frontal eminence of the skull. The supra–orbital nerve runs close to this.

7. KUMBIDU KALAM

It is the region of glabella of the skull. This area is supplied by supra-trochclear nerve.

8. NATCHATHRA KALAM

It is in the middle of the lateral margin of the orbit. The zygomatical frontal suture is here.

9. BALA VARMA

It is the region of the medial angle of the eye.

10. MEL THADI VARMAM

It is in the region of the incisive fossa of the lower jaw. Mental (chin) nerve supplies this area.

11. MUN SWATHI VARMAM

It is in the forehead, in the middle line, 10 cms. above the Kumbidu Kalam.

12. NEMAI VARMAM

It is in the middle of the supra-orbital margin. The supra-orbital nerve and artery emerage from the orbit at this point.

13. MANTHIRA KALAM

It is the region into the orbit, below the eye-ball.

14. PIN VATTI KALAM

It is the middle of the infra-orbital margin, just below the Manthira kalam.

15. KAMPOTHI KALAM

It is the zygomatic region of the face and the zygomatico-facial nerve supplies this zone.

16. UL-NAKKU-KALA VARMAM

It is inside the mouth cavity below the tongue. The ducts of sub-mandibular and sub-lingual salivary glands open here.

17. OTTU VARMAM

It is the sub-mandibular region – the sub-mandibular salivary gland lies in this area.

18. CHENNI VARMAM

It is the middle of the temporal fossa of the skull. The superficial-temporal artery crosses this area.

19. POIGAI KALAM

It is in front of the tragus of the ear. The auriculo-temporal nerve emerges at this point from inside the parotid gland.

20. ALAVADI VARMAM

It is a point behind the ramus of the mandible—below the ear.

21. MOOKADAKI KALAM

It includes the region of the entire nose.

22. KUMBERIKALA VARMAM

It is the tip of the nose.

23. NASI KALAM

It is at the upper end of the Philtrum of the upper lip. The cartilage of the septum of the nose is just above this point.

24. VETTU VARMAM

It is the mental protuberance.

25. ANNAN KALAM

It is below the Vettu Varmam—It is the submental region. The sub-mental lymph glands are located here.

26. ORAKKA KALAM

It is below the angle of the mandible—the hypoglossa nerve crosses deep in this region.

27. KOKKI VARMAM

It is the prominence in the neck due to the thyroid cartilage

28. SANGU THIRI KALAM

It is in front of the middle of the sternocleido-mastoid muscle. The carotid arteries lie deep in this area.

29. SEVI KUTHI KALAM

It is 1 cm. below Poigai Kalam. It is the region of the temperomandibular joint

30. KOMBU KUTHI VARMAM

It is above the ear-behind the chenni Varmam.

31. KAKKATTAI KALAM

It is the supraclavicular region. The brachial plexus is situate deep in this area.

32. THALAI PAHAI VARMAM

It is the circumference of the scalp. (It is the region around which a turban is usually worn)

33. POOTELLU VARMAM

It is about 2.5cms. on either side of the vertex. The parietal emissary foramen may be situated here.

34. PIDARI KALAM

It is the region of the external Occipital protuberance (union) of the skull.

35. POTCHAI VARMAM

It is behind the mastoid process of the skull. The occipital artery crosses this point.

36. SARITHI VARMAM

It is the region of the transverse process of the cervical vertebrae.

37. MOORTHY ADAKKAM

It is the triangular area bounded by the nasion, tip of the nose and the centre of the cornea. The facial artery ends in this region.

38. THALLAL-NADU-KUZHI-VARMAM

It is the sterno-clavicular joint.

39. THIVALAI KALAM

It is the II nd intercostal space at the mid-clavicular line.

40. KAI-PUJA 3rd VARI VARMAM :

It is a point just below Thivalai Kalam, at the level of the IIIrd rib in mid-clavicular line.

41. SULI-ADI-VARMAM

It is in the posterior fold of the axilla.

42. ADAPPA-KALA-VARMAM

It is at the 10th rib in the mid-axillary line.

43. MUNDELLU VARMAM

It is just below the last rib in the mid-axillary line. The subcostal nerve and vessels pass along this line.

44. PERIA ASTHI SURUKKI VARMAM

It is two fingers breadth (5 cms) below the Mundellu Varmam.

45. SIRIA ASTHI SURUKKI VARMAM

It is one finger breadth (2.5 cms) below the Peria Asthi Surukki Varmam. The ilio-inguinal and ilio hypogastric nerves cross this point.

46. LINGA VARMAM

It is the region of ths corona glandis of the glans penis.

47. ANDA KALAM

It is the centre of the perineal region. All the muscles of the perineum are attached to the central tendon situated here.

48. THALIKA VARMAM

It is inside the analorifice.

49. ANANDA VASU KALAM

It is at the region of the 9th costal cartilage. The fundus of the gall bladder is at this point on the right side.

50. UTHIRA KALAM

It is in the middle line (linea alba)–2.5 cms above the umbilicus.

51. PALLAI VARMAM

It is at a point 10 cms to the side of the umbilicus.

52. MOOTHIRA KALAM

It is in the middle-line (linea alba)–5 cms below the umbilicus. The urinary bladder, when full, will be deep to this point.

53. KUTHU VARMAM

It is at the lower end of the linea alba, at the pubic region.

54. KATHIR VARMAM

It is the middle of the body of the sternum.

55. KATHIR KAMA VARMAM

It is the lower part of the body of the sternum. The heart, situated inside the pericardium, lies deep to this area.

56. KOOMBU VARMAM

It is the region of xiphisternum. It is at the upper end of the epigastric region.

57. NER VARMAM

It is in the middle line, 5 cms below Koombu Varmam—it is the epigastric region—region of the stomach.

58. URUMI KALAM

It is in the middle line (linea alba) 10 cms above the umbilicus.

59. AMENTA VARMAM

It is in the umbilicus: 10th intercostal nerve supplies this point.

60. THANDU VARMAM

It is at the root of the penis. The dorsal nerve and vessels of the penis cross this point.

61. KALLADAI KALAM

It is the region of the scrotum. The testis (male sex gland) lies inside this.

62. KAKKATTAI KALAM

It is the region of the acromion. Process of the scapula; near the region of shoulder.

63. PUJA VARMAM

It is the region acromio-clavicular joint. This is crossed by the lateral supra-clavicular nerves.

64. HANUMAR VARMAM

It is in the region of 7th costal cartilage. It is close to the epigastric region of the abdomen, containing the stomach.

65. MEL SURUTHI VARMAM

It is at the point of the spine of the 7th cervical vertebra in the middle line.

66. KAI KUZHI KANTHARI VARMAM

It is the middle of the spine of the scapula.

67. MEL KAI POOTU VARMAM

It is at the medial end of the spine of the scapula. It will be close to the spine of the 3rd thoracic vertebra.

68. KAI--CHEEPU--ENBU VARMAM:

It is at the point 5 cm below the inferior angle of the scapula. It will be at the 9th rib with the 9th intercostal nerves and vessels lying deep to it.

69. POONOOLU KALAM:

It is along the line, in which the 'Poonool" (sacred thread) comes into contact with the body. This lies usually along the line connecting the mid--clavicular point to the opposite lumbar region; both in front and behind.

70 VELLURUMI THALLURUMI:

It is about 7.5 cms from the middle line at the level of the 2nd lumbar vertebra. The kidneys lie deep in this region and the ilio-hypo-gastric, and ilio-inguinal nerves cross behind the kidney at this level.

71. KATCHAI VARMAM

It is around the waist line, along which a belt is worn.

72. KOOTCHA PIRAM VARMAM

It is in the middle line at the spine of the 8th thoracic vertebra.

73. SANGUTHIRI KALAM

It is 10 cms below Kootcha piram Varmam. It is at the level of 1st lumbar spine. It is just opposite to Ner Varmam in front.

74. VALAMPURI–IDAMPURI–VARMAM

It is at the posterior-superior iliac spine. It is at the dimple seen in the back above the gluteal region. It is crossed by the branches of sacral nerves.

75. THALLAI ADAKKA VARMAM

It is deep inside the axilla; can be approached by a finger directed towards the apex of the axilla. All the nerves and blood vessels going to the upper--limb pass through this region.

76. THUTHIKAI VARMAM

It is the point in front of the middle of the wrist joint.

77. THATCHNA KALAM

It is just inside the ball of the thumb; in the palm. Branches of the median nerve lie deep in this area.

78. CHULUKKU VARMAM

It is on the inner side of the root of the upper limb. It is at the level of the neck of the humerus. The nerves and blood vessels of the upper limb cross this point.

79. MUTTU VARMAM

It is the medial epicondyle of the humerus. The ulnar nerve crosses this bone lying very superficial.

80. MOLIYIN VARMAM

It is 2.5cms below Muttu Varmam. At this point ulnar nerve can be pressed against ulna.

81. KAI-KUSATHIDA VARMAM

It is the middle of the front of the forearm.

82. ULLANGAI VELLAI VARMAM

It is the middle of the hollow of the palm. The nerves of the palm and the superficial palmar arch (artery) lies here.

83. THOONGU SATHAI VARMAM

It is in the middle of the back of the upper arm. The muscle underneath is the triceps. Radial nerve crosses deep to the triceps in this region.

84. MANI PANTHA VARMAM

It is the middle of the back of the wrist joint. It is opposite to Thuthikai Varmam.

85. SUNDOTHARI VARMAM

It is in the middle of the 4th dorsal—inter—metacarpal space on the dorsum of the hand. The dorsal branch of the ulnar nerve crosses this point.

86. NADUKAVALI VARMAM

It is between the meta-carpo-phalangeal joints of the middle and ring fingers.

87. SIRU VIRAL KAVALI VARMAM (of hand)

It is at the web between the ring finger and the little finger.

88. MEL MANIKATTU VARAM

It is the middle of the back of the forearm. The posterior cutaneous nerve of the forearm lies here.

89. VISA MANIPANTHA VARMAM

It is the point 5 cms above the Mani pantha Varmam.

90. KAVALI KALAM:

It is in the inter—meta carpal space on the dorsum of the hand. The superficial branches of the radial nerve and the beginning of the cephalic vein cross this region

91. MOTHIRA KALAM

It is the region between the iliac crest and greater trochanter of the femur (see also 110, 111, 112, & 113).

92. PATHAKALAI VARMAM

It is the mid-inguinal point. The superficial inguinal lymph glands lie below this point.

93. AMAKALAM

It is the mid-point, in front of the thigh. It is in front of the middle of the sartorius muscle; and the femoral artery lies deep to this muscle.

94. PAKKA VARMAM

It is on either side of the upper end of the tibia.

95. KOLACHI VARMAM

It is the region around the ankle joint.

96. MUDICHU VARMAM

It is in the middle of the dorsum of the foot.

97. SIRU VIRAL KAVALI VARMAM (of foot)

It is in the web between the 4th and 5th toes.

98. SIRATTAI VARMAM

It is the region in front of the patella. The patellar plexus of nerves supply this area.

99. KAL MUTTU VARMAM

It is on either side of the patella.

100. KAL KANNU VARMAM

It is about 2.5 cms below Kal Kannu Varmam. It is over the medial condyle of the tibia.

101. NAI THALAI VARMAM

It is about 2.5 cms below Kal Kannu Varmam. It is over the medial condyle of tibia.

102. KUTHIRAI MUHA VARMAM

It is the point in the middle of the front of the shaft of the tibia. The tibia can be palpated over this region.

103. KOMBERI VARMAM

It is over fhe shaft of the tibia about 10 cms below Kuthirai Muha Varmam.

104. KANNU VARMAM

It is the medial maleolus of the lower end of the tibia.

105. KONA CHANNI VARMAM

It is the medial side of the Ankle joint. The strong deltoid ligament of the ankle joint is deep in this region.

106. ADAKKA KALAM

It is on the bulging seen in medial border of the foot. The bone here is the tuberosity of the navicular-bone.

107. THIDA VARMAM

It is in the middle of the intermetatarsal space on the dorsum of the foot.

108. KANPUGAL KALAM

It is in the dorsum of interphalangeal joint of the big toe.

109. BHOOMI KALAM

It is the nail-bed of the big toe.

110. IDUPPU VARMAM

It is midway between iliac-crest and the greater-trochanter of the femur.

111. KILIMEGA VARMAM

It is the region of the greater trochanter of the femur; it is about 2.5 cms below the Iduppu Varmam.

112. HIPPIRAI VARMAM

It is about 2.5 cms below the Kilimega--Varmam (111).

113. ANI VARMAM

It is about 2.5 cms below the Ilippirai Varmam.

114. KOCHU VARMAM

It is the middle of the gluteal fold. The sciatic nerve, the biggest nerve in the body crosses this point.

115. MUDAKKU VARMAM

It is the middle of the back of the knee. The popliteal blood vessels and the tibial nerve lie deep to this point.

116. KULIRCHAI VARMAN

It is the point on the lateral side of the neck of the fibula. The common-perponeal nerve can be palpated in this point and pressed against the bone.

117. KUSATHIDA VARMAM

It is on either side of the "calf muscles"

118. UPPUKUTHI VARMAM

It is the region of the calcaneum (heel). The medial calcaneal nerves and blood vessels supply this zone.

119. PATHA CHAKKARA VARMAM

It is the middle of the sole of the foot.

120. PATHAKKUL VARMAM

It is the region of the ischial tuberosity of the hip bone. It is the point through which weight is transmitted during sitting posture.

121. KEEL CHULI VARMAM

It is a point 2.5 cms below the Kochu Varmam. The sciatic nerve and the posterior cutaneous nerve of the thigh are deep to this point.

122. MUNDAGA VARMAM

It is the point in the middle of the back of the leg. The sural nerve crosses this point.

123. MANI ADANGAL VARMAM

It is in the clitoris of the female; which corresponds to the penis in the male.

A SCIENTIFIC APPRAISAL REGARDING THE MODE OF ACTION OF AYURVEDIC DRUGS WITH SPECIAL REFERENCE TO HERBS AND HORMONES

S. N. Tripathi

India is very rich in flora, largely because of it's great dimension and geographical variations. So the plants growing in cold and hot, hills and plains, in humid or in dry weather, all have a fertile atmosphere to grow in our country. Out of this flora more than thousand plants have been recognised for their medicinal value and are used in therapy by Ayurvedic and Unani practitioners as well as in folklore medicine. Becauee of the extensive use of medicinal plants in the treatment, Ayurveda is known in foreign countries as a herbal treatment and Ayurvedic physicians as herbalists. It may not be the whole truth, as Ayurveda is almost a system of medicine based on fundamental principles regarding the concept of positive health, etiology and pathology, symptomatology diseases and pharmacology and therapeutics of drugs. However, there is no doubt that herbs have to play a major role in the Ayurvedic system of medicine.

Pharmacological action of the herbs has been described in the Ayurvedic system of medicine according to the properties and action in the terms of Ras, Guna, Veerya, Vipaka and Prabhava and their effect on Dosha, Dhatu, Mala, Agni, Ama, Ojas etc. But it is not understood by the scientific world. Hence several attempts have been done by Indian as well as

foreign scientists to elucidate the mode of action of these drugs on scientific parameters. It is interesting to record that uptodate many of the drugs have been found to be not effective on scientific parameters and it is difficult to explain the clinical effects observed. Thus, there is ample scope to rethink, postulate and investigate the mode of action of these drugs on new scientific models which have not been tested.

If we reconsider the concept of disease according to Indian medicine all the indigenous are psychosomatic in nature i. e. the somatic disease have their roots in the minor psychic disturbances induced by non-homologous contact of sense objects with sense organs (Asatmya-Indryartha-samyoga). This leads to an increase in Rajas or Tamas, at the level of the psyche. This in turn vitiates the body humors vata, pitta and kapha, the immediate cause of disease. Among them vata disturbances are most likely to follow the neuronal pathways and Paittika disorders are likely to effect the soma through the endocrine system and Kapha is more likely to disturb the immunity mechanism of the body.

1. Psychotropic Drugs (Medhya Rasayana)

These drugs are likely to act at the level of psyche, preventing the pathological effect of non-homologous contact of sense organs by counteracting the effect of hyperactive Rajas and Tamas. These drugs may be labelled as psychotropic drugs and many of our herbs like Bramhi, Mandookparni, Shankhapushpi, Asvagandha. Jatamansi, etc. are known to have psychotropic effects. They are not only indicated to be used for psychic disorders, but are also noted for their preventive and curative effects on somatic diseases. Hence, these herbs re the constituents of several compound preparations used for systemic diseases. Of course, their effect is through the mind.

2. Drugs Acting on Vata System

Some drugs may have direct ant'-Vata effect, acting on neuronal pathways by increasing or decreasing the conductivity

of nerves. They may be affecting the neurohumours governing the neuronal activity and the drugs described above, having psychotropic action, are also likely to have influence on the nervous system. In addition, all the Sneha dravyas, as the drugs having fats and oils, haveg reat influence on this system. Apart from that, there are some specific drugs which have a healing or stimulating effect on the Vata system, e. g. Kupilu (S. *nux vomica*), Bala, Atibala (Sida group of drugs).

3. Drugs Acting on Pitta System

Pitta and Agni has been considered to be similar substances from the physiological, pharmacological and pathological points of view. The concept of endocrine system is closely correlated with the concept of Agni and Pitta. Agni is supposed to regulate the entire metabolic activity of the body, and the role of hormones in metabolism is well established today. So, a large number of drugs, known to have action on Pitta system, are likely to stimulate or suppress the endocrine activities. Anti-vata and Anti-kapha drugs are also like to have a stimulating effect on the endocrine glands indirectly, as the property of Kapha and Vata is opposite to Pitta.

4. Drugs Acting on Kapha System:

Among the Doshas, Kapha is more obvious and is supposed to cause obstruction of the tiny channels of the body. By this obstruction, there is accumulation of nutrients and fluids at particular places leading to inflammatory changes. The cells are deprived of proper nutrients; hence they also stop functioning properly and thus the action of Kapha is more at the level of microcirculation and at cell membrane. This is probably due to antigen and antibody reaction, either humoral or cellular. Several mechanisms have been involved in developing hyper-sensitivity disorders. For example, due to exposure to different kinds of foods and drinks the body may become sensitive or the body may develop sensitivity to certain endogenous substances i. e. leading to autoimmune disease or

even the stress may induce changes in the immunity function of the body. In some case this may be linked genetically. Thus, the drug having anti-kapha property may be acting on immune mehanism, in different ways. It may increase the body resistance sufficiently to deal with the antigenic substances or it may desensitise the body gradually or it may suppress the immune mechanism itself. Many drugs in Indian Medicine may have such actions: most notable among them are Bhallataka (*Semicarpus anacardium*), Shirisha, Mustaka, Yashtimadhu, Vasa etc.

Drugs Action on Dushyas

Some of the drugs may have direct action on Dushyas, i.e. Ras, Rakta, Mansa, Meda Asthi, Majja and Shukra, which may be promoting or suppressing the growth and metabolism and can be beneficially used for the management of diseases having.

Drugs Acting on Malas:

Broadly, faeces urine and sweat have been recognised as Malas, and their accumulation in the system causes so many diseases. There are many drugs used in Indian medicine as purgatives or laxatives (Virechan), diuretics (Mutral) and diaphrotics (Swedal). On the other hand, in certain circumstances when there is excess secretion of these malas, i. e. diarrhoea, polyuria etc; then drugs which will prevent or minimise their excretion have to be given.

Rasayana Drugs

There is a concept of rasayana drugs in Indian medicine. These drugs have rejuvenative effect on the body. These are supposed to vitalise the body. induce positive health and help one to live his full span or life with good health and vigor The mode of action of these drugs is nothing different from what has been described above. Either they stimulate the digestion and anabolism in the body so that the intake is increased and there is improvement in the health or

they help the body in maintaining the complete homoeostasis by normalizing the hyperactivity of Doshas, or they offer the Dhatus to acquire their optimum functional capacity by improving nourishment and metabolism.

Antibacterial and Antiparasitic Activity

Probable mode of action described above is applicable to endogenous disorders. Apart from this, disease may be exogenous(Agantuka)as well by the infestation of micro organisms and parasites. Several herbs may have antibacterial and antiparasitic properties. But according to the philosophy of Indian Medicine, greater importance is attached to the soil than the seed-there is more emphasis on the treatment of the body than on the prescription of antibacterial and antiparasitic drugs *alone*. In the context of intestinal parasites, Charaka has advised a change in environment of the gut, which will not be congenial for the growth of the parasites (Prakriti Vighata). However, several drugs have been identified and many more can be clinched to have antibacterial and antiparasitic activity.

Thus, the herbs are likely to have their mode of action in one way or the other as described above and it has to be tested in suitable experimental models. It may not be within the reach of routine pharmacological laboratories; hence altogether a new set-up has to be organised to investigate the herbal activity as described in the Ayurvedic system of medicine.

Effect of Certain Herbs on Endocrine Glands

Keeping these facts in view, a small endocrinological laboratory has been established by us in the Department of Kayachikitsa; and an attempt is being made to find out the ef ect of certain indigenous drugs on endocrine glands. These investigations have widened the field of administration of these herbs and have provided a scientific basis for their use. A few examples are given below:

Commiphora mukul (Guggulu) and Thyroid

C. mukul is a known drug for lipid disorders and obesity (Medo-roga) in Ayurveda. We were the pioneers in testing the hypocholesterolemic and hypolipidemic and anti–atherosclerotic activity of this drug, as early as in 1963, in the Department of Kayachikitsa, Institute of Medical Sciences, Banaras Hindu University. There is a great controversy regarding the mode of action of this drug. Considering the pharmacodynamics of this drug, as described in Ayurveda a hypothesis was suggested that propably this drug may be activating the thyroid gland leading to more endogenous production of thyroxine which will accelerate the degradation of cholesterol into bile acids. Thus the body cholesterol is reduced due to enhanced excretion of cholesterol in the stool as bile (Mala pitta).

The action of Guggulu was tested on thyroid gland and it was found to counteract completely the action of neomercazole which is known to suppress the thyroid activity (Tripathi *et al*; 1975) along with reduction in blood cholesterol and blood lipid levels.

Recently the effect of *Commiphora mukul* on thyroid enzymes, participating in the synthesis and release of the thyroid hormones, was studied. It accelerates proteolytic enzyme leading to the release of T_3 and T_4 hormones. It is followed by the acceleration of peroxidase activity, responsible for iodination and coupling steps (Tripathi *et al*, 1984). Thus *C. mukul* has direct action on the thyroid gland in the synthesis and release of hormones.

At present, the drug is being tested on patients with ischaemic heart disease to evaluate its role in the management of C. H. D. Quite a big proportion of patients in this series have been found to have subclinical hypothyroidism. After the administration of the drug for a month and onwards, there was excellent improvement in thyroid function in terms of

I^{131} uptake as compared to initial readings. Simultaneously, along with hypocholesterolemic and hypolipidemic action by 6 to 12 months' treatment, the improvement in E. C. G. pattern of ischaemia has also been observed. Thus, the effect of Guggulu on subclinical hypothyroidism has been identified in human beings also.

Albezzia lebbek (Sirish) and Adrenals

Sirish is a renowned drug in Indian Medicine and is largely recommended for the treatment of Bronchial Asthma, Eczema, Urticaria and other skin diseases. It has been also prescribed for use in insect bites and is claimed to be the best anti-toxic drug in the pharmacopoeia of Indian Medicine. From the above description, we can draw the inference that *Albezzia lebbek* possesses anti-allergic and antihistaminic properties.

In a batch of 60 patients of bronchial asthma, histamine, histaminase, catecholamine and plasma cortisol were estimated. It was observed that blood histamine level was quite high in these patients as compared to control along with rise in plasma cortisol. A positive correlation between histamine and cortisol was also observed. After the administration of the drug, there was significant fall in the blood histamine level but it was associated with further rise in plasma cortisol. In a batch of guineapigs, similar model was used to produce bronchospasm with histamine injection and its treatment with *Albezzia lebbek*. Significant rise in plasma cortisol treated with A. lebbek has been noticed. Histological picture of the adrenal glands is also suggestive of this fact that A. lebbek helps in the adrenal steroid-ogenesis (Tripati et. al, 1979).

This may be the possible mode of A. lebbek in the amelioration of symptoms in the patients of bronchial asthma, eczema and skin disorders and insect bites.

C. tamala (Tejpatra) and Immula recemosa Pushkar moola) in Diabetes

Madhwasawa is a compound drug for the treatment of maturity onset diabetes (Kapha ja and Pitta ja Prameha)as described by Charaka. On a clinical trial, this drug was found to possess potent hypoglycaemic property. The same action was also confirmed in experimental studies on several models (Tripathi et.al, 1972).

An attempt was done to screen the hypoglycaemic property of all the ingredients separately, to identify the herbs having effect on glucose metabolism. Out of 30 ingredients of Madhwasawa about 10 drugs have shown good hypoglycaemic response. Among them I. recemosa and C. tamala have shown most potent hypoglycaemic property (Tripathi et al, 1979).

C. tamala has been tested for its action on insulin metabolism by radioimmunoassay technique. It has been observed that by the administration of alcoholic extract of C. tamala there is a rise in plasma insulin in the patients of maturity onset diabeties.

Thus, the hypoglycaemic action of these drugs may be through their effect on islets of langerhans leading to further release of insulin in patients of independent diabetes. These are the few examples of the work done on the herbs to study their effect as endocrine glands in order to establish their mode of action.

Action of kitchen Spices on Thyroid

Commonly, spices are considered to be a very good flavouring agents making the food more palatable. But these have been used in Indian medicine essentially for their medicinal properties. Most of them are Ushna Veerya according to Ayurveda and usually they are supposed to stimulate/accelerate the digestive and metabolic rate of the body. Hence, five

common kitchen spices were selected and tested for their action on the thyroid gland in Albino rats. These are

1. Kali mirch (Black pepper) - *Piper nigrum*
2. Jeera (Cumin seed) - *Cuminum cyminum*
3. Lal mirch (Red pepper chilli) – *Capsicum annum*
4. Bari Elaichi (Greater Cardamum) - *Amomum subulatum*
5. Dhania (Coriander) – *Coriander sativum*

Iodine uptake, Serum Protein Bound Iodine, Triiodothyromine (T_3). and Tetraiodothyromine (T_4), all have been found to be raised by the use of alcoholic extract of these spices. Histological examination also reveals increased cell height of the thyroid epithelium cell and increased vacuolisation within the colloid. Weight of the thyroid gland was also increased as compared to control. Thus to put it in nut-shell, with some variation all the above five spices having Ushna Veerya properties promote the thyroid function within the physiological limit.

It seems that a large number of Ayurvedic drugs are acting indirectly through the endocrine system, which needs a planned exploration. It may prove to be an altogether new concept of treating constitutional disorders Recently, C. C. R. A. S., New Delhi, has kindly sanctioned a project on Herbs & Hormones to work on this problem which is in progress. I hope it will reveal very valuable observations.

IMMUNOPHARMACOLOGICAL STUDIES ON PICRORRHIZA KURROA ROYLE-EX-BENTH

PART : I ANTI - INFLAMMATORY ACTIVITY

B. L. Pandey. M. Biswas* and P. K. Das*

Abstract

Picrorrhiza kurroa rhizomes have reputed medicinal value in Indian traditional system of medicine, Ayurveda and some clinical trials with crude rhizome-powder had shown its therapeutic potential in patients with immune disorders. Present study in rats and mice examined the anti-inflammatory activity in immunological and non-immunological models with positive results. Experiments carried out with watersoluble fraction of alcoholic extract of rhizomes (PK) reveal a slow onset, dose dependent anti-inflammatory activity mediated partly through the catecholaminergic system and interference with lysosomal enzyme release/activity. No propensity to gastric irritation was exhibited with repeated administration and the extract showed low toxicity. Possibility for existence of physiological or novel mechanisms of action of observed PK effects is discussed.

Introduction

Picrorrhiza kurroa, a small perennial herb growing in the Himalayas and other high altitude zones is known as KUTKI in

vernacular and is a reputed remedy for many chronic ailments in Ayurvedic system of medicine[1]. Folklore claims and reports of some clinical studies indicated effectiveness of the root rhizomes of P. kurroa in rheumatoid arthritis, bronchial asthma and some other disorders involving immune dysfunction[2,3]. An experimental evaluation in laboratory animals for some of these claims on P. kurroa has been taken up. The present report gives disclosure of the studies on anti-inflammatory activity evaluation.

Material & Methods

Chemical Extraction

Apparently healthy dried root rhizomes of Picrorrhiza kurroa were selected from the single lot supplied officialy by CCRIMH They were again testified for identity by both the Ayurvedic and Botany experts. They were powdered by milling and then subjected to extraction with 50% alcohol under reduced pressure boiling at 60° C. The extract was filtered and evaporated again similarly to yield a gummy residue. This residue was only partly soluble in water. A weighed quantity of this residue was taken and tritrated thoroughly with a known volume of distilled water for five minutes. In all, three changes with water were given to ensure near complete separation of water soluble fraction. Solution from the above three changes was pooled and filtered again to give representative solution of the quantity of weighed alcoholic extract and is referred to as *'PK'* throughout the report. This solution was administered orally to rats or mice with the help of gavage tube and syringe and the untreated groups received only equivalent volumes of water. The dose is always referred in terms of mg/kg of the alcoholic extract taken initially.

Evaluation of anti-inflammatory activity in laboratory animals

All the animals were obtained from the central animal house of the institute and were maintained on identical food

and other living conditions in the animal house of this Department. A prior one week aclimatisation period in the departmental conditions was allowed before experimentations. While animals of both sexes were incorporated for screening experiments for activity, only male rats were used for experiments aimed at delineation of the mechanism of action.

Carrageenin induced paw Oedema in albino rats

The method for production of inflammatory oedema in the rat hind paw was the same as described by Winter *et. al*[4]. O. L. ml of 1% carrageenin solution was given in subplanter aponeurosis by injection through 24 gauge needle and paw volume were measured before and 3h. after injection to give the inflammatory oedema as the difference. Volume measurement was plethysmographic involving displacement of mercury column.

Initially an arbitrarily selected dose of PK, 200mg/kg was given to rats 1h. before carrageenin injection. This endeavour did not give any indication of inhibitory action on the oedema of PK. In view of the low doses prescribed in Ayurvedic practice and slow onset of clinical effect reported in studies referred above 2, 3 it was thought worthwhile to see if the drug has any delayed onset of action. Administration of PK was thus started in a daily schedule at 48, 24 and 1 hour before subjecting to carrageenin induced oedema procedure. Results as to be described later in table I. indicated 50mg/kg as the minimal dose with statistically significant inhibitory effect and 100mg/kg was the dose producing roughly as much inhibition as the dose of 200mg/kg. The subsequent studies were thus, conducted with the dose of 100mg/kg administered daily for 3days.

Immunological Inflammation

A. SRBC-challenge paw oedema in primed albino mice:

A modification of the method described by Bhattacharya[5] was adopted. Briefly, albino mice of either sexes were sensitised with 0.2ml of 4% suspension of sheep red blood cells in Alseiver's solution by subcutaneous injection in the nape of the neck. PK treatment started three days prior to sensitization and continued throughout the experimentation period. The animals were then challenged with injection of 0.02 ml of similar suspension of SRBC on day 6 of sensitization in the right hind paw. The paw volumes were determined immediately after injection of SRBC–challenge and at 24th after, by plethysmographic method.

B. Bacillus pertussis induced paw oedema in albino rats.

A modification of Arrigoni-Martelli's method was used[6]. Rats were sensitised by single injections of 2ml of tripple vaccine and 0.5ml of Freund's complete adjuvant given subcutaneously in the nape of neck separately. PK treatment commenced 3 days prior to this sensitization procedure and continued daily thereafter throughout the experimentation period. On day 8 of sensitization, the animals were challenged by injection of 0.1ml of tripple vaccine in one of the hind paws. The paw volume measurements were performed prior to and after 24, 48 and 72h. of challenge injection.

Studies on mechanism of anti-inflammatory action

A. Effect of bilateral adrenalectomy on anti-inflammatory activity of PK in carrageenin induced paw oedema in albino rats.

Albino rats, only males, were subjected to bilateral adrenalectomy by the method of Schultzer[7], under pentobarbitone–sodium 40mg/kg. i. p. anaesthesia. The animals were allowed to recover and were maintained on 5% glucose saline supplementation. 2 days after operation they were divided into 2 groups and the treated group received PK for 3 days. 1h. after the last dose of PK the animals were subjected to carrageenin

induced paw oedema procedure to evaluate the anti-inflammatory activity.

B. Effect of reserpinization on the anti-inflammatory effect of PK in carrageenin induced paw oedema in albino rats.

All male albino rats were given an intraperitoneal injection of reserpine (5mg/kg) and after 24h. of this were divided into 2 groups. The treated group received PK for 3 days, and 1h. after the last dose of PK they were subjected to carrageenin induced paw oedema as described earlier.

C. Effect of chronic administration of PK on adrenal, spleen and thymus weights and gastric mucosa.

100mg/kg daily dose of PK was administered to all male albino rats for 7 days. Controls received water similarly. On eighth day, they were sacrificed by cervical fracture and their thymus, spleen, both adrenals were cleanly dissected out, removed and weighed immediately. The stomach was removed and opened by cutting along the greater curvature and was washed with saline. Mucosa was examined with hand lense for any signs of irritation or ulceration.

D. Effect of PK on lysosomal labilization induced paw oedema produced with Nystatin in albino rats.

Nystatin is used to produce pedal inflammation through lyso somal enzyme release[8]. Nystatin induced paw oedema was produced by the method of Schiatti[9]. Briefly, 0.1ml of 6% suspension of nystatin powder in saline was injected in subplanter aponeurosis in one of the hind paws in rats. The paw volumes were recorded prior to and at 24h and 48h after the injection. PK treatment was given 100mg/kg daily for three doses the last one preceding the nystatin injection by 1h.

Toxicity studies

A. Acute toxicity in mice: Oral doses of 100, 250, 500 and 1000 mg/kg as single administration were given to groups o

adult mice comprising of 2 males and 2 females in each. The animals were observed for 24h to notice any morbid signs in behaviour or lethality.

B. Subacute Toxicity: Two groups of 10 rats in each with equal sex composition were made. The treated received PK 100mg/kg orally daily for 2 weeks and the control received water similarly. Daily food and water consumption, nature of the fur and pretreatment and posttreatment weight measurements were noted.

RESULTS

Carrageenin induced paw oedema in albino rats

PK treated rats showed significant inhibition of paw oedema in doses above 50 mg/kg but the anti-inflammatory effect was near maximal with 100mg/kg dose. As stated earlier, the extract produced anti-inflammatory action with delayed onset appearing on repeated administration for three days and not on single acute pretreatment. The inhibition of paw oedema by 100 mg/kg dose of PK with this schedule was comparable to that of 100 mg/kg dose of aspirin given as single dose oral pretreatment 30 min. before injection of carrageenin (table I).

Immunological Inflammation

Development of SRBC-challenge paw oedema in sensitised albino mice was significantly inhibited by PK pretreatment.

In rats the B. pertussis challenge delayed paw oedema was significantly inhibited by PK pretreatment (table II.)

Studies on mechanism of action

A. Effect of bilateral adrenalectomy.

Bilateral adrenalectomy by itself only caused an insignificant increase in the carrageenin oedema as compared to normal

animals i.e. those in table table. I. PK pretreatment however had an anti-inflammatry activitv persisting despite ablation of adrenals. (table III a).

B. Effect of reserpinisation.

Reserpinisation by itself produced obvious but statisticaly insignificant potentiation of carrageenin oedema as compared to the controls in table I. PK pretreatment persisted to show anti-inflammatory effect in reserpinised animals as well. The degree of inhibition of the inflammatory oedema was reduced however. (table III b).

C. Effect of 7 day-PK treatment on weights of spleen, thymus and adrenals and integrity of gastric mucosa.

There was no evidence of any change in weights of spleen, thymus or the adrenals by PK treatment. (table. IV)

There were also no signs of mucosal irritation in either treated or the control group.

D. Nystatin induced oedema.

Nystatin injection produces near maximal inflammatory oedema at 24h postinjection in our experiments. The PK treated group showed remarkable reduction in inflammation produced by the above lysosomal labilizer. (table. V).

Toxicity studies

A. Acute toxicity in mice

Over the 24th observation period there was no mortality even with the dose of 1g/kg orally. No significant change was apparent even in behaviour of the animals. Groups with 250mg/kg and above however showed passage of stools without bead formation and some showed frank loose stools. All animals were alert during the periods of observation and feeding actively.

B. Subacute toxicity in rats

Over the two week observation period there was no difference in any of the parameters studied in the control and PK treated animals.

Discussion

That traditional systems of medicine had recognised various useful herbal remedies for various disorders is now widely accepted. Often, however, the clinical practices, both diagnostic and therapeutic, in these systems fail to find exacting correlates with those in modern medicine. The disease classification is essentially based on symptomatology and therapy designed with varied preoccupations. It becomes difficult therefore to define with certainty, the pharmacological activity to be evaluated with respect to the traditionally prescribed use of an indigenous drug. Nevertheless presumptions based on nature of traditional use and evaluation of specific beneficial activity of indigenous drugs has been found to be a successful approach in medicinal plant research.[10] Based on the reported use of P kurroa in chronic ailments and encouraged with reports of clincial trials 2, 3 benefiting patients of arthritic and other immune disorders, it was thought worthwhile to explore anti-inflammatoty activity-profile of the herb.

The formulation in which the drug is administered to patients is also important and requires to be considered while taking up work on indigenous drugs[11]. It often becomes difficult, however, to find rationale for peculiar formulation and quite often poses problems in animal studies for pharmacological evaluation. In view of the concept of active chemical principle behind the therapeutic property, the usual practice is to use extracts of plants for pharmacological evaluation and studies with 50% alcoholic extract has been advocated for start work[12]. Picrorrhiza kurroa rhizome are used as crude

powder by clinicians but 50% ethanolic extract was used in present evaluation of anti-inflammatory activity.

The techniques for anti-inflammatory activity used in the study were selected specifically to suit the explorations aimed at, on the basis of traditional use. Thus the widely used screening technique for anti-inflammatory agent namely the carrageenin induced paw oedema described by Winter *et. al*[4]. was used for initial screening for activity. The adult human dose of P. kurroa in chronic disorders used by traditional practitioners ranges from 500mg to 1g daily [13]. An arbitrarily selected high dose of extract namely 200mg/kg was thought adequate for initial study. That, this was ineffective in inhibiting corrageenin induced paw oedema, was soon observed, which conventionally should have led to dropping the drug from any further study. There are agents used in therapy which produce slow action in rheumatoid arthritis like goldsalts, penicillamine etc[14]. A second thought was thus mandatory on the test methodology to reveal anti-inflammatory effect of this traditional drug. PK was thus administered for three days, an adequately long period to establish indiginous drug actions in experience of this laboratory [15, 16]. The approach was fruitful and anti-inflammatory activity was discovered.

Dose response study was then performed that showed 50 mg/kg as the dose producing statistically significant anti-inflammatory effect in the sample size adopted by us and the effect was higher with increase in dose to 100 mg/kg and did not increase further with increase in dosages. The maximal anti-inflammatory effect observed with this schedule was comparable to that produced by 100 mg/kg dose of aspirin given as single dose 30 min. before injection of carrageenin. It would have been better to compare the standard drug by giving it in similar schedule as the test drug, but knowledge of the nature of anti-inflammatory activity of aspirin would not justify that approach here. Comparison with standard slow onset anti-rheumatic agents would have been more appropriate but that

would have brought in need for different methodology particularly sensitive to them. The latter was not justified here as the study is aimed essentially at preliminary confirmation of the activity.

With the anti-inflammatory activity confirmed and schedule of administration standardised, the maximal effective dose was used for subsequent experiments. With need for agents to be effective in treating rheumatoid arthritis and reported specific use of *P. kurroa* in rheumatoid arthritis, only immunological inflammation models were taken for study. Both the models used here, involve delayed type hypersensitivity reaction and have an added benefit of depicting anti-inflammatory activity in two species viz. rats and mice. PK administration was started before sensitization and continued till challenge, the schedule thus covered all the events in development and expression phases of immune response and hence was suitable as a screening method. PK did effectively suppressed the immune inflammatory reaction in both mice and rat models.

The above observations not only lend credence to reported use of *P. kurroa* in inflammatory and immune disorders but also speak of the presence of the active principle in the water soluble fraction of the alcoholic extract that was used in this study. In view of this it was thought safe to proceed with explorations of the mechanism of observed anti-inflammatory action of PK. Though the observed maximal anti-inflammatory effect in our experiments of PK was not more than that of 100 mg/kg of aspirin, studies on mechanism of action were required to forsee if PK has any prospects for developing into an antiarthritic drug in the crowded unsatisfactory armamentarium of anti-inflammatory agents. Only male rats were used in these studies to minimise influence of physiological variables on mechanism studies at this stage.

The delayed development of anti-inflammatory effect of PK makes room for considering possibility of the action being mediated through some physiological mechanisms indirectly.

In this respect the well known physiological mechanisms likely to be involved are the adrenocortical hormones and the neurohumours of the sympathetic nervous system. Experiments were thus performed to uncover their role if any behind the observed anti-inflammatory effect of PK. Bilateral adrenalectomy was thus performed before starting PK treatment in rats and their subsequent submission to carrageenin oedema induction. Adrenalectomy is known to potentiate the carrageenin oedema in rats[17]. Even our results exhibit similar tendency but with the sample studied the results do not reach statistical significance That PK pretreatment continues to inhibit carrageenin oedema in adrenalectomised rats indicates the action to be independent of intact adrernal function. Lack of any change in the weights of spleen, thymus and adrenals also reflect noninterference by PK in adrenal hormone secretion. From results of the present experiments it will be too naive to suggest any relationship o prostaglandin metabolism-alterations with PK treatment. There is for definite, however, no gastromucosal damage even with chronic PK treatment. This finding coupled with the observations of slow onset of action and lack of increase of the effect with increase in doses over that of 100 mg/kg of aspirin makes it unlikely that prostaglandin synthesis may be inhibited by PK. The exact role of prostaglandins in inflammation being itself debatable as pro or anti-inflammatory[18], conclusions in this regard may better be given up at this stage.

Results of studies in reserpinised rats are quite interesting. Reserpinization leads to depletion of catecholamines from the storage sites and effect of any agent acting through increased release of catecholamines should be abolished by reserpinization. In our experiments reserpinization shows a remarkable potentiation of carrageenin paw oedema *per se*. The anti-inflammatory effect of PK still persists but it is of a lesser degree as is obvious from the differences in the magnitude of the same in table I and table III b. It means therefore that the anti-inflammatory effect of PK is at least partly mediated through release of endogenous catecholamines. Further experiments

are underway to uncover the actual shape of this link. Reserpinisation however blocked the anti-inflammatory effect of PK only partly and hence additional mechanisms are also operating besides the catecholaminergic phenomenon.

In view of the above findings next explorative strategy was directed to the cellular events that are important in development of an inflammatory reaction. One of such major events is the release of lysosomal enzymes[19,20]. Nystatin is used to produce paw oedema in rats specifically by labilizing the lysosomal membranes and thus leading to release of proteases[8]. PK pretreatment inhibits oedema in this model also indicating thereby possibility of stabilization of lysosomal membranes or inhibition of proteases, the latter being a common factor in pathogenesis of inflammation and many immunological reactions[20,21,22]. The possibility is also worth consideration as several plant products are known to possess this action[23]. This aspect is also being presently studied.

Short of the ability of the results to provide clear picture of the mechanism of anti-inflammatory effect of PK, one gets encouraged with finding low toxicity of PK in both acute and subacute studies carried out. The present work thus, confirms the anti-inflammatory activity of *P. kurroa* and also validates the experimental strategy adopted to reach the same. Observations reported herein also give indications of presence of physiological or interesting novel mechanism of action of *P. kurroa*, the popular drug in traditional Indian medicine.

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TABLE I: EFFECT OF PK & ASPIRIN ON CARRAGEENIN-INDUCED PAW OEDEMA IN ALBINO RATS
(8 in each group)

Group	Treatment	%Increase in Paw Volume Mean ± Se	P Value
CONTROL	Water×3 Days	33.3 ±3.4	
ASPIRIN	100mg/kg.30min.	14.2 ±2.4	<0.01
PK I	25mg/kg×3 Days	31.75±4.0	—
PK II	50mg/kg×,,	20.9 ±3.7	<0.05
PK III	100mg/kg×,,	17.3 ±3.8	<0.025
PK IV	200mg/kg×,,	18.2 ±3.7	<0.025

TABLE II : EFFECT OF PK ON IMMUNOLOGICAL INFLAMMATION

1. SRBC challenge paw oedema in sensitised albino mice (8 in each group)

2. B. pertussis challenge paw oedema in sensitised albino rats (7 in each group)

Group	%Increase in Paw Volume (Mean ± Se) at Given Intervals Post-Challenge 24h.	48h.	72h.	P Value (in comparison with the respective controls)
1.				
CONTROL	56.5 ±4.7			0.05=*
PK	30.95±4.0**			0.01=**
2.				
CONTROL	26.0	38.0	44.0	
	± 3.8	± 3.7	± 2.5	
PK	14.9*	23.0**	29.9**	
	± 3.3	± 2.4	± 2.5	

TABLE III : SYMATHOADRENAL MANIPULATIONS AND EFFECT OF PK ON CARRAGEENIN-INDUCED PAW OEDEMA IN ALBINO RATS

A. Adrenalectomised rats (7 in each group)

B. Reserpinised rats (6 in each group)

Group	% Increase in Paw Volume Mean ± se	P value
A.		
CONTROL	38.0 ± 5.1	
PK	20.3 ± 3.8	<0.025
B.		
CONTROL	43.8 ± 2.3	
PK	31.4 ± 5.1	<0.05

TABLE IV : EFFECT OF CHRONIC (100 mg/kg daily × 7 days) ADMINISTRATION OF PK ON WEIGHTS OF SPLEEN, THYMUS AND ADRENAL GLANDS IN ALBINO RATS

(10 in each group)

Group	Weight in mg/kg body weight, mean ± se		Adrenal
	Thymus	Spleen	(Both)
CONTROL	115.6 ± 10.9	224.8 ± 29.4	33.2 ± 2.0
PK	122.4 ± 12.3	241.6 ± 32.2	26.4 ± 2.2

TABLE V : EFFECT OF PK ON NYSTATIN INDUCED PAW OEDEMA IN ALBINO RATS
(8 in each group)

Group	% Increase in Paw Volume at Given intervals of Nystatin Injection Mean ± Se		P Value
	24h	48h	
CONTROL	42.5 ±3.2	41.1 ±2.7	
PK	17.0* ±5.2	17.6* ±4.3	<0.001 = *

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PLANT EXTRACTS ECHITAMINE AND PLUMBAGIN POSSESS ANTITUMOUR ACTIVITY

B. Nagarajan and B. Chandrasekaran

Abstract

Plant extracts echitamine from *Alstonia scholaris* and Plumbagin from *Plumbago zeylanica* were screened for antitumour activity on fibrosarcoma growth in rats. This was a transplantable tumour, originally induced with methyl Cholanthrene. It was localised, growing only at the site of implantation. Both the products tend to show about 75% tumour regression. Combined treatment did not significantly alter tumour weight. Though solubility was a constraint, oil suspension of plumbagin exhibited a better tumour inhibiting potential. Pharmacokinetic studies showed subtle differences. Echitamine was absorbed rapidly from the tissues and reached a detectable level in blood with 30 min and a maximum at 2 h. which decreased steadily to almost zero at 6 h. It was detected in urine within 2 h and the excretion was maximum between 2-4 h; almost 90% was out at this stage. In addition to the parent compound, few metabolites were also detected in the urine. However, plumbagin showed a rather slow uptake with an extended period of retention. It was not detected in blood upto 24 h. In urine it was present within 4 h and reached a maximum at 24 h traces of the drug were observed in the urine even after 48 h.

Introduction

Many of the antitumour drug screening studies using plant extracts culminated in successful utilization for the treatment of human tumours. Some of the plant extracts such as Thalicarpine, Ellipticine and Taxol were reported to have antitumour activity (1, 2). We made an attempt to study the effect of echitamine and plumbagin in controlling the growth of fibrosarcoma in rats. Due to unavailability of standard tumour model system, we chose to use fibrosarcoma in rats to serve the purpose of assessing cytolytic action alone.

Materials and Methods

Echitamine and plumbagin were generous gifts from Dr. K. K. Purushothaman, Captain Srinivasa Murthi Research Institute, Madras.

Fibrosarcoma: Fibrosarcoma was induced in Wistar rats by subcutaneous implantation of Millipore filter disc impregnated with a 5% suspension of 20-methyl-cholanthrene in parafin oil (3). Tumours which appeared in about 4 weeks after implantation were highly localized and were maintained by serial transplantation. The tumour was minced and suspended in normal saline. A suspension of about 1×10^6 cells in 0.5 ml of saline was injected into the thigh, subcutaneously. The transplanted tumour became palpable in 4 to 6 days time and measurable on day 9 and then steadily grew up to the end of the second week after which necrosis set in and the animal eventually died in about 4 weeks.

Drugs : Echitamine used was in the form of echitamine chloride; 20 mg of echitamine was dissolved in 1.0 ml of water and 10 mg of plumbagin in 1.0 ml of olive oil under aseptic condition and were injected into rats intramuscularly. The drug was given in divided doses for each rat from day 1 and continued upto day 13. The day on which the tumour was implanted into rat was taken as day 0.

Rats were divided into eight groups and were given echitamine and plumbagin on 1, 5, 9, 13 days (D_1 and D_3) and on alternate days (D_2 and D_4) Ten mg of echitamine was given in 4 divided doses followed by 5 mg of plumbagin in 3 divided doses (D5) on alternate days; 5 mg of plumbagin in 4 divided doses was given followed by 10 mg of echitamine in 3 divided doses (D6). Pretreatment was carried out with 4 doses of echitamine (D7) or plumbagin (D8) followed by 3 doses on alternate days after transplantation. Separate controls were maintained for echitamine and plumbagin. Body weight and tumour weight were measured daily for each rat and continued upto 16 days.

Tumour weight : The resultant solid tumour after subcutaneous implantation is considered to be a prolate ellipsoid with one long axis and two short axes. The two short axes are assumed to be equal. The longest diameter (length) and shortest diameter (width) are measured with vernier calipers. Assuming specific gravity to be approximately one, and to be three, the mass (in g) is calcuated by multiplying the length of the tumour by the width squared and dividing the product by two (4)

$$\text{Tumour weight (g)} = \frac{\text{Length (cm)} \times \text{width (cm)}^2}{2}$$

Tumour weight obtained from vernier calipers measurements of length and width and actual weight measurement of the tumour were found to be nearly the same.

Results and Discussions

Changes in mean tumour weight in the group of rats given echitamine and plumbagin in two dose schedules, in combination therapy and also the pretreatment of drugs are shown in table 1. The body weight of rats did not alter appreciably in drug treated rats from tha of controls. On drug treated rats, the tumour did not disappear totally but the growth of tumour was regressed when compared to that of controls. Proper controls both for echitamine and plumbagin did not show any difference in mean tumour weight. When the mean tumour

weight of each of 8 groups of rats treated with echitamine or plumbagin was compared to that of controls on day 16, rats treated with echitamine on 1, 5, 9, 13 days and on alternate days showed 62.5 and 66.3% regression in tumour weight and plumbagin treated rats showed about 75 and 73.7% regression in tumour weight in groups D_3 & D_4 respectively. Combined therapy with echitamine followed by plumbagin and vice versa did not produce any different effect from individual treatments. Pretreatment of rats with echitamine or plumbagin followed by implantation of tumour cells did not delay the appearance of tumour. However it showed about 53 and 56 7% regression in tumour weight.

Drugs such as 5-fluorouracil and cyclophosphamide have limited use in the management of disease. There is a need for more selective and effective chemotherapeutic agent to control tumour growth. We reported studies on the mechanism of action of this compounds and also methods to estimate the biological levels of echitamine and plumbagin (6). Part of this work on tumour inhibition has been published (7)

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Table 1: Mean tumour weight of rats treated with echitamine (D_1&D_2) and plumbagin (D_3&D_4) on 1, 5, 9, 13 days and on alternate days; combined treated with echitamine followed by plumbagin (D_5) and vice versa (D_6); pretreatment with echitamine (D_7) or plumbagin(D_8)*

Days after drug treatment	Controls	D_1	D_2	D_3	D_4	D_5	D_6	D_7	D_8
9	0.559	0.216	0.188	0.375	0.320	0.214	0.378	0.328	0.272
10	1.230	0.387	0.427	0.612	0.518	0.518	0.492	0.494	0.322
11	1.572	0.521	0.362	0.707	0.869	0.695	0.695	0.513	0.435
12	2.353	0.877	0.808	0.997	1.425	1.231	1.703	0.963	0.836
13	3.887	1.468	1.229	1.235	1.445	1.520	2.021	1.931	1.805
14	4 751	2.169	1.861	1.561	1.585	2.288	2.312	2 589	2.427
15	6.066	2.446	2.245	1.937	1 886	2 302	2.482	3 068	2.963
16	8.010	3.057	2.695	2.069	2.522	2.540	2.554	3.754	3.467

* The data represent mean tumour weight of 6-10 rats. The dose schedule is given under 'materials and methods'. Mean tumour weight for separate controls both for echitamine and plumbagin were nearly the same.

AN *IN VITRO* STUDY OF THE ANTI-INFLAMMATORY ACTIVITY OF SOME FLAVONOIDS BY HRBC MEMBRANE STABILISATION

R. Arivudainambi, D. Sukumar, V. Sethuraman, N. Sulochana and J Sadique

Abstract

An *In vitro* study of the anti-inflammatory effect of some flavonoids (quercetin, hyperoside, rutin, naringenin and naringin) by the HRBC membrane stabilisation was made and the compounds were found to be effective. Most of the compounds showed biphasic effect with a critical concentration at which the membrane stabilisation was maximum.

Introduction

There is positive evidence to show that lysosomal enzymes play an important role in the development of acute and chronic inflammation (1–5). Increased enzyme activity has been reported in certain types of experimental inflammation including rat paw made edematous by phlogistic agents (6–7). The inhibitory effects of non-steroidal anti-inflammatory drugs onlysosomal enzymes have been proposed as an explanation for one of their many mechanisms of action *in vitro* (8). Acidic anti-inflammatory compounds such as phenyl butazone, mefenamic acid and indomethacin havebeen shown to exert their beneficial effect by inhibiting the activities of either released lysosomal enzymes or by stabilising the lysosomal

membrane (9–11). Several other investigations carried out also reveal the ability of the anti- inflammatory drugs to stablise the lysosomal membrane and to inhibit the lysosomal enzymes (12–14).

It has been reported that the structure of RBC is similar to lysosomal membrane components (15). Since lysosomal membranes resemble Human RBC membranes, the lysosomal membrane stabilisation effects have been studied using HRBC. When the RBC is subjected to hypotonic stress, the release of haemoglobin from RBC is prevented by anti-inflammatory drugs because of the membrane stabilisation. So, this HRBC membrane stabilisation by drugs against hypotonicity induced haemolysis serves as a very useful *in vitro* method for assessing the anti-inflammatory activity of compounds.

The anti-inflammatory activity of flavonoidal compounds are well known (16). It has been reported that the flavonoids rutin, tri (hydroxyethyl) rutin, magnesium flavonic chelates exert *in vitro* stabilising effect on the lysosomal membranes (17). In the present investigation, an *in vitro* study of some of the flavonoids by finding the stabilisation of the HRBC membrane against hypotonicity induced haemolysis has been made.

Materials and Methods

Collection of Blood

Blood was collected from healthy human volunteers using sterile 22 gauze hypodermic needle. The collected blood was mixed with equal volume of sterilised Alsever solution (containing 2% dextrose 0.8% sodium citrate, 0.05% citric acid and 0.42% sodium chloride) and stored at 4°C.

Saline

Saline at different concentrations was prepared (Isosaline 0.85% and hyposaline 0.36%).

Preparation of HRBC suspension

The blood was centrifuged at 3000 RPM and the packed cells obtained were washed with isosaline (0.85%; PH 7.2) 3 times and a 10% (v/v) suspension was made with isosaline.

Determination of HRBC membrane stabilisation

Solutions of different concentrations of flavonoids were prepared. Assay mixture contained the drug (flavonoid in concentrations as mentioned in Table I), 1 ml. of phosphate buffer (0.15M; PH 7.4), 2ml of hyposaline (0.36%) and 0.5ml of 10% HRBC suspension. In another tube, instead of 2ml of hyposaline, 2ml of distilled water was taken and this served as the control. All the tubes were incubated at 37°C for 30 minutes. Then they were centrifuged and the haemoglobin content in the supernatant was estimated using a photoelectric colorimeter at 560 nm.

Percentage of haemolysis was calculated, assuming the haemolysis produced in presence of distilled water to be 100%. The percentage of HRBC membrane protection was determined using the formula.

Percentage of protection =

$$100 - \frac{\text{OD of the drug treated sample}}{\text{OD of the control}} \times 100$$

The results obtained were shown in the Table I and the Graph I.

Results and Discussion

In general, the flavonoids were found to be effective in stabilising the HRBC membrane against hypotonicity induced haemolysis and hence would be effective as non-steroidal anti-inflammatory compounds in the control of inflammation.

Within the experimental range of dosages of(10 to 500μg/g ml) among the flavonoid aglycones, quercetin exhibited 76% protection at 10μg dose and at subsequent doses, the protection decreased and reached a minimum at 250μg and then increased very sharply. But in the case of naringenin, the result was slightly reversed. The protection was minimum at 10μg, reached a maximum at 50μg and then decreased.

In the case of flavonol glycosides (rutin and hyperoside), it was found that a relatively low value of protection 10μg and this reached a maximum at 50μg. Then the value fell and was maintained more or less constant at higher doses. In the case of flavanone glycoside (naringin) also this trend seemed to persist. In general, the 50μg dosage seemed to be an optimal dosage at which most of the flavonoids showed maximum HRBC membrane stabilisation effect.

TABLE I : EFFECT OF SOME FLAVONOIDS ON THE HRBC MEMBRANE STABILISATION AGAINST HYPOTONICITY INDUCED HAEMOLYSIS

Sl. No.	Dose (µg/ml)		Percentage of protection			
	Flavonoid	Quercetin	Hyperoside	Rutin	Naringenin	Naringin
1	10	76	43.5	64.5	50	25.2
2	50	64	85.2	72.6	80	61.3
3	100	68	65.8	54.8	—	—
4	250	44	69.4	54 8	50	65.8
5	500	95	69.4	54.8	56	65 8

It has to be noted in this connection that various workers have indicated a biphasic activity in the protection of HRBC lysis by non-steroidal anti-inflammatory drugs (18–20). That is, the protection increases when the concentration of the drug is increased. After a critical concentration the activity slows down. A similar property is found to be exhibited by rutin, hyperoside, naringenin and naringin except quercetin. But in all these cases, at very high concentration, the lowered activity is maintained constant. This property is different from the non-steroidal anti-inflammatory drugs. But in the case of quercetin, the same trend is maintained except that a

higher concentrations the fallen activity climbs up again. So, it is likely that the anti-inflammatory activity of these compounds under *in vitro* experimental conditions may be dependent upon the concentrations of these compounds.

Though it is too early to draw any conclusion as to the structure-activity relationship of various flavonoids, the results indicate that there may exist such a correlation and that this system could be used as an effective model for finding the structure activity relationship among the various flavonoid compounds.

Acknowledgement

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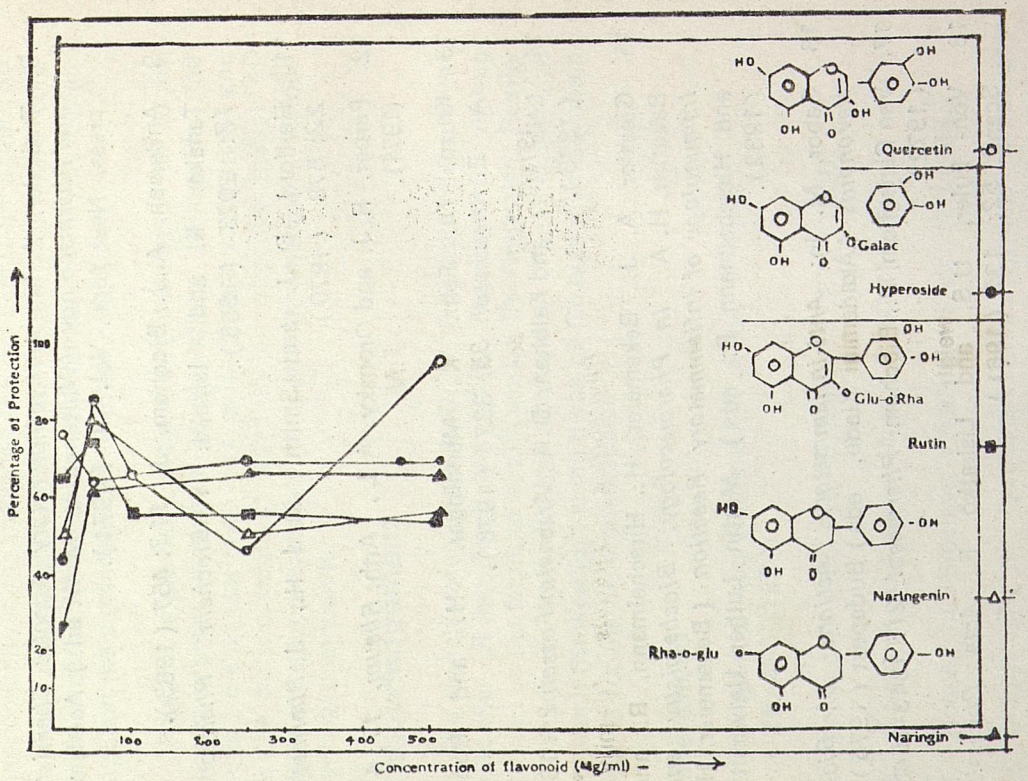
Percentage of Protection
100
80
60
40
20
0
100
200
300
400
500
Concentration of flavonoid (Mg/ml)
Quercetin
Hyperoside
Galac
Rutin
Glu-o-Rha
Naringenin
Rha-o-glu
Naringin

PRELIMINARY PHYTOCHEMICAL AND EXPERIMENTAL ANTI-INFLAMMATORY EVALUATION ON PETROLEUM ETHER EXTRACT OF PHYLLANTHUS FRATERNUS

V. I. Hukeri, G. A Kalyani, H. K. Kakrani, and M. K. Bagi

Abstract

The Phytochemical and experimental anti-inflammatory evaluations were carried out on dried Petroleum ether (40-60° C) extract of *Phyllanthus fraternus* (Family : Euphorbiaceae).

It was found to have β -sitosterol (T. L. C., I. R. & NMR)

The 10% suspension of the extract (with Tween 20) was utilised for the evaluation of local and systemic anti-inflammatory activity in mice and rats. Topical application of xylol to the inner surface of pinna of mice and carrageenin induced rat paw oedema methods were used as experimental models. On intraperitoneal injection (500, 1000 & 2000 mg/kg body weight) and topical application (1, 2 & 3 mg), the extract showed dose dependant (0.65, 18 5 & 45.4%) and (8. 1, 10.4 & 13 4%) anti-inflammatory activity respectively when tested in mice. The i.p. administration in rats did not show this action. However, concomitant injection of drug along with carrageenin in paw showed marked anti-inflammatory action.

Introduction

Phyllanthus fraternus (Synonym : *P. niruri*) of family Euphorbiaceae is an annual herb, growing upto the height of 60 Cm. The herb is bitter in taste and reported to have diuretic, astringent, febrifuge and antiseptic properties. It is used in G. I. T. disorders and some diseases of uro genital system. The fresh roots are said to be beneficial in jaundice. The leaves are made into poultice with rice water for application on oedematous swellings (Anonymous 1973, Dastur Nadkarni 1954, Chopra 1982, Kirtikar and Basu 1933).

The chemical examination of the various extracts o the plant have showed the presence of a bitter substance phyllanthin (Ottow, 1961) hypophyllanthin (Row et al 1966, 1969), lignins (Anjaneyulu et. al. 1973), alkaloids (Rouffiac & Parello, 1969), glycoflavones (Chauhan et. al. 1977), and some other flavonoidal compounds (Chauhan 1979). The component fatty acids of the seed oil of *P. fraternus* is also reported earlier (Ahmad et. al. 1981).

Ramkrishna et. al. (1982) have reported the hypoglycaemic activity of its aqueous extract and Hukeri (1983) noticed the same activity in the flavonoidal glycosides present in ethanol extract of the plant under study. In the present communication, we report the results of preliminary phytochemical examination and evaluation of local and systemic anti-inflammatory activity of petroleum ether extract.

Materials and Methods

A) Plant material: The plant material was collected from the outskirts of Bangalore city, identified by Dr C. J. Saldhana, Head, Dept. of Botany, St. Joseph's Arts & Science College, Bangalore. The plants were freed from adhering soil etc. and dried in shade for 7 days.

B) Preparation of Extract: The dried plant material was coarsely powdered and exhaustively extracted with petroleum ether (40–60° C) for 16 hrs. The ratio of drug and solvent was kept at 1 : 4. The extract was filtered and dried 'in vacuo' in rotary flash evaporator (Toshniwal type) which yielded a dark green waxy residue.

C) Phytochemical Studies: A part of waxy residue (50G) was saponified according to B. P. 1980 procedure. The saponified material was taken into a separator and washed with 100 ml water. The contents of the separator were then extracted with successive quantities of petroleum ether (40-60 C) (30ml X 4). The ethereal solutions were transferred to another separator containing 75 ml distilled water, washed, extracted twice with 25 ml. of 0. 5 N aqueous KOH and washed again till alkali free.

The ethereal layer was then dried 'in vacuo' giving yellowish green residue which was shaken with acetone and quickly filtered off. The filtrate was left overnight in a china dish. Next day white needleshaped crystals were observed on the walls of the dish, which gave positive test for sterols.

These crystals were subjected to T. L. C, using (i) Chloroform (ii) Pet. ether (40–60° C) : Acetone 9:1 as solvent systems. Antimony trichloride reagent was used for spraying the chromatogram.

Purification of isolated sterols was done by column chromatography on alumina (Total column length 35 cm. diameter 2 cm. Alumina height 16 Cm.). The sterol mixture was dissolved in chloroform and column was loaded. Elution was done with various solvents in increasing order of polarity.

D) Pharmacological studies (Evaluation of Anti-inflammatory activity)

A 10% suspension of residue was prepared with Tween 20 and this suspension was utilized for the evaluation using 6 to 8 animals.

i) Xylol induced local inflammation

Local inflammation was produced by topical application of xylol to the mouse ear as per the method of Brown & Robson (1964). Animals were killed 30 minutes after xylol application by decapitation and their ears were amputed. Inflamed portion of ears was cut into equal sizes by cork-borer of suitable diameter and weighed immediately. These circular pieces were dried at 40°C for 4 hours and reweighed.

a) In separate groups of mice the suspension was administered orally (500, 1000 & 2000 mg/kg body weight) 30 minutes prior to xylol challenge. Equal volume of saline was administered in control animals.

b) In the other groups suspension was applied topically in 1, 2 & 3 mg doses, five minutes after xylol, to one ear of mouse. Second ear of the mouse served as control.

ii) Carrageenin induced rat-paw oedema

The inflammation was induced in the hind paw of albino rats by intraplanter injection of 0.05 ml of 1% carrageenin by the technique of Bhatt et. al., (1977) and volume of paw was measured Plethysmographically as well as by the method of Ignatius et. al. (1981). Each rat served its own control.

a) The suspension was administered orally (500, 1000 & 2000 mg/kg b.w.) 30 minutes prior to carrageenin challenge.

b) In an another group of animals the suspension (0.1ml) was injected in paw five minutes after carrageenin administration.

The statistical analysis was done by student's 't' test.

Results

A) Phytochemical Studies

The T.L.C. showed a prominent spot. (Rf.: 0.35 in 1st and 0.44 in second system) which was almost identical to the Rf of β-sitosterol. The Co. T.L.C. using authentic sample of β- sitosterol confirmed the same. Another faint spot (Rf.: 0 6 in first system & 0.75 in second system) was also noticed but could not be identified.

On column chromatography the fractions 35-45 and 45-47 gave single spot on chromatography which was identical with β-sitosterol. Purified sterol (m.p. 136-137°C) was confirmed as β-sitosterol by IR & NMR.

I.R. : (Perkin-Elmer 397 Spectrophotometer In Nujol at I.I.Sc. Bangalore) showed superimposable spectra.

NMR : (Sample in CCl_4 in various H 100, 100 MH_2) revealed sample pattern as of authentic β-sitosterol.

B) Pharmacological Studies

i) Xylol induced local inflammation

a) Orally administered suspension showed dose dependant reduction in wet as well as dry weight of ear of mice as compared to the control (saline) group. (Table - 1, Graph – 1)
b) Topical application of suspension simultaneously to the xylol challenge also reduced the inflamed weight of the mice ear. (Table - I I)

ii) Carageenin induced rat paw oedema

a) Systemically administered suspension did not show any anti-inflammatory activity in carrageenin induced rat paw oedema model.

b) Simultaneous injection of suspension in carrageenin challenged paw however showed some reduction in paw

volume (oedema) but it was not statistically significant. (Students 't' test).

Conclusion

The residue of the petroleum ether extract of *Phyllanthus fraternus* which was found to contain phytosterols showed anti-inflammatory activity on both oral as well as topical application in mice. But such effect was not seen by carrageenin induced rat paw oedema method. The xylol produces increase in weight of ear due to irritant action and the suspension was found to inhibit this action. Thus it can be concluded that petroleum ether extract of *P. fraternus* acts as a better inhibitor of locally produced inflammation.

TABLE I: ANTI-INFLAMMATORY ACTIVITY AFTER ORAL ADMINISTRATION OF P. FRATERNUS SUSPENSION

Dose	Increase in wet weight ear	Percent of control
Control	9.6 ± 0.06	—
500mg	9.2 ± 0.05	95.8
1000mg	8.2 ± 0.05*	85.4
2000mg	4.4 ± 0.03**	45.8

*$P < 0.05$ **$P \leq 0.01$

Dry weights showed insignificant results.

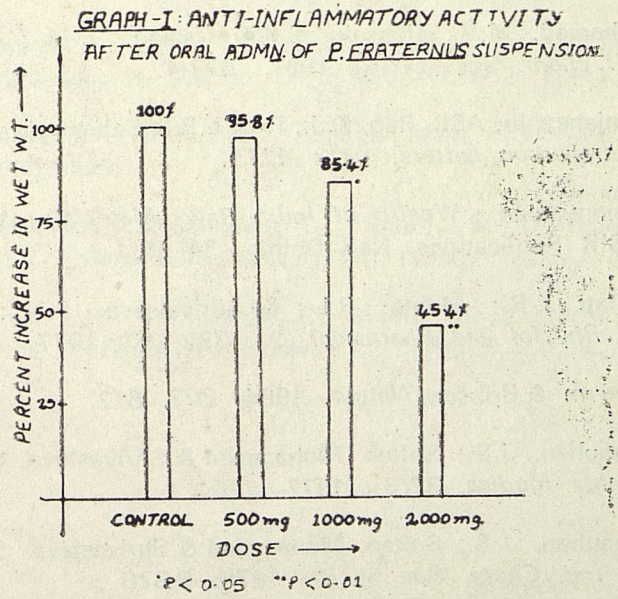

TABLE II: ANTI-INFLAMMATORY ACTIVITY BY TOPICAL APPLICATION OF P. FRATERNUS SUSPENSION

Dose	Untreated	Treated	Difference	Percent Decrease
Wet weight				
1mg.	4.7±0.26	4.28±0.17	0.42±0.02Ns	9.1
2 mg.	7.5±0.22	6.8 ±0.15	0.7 ±0.01Ns	9.3
3 mg.	6.0±0.19	5.1 ±0.25	0.90±0.01*	15.0
Dry Weight				
1 mg.	3.0±0.28	2.6 ±0.24	0.4±0.02*	13.3
2 mg.	7.3±0.27	6.3 ±0.34	1.0±0.12*	13.6
3 mg.	5.2±0.2	4.8 ±0.27	0.4±0.1Ns	7.7

*P<0.01.

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EFFECT OF *W. SOMNIFERA* ON CONNECTIVE TISSUE METABOLISM IN CHRONIC INFLAMMATION

S. Hazeena Begum and J. Sadique

Connective tissue which is the target organ for rheumatic diseases, often suffers the consequences of inflammation. The fundamental components of the ground substance are the collagen and Mucopolysaccharides (1). The root powder of. *W. somnifera* is traditionally used as an anti-rheumatic drug (2). Though its efficacy is known, its mode of action on connective tissue metabolism is not known. Here the study was focussed to elucidate the effect of drug *W. somnifera* on connective tissue metabolism. The model used for connective tissue metabolism is granuloma air pouch.

Materials and Methods (3)

Granuloma pouch was induced by subcutaneous injection of 4.0 ml of 2% carrageenin on the dorsum of male albino rats which were injected (sc) with 6.0 ml of air on the dorsum one day before. Within a few days after the carrageenin injection, a capsule of granulation tissue formed surrounding the air sac. After 10th day the gelatinous mass of tissues was removed and then the changes in the wet weight and the constituents of tissue were determined.

Medication

Animals were divided into 4 groups each consisting of 6 animals. One group was treated as control. The 2nd group was administered with the root powder of *W. somnifera* (100 mg/100 g b.w) and the 3rd and 4th groups were treated with standard drugs hydrocortisone 1.5 mg/100 g.b.w. and phenylbutazone 10 mg 100 g.b.w. respectively. These drugs were administered orally from 7th day to 9th day b.d and the animals were sacrificed on the 10th day and the granuloma was removed for analysis of different constitutents such as collagen and Mucopolysaccharides.

A group of rats used for the study of collagen were injected with ^{14}C proline 50 µci/100 g.b.w. on 9th day and the animals were sacrificed on 10th day. The granulation tissues were removed and used for the analysis of hydroxyproline content and radioactivity. Dried, defatted tissue samples were hydrolysed in a sealed tube with 6N HCl for 24 h. at 110 C After hydrolysis the samples were neutralised with 0.1 N KOH and used for hydroxy-proline estimation and radioactivity analysis using Rojkind method (9).

Another group of rats used for glycosaminoglycans were injected (ip) with 50 µci of $Na_2{}^{35}So_4$ per100 g.b.w. on 9th day and sacrificed on 10th day. The tissues were removed and dried. defatted for the study of ^{35}S incorporation (10) and Glycosaminoglycan (11). Uncoupling oxidative phosphorylation in Mitochondria (12) of granulomatous tissues was also determined.

Result and Discussion

From Table 1 it can be inferred that the wet weight of the granulation tissue is reduced to 28% in *W. somnifera* treated rats. In hydrocortisone treated group it was redcued

to 20%. No significant decrease was observed in phenylbutazone treated group. The explanation is that the drug *W. somnifera* controls the increase in cell number or the fibroplasia of granulation tissue. Table 2, shows that *W. somnifera* reduced the DNA content to 49% and hydrocortisone to 38% and phenylbutazone to 34%. The decresse or reduction in DNA content might explain the decrease in cell proliferation (3). Thus, the *W. somnifera* exerted significant anti-proliferative effect than standard drugs.

Table. 3, shows that the total collagen content was also reduced by *W. somnifera* to 26% but significant decrease was observed in hydrocortisone (41%) treated groups. The effect of phenylbutazone is insignificant.

The effect of drug on collagen metabolism was studied using ^{14}C–proline and its incorporation into protocollagen. The root powder of *W. somnifera* affected the incorporation of ^{14}C–proline into collagen hydroxylproline.

The incorporation of ^{14}C–proline into collagen was decreased to 46.5%, 35.3% and 33% in *W. somnifera*, hydrocortizone and phenylbutazone treated groups respectively (Table.4). This process of inhibition may be due to the interference with proline transport through cell membrane and may affect the proline pool size of the fibroblasts (4). Another possibility may be due to the inhibition of the enzyme propyl hydroxylase activity in granuloma (5).

Another basic substance is the glycosaminoglycan. The drug effect on the mucopolysaccharide synthesis was studied It can be seen from Table. 5 that the mucopolysaccharide content was reduced to 55% in *W. somnifera* treated group and 46% in hydrocortisone treated group and no effect was observed in phenylbutazone treated group. It is highly significant to note that degree of incorporation of labelled sulfate (^{35}S) was reduced to the maximum of 92% (Table 6) during administration of *W. somnifera*. Similarly, the hydrocortisone

showed an inhibition of 43.6% while phenylbutazone exhibited little effect.

Most of the anti-inflammatory drugs affect the mucopolysaccharide by inhibiting the introduction of ester sulfate into the polysaccharide (6). This process is the energy demanding process in which ATP is essential in the activation of sulfate.

Hence, a study was attempted to elucidate the uncoupling oxidative phosphorylation of *W. somnifera*. A significant reduction in the ADP/O ratio (Table. 7) was observed in *W. somnifera* treated groups in the granulation tissue. The uncoupling property was also reported for most of the anti-inflammatory drugs (7) under *In vitro* conditions. Present observation on treatment with hydrocortisone and phenylbutazone showed no marked inhibition of ADP/O ratio.

It can be inferred from the present result mucopolysaccharide synthesis in *W. somnifera* treated groups may be inhibited through the uncoupling of oxidative phosphorylation. So, it is clear from the present studies that the metabolism of connecitve tissue which contains collagen and mucopolysaccharide is deranged during the granulomatous inflammation and the derangement is brought to normal after treatment with anti-inflammatory drugs like *W. somnifera* and other anti-inflammatory synthetic compounds.

TABLE I : EFFECT OF ROOT POWDER OF *W. SOMNIFERA* ON WET WEIGHT CONTENT OF GRANULATION TISSUE IN CARRAGEENIN INDUCED AIR POUCH GRANULOMA

Subject	Drug dose Mg/100 g.b.w.	Granulation tissue wet weight (gms)	Percentage of inhibition
Control	—	11.0±1.5	—
W. somnifera	100	7.9±0.8	28
Hydrocortisone	1.5	8.9±0.5	20
Phenylbutazone	10.0	10.3±0.7	6

TABLE II : EFFECT OF *W. SOMNIFERA* ON DNA CONTENT IN GRANULATION TISSUE IN CARRAGEENIN INDUCED AIR POUCH GRANULOMA

Subject	Drug dose mg/100 g.b.w.	DNA content mg/total tissue	Percentage of inhibition
Control	—	2.77±0.21	—
W. somnifera	100	1.42±0.13	48.7
Hydrocortisone	1.5	1.72±0.16	37.9
Phenylbutazone	10.0	1.84±0.17	33.6

TABLE III : EFFECT OF *W. SOMNIFERA* ON COLLAGEN CONTENT IN THE GRANULATION TISSUE IN CARRAGEENIN INDUCED AIR POUCH GRANULOMA

Subject	Drug dose (mg/100 g.b.w.)	Total collagen (Mg)	Percentage of inhibition
Control	—	80.4 ±7.5	—
W. *somnifera*	100	59.23±4.5	26.3
Hydrocortisone	1.5	47.32±3.2	41.0
Phenylbutazone	10.0	70.0 ±5.0	13.0

TABLE IV : EFFECT OF *W. SOMNIFERA* ON INCORPORATION OF ^{14}c–PROLINE INTO COLLAGEN IN THE GRANULATION TISSUE IN CARRAGEENIN INDUCED AIR POUCH GRANULOMA

Subject	Drug dose Mg/100 g.b.w.	incorporation of ^{14}c–proline into collagen (cpm)	Percentage of Inhibition
Control	—	24390 ± 2258	—
W. somnifera	100.00	13054 ± 1344	46.5
Hydrocortisone	1.5	15776 ± 1040	35.3
Phenylbutazone	10.0	16306 ± 1560	33.1

TABLE V: EFFECT OF *W. SOMNIFERA* ON GLYCOSAMINOGLYCAN CONTENT IN GRANULATION TIS UE (μg URONIC ACID/gm. TISSUE) IN CARRAGEENIN IN DUCED AIR POUCH GRANULOMA

Subject	Drug dose mg/100 g.b.w.	GAG content μg uronic acid/gm tissue	Percentage of inhibition
Control	–	1324 ± 122	—
W somnifera	100.0	376 ± 36	71.6
Hydrocortisone	1.5	720 ± 69	45 6
Phenylbutazone	10 0	1949 ± 151	- 47.0

TABLE VI: EFFECT OF *W. SOMNIFERA* ON ^{35}S (INCORPORATION) INTO GRANULATION TISSUE IN CARRAGEENIN INDUCED AIR POUCH GRANULOMA

Subject	Drug dose mg/100 g.b w.	^{35}S incorporation into granulation tissue (cpm/ 100mg dry tissue)	Percentage of inhibition
Control	—	27562 ± 2100	—
W. somnifera	100.0	2192 ± 180	92
Hydrocortisone	1 5	15541 ± 1200	44
Phenylbutazone	10 0	32257 ± 2500	–17

TABLE VII : EFFECT OF *W. SOMNIFERA* ON UNCOUPLING OXIDATIVE PHOSPHORYLATION IN MITOCHONDRIA OF GRANULATION TISSUE IN CARRAGEENIN INDUCED AIR POUCH GRANULOMA

Subject	Drug dose mg/100 g.b.w	ADP/O ratio
Control	—	1.75 ± 0,15
W. somnifera	100.0	1.0 ± 0.10
Hydrocortisone	1.5	1.4 ± 0 25
Phenylbutazone	10.5	1.5 ± 0.13

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EFFECT OF PHYLLANTHUS NIRURI, LINN. ON CCl_4 INDUCED FATTY LIVER

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and
J. Sadique

Summary

Different doses of dried powder of *Phyllanthus niruri*, Linn. was tested against CCl_4 induced fatty liver in male albino rats. The various biochemical parameters such as alkaline, phosphatase, alanine transferase, gamma glutamyl transpeptidase, lipid peroxide level and albumin, globulin ratio were analysed in serum and liver collected from rats treated with carbon tetrachloride and *P. niruri*. The drug was effective in reducing the elevated activity of enzymes, lipid peroxides at all doses tested; but it was more effective at the dose of 100mg/100g.b.w.

Introduction

The liver diseases constitute a class of the most prevalent chronic diseases in India. The pathological process causing jaundice and other liver diseases are: haemolytic, congenital, toxic, infective, obstructive, drug sensitivity, etc. (1). Drugs or poisons causing liver cell necrosis include cytotoxics, sulphonomides, alcohol, carbon tetrachloride, chloroform, anaesthetics, halothane, etc. (2, 3).

The Siddha system of Medicine is well known to offer cure for hepatic jaundice and other liver diseases and Siddha literatures prescribe a number of herbal drugs such as *Eclipta alba*,

Curcuma longa, Phyllanthus niruri, etc. (4,5). But their beneficial effects, biochemical mode of action, dosage, active principles and toxicity have not been so far clearly established. People mainly depend only on *P. niruri* for all types of jaundice and the plant is known as Bhumyallaki in Sanskrit and Keezhanelli in Tamil (4, 5). For the present study *P. niruri* was selected and the effect was tested on CCl_4 induced fatty liver.

Fatty liver results due to accumulation of lipids, mainly triglycerides. Lipids accumulate for a number of reasons such as exposure to toxic substances such as carbon-tetrachloride or deficiency of lipotropic factors (7) CCl_4 impairs normal metabolic changes by causing necrosis on liver parenchymal cells (8). The fatty degeneration induced in the liver by CCl_4 has been related to impairment of protein synthesis and a consequent fall in lipoprotein formation (9). The effect of CCl_4 is not direct but depends rather on further transformation of molecules. This probably involves the formation of free radicals which may disrupt lipid membranes such as endoplasmic reticulam with the formation of lipid peroxides (10). The metabolism of CCl_4 in liver leads to increased lipid peroxidation and thus induces fatty liver (11). Spironolactone and promethazine treatment inhibited CCl_4 induced lipid peroxidation in liver microsomes (12).

The development of necrosis is associated with a leakage of hepatic enzymes into serum. There is an overall increase in hepatic synthesis of the enzymes such as gamma glutamyl transpeptidase, serum transaminases, alkaline phosphatase, etc. (13). In recent years more reliance has been placed on nczyme determination and it can be useful in showing the severity of the disease and in following its progress by drug treatment.

The aim of the present study is to estimate the level of alkaline phospatase, gamma glutamyl transpeptidase, alanine transferase, lipid peroxide level and serum albumin, globulin ratio during the exposure of CCl_4 on albino male rats and to evaluate the effect of different doses of air dried powder of

P. niruri. Alcoholic extract of indigoferatinctoria was effective against hepatotoxicity induced by CCl_4 (14). Similarly, aqueous extract of *Butea frondosa* flowers, an unani medicine was also found to be effective (15).

Materials and Methods

The fatty liver in male albino rats was induced by injecting (i.p.) CCl_4 at a concentration of 0.05ml CCl_4/100 g.b.w. per day for 5 days. This group was treated as control. To another group of rats treated similarly were given orally different doses of air dried powder of *P. niruri* suspended in 2% gum accacia solution for a period of 9 days. The control group induced with fatty liver received the equivalent quantity of 2% gum accacia solution. Animals were sacrificed on the 10th day, blood and liver were collected for the analysis. Liver was homogenised in ice cold buffer and serum was separated from blood.

Alkaline phosphatase was estimated by the method of Mohan S. Saini *et al*. (16) in serum using P-nitrophenyl phosphate as the sbustrate and in carbonate buffer pH 10. The specific nezyme activity was expressed as µg/nitro phenol released/mg protein/min.

Alanine transferase was estimated by the method of Bergmeyer and Bernt (1974) (17), in serum and the enzyme activity was expressed as µM pyruvic acid released/mg protein/hr. Gamma glutamyl transpeptidase was (18) estimated by the method Rosalki *et al.*, (1970) in the liver homogenate using L-glutamyl-p– nitroanilide as substrate and the enzyme activity was expresssed as µM p-nitroaniline/mw protein/min.

The formation of lipid peroxides in liver homogenate was determined by the procedure of Desai et al., (1964) (19) using thiobarbutric acid. The percentage inhibition of enzyme released or lipid peroxidation by test drugs was calculated by the formula

$$\frac{A - B}{A} \times 100$$

A is a control value, B - drug treated condition. Protein was determined according to Lowry *et. al.*, (20).

Results and Discussion

From the Table. it is seen that there is overall increase in hepatic synthesis of enzymes such as GGTP, serum alanine transferase, alkaline phosphatase and lipid peroxide.

The measurement of serum alkaline phosphatase has been used for over 40 years in the investigation of disease of the liver and biliary system. The level of alkaline phosphatase serves as an index of the liver's excretory function. Serum alkaline phosphatase values more than three times normally, strongly suggests biliary obstructions if bone disease is absent (21). The alkaline phosphatase activity increased in control group than normal and the enzyme activity was also reduced to normal level after the drug treatment.

Alanine Transferase

Increases in both AST and ALT are commonly found in liver diseases, particularly in infective hepatic jaundice and in acute hepatitis. The increase in alanine transferase is more marked than in aspartate transferase. The serum ALT has proved a most useful test for screening suspects in infective hepatitis. It is maximal in early stages of jaundice, then falling to normal when recovery takes place. So, the determinations can be useful in showing the severity of diseases and in following its progress. From the table it can be seen that the enzyme activity was doubled during CCl_4 treatment when compared to normal, and the activity was reduced to normal level after the drug treatment. The drug was more effective at 100 mg/100 g.b.w. concentration.

Gamma Glutamyl Transpeptidase

Rosalki *et al*, (1970) have reported gamma glutamyl transpeptidase to be a more sensitive index of liver changes

in alcoholism and most useful in connection with other liver diseases. Increases are found in all forms of hepato toxicity, the increase being greater in obstructive disorders. GGTP is more sensitve than the other enzymes, The level of GGTP was increased in control group than normal and the level was reduced to normal after the drug treatment. Again the drug was effective at 100 mg/100 g.b.w. dose.

Lipid Peroxidation

Peroxidation occurs during CCl_4 injury in liver. The pathological consequence of lipid peroxidation at cellular level has been associated with alteration of lipoprotein membrane leading to functional damage in cells; lipid peroxide content was increased during CCl_4 injection when compared to normal and the level was reduced during *P. niruri* treatment.

Albumin/Globulin Ratio

A low serum albumin and high globulin concentration are found in severe liver disease due to impaired synthesis of albumin. Although the changes in albumin and globulin concentrations may cancel each other, the albumin/globulin ratio may range from 0.5 to well over 2.5. This is a factor in the development of oedema in liver disease and contributes with portal venous hypertension to the development of ascities. The A/G ratio was very low in (0.55) during CCl_4 treatment and it was 1.39 for normal. The A/G ratio was increased upto 2.5 when *P. niruri* was administered at the dose of 100 mg/100 g.b.w.

From the Table 1, it is seen that the drug was uniformly effective at 100 mg/100 g b.w. in restoring the deranged liver function due to CCl_4 treatment.

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Effect of *Phyllanthus niruri*, Linn. on Carbon tetrachloride induced fatty liver.

Group	Alkaline phosphatase in serum µg p-nitro phenol/mg prot./hr.	Alanine transferase in serum µM pyruvate released/mg prote./ hr.	Gamma glutamyl transpeptidase in liver µM/p-nitro aniline/ mg prot./min.	Liver peroxide level in liver (%)	Albumin/globulin ratio
Normal	48.0 ± 3.5[a]	273.0 ± 22.1[a]	9 06 ± 0.62[a]	57.0±4.1[a]	1.39±0.09[a]
CCl_4 induced (control)	55.8 ± 4.1	600.0 ± 51.8	12.14 ± 0.85	100.0±8.6	0.55±0 04
CCl_4 + *P. niruri treated*					
1. 50mg/100g.b.w.	49.5 ± 2.5[b]	305.0 ± 25.0[a]	9 60 ± 0.52[a]	81 2±7.8[a]	1.08±0.09[a]
2. 100mg/100g.b.w.	31.8 ± 3.0[a]	250.0 ± 23.6[a]	8.51 ± 0 90[a]	57.2±4.5[a]	2.5 ±0.18[a]
3. 200mg/100g.b.w.	48.0 ± 3.7[a]	290.0 ± 22.5	9 06 ± 0.71	81.2±8.1[a]	1.7 ±0 15[a]

a = P < 0.001 b = P < 0.005.

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STUDIES ON PLEIOSPERMIUM ALATUM

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Introduction

Pleiospermium alatum (Wight & Arn.) Single (Syn. *Hespereteusa alata* (Wight and Arn. Alston) belonging to Rutaceae is a tree usually found in the hot dry forests of south India. The leaves and bark of the plant are used for fomentation in rheumatic pains[1]. In the present work, the leaves of the plant have been investigated for their palyphenolic constituents and also for anti-inflammatory activity.

Experimental

Shade dried leaves of *P. alatum* (500 gms), collected from Kotti Hills during the month of October, were extracted with 80% EtOH and fractionated in the usual way[2]. A yellow solid that separated from the EtOAc fraction was characterised as a flavonoid glycoside on the basis of colour reactions, Rf, etc., It had max (MeOH) 271, 326 nm; (NaOMe)+64 nm; ($AlCl_3$/HCl) nil; (NaOAc) (band II) and (NaOAc/H_3Bo_3) nil. On these basis, the flavonoid was concluded as apigenin glycoside.

The methanolic solution of the solid (M.P. 229-31°) on hydrolysis (5% H_2SO_4, 100°, 2 hrs) yielded an aglycone which was characterised as apigenin (Co-Pc, UV data and

Rf) and the sugar molity was identified as glucose. The estimation of sugar indicates that the flavonoid is a bioside, thus confirming the glycoside to be apigenin-7-O-diglucoside. The identity of the compound was further confirmed by direct comparison with authentic sample.

Albino rats of both sexes (150–170 gms.) were used as experimental models. The crude aqueous concentrate of *P. alatum* containing the flavonoid was given at doses of 50, 100 and 200 mg/kg.b.w. intraperitoneally to three different groups of animals (5 in each group). Phenyl butazone, the standard reference drug was injected (100mg/kg.b.w., i.p.) to another group while another group served as control. The method of *Winter et al*[3], was adopted to evaluate the anti-inflammatory activity. The results were calculated from decrease in paw volume in ml. after drugs treatments in comparison to control value (Table: 1).

Blood samples from experimental rats were drawn by heart puncture. Serum was separated after one hour by centrifugation and it was stored at 4 C. GGTP was estimated in blood serum by the method of Bergmeyer and Bernt[5] in serum and the enzyme activities were expressed as pyruvic acid released/mg protein/min./litre. as can be seen in Table: 3. Assay of lipid peroxide formation in liver was also done using the method of Desai *et. al* [6] which showed the same percentage of inhibition (40%) for both *P. alatum* as well as phenylbutazone.

Conclusions

From the leaves of *P. alatum*, a flavonoid glycoside namely apigenin-7-O-diglucoside was isolated. Further, it was found that the aqueous concentrate of *P. alatum* containing the above said glycoside produces a dose dependent inhibition of carrageenin induced rat paw oedema. At a dose of 200 mg/kg.b.w. *P. alatum* shows significant activity comparable to that of phenylbutazone the reference drug.

It has been reported[7] that gamma glutamyl transpeptidase showed an increased activity in carrageenin oedema and the level of this enzyme was suppressed in a dose dependent manner by anti-inflammatory drugs. In the case of *P. alatum* also, as can be seen from the Table: 2, the activity of GGTP was inhibited by the aqueous concentrate.

Similarly, the activities of alanine and aspartate transferases [8,9], are maximum in inflamed condition and anti-inflammatory drugs suppress the activities of these enzymes. Like the phenylbutazone, the reference drug, *P. alatum* also suppressed these enzyme levels (Table: 3).

In liver tissue there was a reduction (40%) in the content of lipid peroxide, the extent of reduction being the same for phenylbutazone also. According to Bonta *et. al* [10] the lipid peroxides may be pro-inflammatory and they damage the tissues directly. So *P.alatum* as well as phenylbutazone may prevent the formation of lipid peroxide by acting as free radical scavangers or antioxidates.

These results offer a significant predictive value for clinical usefulness of *P. alatum*. Further, the study of biochemical parameters throws light on the mechanism of action of *P. alatum*. From the chemical investigation it can easily be concluded that the anti inflammatory activity of *P.alatum* is due to the presence of apigenin-7-0-diglucoside.

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TABLE I : EFFECT OF P. ALATUM AND PHENYLBUTAZONE ON CARRAGEENIN INDUCED RAT PAW OEDEMA

Treatment	Dose in mg/k. g.b.w.	Mean increase in paw volume ± SEM	Percentage inhibition
Control	—	0.7747 ± 0.011	—
Phenylbutazone	100	0.4617 ± 0 010	42.98
P. alatum	50	0.7707 ± 0.01	—
	100	0.6641 ± 0.11	14.27
	200	0.5140 ± 0.012	33.65

TABLE II : EFFECT OF P. ALATUM ON GAMMA GLUTAMYL TRANSPEPTIDASE (in terms of m. moles of p-nitroaniline formed/min/mg protein)

Treatment	Activity of GGTP
Control	2.21
Normal	1.87
Phenylbutazone	1.99
P. alatum 100 mg./kμ g. b.w.	1.99
200 mg./k g.b.w.	1.91

TABLE: 3 EFFECT OF P. ALATUM ON ALANINE AND ASPARTATE TRANSFERASES

(Activity in terms of pyruvate formed/min/litre of the serum)

Treatment	Alanine transferase	Aspartate transferase
Control	188 88	74.07
Normal	146.66	46.29
Phenylbutazone	146.66	60.18
P. alatum		
100 mg/kg. b.w.	162.03	64.81
200 mg/kg. b.w.	146.8	46.49

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EFFECT OF MANDUR BHASMA ON LIPOLYTIC ACTIVITIES OF LIVER, KIDNEY AND ADIPOSE TISSUE OF ALBINO RAT DURING CCl_4 INDUCED HEPATIC INJURY

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Abstract

An Ayurvedic preparation of iron, 'Mandur bhasma' is used in the traditional medicine against hepatitis. In the present study the hepatoprotective property of this drug was tested in albino rats during CCl_4 induced hepatic injury CCl_4 (0.4 ml/100 gm body weight) was given subcutaneously for 11 days. On biopsy after 11 days, acute hepatic necrosis was observed. Mandur bhasma was given orally concomitantly with CCl_4 treatment.

The lipolytic enzymes play important role in the lipid metabolism. The effect of mandur bhasma on the activities of lipolytic enzymes of rat liver, kidney and adipose tissue was studied during CCl_4 induced hepatitis The activities of acid lipase, alkaline lipase, lipoprotein lipase and hormone sensitive lipase exhibited significant alterations during CCl_4 induced hepatic injury. indicating role of these enzmes in the mobilization of fat from adipose tissue and accumulation of fat in liver and kidney. Simultaneous treatment with mandur bhasma and CCl_4 did not show any significant alterations in the levels of enzyme activities. These results suggest the hepato-

protective role of mandur bhasma during CCl_4 induced hepatic injury.

Key words - Acid lipase, alkaline lipase, hormone sensitive lipase, lipoprotein lipase, CCl_4, mandur bhasma, kidney, liver, adipose tissue.

Introduction

Lipolytic enzmes play a very important role in the biological turnover of lipids. Various forms of lipases have been reported (Brockerhoff and Jensen, 1974). Lipoprotein lipases have been detected in many tissues, adipose tissue, mammary tissue, muscle, heart, aorta, liver, kidney, lung, spleen, medulla, diaphragm and fluid (plasma and milk) (Desnuelle, 1972; Fredrickson and Levy, 1972).

Hepatic triglyceride lipases have been reported in liver homogenates (Varinkova and Mosinger. 1965). and in plasma membrane, cytosol microsomes and lysosomes (Hayashi and Tappel, 1970; Assmann *et. al.*, 1973; Teng and Kaplan, 1974, Debeer *et.al*; 1979). The cellular fractions show alkaline pH optima for lypolytic activity except the lysosomal preparation which has an optimum pH 4 to 6.

Mahadevan and Tappel (1968) reported the lysosomal and microsomal lipases rat kidney. Similarly Matsumura *et. al*; (1976) reported three different forms of lipases in rat adipose tissue viz., lipoprotein lipase, hormone sensitive lipase and triglyceride lipase with alkaline pH. In our laboratory we have detected the lipolytic activity having acidic pH 4.2 (unpublished data).

It is well known that treatment of CCl_4 to rats causes centrolobular hepatic necrosis leading to the accumulation of fat in liver and kidney. It was suggested that fats from peripheral adipose tissue are translocated to the liver and kidney for accumulation during toxicity (Roullier, 1963).

Mandur bhasma an Ayurvedic preparation of iron has long been used in the treatment of liver diseases (Sharma, 1977) but presently detailed pharmacological studies are not available. Therefore in the present investigations attempts have been made to find out the effect of CCl_4 on lipolytic enzymes of liver, kidney and adipose tissue and the protective effect of mandur bhasma during CCl_4 induced hepatic injury.

Materials And Methods

Male albino rats reared in the animal house of the department were used for the experiments. The rats weighing 125-150 gms were maintained in the cages. Rats were fed with standard laboratory food (Hindustan Lever Ltd., Bombay) and watered ad libitum.

Exprimental protocol—Experiments were run in three sets. Five rats were used in each group.

Experiment No. I—Paraffin (0.1 ml/gm body wt.) was injected subcutaneously for 11 days.

Experiment No. II—In second set 0.3 ml CCl_4 in liquid paraffin (3:1 v/v) per 100 gm body wt. was given subcutaneously for 11 days.

Experiment No.III—In third set 0.3 ml CCl_4 in liquid paraffin (3.1 v/v) per 100 gm body wt. was given subcutaneously concomitant with the oral administration of mandur bhasma (1 mg/100 gm body wt.).

Group of 5 normal rats was treated as control animals.

Livers of the exprimental animals were biopsied on 5th and 11th day to check the hepatic necrosis. Acute necrosis was observed on 11th day in the livers of Expt.2 rats. All the animals were sacrificed on 11th day by a sharp occupital blow. Liver kidney and adipose tissue were dissected out and used for the assay of lipolytic activities. Hormone sensitive lipase,

lipoprotein lipase and alkaline lipase were assayed according to Matsumura *et. al.*,(1976) using triolein as substrate At the end of incubation, the enzyme activities were inhibited, and liberated free fatty acids were estimated as described ea lier (Patil *et.al.*, 1983). The acid lipase activity was determined by the method of Mahadevan and Tappel except for the fatty acids which were described as per Patil *et.al.*, (1983). Protein of liver and kidney was determined using Folin-Ciocaltue phenol reagent (Lowry *et.al.*, 1951) while protein of adipose tissue was measured using the method of Tornquist and Belfrage (1976).

Results

Alterations in the lipolytic activities of liver of albino rats of Expts. I-III are represented in Table 1. Lysosomal and lipoprotein lipase activities of liver of Expt.I and II rats showed decrease, except the lipoprotein lipase activity of Expt. II rats which had exhibited an enhancement. The enzyme activities when expressed per mg protein paralleled the changes in activites after expressing per mg. wt. of liver indicating the alterations in enzyme proteins. Alkaline lipase activity was significantly increased in rats of Expt. I and II. The enzyme activity after expressing as per gm wt. of liver and per mg. protein showed similar variations when mandur bhasma was given simultaneously with CCl_4 treatment (Expt. III). There was rise in all enzyme activities as compared to Expt. II rats on expression as both per gm liver and per mg protein while these enzyme activities per mg protein were higher than control animals.

Table II shows the changes in the lipolytic activities of adipose tissue under given experimental conditions Significant increase in the activities of all lipolytic enzymes have been observed except the lipoprotein lipase activity of Expt. II rats. The parallel alterations were noticed on expression as per mg protein and per gm wt tissue. After simultaneous treatment of mandur bhasma, conspicuous fall in acid lipase and hormone sensitive lipase activities, while increase in

lipoprotein lipase activity was observed when compared to the activity of lipoprotein lipase from Expt. II rats. Alkaline lipase activity exhibited a decrease on expression per gm fresh wt., while showed an increase on expression per mg. protein. The activities of all the enzymes were higher than those of control rats.

Variations in lipolytic activities of kidney in Expt I to III, are shown in Table III. The enzyme activities declined as compared to those of control-animals. However, the reductions in enzyme activities were more in Expt. I rats than in Expt. II rats when mandur bhasma was given simultaneously with CCl_4 treatment lysosomal lipase activity was appeared to be protected. Lipoprotein lipase and alkaline lipase were increased than in Expt. II rats. Alkaline lipase showed about 2.6 fold increase than that of normal rat. While though the lipoprotein lipase activity was enhanced than Expt. II rats, the activity was about 50% than in normal rats.

Discussion

Lipolytic enzymes are indispensible for the biological turnover of lipids. Lipoprotein lipases play a role in the hydrolysis of lipoprotein triglycerides releasing free fatty acids which are uptaken mainly by adipose tissue and liver for storage as energy reserves. (Robinson, 1963); or utilized as an important component in complex lipids necessary for the structural and functional integrity of biological membranes (Scow and Chernick, 1970); on the contrary lipases hydrolyse the cellular triglycerides to free fatty acids which are utilized for the metabolic processes. Similarly, these lipases are responsible for the mobilization of lipids from adipose tissue during metabolic demand. From the results obtained in the present investigation, it appears that during CCl_4 intoxication triglycerides from adipose tissue are mobilized and are accumulated in liver and kidney. Roullier (1964) has postulated similar hypothesis. Similarly, lipid accumulation was reported in the kidneys of mice (Estler *et. al.*, 1973) and chicks (Whitehead *et. al.*, 1974) poisoned with CCl_4.

The decreased lipoprotein lipase activity in all the tissues studied, suggests the impaired secretion of lipoproteins The decrease in liver and kidney lipases and increase in adipose tissue lipases suggests the mobilization of triglycerides from adipose tissue for accumulation in liver and kidney during CCl_4 intoxication. Liver alkaline lipase activity was increased by 6 fold. This lipase may be responsible for the hydrolysis of cellular triglycerides resulting in enhanced lipid peroxidation. Triglycerides must be broken down to fatty acids before they undergo oxidation (Farverger 1963). Thus, alkaline lipase of liver may play very important role in drug metabolism by liberating free fatty acids for lipid peroxidation.

When rats were simultaneously treated with CCl_4 and mandur bhasma the enzyme activities observed to be protected. The higher lipoprotein lipase activity in Expt III rats than in Expt. II rats suggests the increased secretion of liver lipoproteins and rapid uptake of fatty acids by adipose tissue. The acid and hormone sensitive lipolytic activities were significantly lowered. From these observations it appears that the rate of lipolysis was less than uptake of fatty acids by adipose tissue in Expt. III rats. While liver and kidney lysosomal lipase activities were protected by mandur bhasma. Surprisingly, alkaline lipase activities of all the three tissues were significantly higher than those observed in Extp. II and control rats. The question arose how this alkaline lipase play role during the CCl_4 toxicity and during the protection by mandur bhasma because it was observed that when liver homogenate was incubated in the presence of mandur bhasma, the rate of lipid peroxidation was significantly lower when compared with the lipid peroxidation in absence of mandur bhasma.

It is possible that this increased alkaline lipase in Expt. III rats may be responsible for synthesis of complex lipids of membranes and other cellular components of these tissue for regeneration of new cells rather than lipid peroxidation. Histologically liver and kidneys were not damaged significantly

and new regenerating hepatic regions were obsvered in the region of necrosis.

Further studies are being carried out in this laboratory on the chemical nature of mandur bhasma and on the mechanism of its hepatoprotective action during hepatopathology.

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TABLE I: EFFECT OF CCl_4 ON LIVER LIPASES. VALUES ARE MEAN ± SE OF 5 ANIMALS

Treatment	Lipolytic Activities					
	Acid Lipase		Alkaline lipase		Lipoprotein lipase	
	K units/gm wet wt.	Units/mg protein	K units/gm wet wt.	Units/mg protein	K units/gm wet wt.	Units/mg protein
1. Control	10.0 ±0.588	33.33 ±2.33	2.0 ±0.11	66.7 ±3.1	6.0 ±0.26	20.0 ±0.86
2. Expt. I	7.2 ±0.48[a]	31.30 ±1.59[d]	7.86 ±0.41[b]	34.17 ±1.48[c]	7.8 ±0.47[a]	33.91 ±1.30[b]
3. Expt. II	3.84 ±0.18[c]	16.70 ±0.61[b]	12.50 ±0.462[c]	54.35 ±2.75[a]	2.98 ±0.12[b]	12.78 ±0.44[a]
4. Expt. III	7.2 ±0.56[a]	38.91 ±1.88[a]	15.6 ±0.91[c]	84.31 ±3.16[b]	9.46 ±0.85[a]	51.13 ±2.03[c]

a—$p<0.05$, b—$p<0.01$, c—$p<0.001$, d—$p>0.05$ compared to the control group

TABLE 2: EFFECT OF CCl_4 ON ADIPOSE TISSUE LIPASES. VALUES ARE MEAN ± SE OF 5 ANIMALS.

Treatment	Acid lipase		Hormone sensitive lipase		Alkaline lipase		Lipoprotein lipase	
	K units/gm wet wt.	Units/mg protein	K units/mg wet wt.	Units/mg protein	K units/gm wet wt.	Units/mg protein	Kunits/gm wet wt.	Units/mg protein
1. Control	1.96 ±0.082	9.8 ±0.46	8.99 ±0.52	44.95 ±1.94	16.18 ±0.70	80.9 ±3.85	8.34 ±0 67	41.7 ±2 3
2. Expt. I	27.57 ±1.19^{c}	119.87 ±4.43^{c}	27.51 ±2.3^{c}	119.61 ±5.1^{c}	17.8 ±0.93^{d}	77.39 ±4.07^{d}	17.82 ±1.2^{b}	77.48 ±3 62^{d}
3. Expt. II	60.92 ±2.43^{c}	202 73 ±6.53^{c}	47.96 ±3 2^{c}	159.87 ±6.14^{c}	31.76 ±1.84^{b}	105.67 ±4.82^{a}	1 05 ±0.02^{c}	3 5 ±0.3^{c}
4. Expt. III	7.13 ±0.37^{c}	31.01 ±5.71^{c}	15.95 ±0.83^{b}	69.31 ±2.77^{a}	28.22 ±0.05^{b}	127.70 ±5.92^{b}	13.10 ±1.06^{a}	56.44 ±2.86^{a}

P values are as reported in table 1.

TABLE 3 : EFFECT OF CCl_4 ON KIDNEY LIPASES. VALUES ARE MEAN ± SE OF 5 ANIMALS

Treatment	Acid lipase		Alkaline lipase		Lipoprotein lipase	
	K units/gm wet wt.	Units/mg Protein	K units/gm wet wt.	Units/mg Protein	K units/gm wet wt.	Units/mg Protein
1. Control	13.6 ±0.57	68.0 ±4.5	13.6 ±0.78	68.0 ±4.13	12.0 ±0.76	60.0 ±3.82
2. Expt. I	3.76 ±0.13[c]	18.80 ±0.75[c]	10.2 ±0.52[a]	51.0 ±2.05[c]	0.9 ±0.06[c]	4.5 ±0.22[c]
3. Expt. II	5.4 ±0.21[b]	29.19 ±1.61[b]	10.4 ±0.66[a]	56.22 ±3.14[a]	1.8 ±0.08[c]	9.73 ±0.51[c]
4. Expt. III	14.46 ±0.81[d]	72.3 ±4.9[a]	34.8 ±1.83[c]	174.0 ±5.53[c]	6.4 ±0.35[b]	32.0 ±1.27[b]

P values are as reported in table 1.

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BUREAUCRATIC FUNCTIONING - THE BUGBEAR OF BIOMEDICAL RESEARCH BODIES

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"Teach us O'Lord to reverence
Committees more than common sense;
Impress our minds to make no plan
But to pass the baby when we can!

Although Max Weber tried to create an ideal type of bureaucracy, the present day officialdom in some governmental scientific institutions has been reduced to creeping along the groove of set rules and regulations, resulting in an imposed restrictive attitude towards scientific personnel and stultification of creativity and efficiency. Further, it has been proven to be totally inadequate with regard to bureaucracy's other face—the informal organisation. Of late, in business establishments, a system of management that sees human relations as the primary method by which management could successfully weld people into an effective organisation has come up. Human relations research has broadened the traditional organisation theory by taking cognisance of human factors in management. In industrial establishments, such *humanism* has sought to indicate ways and means by which mangement can manipulate human factors for suitably moulding workers to the organisational goals.

There has been little, if any, attempt towards changing the traditional bureaucratic set-up in our biomedical research

institutions. It is being increasingly recognised that the traditional type of bureaucratic organisation tends to work against the development of scientists and science in general. In large stiffly formal organisations, individuals, have minimal control over their work situation, are expected to be passive in their work approach, encouraged to set their sights on short-time perspectives. They are permitted to develop, if anything, only a few specialised skills. Obviously, in such research institutions, where the background knowledge and intelligence level of scientists are appreciable, such a set-up is bound to retard the progress of research The traditional rigid bureaucratic system is fraught with the danger of jeopardising the very objective of creative research for which such institutions are established.

The orthodox bureaucratic system of routing all correspondence 'through proper channel' is being machanically applied to research institutions as well. For example, a scientist is asked to submit all research proposals in this manner, leading to inordinate delay at every stage of its travel and scrutiny upwards and downwards (and sometimes sidewards!) through various hierarchical tiers. It is an accepted management adage that the greater the number of levels of scrutiny and approval through which a particular matter is made to pass, the longer the time lag between the initial thought and its successful decision/implementation. Such delay also results in frustration and job dissatisfaction. The creative and enthusiastic scientist may be compelled to reduce or restrict his performance level and thus develop positive apathy to his work on account of discouraged personal identification with the organisational goals. It is not appreciated that it is this factor of lack of control over his work environment, rather than the more publicised 'inadequate' salary and professional facilities, that is responsible for the steady exodus of scientific personnel away from governmental scientific institutions in our country.

It is the usual practice, for instance, that research proposals are required to be sent through a departmental head

with the latter's comments or recommendations (Fig. 1). Often a departmental head is not fully conversant, or perhaps even ignorant, of the scientific contents of a research proposal, because of increasing sub-topic superspecialisation and rapid advances in biomedical technology. Subsequent decision is still taken on the basis of his 'recommendations' such as 'not recommended' or 'strongly recommended', etc. Such comments are always at risk of being based on interpersonal relationships (e. g. envy, sycophancy) rather than on the scientific merits of a given proposal (Fig.2). Even when a proposal is rejected, it is limited to cryptically worded statement to that effect, without detailing arguments back to the proposer as to the reasons for its negation. Whereas reputed international scientific journals give detailed comments, including appropriate references, when a submitted article is found unsuitable for publication, the bureaucratic approach generally existing in the higher echelons of Indian Scientific institutions leaves the scientist not only confused regarding the validity of his hypothesis, but also doubtful about possible prejudice or arbitrariness having influenced the decision against his project. It should be drummed into the decision-making authorities that the individual scientist in an organisation has a right to know the details of scientific evaluation on the basis of which the particular research proposal was rejected. This would help to improve upon performance and motivation towards generation of more scientific ideas from such a creative individual.

The review process of a research proposal in a bureaucratic set-up usually takes a long time (as long as 12 months, if not more) by which time some of its ideas content becomes obsolete. Similarly, projects which were originally sanctioned after all the formalities were completed, have to be routed through rigidly preordained channels for renewal. So is the case for sanction of project funds. In a particular instance we are aware of, the scientist received the renewal funds seven months *after* the starting date of a time bound project.

This resulted in delayed payment to supplying firms besides delay in completion of the scheme.

In a bureaucratic set-up, the individual scientist's opportunity to contribute towards organisational goals, to acquire or develop newer skills, to undertake additional projects, and most importantly, to innovate are often at the caprice and whim of a departmental head. If the latter decides wrongly not to recommend a particular innovative idea of a scientist placed in a subordinate capacity, there is no provision for timely undoing of such wrong which in turn retards the progress of science. Many a brilliant scientist's self-confidance, idea and career may have been wrecked by such a working superior's attitude.In one instance, a departmental head of an institution failed to circulate on time a notice regarding research proposals to be submitted for consideration by an international sponsoring agency. Not only did he deprive the scientists working 'under' him of an opportunity for the materialising of their innovative thoughts. but perhaps, by his indifference, also hampered the progress of that department and science in general. He has only to show such lack of accountability just a few times more each year and there have to be but a few more like him in an organisation, to complete driving the nail into the career coffin of any enthusiastic rising research scientist! The sponsoring agency, be it remembered, was also deprived of many original ideas of a team of scientists and opportunity to utilise their talents and expertise. As all of us are well aware, such happenings are not restricted to one department or to one institution.

Hence 'debureaucratisation' is urgently called for in biomedical research institutions. Some of the important aspects of debureaucratisation are listed in Table 1. It may be stated as a law that 'greater the cooperation, greater the chances of survival of any species, and greater the happiness of its individual members'. Illustrative examples for the working of a team of scientists *before* and *after* debureaucratisation are provided in Table 2. The motivators involved in the various steps

of debureaucratisation are listed in Table 3. All these measures are *easy* to implement and hardly involve any financial burden on the organisation. A departmental head should not see himself as an exalted egocentric leader, but as a member of a team with the responsibility to produce the right working environment, so that his fellow scientists can give of their best. If there is no delegation of responsibility from the top brass to their co-workers, there will be timidity in taking of responsibility at the lower levels and consequently, no feeling of collective responsibility to help achieve the objectives for which the scientific institution stands.

To summarise, Max Weber described the pure bureaucratic structure of the ideal type as corresponding to a pole at one end of a continuum; the reality lies along the continuum. Debureaucratisation, in essence, is a process by which an organisation attempts to keep its processes and options open to reality. This permits swift, successful and continual adaptation demanded by the crises and changing situations in thought and action so characteristic of a biomedical institutional milieu. Positive steps towards the latter functional style of biomedical research institutions are urgently called for. Otherwise, as William Burke put it, 'The only thing necessary for the triumph of evil is for good men to do nothing'.

TABLE I
DIFFERENT ASPECTS OF DEBUREAUCRATISATION

1. Decentralisation and delegation of authority
2. Participative management
3. Self evaluation of performance semi annually as an open system instead of the present annual confidential report.

4. Matrix organisational system instead of orthodox hierarchical bureaucratic system

5. Job enlargement and job enrichment

6. Adoption of theory 'Y' instead of theory 'X'

7. Full and free upward and downward communication based on functional expediency and efficiency rather than only rank and conferred power of any individual.

8. A reliance on consensus rather than the more customary form of Coercion to manage conflicts.

9. The Idea that influence is based on technical competence and knowledge rather than the vagaries of personal whims or prerogatives of power and hierarchical Placement.

10. A basically human bias that accepts the inevitability of conflicts between the organisation and an individual, but that is willing to cope with and mediate such conflicts on rational persuasive grounds

TABLE II

WORKING NORM OF A TEAM OF SCIENTISTS BEFORE AND AFTER DEBUREAUCRATISATION

Bureaucratic set-up	After Debureaucratisation
1. It was mandatory for each scientist to consult departmental head for any problem in his project work.	1. Scientists are encouraged to consult each other freely in research matters which may obviate the need for consulting departmental head for every problem.

2. Departmental head signs all correspondence pertaining to research work of all scientists working in his department.	2. Individual scientist signs the correspondence related to his research idea and establishes link promptly with sanctioning body without any unnecessary Intermediaries. Information only regarding proposed or running project need be supplied to superior.
3. Departmental head was responsible for all the on-going research work in the department.	3. Individual or study group scientists are responsible for the research work being undertaken by him/collaborators.
4. All correspondence had to be routed 'Through proper Channel'	4. Individual scientist or chief investigator of group writes directly to the sanctioning person / agency concerned after ethical clearance, if such is judged to be required.
5. There was 100% verification and supervision by departmental head.	5. Verification and supervision reduced to 10% or even less.
6. Correspondence are written with a formal approach.	6. Individual scientists are encouraged to answer project question pertinent to their ideas/skills in a more personalised way.
7. Departmental head constantly reminded his subordinate scientists of the work to be done.	7. Individual scientist starts taking pride in his work and is motivated to complete it. Steady use of the whip is no longer required.

TABLE III
MOTIVATORS INVOLVED IN VARIOUS STEPS OF DEBUREAUCRATISATION

Step	Motivator involved
1. Removing some restrictive rules (controls) while retaining accountability.	1. Responsibility and Personal Achievement
2. Increasing the accountability of individual scientist for his work	2. Responsibility and recognition
3. Giving a scientist independence for executing the total research project (job freedom).	3. Responsibility, Achievement and Recognition
4. Encouraging individual scientists to take on more specialised tasks.	4. Responsibility, Growth and Advancement
5. Making periodic assessment reports on research available directly to the researcher rather than to the departmental head or other intermediary unconnected with a given project.	5. Internal Recognition

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EFFECT OF BITTERGOURD JUICE ON ALLOXAN INDUCED DIABETES IN RATS

J. Giri, T.K. Sakthidevi, and A. Palaniammal

Summary

The present study reveals that *Momordica Charantia* the small variety, has antihyperglycemic and antiglycosuric qualities. However, it does not promote liver glycogen formation. It also prevents intestinal absorption of glucose. Hence, its juice should not be taken by diabetics daily over a long period. But it will be definitely effective, to keep in check the levels of sugar in blood and urine when the diabetic is tempted to take sweets or a heavy meal which will induce hyperglycemia and glycosuria. A little bittergourd juice may be taken immediately after food, by the diabetic in such a situation.

Key Words

Diabetes, Bittergourd, Ayurvedic medicine, Treatment of diabetes.

Introduction

Diabetes is a chronic disease and needs life time treatment. In the developing countries like India, the modern medical treatment is often expensive, elaborate and beyond the means of the majority of the people. Hence there is need to find simple, safe, relatively non-toxic and effective indigenous remedy for diabetes.

In the Ayurvedic system of medicine, bittergourd juice is claimed to be a cure for diabetes. *Momordica Charantia* (the small variety) is a plant cultivated throughout India. Further it is inexpensive and easily available. The present study is an attempt to understand the effect and mechanism of action of *Momordica Charantia* on blood glucose.

Materials And Methods

In the present investigation three experiments were conducted. They are described in the following sequence:

Experiment-1

36 male albino rats of Wistar strain weighing 170–210g were selected and divided into groups I and II. Group I consisting of 12 rats, formed the basal control group. This group was fed on stock diet and not given either alloxan or bittergourd juice. Group II consisted of 24 rats. This group was given alloxan, after 48 hours fasting (Weinhouse, 1963), subcutaneously (140 mg/Kg body weight). Diabetes was found to be induced in 2 days. But rats were left for 30 days without any treatment to make sure that diabetes was permanently induced. After 30 days, group II rats were divided into groups A and B, each consisting of 12 rats. Group A was used as experimental control, while group B formed the experimental rats. Group B was given bittergourd juice by forced feeding for 15 days(2ml. of 100% solution). At the end of this period group B was further divided into groups B1 and B2 consisting of 6 rats each. Group B2 rats were sacrificed by decapitation, on the 16th day. The liver was collected for isolation and estimation of glycogen (Oser, 1965 and Remontgonery, 1959). Group B1 rats were not given any bittergourd juice and checked for the level of blood sugar for a further period of 15 days. On the 16th day after discontinuing bittergourd juice administration, they were sacrificed; the liver was collected as in the case of group B2.

As for the experimental control (group A) rats, they were not given any bittergourd juice. Six of them were sacrificed on

the 16th day along with group B2 rats and the remaining six were sacrificed on the 32nd day along with group B1 rats for analysis of liver.

Group I which formed the basal control group was not given alloxan or bittergourd juice. Six of them were sacrificed on 46th (30 + 16) day and the remaining six were sacrificed on 62nd (30 + 32) day along with groups B2 and B1 rats respectively. All the 36 rats (Groups I and II) were fed the stock diet during the entire period of this study and given water *ad libitum*.

Every fifth day, blood samples were collected from all the 36 rats by cutting the tail at the tip by about 0.1 Cm. Blood glucose was estimated by Folin-WU method (Varley, 1976).

On every fifth day, after 12 hours fasting, the urine was collected from 6a m to 10 A.M. and the urine glucose level was estimated by Folin-Wu method.

Faeces were collected for three days prior to (each) blood collection. They were ground well with water, to get a homogeneous solution and filtered. The filtrate was used for the estimation of faeces sugar by Folin-WU method.

Experiment –2

In this experiment, the effect of bittergourd juice on the pattern of GTT curves in alloxan diabetic rats was studied.

Twelve male albino rats (Wistar strain) weighing 175-200g. were taken and divided into two groups A andB. Diabetes was induced in them as described earlier. After 30 days the animals were used for experiment.

Each rat in group A was fed with 0.4g. (2g/Kg. body weight) of glucose (Varley, 1976). The glucose was dissolved in 2 ml. of water and given to the rats by forced feeding. Blood samples were collected initially, just before the administration

of glucose and after feeding glucose, at intervals of half an hour for 2½ hours, from the tail as described under experiment I. Glucose was estimated by Folin-WU method.

Fasting blood samples were collected from Group B rats. 2 ml. of 100% bittergourd juice was mixed with O.4g. of glucose and this mixture was fed to all the rats in group B by forced feeding. Blood was collected and estimated as for group A.

Experiment –3

In this experiment an *in vitro* study of the absorption of glucose by the intestine was conducted to study the effect of bittergourd juice on glucose absorption (Albanese, 1963). The intestine was filled with Krebs Ringer phosphate buffer solution and in the outer tube was taken the same buffer solution but containing 0 5 % glucose. The intestinal fluid was collected at intervals of 10 minutes for 50 minutes and used for the estimation of glucose by Folin–WU method.

A similar experiment was conducted, by taking in the outer tube 10 ml. of Krebs Ringer phosphate buffer containing 0.5% glucose and bittergourd at 100% concentration (bittergourd was homogenised with Ringer solution to produce 100% solution).

RESULTS

Experiment: 1 The results of experiment I are given in Tables I and II.

At the commencement of the experiment blood and faecal glucose values of the three groups A, B & C when compared showed no statistically significant difference; the initial urine sugar value was Nil in all the three groups.

After induction of diabetes in groups B & C the blood sugar value is increased three fold; sugar is detected in urine in significant amounts but the faecal sugar is decreased to less than 40% when compared to the basal control group.

After treatment with bittergourd juice for 5, 10 and 15 days, the blood and urine sugar values of the experimental group are decreased and the faecal sugar value was increased significantly when compared to the experimental control. All these changes which progress gradually from 5 to 15 days are significant in all stages.

When bittergourd juice was discontinued for 15 days, blood and urine sugar values were gradually but significantly increased and the faecal sugar was decreased in the experimental group.

From Table 2 it is evident that the liver glycogen value was lowest in the experimental group and highest in the basal control group. On discontinuing bittergourd juice administration the liver glycogen values significantly increased in the experimental group.

Experiment–2

The blood glucose (Table-3) of group B rats which received bittergourd juice with glucose solution recorded significantly low (at 1% level) values at all time intervals when compared to group-A, which received only glucose solution.

Experiment–3

A comparison of the absorbed glucose values of group A and group B rats, at different time intervals (Table: 4) indicate a lowering of the glucose values when bittergourd juice was added fo glucose in the outer tube.

TABLE I: BLOOD CLUCOSE LEVELS IN DIFFERENT STAGES OF THE EXPERIMENT

in mg/100ml.	Based control Mean ± SD (A)	Experimental control Mean ± SD (B)	Experimental group Mean ± SD (C)
At the commencement of the experiment			
Blood sugar in	56.2 ± 2.9	55.8 ± 2.8	56.8 ± 2.7
Urine Sugar	Nil	Nil	Nil
Faecal sugar	635 ± 24.3	639 ± 21.8	643 ± 21.8
After the induction of diabetes			
Blood sugar	55.8 ± 3	180 ± 26 9	181 ± 8.8
Urine sugar	Nil	17.92 ± 2.3	19 ± 3.6
Faecal sugar	638 ± 19.6	250.8 ± 19.8	248 3 ± 23.3
After 5 days bitter-gourd juice treament			
Blood sugar	53.2 ± 5.4	186.2 ± 10.3	73.7 ± 5.5
Urine sugar	Nil	17.5 ± 1.3	2.7 ± 0.8
Faecal sugar	630 ± 24.9	265 ± 18.8	308 ± 22.1
After 10 days bitter-gourd juice treatment			
Blood sugar	54.2 ± 3.9	188.2 ± 11.0	65.0 ± 3.8
Urine sugar	Nil	17.2 ± 1.2	1.8 ± 0.3
Faecal sugar	635 ± 25.8	260 ± 21.7	445.8 ± 22

After 15 days bitter-gourd juice treatment			
Blood sugar	57.8 ±3 4	187.7±10.2	47.5± 2.7
Urine sugar	Nil	17.2± 1.4	Nil
Faecal sugar	639.12±4.7	259.2±24.7	711.6±29.0
After 10 davs without treatment			
Blood sugar	57.3 ± 3.7	187 ±10	91±2.8
Urine sugar	Nil	17.6 ±1.3	4.5±0.2
Faecal sugar	650 ±14.1	250 ±25.8	617±20.3
After 15 days without treatment			
Blood sugar	57.3 ±4.1	188.7±8.7	136±6.3

TABLE II : LIVER GLYCOGEN VALUES OF DIABETIC RATS

	Glycogen in g/100 g of liver		
	Basal control Mean±SD (A)	Experimental control Mean±SD (B)	Experimental group Mean×SD (C)
After 15 days treatment with bitter gourd juice	2.4±0.2 (A_1)	1.6±0.2 (B_1)	0.8±0.02 (C_1)
15 days after discontinuing the administration of bittergourd	2.4±0.06 (A_2)	1.7±0.08 (B_2)	1.4±0.1. (C_2)

TABLE III: CHANGES IN BLOOD GLUCOSE VALUES OF DIABETIC RATS IN PRESENCE OF GLUCOSE AND GLUCOSE+BITTERGOURD JUICE

Time in Minutes	Mean blood glucose values with glucose solution in mg% Mean ± SD (Group-A)	Mean blood glucose values with glucose solution and bitter-gourd juice Mean ± SD (Group-B)	't' Value AVs B
Fasting level	139 ± 1.4	142 ± 3.5	1.14NS
30	242 ± 2.8	198 ± 2.8	15.77**
60	286 ± 2.8	237 ± 3.7	14.71**
90	160 ± 1.4	133 ± 1.4	19.05**
120	135 ± 1.4	113 ± 4.5	6.87**
150	118 ± 3.2	94 ± 2.8	8.03**

NS – Not significant
** – Significant at 1% level

TABLE IV: GLUCOSE VALUES IN SEROSAL FLUID

Time in Minutes	% of glucose absorbed in presence of	
	Glucose Group A	Glucose + bittergourd juice Group B
10	5	3.5
20	9	7.0
30	13	9.9
40	16.6	13.6
50	20	14 6

Discussion

Experiment–1

Initial glucose values indicate that all the three groups of rats selected for the experiment were normal, and did not vary significantly in the mean glucose values of blood, urine and faeces.

After induction of diabetes, hyperglycemia and glucosuria developed in both experimental control and experimental groups, to the same extent.

When bittergourd juice was given to the diabetic rats it reduced the sugar level and stopped its excretion in urine. But faecal excretion was increased. These results suggest that bittergourd juice has hypoglycemic activity and its mechanism of action is by preventing glucose absorption. The unabsorbed glucose gets excreted in the faeces.

To make sure the hypoglycemic activity of bittergourd, the administration of bittergourd juice was stopped for 15 days and during this period the blood, urine and faecal sugar values of the experimental rats recorded a reverse process i.e. the blood sugar level gradually rose while the faecal sugar level gradually decreased. Sugar appeared in the urine. All this proved the hypoglycemic action of bittergourd juice.

The experimental controls maintained the diabetic state throughout the experiment and served as very good controls for the experiment.

Diabetes depletes liver glycogen but bittergourd juice seems to further reduce it. On discontinuing bittergourd juice administration, the liver glycogen value increased significantly, which confirms the earlier observation that bittergourd juice prevents absorption of glucose and thereby prevents glycogen formation.

Experiment– 2

The observations are additional proof forthe hypoglycemic activity of bittergourd juice.

Experiment— 3

The percentage of glucose absorbed by the intestine is less in the presence of bittergourd juice. This confirms the inhibitory action of bittergourd juice on glucose absorption. The inhibitory action may be by blocking the glucose receptors in the mucosal membrane. Further studies need to be done, to understand the exact mechanism.

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EFFECT OF TULASI LEAF EXTRACT ON DIABETES MELLITUS

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Summary

In the present study an attempt has been made to determine quantitatively the effect of tulasi on blood sugar level and its possible use as a substitute for oral hypoglycemic drugs. There was a significant fall in the levels of blood glucose, blood urea, serum cholesterol, serum triglyceride and liver glycogen when alloxan induced diabetic rats were treated with tulasi leaf extract for 15 days. Tulasi leaf extract was found to have an inhibitory action on glucose absorption in the intestine. The present study also reveals that tulasi leaf extract decreases glycogen formation in the liver.

Introduction

Diabetes a disease of great importance from the socio-medical point of view. It is a disease of complications. The disease is very common in India. The incidence ranges from 2.53 to 2.7% in different regions of India (4). Although the modern allopathic system of medicine is greatly accepted in the treatment of diabetes throughout the world, it has not been able to reach the remote rural areas for various reasons (3). In our country a large majority of our people cannot afford the expenses of elaborate methods of treatment (1). Because of the local availability of herbs, treatment according to traditional system of medicine is often cheaper(6). Hence this study was

carried out to assess the effect of tulasi which is known in Ayurvedic System of medicine for its antidiabetic action (2).

Material and methods

40 male albino rats of wistar strain weighing 150–190g were divided into groups I and II. Group I consisted of 15 rats and group II of 25 rats. All the rats were fed with stock diet throughout the experimental period and given water ad libitum. Group I rats formed the basal control. Group II rats were given alloxan after 48 hours fasting (wein house, 1963) subcutaneously (140 mg/kg body weight), Diabetes was found to be induced in 2 days. But the rats were left for 30 days without any treatment to make sure that diabetes was permanently induced After 30 days 5 rats were sacrificed from group II and the rest were divided into sub–groups group II_A and group II_B consisting of 10 rats each. Group II_B rats (experimental) were given 2.0 ml of 100% solution of tulasi leaf extract for 15 days by force feeding daily in the morning. Five of the group II_B rats were sacrificed by decapitation on the 16th day. Blood was collected from the jugular vein for biochemical analysis. The liver was cut out and used for isolation and estimation of glycogen. The remaining five rats of group II_B were not administered tulasi leaf extract for the next 15 days and on the 31st day they were sacrificed and blood and liver samples were collected as described earlier.

As for the experimental control group II_A rats. they were not given any tulasi leaf extract. Five of them were sacrificed on the 16 th day and the remaining five were sacrificed on the 31st day; blood and liver samples were collected and subjected to analysis.

Group I which formed the basal control group was not given alloxan or tulasi leaf extract. Five of them were sacrificed on the day (1st day) the tulasi leaf extract was administered to group II_B rats. The remaining rats were sacrificed on the 16th

and 31st days, five each time. In each case, blood and liver samples were collected and subjected to analysis.

Effect of tulasi leaf extract on absorption of glucose

An *in vitro* study was conducted to study the effect of tulasi leaf extract on glucose absorption in the intestine (Albanese, 1963). The intestine was filled with Krebs Ringer phosphate buffer containing 0.5% glucose and tulasi leaf extract at 100% concentration (Tulasi leaf extract was homogenised with Ringer solution to produce 100% solution).

Biochemical Analysis

Blood glucose, blood urea, serum triglycerides and serum cholesterol were estimated according to Varley (1980).

Liver glycogen was isolated and estimated by the methods of Oser (1965) and Rex montgomery (1959).

Observations

The results of the present study are presented as follows:

Table 1 shows the blood glucose and urea values of normal, diabetic and diabetic rats treated with tulasi leaf extract for 15 days and 15 days after discontinuing the treatment with tulasi leaf extract.

Table 2 shows the serum cholesterol and triglyceride values of normal rats, diabetic rats, diabetic rats treated with tulasi leaf extract for 15 days, and also in rats after discontinuing the treatment.

Table 3 gives the liver glycogen content of the rats in different experimental conditions, that is normal rats, diabetic rats diabetic rats treated with tulasi leaf extract for 15 days, and after discontinuing the treatment for 15 days.

Table 4 shows the glucose value in serosal fluid with and without tulasi leaf extract.

Discussion

Effect on blood glucose & urea

The mean blood glucose level of the experimental control and experimental group rats were raised more than 3 fold compared to the basal control group (Table 1)

The mean blood glucose value of the experimental group affer 15 days treatment with tulasi leaf extract was reduced by43% while in the experimental control group the mean blood glucose value had further increased on discontinuing the treatment for 15 days. When comparing the mean blood glucose value of experimental group rats with the value of the same group after 15 days treatment, the decrease in blood glucose was statistically significant.This shows that tulasi leaf extract has hypoglycemic effect.

The mean blood urea value of the experimental group after 15 days treatment with tulasi leaf extract was reduced by 40% (Table 1). The basal control and the experimental control groups had shown no statistically significant change.

Effect on cholesterol and triglyceride

From the values presented in Table 2 it is seen that the mean serum cholesterol value of the experimental group after 15 days treatment with tulasi leaf extract was reduced by 26%. On discontinuing the administration of tulasi leaf extract to diabetic rats for 15 days the mean serum cholesterol level recorded a rise in the experimental group. This shows that tulasi leaf extract has hypocholesteremic effect.

The mean serum triglyceride value of the experimental group after 15 days treatment with tulasi leaf extract was reduced by 39% (Table 2) In the experimental group the mean serum triglyceride level had again increased by about 15% on discontinuing the administration of tulasi leaf extract to diabetic rats for 15 days. This shows that tulasi leaf extract lowers triglyceride level also in serum.

Effect on liver glycogen content

It can be seen from Table 3 that the mean liver glycogen content of the diabetic rats, i. e. the experimental control and experimental group rats, was lower than that of the basal control. After 15 days treatment with tulasi leaf extract the mean liver glycogen content of the experimental group was further decreased.

In the experimental group the mean liver glycogen content showed an upward trend (from 1.0 ± 0.0894 to 1.25 ± 0·1415 g/100mg) on discontinuing the administration of tulasi leaf extract for 15 days. But the value was still lower than that of the experimental control group.

Effect on absorption of glucose

From table 4 it is evident that the percentage of glucose absorption was lowerd when tulasi leaf extract was added to glucose.

This probably is the reason why glucose level in the blood decreases with the administration of tulasi leaf extract.

But further studies need to be done to understand the mechanism of hypoglycemic action of tulasi leaf extract.

TABLE I: LEVELS OF BLOOD GLUCOSE AND BLOOD UREA IN RATS

Experimental conditions	Glucose in mg/100 ml Mean ± S.D.			Urea in mg/100 ml Mean ± S.D.		
	Basal control	Experimental control	Experimental	Basal control	Experimental control	Experimental
Diabetic	56 ± 5.656	183.2 ± 43.9	183 ± 43.9	23.2 ± 4.099	59 ± 19.32	59 ± 19.32
After 15 days treatment with tulasi leaf extract	59.2 ± 2.993	194.4 ± 13.99	103.2 ± 9.926	25.2 ± 2.993	63 ± 5.291	35 ± 3.687
After discontinuing the treatment with tulasi leaf extract for 15 days	60 ± 5.656	197.6 ± 12.02	128 ± 5.656	26.8 ± 3.71	66 ± 8.484	46.8 ± 5.741

TABLE II : SERUM CHOLESTEROL AND TRIGLYCERIDE VALUES OF RATS

Experimental conditions	Cholesterol in mg/100 ml Mean ± S.D.			Triglyceride in mg/100 ml Mean ± S D.		
	Basal control	Experimental control	Experimental	Basal control	Experimental control	Experimental
Diabetic	94 ± 16.55	276 ± 10.21	276 ± 10.2	41.75 ± 2.318	165.25 ± 4.359	165.25 ± 4.359
After 15 days treatment with tulasi leaf extract	99 ± 14.29	280 ± 7.071	204 ± 18.81	42.75 ± 2.358	169.75 ± 3.652	100 ± 4.031
After discontinuing the treatment with tulasi leaf extract for 15 days	99 ± 19.07	284 ± 10.68	234 ± 10.68	43.5 ± 4.404	179.8 ± 4.203	131.2 ± 4.445

TABLE III : LIVER GLYCOGEN CONTENT OF RATS

Different Experimental conditions	Glycogen in g/100 g of tissue		
	Basal control	Experimental control	Experimental
Diabetic	2.3± 0.3347	1.3±0.1095	1.3±0.1095
After treatment with tulasi leaf extract for 15 days	2.38± 0.2315	1.34±0.1020	1.0±0.08943
After discontinuing the treatment with tulasi leaf extract for 15 days	2.38± 0.2315	1.35±0.1484	1.25±0.1415

TABLE IV : GLUCOSE VALUES IN SEROSAL FLUID WITH AND WITHOUT TULASI LEAF EXTRACT

Time in mts	% of glucose absorbed in presence of	
	Glucose	Glucose + tulasi leaf extract
10	2.8	1.8
20	5.8	3.3
30	8.8	4.7
40	12.0	6.2
50	15.0	8.0

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A PILOT STUDY OF "NAAYURUVI KUZHI THAILAM" IN ERAIPPU NOI (BRONCHIAL ASTHMA)

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Introduction

In India where the life style of the people is changing into mostly industry oriented the incidence of allergic disorders is increasing in their daytoday life Day by day the environmental pollution and other inexplicable factors contribute largely towards this high incidence Bronchial asthma is one of these allergic disorders; and it is defined as diffuse reversable obstructive air way disease (Charles Hiller et al. 1984).

Even from very early times attempts have been made to cure and manage this disease. In Siddha system of medicine, this is described under the disease entity "ERAIPPU NOI" (Kuppusamy Mudaliar, 1954). Extensive references are seen as to how to diagnose and treat patients suffering from bronchial asthma. In this paper an attempt is made to examine the efficacy of the Siddha drug "NAAYURUVI KUZHI THAILAM" in which *Achyranthus aspera* (Naayuruvi) roots are the primary constituent in the management of the disease "ERAIPPU NOI" (Br. asthma).

Materials and methods

This study was carried out at the O. P. D. level at the Central Reasearch Institute for Siddha, Madras. Altogether 23

cases from both sexes were treated and followed up. The following symptoms like wheezing, gasping, dyspnoea, sneezing, cough, sputum with cough, husky voice and hydrosis were taken as criteria for the selection of the cases. The clinical investigations like blood Total Count (T.C.), Differential Count (D.C.), Erythro Sedimentation Rate (ESR) were also done and recorded. The total duration of the treatment was fixed as 45 days. The marital, educational, social status of the patients along with the age and sex were also recorded. Even after the treatment, the investigations mentioned above were repeated and recorded.

Selection of the drug:

The drug Naayuruvi kuzhi thailam as referred in "Yaakoppu Vaithiya Chinthamani" was prepared at the Pharmacy of the Central Research Institute, Madras.

Ingredients

Roots of Nayuruvi *(Achyranthus aspera)* Cow's urine

Method of Preparation

Roots of *Achyranthus aspera* (Naayuruvi ver) are cut into pieces and soaked in cow's urine for a day and then dried in the sun. They are put into the pot of kuzhi pudam and the oil is collected.

Dose

1 to 3 drops

Mode of administration

Two drops of thailam is smeared on betal leaf and administered twice or thrice a day

Observation

Information recorded in the proforma were analysed and tabulated

Dicussions

Age, sex or marital status, can not be considered as a factor for the incidence of this disease. Table No. III shows that this disease is more common among tobacco addicts than others. Table IV shows that most of the patients had all the symptoms taken as criteria for the selection before the treatment, and most of the symptoms were observed to be absent after the treatment, Table V shows that the fall in blood Total Count (T.C.), Erythro Sedimentation Rate (ESR) and Eosinophilia Count were observed which were statistically significant $p < 0.05$, $P < 0.01$ and $p < 0.05$ respectively.

Conclusion

The Siddha drug "Naayuruvi kuzhi thailam" which was not in the use either in the Hospital or by most of the practitioners, was found to be quite effective in the management of the disease "Eraippu noi" as referred to in "Yaakoppu Vaithya Chinthamani". This type of research will provide a better scope in solving the complicated and challenging disease like Br. asthma.

Acknowledgement

The authors are very greateful to the Director, CCRAS for financial sanction and approval. Thanks are also due to the staff of the pharmacy, CRIS who supplied the thailam promp ly and the other staff of CRIS who helped in conducting this trial.

CLINICAL EVALUATION OF NAAYURUVI KUZHI THAILAM IN THE TREATMENT OF ERAIPPU NOI

TABLE: I AGE AND SEX CLASSIFICATION

Age in years	Male		Female	
	No	%	No.	%
20–30	5	33.33		
30–40			2	66.66
40–50	2	13.33	1	33.33
50–60	4	26.66	—	—
60–70	1	6.66	—	—
Total	12		3	

TABLE: II CLASSIFICATION OF CASES ACCORDING TO MARITAL STATUS

Marital status	Male		Female	
	No	%	No.	%
Married	10	66.66	3	100.00
Unmarried	2	33.33	—	—
Divorced	—	—	—	—
Widowed	—	—	—	—

TABLE: III CLASSIFICATION OF CASES ACCORDING TO PERSONAL HABITS

	Dietetic Habits	No.	%
1.	Vegetarian	2	13.33
2.	Non-vegetarian	13	86.66
	Addictions		
	1. Tobacco	11	73.33
	2. Alcohol	9	60.00

TABLE IV SIGNS AND SYMPTOMS

Sings and Symptoms	Treatment Before				Treatment after			
	Present		Not Present		Present		Not present	
	No.	%	No.	%	No.	%	No.	%
Wheezing	15	100.00			2	13.33	13	86.66
Gasping	15	100.00			1	6.66	14	93.33
Dyspnoea	15	100.00			–	–	15	100.00
Sneezing	15	100.00			2	13.33	13	86.66
Cough	15	100.00			4	26.66	11	73.33
Sputum with cough	13	86.66	2	13.33	–	—	15	100.00
Husky voice	11	73.33	4	26.66	–	—	15	100.00
Hydrosis	15	100.00			–	—	—	—

TABLE : STATISTICAL SIGNIFICANCE

	Before treatment vs After treatment	Significance
Blood		
T.C.	1 t/ = 2.2708 2.15	
	P∠0.05	Significant
E.S.R.	1 t/ = 3.7603 2.98	
	P∠0.01	Significant
Eosinophilia	1 t/ = 2.557 = 2.15	
	P 0.05	Significant

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THE SKIN DISORDORS AND VITILIGO – A CASE STUDY

G.D. Mukherjee

Abstract

Vitiligo is a prominent skin disease appearing mostly on the exposed parts of the body such as the lips. eyelids, forehead, root of the ears, root of the nails of both the upper and lower extremities, fore limbs and hind limbs. It appears on the hidden parts also as the neck, chest and genitalia. This disease creates a special stigma. The treatment is time consuming, expensive and the prognosia is most uncertain It is chronic from the very onset and produces several other ill effects which can be named as mental changes. The psychological abnormalities that appear in cases suffering from vitiligo are inferiority complex, development of depression, anxiety, psychosis and aggressiveness and sublimative in nature A belief still persists among some people in society that it is a type of Leprosy and therefore untouchable and people afflicted with it should be avoided and thus no social and familial relationships are built up. But the fact that it is not true. It is not at all a disease of bacterial origin, nor is it an infectious disease. It occurs only due to depigmentation or lack of melanin pigmentation which is true, is due to cosmetic reason.

The diseases and disorders of the skin are a common occurrence. A survey among the school children reveals that about 24% of the students of either sex in the rural and tribal areas in our country are suffering from various types of skin diseases and disorders. Although in general the morrality rate among skin patients is not, so high, yet there are skin diseases which

In the long run create permanent disability to the patient and necessitate vocational rehabilitation. Vitiligo is such a type of skin disease which is creating a social stigma to the patient, who develops some abnormal psychological phenomena which invariably create a social and familial problem.

So before discussing about vitiligo according to the concept of Ayurveda, it would be proper to explain briefly, by the concept of the skin. As per modern Anatomy, the different layers of the skin are five in number and these are the stratum cofneum, stratum lucidum, stratum granulosm, rate mucosum and cutis vera. Ayurveda also mentions six layers (as per charaka). Sushuruta classified it into seven layers which may be considered a more detailed classification than that of charaka. The layers of skin, as stated by the author are Abavasini, Lohita, Sweta, Tamra, Vedini, Rohini and Mamsa Dhara. Abavasini layer is the outer most layer of the body surface and is responsible for melanin production and actually maintains the normal pigmentation of the body. Tamra and vedini type of layers which contain granules of pigment which occurs largely in coloured races due to exposure to sunlight specially in the tropical countries.

The factors which confirm on the skin its chaiacteristic normal colour, are metabolically produced by the specialised cells in the skin by the enzyme (Dopa-oxidase). Mukherjee G. D. reported during the year 1966, that there exist in Abavasini layer a pittya, known as Bharjaka pittya which provides the skin with the pigment that lends the normal colour and enables the function of the skin, as performed generally by melanin.

Methods and Materials

Various types of diseases and skin disorders, as defined in different texts are nearly seventy five in number. Of course, all these varieties of diseases are not found in a particular place or country, but they vary from race to race, country to

country, diet habits of the population and the climatic conditions of the country. There are several skin diseases which are very common in the tropical countries and some are found in extreme climatic condition. So considering the above facts; all the varieties of skin diseases may be grouped as follows.

1. Due to Avitaminosis: There are some skin diseases which are due to avitaminosis or deficiency of vitamins Vitamin 'A' deficiency may lead to Acne vulgaris, Keratoderma, Lichen, Spinulosum, Pellagra, Herpes simplex, Angular stomatitis, Herpes zoster may develop due to want of vitamin B-Complex. Bleeding dermatoses and Scurvy are due to the deficiency of Vitamin-C, Keratoderma and collagn diseases may develop due to want of Vitamin-E,. and Haemorrhagic drug eruptions may be due to deficiency of Vitamin-K and E.

1. Due to Infection and Contact: Poxes, eczema, boils, curbuncles, syphillis and leprosy.

3. As Complication of other diseases: Herpes, lisminosis and other metabolic diseases such as puritus genitalia.

4. Wanton and Exaggeration of normal physiological activities as Vitiligo, Keloid etc.,

5. Endocrine defects in the Pituitary, Thyroid, Adrenals, Ovaries, and Androgens.

6. Neoplastic - Tumours (as benign, malignant sarcomas and reticulosis) etc.;

7. Other factors - as wats, prickly heat and allergic conditions are due to side effects of medicines.

8. Psychological factors - It has got no effect directly but often aggravates the condition, as in the case of Vitiligo.

So far as the signs and symptoms of the above said diseases are concerned, there are a few common manifestations

prevalent in majority of the cases. The commonest symptoms are itching, pain, burning, stinging, hypersensation and loss of sensation (either local or general) etc. Macula, Papule, vesicle, weal and pustule are the most common and prominent signs.

Observations

On close observation of long standing cases suffering from vitiligo, it has been found that majority of them suffer from various psychological disorders which on the one hand virtually prevent improvement and on the other aggravate the condition. Indeed it has also been observed that persons who frequently come into contact with such cases have been found to develop abnormal behaviour and, in the long run, they also become suceptible to the disease. Persons suffering from hysteria, epilepsy etc. having already got serious psychological disorders may not be susceptiable to the particular disease, but a person suffering from vitiligo or other skin diseases develop some sort of behavioural disorder. Now the question may arise as to how psychological factors act predominently in etiopathogenesis of skin diseases.

In explaining the relationship between the brain and the skin Dr. P.N. Bahl reported that embryologically the relation ship of the skin to the brain is based on the fact that both are derived from the epiblast. It is by the sense of touch that a baby or an animal can recognise affection or anger or is able to differentiate between pleasant and unpleasant sensation. And it is an essential part of the individuals temperament. The state of mind and the state of skin affect each other reciprocally, and the individuals reaction can always be determined with the help of his skin condition because emotion like, fear, anger. and embarrassment are always reflected on the skin.

So it is always desirable to study the psychology of individual cases, when the physician undertakes the treatment of any type of skin disease. The author in the course of his

study of vitiligo cases found evidence to corroborate the above statement.

As a matter of fact, Leucoderma is a prominent skin disease which appears mostly on the exposed parts of the body and sometimes on the hidden parts also. The disease creates a social stigma. The treatment is time consuming, expensive and sometimes uncertain. It is chronic from the very onset and produced several other ill-effects, some of which may be called mental changes. The most common mental or psychological abnormalities that were observed in these cases are:

1. Inferiority Complex: It develops immediately following the onset of the disease. The patient considers himself or herself inferior to those with whom he was earlier at par. Naturally,at the begining the patient tries to hide the patches or lesions and failiure in this effort leads to avoidance of relatives and friends, as far as possible, on the part of the patient

2. Idea of reference: Whenever he or she sees some persons talking at a distance, he or she thinks that they are talking definitely about his or her disease which is certainly not a fact.

3. Depression: The disease is chronic from the very onset and when a vitiligo case feels or comes to know that the disease is chronic and often incurable, then the person becomes gradually depressed, and this tendency may even lead to suicide.

4. Anxiety: As the disease spreads, it may give rise to a state of acute anxiety in the patient leading to insomnia mixed with depression.

5) Psychosis: As the patient tries to fight shy of the surrounding environment, he or she may gradually feel more lonely and withdrawn, ultimately plunging into a psychotic state. Such a patient may have delusions (false beliefs)

suspicion or doubts, that his or her spouse is indulging in adultery, thus causing even marital disharmony.

6. Aggression or sublimation: He or she may either develop a disbelief in God and become aggressive in nature in his or her interpersonal behaviour, or he or she may choose the path of sublimation and resort to leading a religious life as a possible escape from his/her cruel fate.

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THERAPEUTIC TRIAL OF CERTAIN HERBAL PREPARATIONS BASED ON AYURVEDIC CONCEPT OF ETIOPATHOGENSIS OF RHEUMATOID ARTHRITIS (AMAVATA)

Prem Kishore, M. M Padhi, S. N. Banerjee

Rheumatoid arthritis, the most painful disease, has remained a great crippler in spite of tremendous scientific developments This state of affairs is primarily due to lack of specific knowledge of its etiopathogenesis. The Ayurveda, the ancient Indian Science of Medicine, has propounded many original and scientific concepts on the various aspects of medical science. The concept of the etiopathogenesis of the diseases in general as well as of several specific diseases, is based on thorough understanding of the various aspects of human environment and process of production of disease understood by them. An unique conept of pathogenesis of Rheumatoid arthritis has been put-forth in Ayurveda around 900 A. D. by *Madhava.* This disease has been considered to be the consequence of product of *'Ama'* in the human body due to a variety of reasons, the gastro-intestinal dysfunction being the main cause. (Tripathi et. al 1965) The clinical manifestation of this disease discussed in Ayurveda highlights the features of gastro-intestinal dysfunctions in addition to the features related to the joint inflammation. So much so, that enteropathy (Grahani Roga) (Yogaratnakara) and Ulcerative colitis (Amatisara) (Harita) have been identified as the manifestations of this disease. The principle of treatment and the drug recommended for this disease are also directed towards augmenting the impaired gastrointestinal function. (Shastri, 1961).

In the present Era the published reports also confirm the impairment of gastro-intestinal function by way of lowered acid secretion, impaired intestinal absorption, deranged liver function and atrophy of villi (Gaspardy and Vida, 1964, Morace et. al. 1964, Peliven et.al. 1961. Shatin, 1964, Tewari et.al. 1979). These aspects have also been gradually recognised by the modern sciences and a new term 'intestinal arthritis' has been putforth to indicate the arthritis associated with certain intestinal disease (Keily et.al 1981). The preliminary studies taken up by the author also confirm the reduced acid secretion, below normal liver function, diminished absorption of protein and carbohydrate (Kishore, 1966). The improvement of the impaired gastro-intestinal function has also been observed in certain cases by treatment with Ayurvedic gastrointestinal stimulant drugs (Kishore & Tripathy, 1965).

Selection of drug

Keeping in view the facts discussed earlier, efforts have been made to study the effect of *Sunthi* – Ginger, in combination with certain other drugs to assess its efficacy in the treatment of Rheumatoid arthritis. This drug has been considered an important agent in preventing/checking the formation of *Ama* and alleviating the *'Ama'* already formed in the body. In addition, it also augments the gastro-intestinal function (Bhava Prakasha).

The paper presents observations on four separate trials with the preparations having *Sunthi* as a major ingredient. The *Guduchi*, *Guggulu*, *Nirgundi* and *Rasona* have been taken up for evaluation alongwith *Sunthi*. Prevalent combinations of Ayurvedic drug formulations have also been tried in separate groups of patients to compare the efficacy.

Materials And Methods

The patients for trials were selected on the basis of ARA criteria (1959) and only clinical findings as morning stiffness,

pain in motion, swelling of one joint, swelling of another joint, symmetrical involvement of joints, sub-cutaneous nodules over bony prominences alongwith radiological reports were taken into account. After admission, the patients were subjected to detailed clinical examinations pertaining to availability of relevant findings, their intensity as well as certain functional tests and measurement of joints. A specific proforma evolved was filled up for each patient. In some cases photographs of the affected joints were also taken.

Assessment and classification of results :

The assessment of the results has been done according to the changes in clinical findings In addition, the changes in ESR test, functional tests and measurement of the joints have been noted. The results of the treatment have been classified as follows:

Complete Relief:

Completely free from signs/symptoms of joint inflammation with free movement of the joints except those due to irreversible changes.

Partial relief

Reduction of signs/symptoms of joint inflammation and improvement of joint movement to a major extent, but not fully.

No relief

No response at all or only marginal improvement of the condition.

Drop out

The patients who discontinued the treatment before stipulated period.

Observations

The observations on 265 patients in four separate trials have been taken up for a period of more than six years to assess the role of *Sunthi* and certain other drugs in the treatment of Rheumatoid Arthritis. The observations on the general clinical profile of patients have been discussed first and the effect of each combination of *Sunthi* in different trials have been discussed separately.

The general clinical profile

The observations indicated that the disease affects the individuals of either sex in all age groups, though the incidence appears to be maximum in the age group of 21–30 years (Table-2).

The patients have been suffering from the disease mostly for less than one year duration. though many chronic cases of more than 10 years duration were also observed. The knee joints, ankle joints and wrist joints were most commonly affected. Certain patients where X-ray of joints was taken, showed varying degree of changes ranging from Oeteoporosis to Anklyosis and fusion of bones were also observed. The overall classification of cases taken up for trial as per the ARA criteria has been observed as either 'Definite or Classical'. The joint involvement is invariably poly–articular and symmetrical. The ESR has been found to be raised in most of the patients. Though most of the patients were having Gastro-intestinal symptoms such as constipation, loss of appetite, etc., certain patients with chronic diarrhoea were also observed. It was also noted that the intensity of the disease was directly related to the intensity of the chronic diarrhoea.

Therapeutic efficacy

(i) Sunthi-Guduchi

The trial of a 12 weeks course of *Sunthi-Guduchi* in the form of decoction in the dose of 25ml. - 50ml. three times a day

in comparision to a combination of *Yogaraja Guggulu, Vataga jankusa Rasa* and *Maharasnadi Kvatha* has been taken up in 77 patients in two groups. The treatment gradually showed improvement in the pain, swelling and restriction of movement, the cardinal manifestation of the disease in both the groups of treatment. The effect of *Sunthi-Guduchi* has been relatively better since the percentage of patients with no relief and drop out has been much less than the other set of the treatment and many more patients have been reported partial Relief (Table-3).

The ESR have also shown significant reduction in the patients treated with *Sunthi-Guduchi* and in most of the cases it has come within normal limit after treatment.

(ii) Sunthi-Gugglu (A)

A clinical trial of *Sunthi-Guggulu* in comparision to *Yogaraja Gugguiu, Amavatari Rasa* and *Maharasnadi Kvatha* was taken up on 63 patients in two groups. 36 patients were treated with a six week course of *Sunthi-Guggulu* in the dose of 2gms., three times a day, whereas the 2nd group of 27 patients were treated with the other combination mentioned above. Remarkable improvement was observed within a short period of treatment with Sunthi-Guggulu and the percentage of patients who reported complete relief and partial relief have been much more with the treatment by *Sunthi-Guggulu* than the other combination mentioned above (Table-4).

(iii) Sunthi-Guggulu (B)

Keeping in view the better efficacy of *Sunthi-Guggulu* combination, efforts have been made to further asses its effect in a larger series of patients. As such the trial of a six week course of *Sunthi-Guggulu* alongwith local external treatments have been taken up on 75 patients. The efforts of the drugs have been quite significant and it has been observed that all most all the cases who completed the course have shown definite improvement, though complete relief was observed

in a small proportion of cases. Partial relief, i. e. more than 50%, was observed in 42 cases. It was an important observation that the patients in the early stage of the disease in younger age groups and the males showed better etfect of the treatment (Table-5).

(iv) Rasonadi Kvatha

A clinical trial of six week course of *Rasonadi Kvatha* combination of *Rasona, Sunthi* and *Nirgundi* has been taken up on 50 patients. The treatment showed good effect since of the patients who completed the full course of treatment showed definite improvement-28% Complete Relief and 46% partial Relief. It was observed that the drug was more effective in female patients (Table-6).

Discussion

In view of the Ayurvedic concept of Gastro-intestinal etiology of this disease; an attempt has been made to assess the effect of *Sunthi* in the treatment of this disease. This drug has been said to regulate the bowel movement by way of controlling loose and watery motions as well as relieving constipation. The digestive stimulant action of the drug has been well established. Thus, this drug will be able to alleviate the 'Ama, the chief causative agent of the disease according to Ayurveda, This conception has been put to test on a series of four trials with the various combinations of *Sunthi* as a major ingredient. The effect of its combinations has been better than that of the prevalent Ayurvedic preparations such as *Yogaraja Gugglu, Vatagajankusa Rasa,* Amavatari Rasa and *Mahatasnadi Kvatha.* The effect of the combination of *Sunthi* may be attributed primarily to its effect on gastro-intestinal tract, it being a major ingredient in all these combinations as well as of sufficient dose. According to Ayurvedic pharmaco-dynamic principles the drug Sunthi possesses *'Katurasa'* that is combination of *Agni* and *Vayu Mahabhutas* (Sherma 1976) Since the properties available in the drugs also exist in the human

body (Susruta), when ingested it enhances the strength of *Agni* due to similarity. So the *'Dhatvagnis'* and *Bhutagnis* nourished by *Panchakagni* (Charaka) act in a proper manner throughout the body including *'Srotas'* to convert the *'Ama'* already produced and to prevent its production. When major features of this disease like inflammation and morning stiffness are said to be due to accumulation of oedema fluid within inflammed tissues, it is supposed to remove this due to its *'Dravasosaka'* action. Further more, it alleviates *'Kapha'* because of its properties like *'Usna'*; *'Tirsna'* and *'Usnavirya'* as well as *'Vata'* for its *'Madhura Vipaka'*, those two take dominant role in pathogenesis of this disease. The efforts to evaluate a potent Ayurvedic gastro - intestinal drug in the treatment of Rheumatoid Arthritis has indicated that the treatment may act on the process of etiopathogenesis of this disease and prevents/alleviates the formation of *'Ama'*. These observations further confirm the Ayurvedic concept of gastro-intestinal origin of the disease by providing therapeutic evidence.

Summary

The Ayurvedic concept of the etiology of Rheumatoid arthritis lays great emphasis on the role of digestive dysfunction. The treatment of this disease is also directed towards corrections of such abnormalities which lead to production of *'Ama'*. In the present paper a series of four clinical trials have been taken up to assess the efficacy of gastrointestinal stimulant drug *Sunthi* in the treatment of this disease. The observations indicate that the effect of *Sunthi* combinations have been relatively better than the conventional approach of Ayurvedic treatment consisting of *Yogaraja Guggulu Vatagajankusa Rasa, Amavatari Rasa* and *Maharasnadi Kvatha*, etc. The observations further augment the concept of etiology of this disease in Ayurveda: An attempt has also been made to analyse the possible mehanism of action in accordance with the Ayurvedic Pharmaco-dynamic principles.

TABLE–1. SHOWING GROUPWISE TREATMENT AND NUMBER OF PATIENTS IN EACH GROUP.

Trial No.1.

A.	Yogaraj Guggulu–1gm. Vatagajankusa Rasa–250mg. Maharasonadi Kvatha 50ml.	Thrice daily	40 patients
B	Sunthi–Guduchi Kvatha 25–50ml.	Thrice daily.	37 patients

Trial No. 2.

A.	Sunthi–Guggulu–2gms.	Thrice daily	36 patients
B.	Yogaraj Guggulu–2gms. Amavatari Rasa–½gm. Maharasonadi Kvatha 25ml.	Thrice daily	27 patients.

Trial No. 3.

Rasonadi Kvatha–25ml.	Thrice daily	50 Patients.

Trial No. 4.

Sunthi–Guggulu–2gms. each	Thrice daily	75 Patients

In addition to the above medicines, Baluka Sveda and Lepa were given in the acute stage of the disease.

TABLE 2 : SHOWING THE AGE AND SEX

Sex	Age in years							Total
	1–10	11–20	21–30	31–40	41–50	60–61	and above	
Male	4	34	49	16	16	17	7	145
Female	2	22	25	24	22	14	11	120
Total:-	6	56	74	42	38	31	18	265

TABLE–3.

Results	Yogaraja Guggulu Vatagajankusa Rasa Mahara-snadi kvatha	Sunthi-Gudichi	Total
Complete Relief	11 (27.5%)	10 (27.2%)	21 (27.2%)
Partial Relief	10 (25%)	15(40.54%)	25 (32.46%)
No Relief	5 (12.5%)	2 (5.40%)	7 (9.9%)
Drop out	14 (35%)	10 (27.02%)	24 (31.16%)
Total	40	37	77

TABLE–4

Results	Yogaraja Guggulu Amavatari Rasa Maharasnadi Kvatha	Sunthi-Guggulu	Total
Complete Relief	8 (27.62%)	12 (33.3%)	20 (31.74%)
Partial Relief	8 (22.22%)	12 (33.3%)	18 (28.57%)
No Relief	—	—	—
Drop out	13 (48.14%)	12 (33.3%)	25 (39.68%)
Total:–	27	36	63

TABLE 5 : SHOWING THE RESULTS IN RELATION TO AGE

S.No.	Age in years	Results				Total
		Complete relief	Partial relief	No relief	Drop out	
1.	11-20 years	5	6	—	3	14
2.	21-30 years	6	6	—	5	17
3	31-40 years	—	11	—	4	15
4.	41-50 years	3	8	—	2	13
5	51-60 years	—	6	—	2	8
6.	61 years & above	1	5		2	8
	Total:-	15	42	—	18	75

TABLE–6

S. No.	Results	Male	Female	Total
1.	Complete Relief	5(19.23%)	9(37.5%)	14
2.	Partial Relief	12(46.1%)	11(45.83%)	23
3.	No Relief	2(7.69%)	1(4.16%)	3
4.	Drop-out	7(26.92%)	3(12.5%)	10
	Total	26	24	50

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RAPID COMMUNICATION

EFFECT OF AN INDIAN MEDICINAL HERB ON RAT FOOT OEDEMA

A. K. Khare, M. K. Sharma

Nyctanthes arbor tristis Linn. (Hindi name : Harsingar) has been used on empirical basis by practitioners of Indigenous Medicine in India for the treatment of obstinate sciatica, chronic arthropathies and pyrexia. It is a popular anti-arthritic drug in traditional system of medicine[1]. However, epxerimental evidence in support of its use is lacking. Therefore, the present study was undertaken to evaluate anti-inflammatory activity or the herb against experimentally induced rat foot oedema, a common model for assay of anti-inflammatory drugs.

Leaves of *Nyctanthes arbor tristis* Linn. were locally procured, batanically identified, shade dried and pulverised in a mixer grinder in our laboratory. Powdered leaves were successively extracted with petroleum ether and 95% ethyl alcohol in a Soxhlets's apparatus by the method of Devis as described in one of the earlier communications[2]. Extract thus obtained was evaporated to dryness in a vaccum dessicator (over anhydrous calcium chloride) and water soluble portion was used in oral dose (administered with a metallic rat feeding canula) of 500 mg. per kg. of body weight which were administered one hour prior to the injection of phlogistic agent in rat hind paw.

Study was conducted on 60 Albino rats of either sex, weighing 80--120 gms. fed on standard laboratory diet and housed in identical environmental conditions. Animals were divided in to four groups of 15 each. Inflammation was experimentally induced by subplantar injection in right hind paw of rats, of following phlogistic agents:--

A	Carrageenin	(1% soln, in N. Saline)[3]	... 0.1 ml.
B.	Hyaluronidase	(1500 i. u./ml.)[4]	... 0.1 ml.
C.	Histamine	(0.1% soln, in N. Saline)[5]	... 0.1 ml.
D.	Serotonin	(0.1% soln, in N. Saline)[6]	... 0.1 ml.

Each of the above groups (A,B.C&D) were subdivided into three subgroups I, II & III for administration of the drugs. Subgroup I received normal saline and served as control (0.5 ml.) while II and III received Sodium salicylate (500mg./kg. B. W.) and drug under investigation (500 mg./kg. B.W.) respectively.

Initial paw volume was measured by the micropipette method[7] Increase in rat foot volume was determined by taking final reading of paw volume after 3 hours, 20 min., 1 hour and 4 hours in groups A, B, C and D respectively. In all the groups, mean increase in paw volume of control group (Subgroup 1) was compared with subgroups II and III receiving standard and test drugs in order to determine anti-inflammatory activity of both, test and standard drugs.

Results of the present study indicated that water soluble portion of the alcoholic extract of the herb exerted marked anti-inflammatory activity in all the experimental model used in the study. Its anti-inflammatory activity was 36.2% against carageenin induced rat foot oedema, while in Hyaluronidase, Histamine and Serotonin induced oedema it was 28.9%, 47.8% and 32.5% reepectively. Sodium salicylate in corresponding dose showed anti-inflammatory activity 38.9%, 33.3%, 34.0% and 32.5% in groups A, B, C and D respectively. So it could be concluded from the present study that the test drug exhibited anti-inflammatory activity in all the models of experimental inflammation employed and was equipotent with standard drug (Sodium salicylate) except in Histamine induced oedema where test drug was found to be far more potent than the standard drug. On statistical analysis of date by student's 't' test of significance, all the results were found significant (Vide accompanying table).

TABLE SHOWING EFFECT OF WATER SOLUBLE FRACTION OF HARSINGAR AND SODIUM SALICYLATE ON RAT FOOT OEDEMA INDUCED BY VARIOUS PHLOGISTIC AGENTS

S. No.	Group/Sub-groups	Mean initial paw Vol. (ml)	Mean final volume of paw (ml)	Mean increase in paw volume (ml) ± S.E.	Anti-inflammatory activity (P.C.)	P. Value (at df 18)
1.	Group–A					
	i. Control	0.64	1.15	0.51 ± .062	—	—
	ii. Test	0.56	0.88	0.32 ± .026	36.2	∠.05
	iii. Standard	0.62	0.93	0.31 ± .033	38.9	∠.05
2.	Group B					
	i. Control	0.61	1.12	0.51 ± .056	—	—
	ii. Test	0.56	0.92	0.36 ± .032	28.9	∠.05
	iii. Standard	0.63	0.97	0.34 ± .041	33.3	∠.05
3.	Group C					
	i. Control	0.55	1.05	0.50 ± .045	—	—
	ii. Test	0.62	0.88	0.20 ± .020	47.8	∠.01
	iii. Standard	0.57	0.90	0.33 ± .027	34.0	∠.01
4.	Group D					
	i. Control	0.56	0.92	0.36 ± .041	—	
	ii. Test	0.60	0.84	0.24 ± .032	32.5	∠.05
	iii. Standard	0.53	0.77	0.24 ± .027	32.5	∠.05

N. B.:

Oedema was induced by:

1. Carageenin in gr. A 2. Hyaluronidase in gr. B 3. Histamine in gr. C and 4. 5-Hydroxytrypatamine in gr. D.

2. Final volume was measured after three hours, one hour, twenty minutes and four hours in groups A, B, C and D respectively.

3. Each sub-group comprised of 10 animals of either sex and drugs (Harsingar and Sodium Salicylate) in oral dose of 500mg./kg. B.W. one hour before injection of phlogistic agent.

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THE EFFECT OF LAWSONIA INERMIS. LINN. (LYTHRACEAE) EXTRACT ON SKIN INFECTIONS AND DISORDERS

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Introduction

Traditionally, from very early times mankind has utilized plants in an attempt to cure diseases, and disorders, and to get relief from physical and physiological sufferings. Primitive, peoples of all ages have had some knowledge of drug plants, derived as a result of the trial and error method. In general, plants are one of the important sources of medicine. Chinese were the first to use natural vegetation such as herbs, shrubs and trees as medicine. The practice of utilizing plants for medicine is as old as 5000 to 4000 BC. Greeks have given enormous information about medicinal plants. In India, the earliest references of the curative properties of plants appear in Rig Veda composed between 3500–1600 BC. The later Veda Atharva, describes, the uses of large number of drugs, Investigations uptodate have brought up the number of drug plants, to about 2000.

Studies of medicinal plants based on ancient literature and their investigation in accordance with modern methods constitutes a special field of study called Ethnology. The other term used in this context is Pharmacognosy, which is a branch of medicine (Trease, 1952) dealing with history, commerce, collection, selection, identification and preservation of crude drugs and raw materials (Allport, N. L., 1944). Most of the

drug plants from wild in the tropics and a few of them have been cultivated (Bailey L. J. 1949), The medicinal value of drug plants is due to the presence in the plant tissues of some chemical substance or substances that produce a definite physiological action on the human body. (See; Albert F. Hill, 1983)

The pharmacology and clinical studies on the effect of various traditional medicines on diverse diseases such as asthma, cancer, diabetes mellitus, heart diseases, rheumatism, skin disorders and others lane made rapid progress (Krishnan V. R. 1977). The various Tamil medicines for fever, piles, dysentery, diarrhooa, stomach ache, gas trouble, asthma, vomiting, eye sore, jaundice, snake-bite, dog-bite, spider-bite, scabies, burns, abrasions, nervous weakness, breast pain, tooth ache, head ache, indigestion and for other disorders too. are under constant research and are making rapid progress in competition with drugs used in western medicine (Viswanatha K.A.P. 1962),

Among the various afflictions the mankind is subjected to those of the skin may be considered very important because the skin is most susceptible to contagious diseases, due to the fact that it is the outer most part of the body with a wide surface area exposed constantly to the external enviornment. Skin consists an outer layer called epidermis and inner layer called dermis. Besides serving as a protective covering for the body, the skin also protects the body from invading parasites and in other ways. With this aspect in view, a therapeutical study was carried out on various skin disorders with many disorders with many traditional medicinal plants with particular reference to its pharmacology and clinical studies.

Materials And Methods

The chosen cases skin disorders were treated with the materials as such and with certain by-products of the following

plants. The various parts of the plants used for the preparation of medicines were the leaf; bark, flower, seed, wood, nut. fruit, pulp etc., (Pandey, B.P 1980). The pharmacognetic aspects of the plants used for study are tabulated here in detail

For the given fifteen types of skin disorders, varied type combinations of plant products were used in different forms in specifically different proportions. The various specific actions of drug combinations are astringent effect, curing effect on skin itches, eczema, insect bite, antipyretic effect, nail bed rot, nail root rot, nail fold rot. nail eponychium rot, dry and moist gangrene, pruritus, dandruff and elephantiasis and also abrasions, abscess (boils), mite itches and scabies.

Method

For the preparation of leaf, flower, rhizome and or bark powders, moisture free dry materials were taken and made into amorphous grain free powder with the help of germfree mortar and pestle.

Normally the fatty oils are liquid at ordinary temperatures and usually contain oleic acid. They are some times called fixed oils, because unlike the essential oils they do not evaporate (advantageous feature for treatment to keep the skin smooth and moist). Chemically the fatty oils consist of glycerine in combination with a fatty acid. However, the fats are solid at ordinary temperatures and contain stearic acid and palmitic acid. Usually the fatty oils are stored up in seeds of the plants belonging to many families. Sometimes to a less extent, they are also stored in fruits, stems and other plant organs.

Extraction of fatty oils

The seed-coats are removed and the material is converted into a fine meal. The oils may be removed by solvents or by hydraulic pressure. The hydraulic pressure method is

commonly used for extracting the edible oils. The pressure causes the cell wells to break and the fatty oils escape These oils are filtered and purified (method used by authoritative agencies). The various oils were obtained from various agencies of ISI standard. The raw materials were rolled, crushed, hydraulically pressed/expeller pressed and steam distilled, depending on the need of the material. In the case of preparation of paste, lotion and emulsion, variable but specific percentage of weight/volume of materials were taken and prepared.

Results

Lawsonia inermis leaf extract as such had differential impact on the various skin abnormalities. Depending on the severity of the disorder or infection and the stage of the illness, the effect of this leaf extract varied. Also, in combination with other medicinal plants and their by-products, the curing effect was found to be fast and appreciable, irrespective of the severity of the skin disorder concerned. The form of application of the medicine may be in any one of the following forms: cream, paste, powder, lotion, emulsion or liniment

The varying role of the leaf extrat *Lawsonia inermis* alone in the selected disorders, namely, skin itches, abrasions (wounds), abscess (boils), mite itches, scabies, eczema, insect bite, antipyretic, astringent, nail rot, gangrene, pruritus, dandruff and elephantiasis is quite characteristic.

In the cases of abscess (boils) the influence of *Lawsonia* leaf extract alone can cure only about 45% At the same time when the extract is prepared by adding camphor *(Cinnamomum camphora)* (Krishnamoorthy, 1953) 10% by weight, the curing effects was found to be more, about 53%. With the addition of seasame seed oil *(Seasamum indicum)*, the result showed a further increase of 11% effects (Table 1). This type of enhanced effect due to differential composition is anaiysed in the discussion part of the paper.

For mite itches, *Lawsonia* extract alone plays a curing role for about 30%. When the extract is prepared by mixing the powder of *Curcuma longa*, the relieving effect was found to have increased to 66%. The effect was further increased (76%) by incorporating 20% volume of Arachis oil *(Arachis hypogea)* to the earlier mixture (Table 2)

Treatment of scabies with *Lawsonia* and others exhibited distinct variations, The *Lawsonia* leaf extract alone was found to be effective upto about 32%. When the dried flowers of *Leonetis neptifolia* were added for the purpose of the treatment the irritation and other causative factors were reduced and 51% relief was obtained. In *Bauhinia variegata* tree's bark was mixed in powder form and the illness was treated the relief increased to 62%. Further good results (78%) were exhibited when chaulmoorga oil of *Hydnocarpus kurzii* (*Terak-togenos Kurzii*) (Chopra, 1933) was added to the mixture of the above components (Table 3)

The other type of skin infection taken for study was eczema. Eczema is a superficial inflammation of the skin mainly affecting the epidermis. Eczema causes itching with a red rash often accompained by small blisters that weep and become crusted. Subsequent scaling, thickening and dis-colouration of the skin may occur. The drug used with the *Lawsonia* leaf extract, sandal wood oil (*Santalum album)* (Pandey, 1980) or olive oil *(Olea europea)*, leaf of *Cassia alata*, pepper *(Piper nigrum)* and Chaulmoorga oil of *Hydno-carpus kurzii* (Kanny Lall dey, 1896) composition showed some corticosteroid effect and the curing feature was found to be faster and good (Table 5)

The skin *in toto* has various derivatives. One among them is the nail. It is a horny structure composed of keratin, formed from the epidermis on the dorsal surface of each finger and toe. The exposed part of the nail is the body, behind which is the root. Growth of the nail occurs at the end of the nail root by division of the germinative layer of the underlying

epidermis. Nail has some important sensitive structures namely lunula, nail bed, nail fold and eponychium. People with affected nails were given treatment with the mixture of *Lawsonia inermis* leaf extract (paste), *Curcuma longa* powder and the skin juice of *Citrus medica*. With the first paste alone the 50% cure was observed. Simultaneously when curcuma rhizome powder and *citrus medica* juice were added to the *Lawsonia* leaf extract for treatment, the healing effect was profound and notable (Table 6)

Just as nail is an epidermal derivative on the head also there is another derivative,the hair. The scalp is such disturbed by a special type of infection called scurf or dandruff. It is a common condition in which the scalp is covered with small flackes of dead skin. The flakes, which come away when the hair is brushed or combed, represent an increase in the normal loss of the outermost skin layer. If too little sebum is produce the hair becomes dry and brittle with the formation of white skin flakes; too much of sebum gives greasy hair and yellow flakes. The treatment is carried out with the *Lawsonia inermis* leaves and *Leonetis neptifolia* leaves by mixing coconut oil (*Cocos nucifera*). It is prepared as a cream and applied as a paste. Subsequently, by regular washing with the mixture of *Lawsonia* extract and *citrus* juice, dandruff free skin and hair were developed (Table 7)

Discussion

The diverse combinations of various medicinal plants and their by-products with *Lawsonia inermis* (Henna) were given for the treatment of various cutaneous disorders and related abnormalities and infections. An analysis was carried out to ascertain the central role of *Lawsonia inermis*. In all the experimental treatments the drug without its combinations resulted in 'zero reaction' and the healing effects was found to be poor and almost nil so the role of its extract varried when combined with other medicinal plants or their exctracts showing increased healing effect the skin infections.

As astringent drugs they are more curative and act as antitoxic agents. It was due to the presence of curcuma. In healing skin itches they protect and harden the skin Itchy skin is also protected from skin irritation. Towards curing abrasions they are anti-haemorrhagic and stop bleeding. In the case of boiling abscess, camphor strengthens the action of *Lawsonia inermis* (Henna) leaves and acts as an anti-inflammatory drug and also absorbs the pus and fluid from the boil and any type of infected part of the skin with unwanted fluid accumulation.

The combined drug given for mite-itches kills the mite larva and also helps the patient by giving relief from irritation. In the case of treatment for scabies, the characteristic observations were made regarding its healing role. The medicine protects the soft skin from secondary infection and also inhibits the hatching of mite-eggs and denatures the eggs and related substances With reference to eczema and insect bite, the medicine combinations play an anti-inflammatory and astringent role and act as effective curative agents In the nail-rot disease, they are the best curatives and kill the germs. Secondary infection is also retarded and simultaneously fast growth rate of nail was observed.

For moist gangrene, henna powder was applied as a dehydrating agent But in contrast to this, for dry gangrene treatment, olive oil was mixed for the distinct healing effect. In the pruritus, the medicine in the form of emulsion was applied for an emmollient effect. In general, pruritus is nothing but an itching caused by local irritation of the skin or some times nervous disorders. Severe itching is often a symptom of some forms of jaundice. Pruritus of the vulva in women may be due to vaginal infection, in some cases caused by yeast organisms that flourish in diabetes, when the urine contains sugar. Pruritus of the anal region may be due to poor hygiene, haemorrhoids in the presence of intestinal worms.

In the case pruritus, the admixture of the medicine acts as a demulcent agent. For the above types of infection the

result was evidently favourable. In the treatment of dandruff the henna combination acts as an emmollient agent. The henna emulsion given for elephantiasis dehydrates and acts as an anti-inflammatory agent. In the laboratory culture, the mites and mite larvae including filaria larvae were retarded and were killed within a short period when the *Lawsonia inermis* leaf extract was added. They have a multiple action at the level of the skin as well as at the level of the disease causing or desease carrying organisms such as mite or other larvae or microorganisms responsible for the contagious diseases and other skin disorders

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TABLE : I MEDICINAL FLORA USED IN THE PRESENT STUDY

S. No	Plant's Botanical Name	Part used	Status	Family	Distribution
1.	*Lawsonia inermis*	Leaf	Shrub	Lythraceae	India, Arabia Egypt
2.	*Bauhinia variegata (candida)*	Bark	Tree	Caesalpiniaceae	India
3	*Cassia alata*	Shrub	Leaf	do	Tamilnadu, W.Bengal
4.	*Leonetis neptifolia*	Herb	Flower	Labiatae	Tamilnadu
5.	*Hydnocarpus kurzii* (*Taraktogenos kurzii*)	Seed	Tree	Flacourtiaceae	Assam, E. Bengal
6.	*Cinnamomum camphora*	Wood	Tree	Lauraceae	Nilgiris, Mysore
7.	*Sesamum indicum*	Seed	Herb	Pedaliaceae	India, Africa
8.	*Arachis hypogea*	Seed	Herb	Leguminosae	Brazil, India, China
9	*Curcuma longa*	Rhizome	Herb	Zingiberaceae	Tamilnadu, Orizza
10.	*Cocos nucifera*	Nut	Tree	Palmae	India
11.	*Piper nigrum*	Seed	Shrub	Piperaceae	India, Ceylon
12.	*Santalum album*	Wood	Tree	Santalaceae	Tamilnadu, Kerala
13.	*Olea europea*	Fruit Pulp oil	Tree	Oleaceae	North India
14.	*Citrus medica*	Fruit	Tree	Rutaceae	Assam, Punjab, Sikkim
15.	*Penicillium griseofulvin*	Criseofulvin			

TABLE II : INFLUENCE OF *LAWSONIA INERMIS* AND OTHER COMBINATIONS ON CURING EFFICACY OF ABSCESS OR BOILS (FURUNCLE)

S.No.	Materia medica	Composition	Healing%
1.	*Lawsonia inermis* & Dis. Water	85 : 15	45
2	*Lawsonia inermis* & *Camphora* & Dis Water	80 : 10 : 10	58
3.	*Lawsonia inermis* & *C. camphora* & Sesamum oil.	75 : 15 : 10	69

Boil : Tender inflamed area of the skin containing pus. The infection is usually caused by the bacterium *Staphylococcus aureus* entering through hair follicle or a break in the skin and local injury or lowered constitutional resistance may encourage the development of boils. Boil is medically called as Furuncle.

TABLE III : INFLUENGE OF *LAWSONIA INERMIS* AND OTHER COMBINATIONS ON CURING EFFICACY OF MITE ITCHES :

S No.	Materia medica	Composition	Healing%
1.	*Lawsonia inermis* & D. Water	80 : 20	30
2.	*Lawsonia inermis* & *Curcuma longa* & D. Water	70 : 15 : 15	66
3.	*L. inermis* & *Curcuma longa* & Archis oil	65 : 15 : 20	76

TABLE IV : INFLUENCE OF *LAWSONIA INERMIS* AND OTHER COMBINATIONS ON CURING EFFICIENCY OF SCABIES:

S. No.	Materia medica	Composition	Healing%
1.	*L. inermis* & D. Water	90:10	32
2.	*L. inermis* & *Lenonetis neptifolia* D. Water	55:30:15	51
3.	*L. inermis* & *L. neptifolia, Bauhinia variegata* & D. Water	50:25:15:10	62
4.	*L. inermis* & *L. neptifolia* & *B. variegata* & Chaulmoorga oil & D. Water	50:20:15:10:5	78

Scabies: a skin infection caused by the itch mite, *Sarcoptes scabie*. Scabies is typified by severe itching (nights) red papules and often secondary infection. The female mite tunnels in the skin to lay her eggs and newly hatched mites pass easily from person to person by contact. The intense itching is caused by the mites secretion, commonly infected areas are the groin, penis, nipples and the skin between fingers, (Families with mass application habit of Lawsonia paste as the nail decorative are not showing this abnormalities)

TABLE : V INFLUENCE OF *LAWSONIA INERMIS* AND OTHER COMBINATIONS ON CURING EFFICIENCY OF ECZEMA

S.No	Materia medica	Composition	Healing%
1.	*Lawsonia inermis* & Sesamum Oil & D. Water	85 : 10 : 5	46
2.	*L. inermis* & D. Water	90 : 10	32
3.	*L. inermis* & *Cassia alata* & Sesamum oil & D. Water	75 : 15 : 5 : 5	51
4.	*L. inermis* & *C. alata* & Sesamum oil & *Piper nigrum* & D. water	70 : 10:5 : 8 : 7	72

Eczema: a superficial inflammation of the skin affecting the epidermis. After the occurence of eczema subsequent scaling, thickening or discolouration of the skin may occur and endogenous eczema which occurs with out any obvious external cause.

TABLE: VI INFLUENCE OF *LAWSONIA INERMIS* AND OTHER COMBINATIONS ON CURING EFFICIENCY OF NAIL ROT DISEASES

S.No	Materia Medica	Composition	Healing%
1.	*L. inermis* & D. Water	90:10	50
2.	*L. inermis* & *Curcuma longa* D. Water	80:10:10	72
3.	*L. inermis* & *Curcuma longa* & *Citrus medica* & D. Water	75:13:5:7	96

TABLE: VII INFLUENCE OF *LAWSONIA INERMIS* AND OTHER COMBINATIONS ON CURING EFFICIENCY OF DANDRUFF OR SCURF

S.No	Materia medica	Composition	Healing %
1.	*L. inermis* & D. water	90:10	28
2.	*L inermis* & *L. neptifolia* & D. Water	15:40:15	40
3.	*L. inermis* & *L. neptifolia* cocos oil & D. water	50:40:5:5	79
4.	*L. inermis* & *Citrus medica* Extract	63:35	90

Sucrf : (Pityriasis capitis) A common condition in which the scalp is covered with small flakes of dead skin. The flakes which come away when the hair is brushed or combed represent an increase in the normal loss of outermost skin layer. Some types of dandruff are accompained by inflammation of the scalp to give a type of seborrhoeic dermatitis.

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A PRELIMINARY REPORT ON USE OF A COMPOUND PREPARATION IN PATIENTS OF MALIGNANCY CERVIX

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Abstract

'Geriforte' (Himalaya Drug Co.) a compound preparation containing a number of herbal ingredients to India has been recommended in a number of wasting diseases as nonspecitic resistant increaser (NSRI) or anti-stress substance.

Encouraged by these reports and experimental work done on the above referred drug, we considered it worthwhile to use it in patients of malignancy cervix to evaluate its antistress effect in human beings. 110 patients were selected for the study, out of which 65 patients received 'Geriforte' 2 tablets thrice a day for one month. Treatment was started at the one set of radiotherapy/chemotherapy. All the selected patients were clinically and histologically proved cases of cancer cervix stage III and received chemoiherapy and radiotherapy according to same standard regimen.

Mean weight loss, mean period of toxemia, mean decline in haemoglobin *titre*, mean hours of sleep, grade of loss of appetite, tolerance to chemotherapy and radiotherapy were considered parameters for evaluation of antistress activity. Results indicated marked difference in the above parameters which was found significant on statistical analysis. We have concluded from our study that the drug under study had definite antistress effect.

Introduction

Some indigenous substances have been recognised as antistress adaptogenic substances,[1,2]. In other words they are called non-specific resistance increasers (NSRI) which enable the animal to meet stress of diverse nature more efficiently. 'Geriforte' (Himalaya Drug Co.) an indigenous preparation having a number of herbal remedies which have been used on empirical basis in disorders of chronic nature. Some recent experimental[3] and clinical[4,5] studies have shown that this drug possesses antistress adaptogenic properties. We were encouraged by these reports and considered it worthwhile to conduct a trial of drug in patients of carcinoma of cervix stage III.

Material and methods

Patients

110 patients of carcinoma cervix clinically and histologically proved were taken for the study from the patients attending our O.P.D. These patients were in the age group of 40–50 years.

Treatment

Patients were put on chemotherapy* and radiotherapy** for one month after diagnosis was established. All the patients were randomly divided in two groups I and II consisting of 45 and 65 cases respectively. Patients of group I were given placebo 2 tablets T. I. D. (obtained from M/S Kumar Pharma, Kanpur) and those of other group were given Geriforte 2 tab. T.D.S. for one month. All the patients received same chemotherapy and radiotherapy at our hospital.

* Chemotherapy consisted of inj. Endoxon 500mg I. V. on day 1, 3, 5 and inj. Neotrexate 50 mg. I, V on days 2, 4, (5 days).

** Radiotherapy followed chemotherapy after 1 week and consisted of Co 4500 r X 4 weeks. (20 exposures).

Parameters

In one month of study following parameters were used for evaluation of antistress activity of 'Geriforte'.

1 Mean weight loss in one month :

Body weight was recorded before starting the treatment and at the end of the treatment i. e. on first follow up to ascertain mean weight loss by patients of each group.

2. Mean period of toxaemia :

After starting the treatment, period of toxaemia (anorexia, nausea, vomiting, fever, dehydration, disorientation, lethargy and disturbed sensorium) was noted in all the patients of each group.

3. Mean decline in Hb *titre in one month :*

Hemoglobin was weekly checked and difference between reading taken at outset of treatments and at the end was considered for calculation of the above.

4. Mean hours of sleep :

At the end of treatment every patient of both groups was interrogated about average hours of sleep (day and night) to assess anxiety state.

5. Loss of appetite :

Patients were interrogated about loss of appetite in terms of 25, 50, 75 and 100% loss and mean of each group was calculated.

6. Tolerance to chemotherapy :

Patients were closely examined for adverse reactions e. g. nausea, vomiting, diarrhoea, fever, leucopaenia, alopecia cystit s etc. and according to severity of these reactions, they were put in 3 g·oups i. e. good, fair and poor.

7. Tolerance to Radiotherapy :

Patients were assessed for tolerance to radiotherapy on the basis of severity of radiation reactions and fell into catagories of good, fair and poor.

Results and Discussion

Results are shown in table which indicate that Geriforte had significant effect on mean weight loss in one month, mean period of toxaemia after starting the treatment, mean decline in Hb titre in one month, as these parameters are much less affected in group II. Results analysed by students 't' test of significance were found significant. Mean hours of sleep in group I and II at the end of one month treatment were also considered and it was found that in patients receiving 'Geriforte', anxiety was less in comparison to other group receiving only placebo as the difference in mean hours of sleep in two groups was significant. Average loss of appetite in group I was 41% while in group II it was only 22%. Grossly speaking, data are significant. Table shows that in patients of group I about half the patients had poor tolerance to RT while in group II only 1/3 patient had poor tolerance to RT. Similarly tolerance to CT was poor in the more than half the patients of group I while it was so in less than 1/4 patients of group II.

We have taken patients of carcinoma cervix (stage III) for evaluation of antistress activity of the drug because all the patients have similar problems and are falling in to the same age group i e. 40–50. Moreover. as cancer is the most notorious wasting disease and about 3/4 of women patients

TABLE SHOWING ANTISTRESS ADAPTOGENIC EFEECT OF COMPOUND INDIGENOUS PREPARATION (GERIFORTE) ON VARIOUS PARAMETERS IN PATIENTS OF CARCINOMA OF CERVIX (STAGE III).

S.No	Parameter	Group I	Group II
1.	Mean weight loss in Kgs. in one month period	6.6 ± .95 kgs.	2.9 ± .42 kg. **
2.	Mean period of toxaemia in days after starting the treatment	12.5 ± 1.5 days	7.2 ± 1.2 day **
3.	Mean decline in Hb titre in one month (gm. per 100 ml.)	2.48 ± .32 gm%	1.00 ± .2 gm%**
4.	Mean hours of sleep (at the end of treatment)	6 5 ± .55 hrs.	8 6 ± .82 hrs *
5.	Mean loss of appetite (in %)	41.5 ± 8.5%	22.5 ± 4.2*
6.	Tolerance to Radiotherapy		
	a) Good	5	10
	b) Fair	16	45
	c) Poor	24	20
		45	65
7.	Tolerance to chemotherapy		
	a) Good	8	12
	b) Fair	12	15
	c) Poor	25	38
		45	65

P∠.05 (significant) **P∠.01 (highly significant)

attending our O. P. D were suffering from this lesion, we considered it worthwhile to evaluate antistress adaptogenic effect of compound indigenous prepations on these patients.

Our study is only a preliminary report showing antistress adaptogenic activity in 'Geriforte' which requires further experimental work of clinical trial on patients of other chronic disorders to substantiate our claim.

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