PART I

APHRODISIAC ACTIVITY OF

VENTHAMARAI MAGARANTHA CHOORANAM

(*Nelumbo nucifera,Gatern*)

&

PART II

BRONCHO DILATOR AND ANTI-HISTAMINIC ACTIVITY OF

" MARICHIYATHI MATHIRAI"

The dissertation Submitted by

S.M.VAHITHA BI

Under the Guidance of

Dr. M.PICHAIH KUMAR, M.D(s)

Dissertation submitted to

THE TAMILNADU DR. MGR MEDICAL UNIVERSITY

CHENNAI-600032

In partial fulfilment of the requirements

for the award of the degree of

DOCTOR OF MEDICINE (SIDDHA)

BRANCH-II-GUNAPADAM

POST GRADUATE DEPARTMENT OF GUNAPADAM

THE GOVERNMENT SIDDHA MEDICAL COLLEGE

CHENNAI – 106.

APRIL 2012

CONTENTS

PART-I

PART-II

PART-1

PART-2

NO	TITLE OF FIGURES

ABBREVIATIONS

VMC	venthamarai magarantha chooranam
GTP	Guanosine Tri Phosphatase
GMP	Guanosin mono Phophatase
cGMP	Cyclic guanyl mono phosphatase
NO	Nitric oxide
PDE5	Phospho di esterase 5
ED	Erectile dysfunction
GABA	Gama amino butric acid
ANS	Autonomic nervous system
LC	Locus coeruleus
DPPH	Dia phenyl picryl hydrazyl
ROS	Reactive oxygen species
ONOO	Free radical formation in the peroxynitrous acid (ONOOH)/peroxynitrite (ONOO-) system
NN	Nelumbo nucifera
MAPA	Medicinal and aromatic plant abstract
RLAR	Rat lens aldo reductase
MIC	Minimum inhibitory concentration
TLC	Thin layer chromatography
OECD	Organisation of economical co operative development
CMC	Corboxy methyl cellulose
SHBG	Sex hormone binding globulin

AT	After treatment
BT	Before treatment
MF	Mounting frequency
ML	Mounting latency
IF	Intromission frequency
IL	Intromission latency
EL	Ejaculation latency
PEI	Post ejaculatory interval
L	Lymphocyte
Alb	Albumin
E	Eosinophil
Dep	Deposits
TC	Total count
ESR	Erythrocyte sedimentation rate
FPC	Few Pus Cells
DC	Differential count
CL	Cholesterol
PCS	Pus Cells seen
P	Polymorphs
Hb	Haemoglobin
MM	Marichchiyathi Maaththirai
FEV1	Forced Expiratory Volume
PEF	Peak Expiratory Flow
CCB	Calcium Channel Blocker
FTIR	Fourier Transform Infrared Spectroscopy

ICP-OES	Inductively Coupled Plasma Optical Emission Spectrometry
SEM	Scanning Electron Microscope
MCV	Mean Corpuscular Volume
MCH	Mean corpuscular Haemoglobin
MCHC	Mean corpuscular Haemoglobin Concentration
AST	Aspartate Amino Transferase
ALT	Alanine Amino Transferase

ACKNOWLEDGEMENT

First of all, I thank God for giving the lovable parents and expresses my whole hearted gratitude to my parents for their valuable support and encouragement and blessing in my career, from the very beginning.

I would like to acknowledge and extent my heartfelt gratitude to the following persons who have made the completion of this dissertation study possible.

I feel pleasure to offer my deep sense to gratitude to my responsible learned guide to **Dr.M.Pitchiah kumar M.D (Siddha),** Lecturer and Research guide in this study, for his valuable guidance of my whole study.

I express my sincere thanks to our principal prof. **DR.A.M. ABDUL KHADER, M.D. (S),** Govt. Siddha Medical College, Chennai for his permission to perform this study.

I express my sincere thanks to vice principal prof. **Dr.V.Banumathi M.D. (S),** Govt. Siddha Medical College, Chennai for her permission to perform this study and also for her valuable suggestions and encouragement throughout the course of the study.

I wish to express my profound gratitude to prof. **Dr.A.Kumar M.D (Siddha),** Head of the Dept of PG Gunapadam, Govt Siddha Medical College, Chennai for his valuable guidance, encourangement and offered good advice during the course of my study.

I feel intensely grateful to **Dr. V.Velpandian, M.D. (S)**, lecturer, **Dr.S.Ayyasamy, Ph.D,** Assistant lecturer, PG - Gunapaadam Department, Govt. Siddha Medical College, Chennai-106 for their passionate encouragement and precious suggestions in pre clinical and clinical studies.

I wish to express my sincere gratitude prof. **Dr.B. Malarvizhi, M.D. (S),** Head of the Department, Anatomy department, Govt. Siddha Medical College, and Chennai-106, for her excellent guidance for selection of dissertation drugs and preparation and support in completion.

I also express my thanks to **Dr.R.Sivagami, M.B.B.S., M.D (Pharm),** senior assistant professor, Department of Pharmacology, Kilpauk Govt Medical College, and Chennai-10, for her assistance and guidance in modern Pharmacological studies.

I wish to express my profound gratitude to Former Head of the Dept of PG Gunapaadam prof. **Dr. M.Allimuthu, M.D. (s),** principal, Govt. Siddha Medical College, Palayamkottai for His valuable Guidance and Encouragement.

I express my sincere thanks to prof. **Dr. P.Kumar, M.D. (s),** state level licensing authority (IM) for his valuable suggestions and encouragement.

I express my special thanks to **Mrs. Girija Srinivasan,** Assistant Professor in Medicinal Botany, Govt. Siddha Medical College Chennai-106 for her valuable suggestions and help towards the successful completion of the entire Study.

I express my sincere gratitude to **Dr. Sutha B.S.M.S. Ph.D**, Surgery Dept, GSMC, Chennai, for her valuable suggestions and encouragement in completion of the study.

I am also thankful to **Dr. Prof. Selvaraj, HOD,** Biochemistry dept, and Lab assistant Mrs. Rajalakshmi, for helping me to carry out the Bio-Chemical analysis studies of the trial drug.

I acknowledge my thanks to **Dr. T.Anandan,** Assistant Director In-charge, CRIS, Chennai-106 and **Dr.Sasikala Ethirajulu, M.Sc., Ph.D.**, CRIS, Chennai- 106 , for their help in doing pharamacognostical studies and other guidance to do the research work.

I am also thankful to my college staffs for their kind co-operation for my study.

I am also thankful to **Mr. Abdul kadhar M.Sc.** Lecturer Herbal botany for his valuable advice in Botanical aspect of this study.

My sincere and heartful thanks to **Mrs. Shagila, Research officer**, CRIS, Chennai-106 for do quantitative studies.

I convey my thanks to **Dr. V. Murugesan,** Director, Sophisticated analytical instrument facility, IIT-Madras for his help and to do quantitative and qualitative studies.

I extended my gratitude to the animal **Ethical committee members** for their approval to do animal studies in pre clinical studies.

It will be a indulgence if I Don't be thankful for **Dr. Anbu, M.Pharm, Ph.D,** Vel's college of Pharmacy Chennai for helping in the pharmacological study. It was under his direct supervision that the work contained in the dissertation was performed. His patience and willingness to discuss the minutiae of the different obstacles I encountered during the animal studies were invaluable.

I am also my thankful to our Librarian **Mr.V.Dhandayuthapani, B.Com, M.Libsc** and staffs for their kind co-operation for my study.

I extended my gratitude and acknowledgement to Dr.Tamilnadu M.G.R.University for providing an opportunity to pursue this dissertation study.

I full-heartedly thank **My Patients** for their sincere dedication and co-operation throughout the course of the clinical study.

I should express my gratefulness to **All My Classmates** and **PG Gunapaadam students** for lending their helping hands whenever needed during the course of the study.

I wish to thank my entire family for providing excellent environment for me. My special thanks to my lovable husband **Mr. A. Kadhar** who has taken great efforts in molding my research work and for the encouragement given by him throughout my career.

Lastly but most importantly, I acknowledge my son **K. Javeed kalam** for his lovable adjustments and co-operation during the study period, to him I dedicate this Dissertation.

PART –I

APHRODISIAC ACTIVITY OF VENTHAMARAI MAGARANTHA CHOORANAM

1.INTRODUCTION

Siddha medicine, being the oldest traditional system in the world has a strong significance in detoxification, anti-oxidation, immune modulation and metabolic balance. It is a carefully guarded medical system given away incredible and rapid outcomes in various unremitting ailments. During the period of siddhars there was not even a microscope, but were able to identify, as many as 3500 herbs, their properties, purification process, also administered plant based and mineral-based medicine with suitable adjuvant and they documented all these things. The therapeutic effect has been proved for thousands of year that were never changed for centuries. Like other medical systems based on the foundations of logic and scientific methods, siddha medicine had theoretical foundations as well as deserves to be called a medical science.

Since, siddha medicine, based an individualistic medicine, on patients constitution and syndrome differentiation that we cannot make use of modern medical system as a standard to explain in all levels. Our siddha medicine not only pay attention to the preventive and curative methods, but also focused on the physical, mental, spiritual and psychological well-being thus giving a total perfection in life.

Ancient India is the creator of sexual education. The sex is considered as a part of life. It was wide-open in all kind of arts, like literatures, sculptures etc. An American professor Wendy Doniyer, dept. of the history of religions, states: that,"For Hindus, the phallus in the back ground, the archetype of which their own penises are manifestations, is the phallus (called the *lingam*) of the god *Siva*".

The *lingam* is a representation of the *Hindu* deity *shiva* used for worship in temples. As the symbol of the male creative energy, the *lingam* is often represented with the *yoni*, a symbol of the goddess or of *shakthi*, female creative energy. The union of *lingam* and *yoni* represents the"indivisible two-in-oneness of male and female". A complementary theory suggests that the *lingam* represents the beginingless and endless *sthambha* pillar, symbolizing the infinite nature of *shiva*. The *lingam* and the *yoni* have been interpreted as the male and female organs since the end of the 19 century by some scholars, while to practicing Hindus they stand for the inseparability of the male and female principles and the totality of creation.

Sexual feelings are an inevitable part of life. The basic and fundamental purpose of sexuality is the "continuation of progeny" and the survival of human race. However unfortunately, there has been lot of ignorance, wrong information, fear and negative attitude as for as sex is concerned. Fiction and misestimation are uncontrolled and are passed on from generation to generation.These sexual fiction can result in sexual dysfunctions, depressed, silent suffering, disturbed interpersonal relationships and even divorce. Sexual ignorance is a social disease and can only be through comprehensive sex education, which can increase awareness and improve the quality of life.

The term impotence has traditionally been used to describe the inability of the male to attain and maintain an erection adequate for sexual intercourse. Although the term has been used for centuries, as will be described in this article, it generates much confusion and has been replaced by 'erectile dysfunction' since 1992. One of the main aims of marriage is the procreation (reproduction) and more importantly for sexual fulfilment of both partners. For life to continue, an organism must reproduce itself before it dies. In *Homosapiens*, reproduction is initiated by the mating of a male with a female in sexual intercourse, which facilitates the coming together of sperm and ovum for the purpose of fertilization. For that there to be a normal sexual intercourse and sexual fulfilment in males, the male sexual organs (the copulatory organ, the penis) and factors relating to erection must function normally. Inability to perform this function effectively is a major problem facing the reproductive process. This is known as sexual dysfunction. This condition, which is of various types, can be managed by the use of aphrodisiacs. An aphrodisiac can therefore be described as any substance that enhances sex drive and/ or sexual pleasure. Aphrodisiac can also be viewed as any food, drug, scent or device that can arouse or increase sexual drive or libido.

Sexual dysfunction is a serious medical and social symptom that occurs in 10-52%, of men and 25-63% of women. It is the repeted inability to achieve normal sexual intercourse. Male impotence is a significant problem that may contribute to infertility function decreases spontaneously with advanced aging.It occurs commonly in middle aged and older men.

Research during past two decades has an unfolded focus on impotence (erectile dysfunction), pre mature ejaculation and male infertility. There are a number of prescription drugs which may act as sexual stimulant and enhancing the sexual desire and activity, the use of medicines have not shown significant improvement in treating sexual disorders, at the

same time there are large number of side effects. These include arrhythmias, suicide tendency, mental confusions and tremors etc…

A recent study estimated that 152 million men worldwide experience some degree of impotence. In addition, based on population projections, it is likely that the prevalence of the condition will more than double over the next 25 years. The history of impotence has taught us that until only a few years ago, this condition was still considered to be of psychological or supernatural origin. Today, the development of numerous treatments has allowed the social stigma to subside and both the patient and the physician some choice in how to manage the condition.

Sexual function is an important component of quality of life and subjective well-being in humans. Sexual problems are widespread and adversely affect mood, well being, and interpersonal functioning. Sexual problems are related to sexual desire and male erectile dysfunction. Successful treatment of sexual dysfunction may improve not only sexual relationships, but also the overall quality of life. This is very important because of the side effect associated with other treatment options and the readily available drugs. The increasing incidence of male sexual dysfunction is necessitating more and rapid search into drugs with aphrodisiac potentials with negligible side effects.

Aphrodisiacs are the substances which are used to increase sexual activity and help in fertility. There are many aphrodisiacs in siddha medicine which are given for many years. Except few, most of the drugs were not yet validated scientifically. Among them Lotus is one of the known Aphrodisiac, lined in classical siddha literature and also known as *Karpam.*

Lotus is the national flower of India. It symbolizes purity, beauty, majesty, grace, fertility, wealth, richness, knowledge and serenity. The Lotus is a sacred flower for Hinduism and Buddhism. The Lotus flower is quoted extensively in *Puranic* and *Vedic* literature. Lotus means estranged love, the state of spiritual perfection and total mental purity. Lotuses are also used to represent chakras, or the body's energy centers. A lotus is often used analogously for how people should live.

Lotus has been a divine symbol in Asian traditions representing the virtues of sexual purity and non attachment. Lotus grows with cultural background, and included with life style of Dravidian culture. .

“G+tpDf;F mUq;fyk; nghq;F jhkiu”

“G+ntdg; gLtJ nghwptho; g+Nt” -fgpyu; FwpQ;rpg;ghl;L

By the literature evidence and the scientific background all parts of the lotus flower are medicinally useful, in that the stamens are particularly mentioned for male impotence in *Gunapadam mooligai vaguppu, Theran porut panbu nool*. So I have chosen the stamens of *venthaamarai magarantha chooranam* (stamens of *Nelumbo nucifera)* which is male part of flower in my present study for *Samboga vaatham* (Male impotence). This study is intended to provide adequate information on the screening of *Venthamarai magarantha chooranam* with sex enhancing potentials since attention is now being focused on the use of siddha drugs as Indian traditional medical practice in the management of this high rising incidence of sexual dysfunction.

2. AIM AND OBJECTIVES

Aim

Sexual dysfunction, Impotence, and other related problems are eluding scientific community and medical practitioners since time memorial. Sexual dysfunction may have psyco social implication affecting men in manyways.There has been constant exploration for newer medicines or herbs to overcome these age-old problems of sexual dysfunction. A variety of plants have been used as sex stimulants in siddha medicines. Lotus was a symbol of immortality and love. There is no scientific evaluation on *Venthamarai magarantham* substantiating its usage as sexual stimulant.

The main aim of this dissertation is to do a scientific review, to validate the safety and efficacy of the *venthaamarai magarantha chooranam* for *sambogavaatham* (Erectile dysfunction).

Objectives

- Besides the scientific study of siddha science and medicine also our aim, the following methodology was adopted to evaluate the safety and efficacy of the test drug.
    - ❖ Identification of the herbal drug *Venthamarai*
    - ❖ Collection of various siddha and modern scientific literature.
    - ❖ Preparation of drug according to the text.
    - ❖ Physio chemical analysis of *Venthamarai magarantham.*
    - ❖ Phyto chemicals analysis test drug.
    - ❖ Evaluation of the toxicity of test drug.
    - ❖ Evaluation of Aphrodisiac activity of test drug
    - ❖ Clinical assessment of *Venthamarai magarantham* on Impotence

ntz;jhkiu (*Nelumbo nucifera*)

Figure: 3.2.1

Njd; (Honey)

Figure: 3.2.2

3. REVIEW OF LITERATURE

The literature support for my trial drug were collected from the Siddha text books, classical literatures of Siddha, Materia medica, Compendium of Medicinal Flora, Wealth of India, Chemical Abstracts, MAPA, Internet Journals and Search web sites.

3.1. BOTANICAL ASPECT

Botanical name: ***Nelumbo nucifera, Gaertn***

Taxonomical classification:

According to Bentham and Hooker's classification (1862-83)

Kingdom - Plantae

Division - Angiosperms

Class - Dicotyledons

Subclass - Polypetalae

Series - Thalamiflorae

Order - Proteales

Synonyms:

- *Nelumbium speciosum Willd.*
- *Nymphaea nelumbo*

Vernacular Names:

Tamil - *Tamarai, Bathumam*

English - Sacred lotus

Hindi - Kanwal

Urud - Kanwala

Malayalam - *Tamara, Aravintham*

Sanskrit - Kamala , Svetakamala ,Pankaja

French - Nelumbo

German - Indische Lotosblume

Persian - Nilufer

Occurrence and distribution:

A very small genus of aquatic herbs distributed in Asia, Australia, America. One species occurs in India. Common throughout the warmer part of India, Africa, Hungary, Java and Philipines.

Description:

A handsome aquatic herb with stout, creeping rhizome found throughout India, ascending up to 1800 m, leaves peltate,60-90 cm or more in diameter , orbicular, glaucous petioles very long, smooth or with small prickles. Flowers solitary, large, white or rosy .Fruit-torus large, top shaped 5-10 cm. Spongy with many uni ovulate carpels sunk separately in cavities on the upperside. Carpels maturing in to ovoid nut like achenes. The Fruiting torus is often sold for the edible carpels embedded on it. The carpels are round, oval or oblong, hard and dark brown. They are eaten after removing the outer covering and also the embryo which is intensely bitter. They are sweet and tasty and may eat raw, roasted, boiled, candied or ground in to flour.

Botanical history:

The lotus is an Asian water lily known for the delicate beauty of its water flowers. It possesses an amazing ability to flourish in a variety of environments ranging from clear ponds to muddy marshes. It is also known for its exceptionally hearty seedpods, which often plant themselves far from its source, bringing the beauty of the lotus blossoms everywhere.

Most seeds remain quiescent during a cold or dry season and germinate only with the coming of favourable growing conditions. Seeds that require special treatment to germinate, even when presented with adequate water and oxygen and favourable temperatures, are said to exhibit dormancy. Seeds with thick or waxy coats, which inhibit the entry of water and oxygen, may remain in a prolonged quiescent state. Seeds of the Indian lotus can germinate 200 years after they are shed. Most seeds, however, lose the ability to germinate within several years of shedding. Following the return of the rains, primitive peoples witnessed the rise of the undefiled water lily from the bottom of dried-up watercourses and considered the living blooms symbols of immortality and resurrection.

Lotuses are 5 species of water lilies, three in the genus Nymphaea and two in Nelumbo; both genera are members of the water-lily family, Nymphaeaceae. Lotus is also the name of a

genus in the pea family, Leguminosae, which contains such plants as the bird's-foot trefoil, Lotus corniculatus. Nymphaea lotus, the Egyptian white lotus, is believed to be the original sacred lotus of ancient Egypt.

The white lotus is a shallow-water, night-blooming plant with a creeping rootstock (rhizome) that sends up long-stalked, nearly circular, dark green leathery leaves, which float on the surface. The flowers, up to 25 cm (10 in) across, remain open until midday. The East Indian lotus, N. nucifera, found in southern Asia, was introduced into Egyptabout 2,500 years ago but is no longer found in the Nile region. The Buddhists of India, Tibet, and China consider its flowers sacred. The lotus, Nymphaea lotus, bears many-seeded, berrylike fruit and leathery, floating leaves that may reach 50 cm (20 in) across. The cup-shaped flowers of the lotus were often represented in ancient Egyptian art and architecture.

ntz;jhkiu kfue;jk;

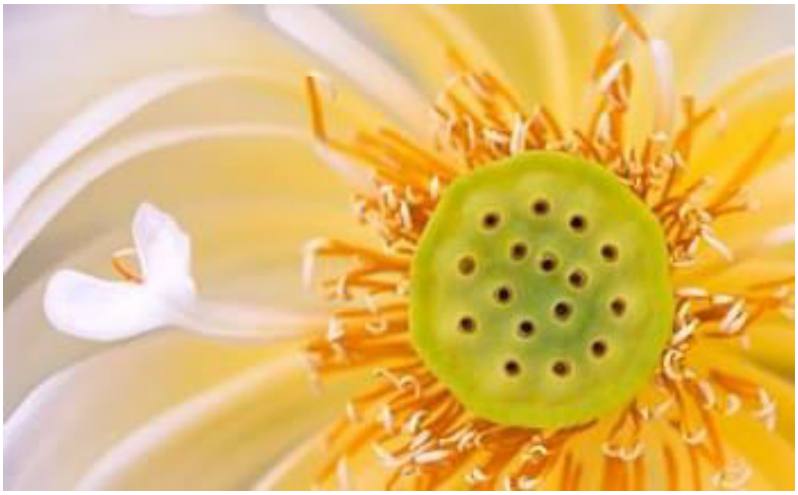


Figure: 4.1

Figure: 4.2

3.2. GUNAPADAM ASPECT:

ntz;jhkiu:

Nelumbo nucifera, Gaertn

NtW ngau;fs;:

nts;isj; jhkiug;Ngiu tpsk;gf;NfS

kpLf;fhdgj;k fhwzpahFe;

jps;isj;jhd; jprhuhgj;Jkh

ePahd thu;gprQ; rhulhthy;

nfhs;sj;jhd; nfe;jkhy jrkhFq;

fpsu;e;jNjhu; yl;Rkp rpNu\;lhthFQ;

Rs;sj;jhd; ryG\;gyh tkhFQ;

nts;isj;jhkiug; Ngu;nrhy;yyhNk.

-NghfKdptu; epfz;L- 1200 ghly;919

mutpe;jk;> gJkk;> espdk;> #upa el;G> fkyk;> fQ;rfk;> **tpe;jk;>** gq;frk;> mk;;Grk;> Gz;luPfk;> Kz;lfk;> khYe;jp> el;G> jgdd; Nghd;wit.

jhkiuj; jhJtpd; ngau;:

"jhkiuj; jhJg; ngaiu rhj;jf;NfS

jd;ikahk; gj;Jk Nrhkh\khFk;

fhkiufpQ; ryf;fpr khq;Nf ruq;

fhQ;rde; JjTkhFk;

Mkiu mf;fpdhutf; fPjk;gj;jpk;

kofhd gj;Jkpdp NffhrkhFQ;

rhkiu rhypdpdk; kpWdhdp rkhFQ;

rhj;jpaNjhu; Ngnuy;yhk; jhJthNk"

-

NghfKdptu; epfz;L 1200 ghly; 911

gad;gLk; cWg;Gfs; **:** kyu;,tpij> fpoq;F> kfue;jj;jhs;.

Rit (taste) **:** ,dpg;G> Jtu;g;G

jd;ik (Potency) : rPjk;

gpupT(Bio-transformation): ,dpg;G

nra;iffs;

Fspu;r;rpAz;lhf;fp - Coolant

cs;soyhw;wp - Demulcent

Jtu;g;gp - Astringent

euk;Gukhf;fp - Nervine tonic

Nfhioafw;wp - Expectorant

Ngh\zfhhp - Nutrient

jhJntg;gfw;w[p] - Sedative

ntz;jhkiug;g+ :

NtW ngau;: ,uhrPtk;> ,Wk;G> kiug;g+

nghJ Fzk;:

“gUj;jew; whkiug;g+ gy;the;jp Nehiaj;

Juj;jpLk; ,d;DQ; nrhy;Nth-fuj;jpy;

vLj;jizf;ff; fz;FspUk; VFQ; RuKk;

vLj;jtp jhfKk;Nghk; vz;”

-

mfj;jpau; Fzthflk; gf;fk; 135

jhkiug;g+tpdhy; the;jp Neha;> ntg;gj;jhy; gpwe;j tpop vupr;ry;,Ruk;,ePu; Ntl;if ,itfisg; NghFk;.

ntz;jhkiug;g+ Fzk;:

“<uiyg; gw;wpkpf VWfpd;w ntg;gKk;Nghq;

Nfhu kUe;jpd; nfhLikaWk; -ghUyfpy;

jz;lh kzj;ijAs;s jho;FoNy! fhe;jy;tpLk;

ntz;lh kiug;g+thy; tps;”

-

Njiuau; Fzthflk; gf;fk; 201;

ntz;jhkiug;g+tpdhy; <uypid gw;wp tUfpd;w ntg;gKk>; ntg;gKs;s kUe;Jfspd; cl;#Lk; jPUk;.

fw;gk;;:

“rz;lidAQ; rz;lidAe; js;sky Us;SiwAz;

rz;lidAQ; rz;lidAQ; rhu;…”

-Njiuau; akfntz;gh

rz;ld; - Ngbj;jd;ik> mypj;jd;ik ,tw;iwf; Fwpf;Fk;>

kyu; cs;Siw- jhkiug;g+tpd; kfue;jg;nghb

rz;lidAQ;- rz;l ieAk;-vkDk; tUe;Jthd;>

rz;jidAQ; rhu;-MW khjk; tiu Grpf;FkhW $wg;gl;Ls;sJ.

-fof

jkpo; mfuhjp gf;fk; 422

jhkiug;g+tpd; kfue;jg;nghbAld; Njd; $l;b> epj;jpag;gb gj;jpaj;Jld; Grpf;f myp vd;fpw Ngbj;jdk;> **Mz;ik ,d;ik** vd;git jPUk;. MW khjk; tiu Grpf;f Ntz;Lk; vd;W $wg;gl;Ls;sJ.

tpij:

“ke;jj; Jtkfw;Wk; ty;yUrp ePf;fptpLk;

ke;jj; JiwjhJ tpw;flNy- je;jpLk;gpd;

Dd;dpypd;De; NjhlFzk; ahTNkhl; LQ;ryre;

jd;dpyz; Zf;fpuTQ; rk;”

-Njiuau; Fzthflk;

jhkiu tpijapdhy; myrk;> Ritapd;ik jPUk;. Mz;ikg; ngUf;fj;ij cz;lhf;Fk;.

fpoq;F:

“fz;Zf;nfhspnfhLf;Fq; fhrgpj;jk;Nghf;Fk;

vz;Zq; Fspu;r;rpjUk; Ve;jpioNa! – Gz;Zfspy;

J}kiug;Gz;Zk; Nghf;Fe; njhe;jpf;f Lg;gfw;We;

jhkiuf; fe;jkJ jhd;”.

-mfj;jpau; Fzthflk;

fz;xsp> Fspu;r;rp ,itfisj; jUk;. ,Uky;> jtisr;nrhwp> tapw;Wf;fLg;G Mfpatw;iw ePf;Fk;.

tof;F Kiwfs;;:

- jhkiug;g+tpd; Njd; fz; Neha;fisg; Nghf;Fk;.
- G+it kzg;ghF nra;JFUjpg;Nghf;F>FUjp%yk;>rPjf;fopr;ry; ,itfSf;F nfhLf;fyhk;.msT 17 Kjy; 35 fpuhk; vil.
- jhkiu tpijiag; nghbj;J 1-2 fpuhk; vil cs;Sf;Ff; nfhLf;f clw;F td;ikiaj; jUk;
- tpiuiaj; Njd; tpl;liuj;J ehf;fpy; jltp tu> the;jp> tpf;fy; epw;Fk;. ,jd; ,iyahy; rq;F gw;gkhFk;.
- ntz;jhkiu - #jk; fl;Lk;.
- jhkiu tpij - Rf;fpyj;;jpid tpUj;jp nra;Ak;.
- g+ - Njf #L>ePu; vupT>Ruk; jPUk;.
- fpoq;F - fz;fisg; gpufhrpf;fr; nra;Ak;.

-gpuhz uf;\hkpu;j rpe;J gf;fk; 30

“Rfkhd jhkiujhd; fz;Fspu;r;rp>
jhkiu tisak; eQ;nry;yhKwpf;Fe;
jhkiuapd; kzpjhDk; trpfukhFk;
Rthrjh kiuj;jhJ Nkfk; Nghf;Fk;
Mdjh kiuf; fpoq;F Mz;ikAz;lhFk;”

-Nghfu; fUf;fpil epfz;L-500 gf;fk;

jhkiu - fz;Fspu;r;rp

jhkiu tisak; - eQ;R Kwpf;Fk;

jhkiu kzp - trPfu rf;jp

jhkiuj; jhJ - Nkfk; Nghf;Fk;

jhkiuf;fpoq;F - Mz;ikAz;lhf;Fk;

jhkiug;g+ NrUk; gpw kUe;Jfs;;;:

fy;ahzf;fpUjk; - euk;G gyg;gLk;.

c\;zRuf;f\hak ; - Ruk; jPUk;.

kfh Rju;rd #uzk; - cly; td;ik gLk;.-rpfpr;rhuj;d jPgk; gf;fk; 119

tpNdhj fz; ijyk; - fz;Nuhfk; 96jPUk;.

-mDNghf itj;jpa etePjk; 2 gf;fk;252

fz; Nuhf ijyk; - nts;nsOj;J jPUk;.

-%ypif ku;kk;

- mg;gpufrj;J gw;gj;Jld; jhkiug;g+r;rhW kw;Wk; Njd; ,it Nru;j;J cz;z gpuNkf Neha;fs; jPUk;.
- nts;tq;f gw;gj;Jld; jhkiug;g+r;rhW kw;Wk; Njd; ,it Nru;j;J cz;z FUjpf;fopr;ry;> #l;Lf;fopr;ry; jPUk;.
- nts;spgw;gj;Jld; ntz;jhkiug;g+r;rhW kw;Wk; nfl;bj;Njd; ,it Nru;j;Jz;z ,Uja Neha; jPUk;> ,uhr fUtpfs; gyg;gLk;.

-mDNghf itj;jpa etePjk; ghfk;5 gf;fk; 19

- jhsff; fWg;G - ntz;jhkiug;g+tpjo; NrUfpwJ. fg Neha;fs; jPUk;.
- fq;fhju #uzk; - kJNkfk;> ghy;tpid Neha;fs; jPUk;.

-Nkfepthuz Nghjpdp gf;fk;71

tpNdhj fz;ijyk;:

nre;jhkiug;g+ - 9 gyk;

nre;jhok;g+ - 1 gyk;

nul;il ee;jpahtl;il - 4 gyk;

Gspg;G khJsk;g+ - 4 gyk;

G+f;fis ,bj;J urk; gpope;J me;j urj;Jld; vs;nsz;nza; 2½ gyk; tpl;L ,sk; gjkhff; fha;r;rp tbj;j ijyj;jpy; g+j;Njd; 4¼ gyk; ,ytq;fk; g+ ePf;fpaJ 1 tuhfd; ,itfis Nkw;gb ijyj;jhy; ikNghy miuj;J Nru;j;J xU Fg;gpapylf;fQ; nra;J itj;Jf;nfhz;L fz;zpy; fhiy> khiy jPl;l fz;Nuhfk; jPUk;.

- mfj;jpau; itj;jpa rpe;jhkzp 4000 gf;fk;252

jhkiuf;FbePu;:

10 fpuhk; jhkiug;g+ ,jo;fis xU ypl;lu; ePupy; ,l;Lf;fha;r;rp> ¼ ypl;luhf;fp tbfl;b> fhiy>khiy rhg;gpl;L tu cly; #L FzkhFk;.

jhkiu kzg;ghF:

epoypy; cyu;j;jpa ntz;jhkiu ,jo;fs; 1 fpNyh msT> 3 ypl;lu; ePupy; ,l;L> Cw itj;J>kWehs; xU ypl;lu; msthff; fha;r;rp> tbfl;b 2 fpNyh ru;f;fiu Nru;j;J Njd; gjkhff; fha;r;rp itj;Jf;nfhz;L> 2 Njf;fuz;b rpwpjsT ePUld; fye;J rhg;gpl;L tu cly;#L> jhfk; FiwAk;.fz;fs; Fspu;r;rpailAk;.

,uj;jf;nfhjpg;G fl;Lg;gl:

ntz;jhkiu ,jo;fis ed;F cyu;j;jp nghb nra;J nfhz;L 1½ Njf;fuz;b msT> Njdpy; Fioj;J rhg;gpl Ntz;Lk;.

-gjhu;j;j Fzrpe;jhkzp gf;fk; 112

,uj;j gpj;jj;jpw;F:

- ❖ jhkiug;g+it fOePupy; miuj;J nfhLf;fNtz;Lk;.
- ❖ fLf;fhAld; jhkiug;nghb Nru;j;J Njdpy; Fog;gpf;nfhLf;fNtz;Lk;.

tPupatpu;j;jpf;F:

jhkiug;g+Tld; Vyhjpr;#uzk; Nru;j;Jf;nfhLf;f Ntz;Lk;.

-ruNge;jpuu; itj;jpa Kiwfs; gf;fk;156-;168

“ryNjh\q; fhkhiy rj;jptpf;f yhd

gyNjh\q; fl;Fkplu; gz;Zq; - fiyahf;

fgKupar; rhLkpF fharpj;jp ahFk;

jgddl; ghFkk;G rk;”.

-jd;te;jpup Foe;ij thflk; gf;fk;170

xs\j Ntfk; vl;Lk; jPUk;. c\;zk; FiwAk.;

rq;f fhy ,yf;fpaj;jpy; jhkiu:

“kd;capu; mwpahj; Jd;mUk; nghjpapy;

#Uil mLf;fj;J Muk; fLg;g

NtdpyhNd jz;zpas;: gdpNa>

thq;Ffjpu; njhFg;gf; $k;gp>Inad>

myhq;F ntapy; nghjpe;j **jhkiu**

cs;sfj;jd;d rpW ntk;ikaNs”

-376 nea;jy; ghly; GwehD}W

jiytd; jd; neQ;Rf;Ff; $wpajhf mike;j ,g;ghlypy; jiytpapDila eyj;ij kdjhy; epidj;J jdJ nghUs; NjLk; Ntfj;ijf; fl;Lg;gLj;Jfpwhd;.

,q;F ehk; mwpag;gl Ntz;ba ,aw;if El;gk; vd;dntd;why; jhkiuf;Fsk; kpFe;j Fspu;r;rpiag; ngw;wpUf;fpwJ. MdhYk;> me;j Fspu;r;rpapd; jhf;fk; jhkiuiar; #o;e;j NghjpYk;> mjw;F khwhf cl;Gwj;jpy; rpW ntk;ikAld; ntJntJg;ghf (85^0- 95^0 ghud;`Pl;) vg;nghOJk; jd;dfj;Nj nfhz;Ls;sJ kpf El;gkhf gjpT nra;ag;gl;Ls;sJ. kw;iwaj;jhtuq;fSf;F ,y;yhj gz;ghfj; jhkiu jd;kyupDs; **rpW ntg;gj;ij** capu;fs; tho;tjw;F Vw;g cUthf;fp> mtntg;gj;ijj; jd;dfj;Nj nfhz;Ls;sJ.

,jdhNy jhkiu kyupDs; ,uthdhYk; Njd;cz;l **g+r;rpapdq;fs**; mq;NfNa cwq;Ffpd;wd. Vnddpy; ,jkhd ntg;gj;jpdhyhd fjfjg;G mit **kfpo;Tld;** jq;f Vw;w tifahf cs;sJ.

“cyfk; ctg;g tyd; Vw;G jpupjU

gyu; Gfo; QhapW flw;fz lhq;F”

-ef;fPuu; jpUKUfhw;Wg;gil ghly; 123

,uT Neuq;fspy; tz;Lfs; jhkiug;g+tpy; cwq;fp tpl;Lf; fhiyapy; g+ ,jo; tpupj;jJk; ntspNaWtjhfj; njuptpj;jpUf;fpwhu;.

mWrpy; fhy tQ;rpiwj; Jk;gp

E}w;wpjo; **jhkiug;** g+r;rpid rPf;Fk;

fhk;Gfz; Id;d J}k;Gil Ntoj;J….

-Iq;FE}W Ntog;gj;Jghly; 22

may; kfue;jr;Nru;f;if gw;wp tpsf;fg;gl;Ls;sJ.

“gy; kyu;g; godj;j ghrilj;**jhkiu**

,d;kyu; ,kpu;G CJk; Jiz Gzu; ,Ue;Jk;gp

cz;Jiw cile;j g+g; Gdy; rha;g;g Gye;J

Cb gz;Gil ey; ehl;Lg; gif jiy te;jd”.

-mfehD}W ghly; 118

tz;Lfs; JizAld; te;J $b kfpo;tjw;F Vw;w gs;spaiwahfj; jhkiuapd; cs;sfk; jpfo;fpwJ vd gjpT nra;ag;gl;Ls;sJ.

“Ez;jhJ nghjpe;j nrq;fhy; nfhOKif Kz;lfk;”

jhkiu kyu; tpupe;j nghOJ gpufhrj;jpw;Fk; kw;Wk; Ftpe;j epiyapy; Rlupd; tbtj;jpw;Fk; ctikahff; fhl;LtJ rq;fg;Gytu;fspd; kughf mwpag;gLfpwJ.

“tpsf;fpd; md;d Rlu;tpL **jhkiu”**
- ew;wpidg;ghly; 310

“Rlu; g+e;**jhkiu”**

- kJiuf;fhQ;rp 249

“Rlupjo;j; **jhkiuj**; jhJgL ngUk;NghJ”

“Ks;siuj; **jhkiu** Kfpo;tpup ehl;NghJ

nfhq;Fftu; ePyr; nrq;fl; nryT

kjpNruhtpd; khdj; Njhd;Wk;”.

-

gj;Jg;ghl;L rpWghdhw;Wg;gil ghly;184

topghl;L ,lq;fSf;F Kd;G ePu;epiyfis mikg;gJ jkpou; kughfj; njupfpwJ. me;ePu; gy;NtW gad;ghl;L epiyapYk; J}a;ikahf ,Uf;f Ntz;Lk; vd;nwz;zpNa Fwpg;ghfj; jhkiu kyu;fisf; Nfhapy; Fsq;fspy; tsu;j;Jg; Ngzpajhf vz;z ,lk; ,Uf;fpd;wJ (anti-microbial activity). rhd;W: nghw;whkiuf;Fsk;> rpj;jd;d thry; rpj;jpuq;fs;. rq;ffhyj;jpy; ngUik nfhz;ljhf jhkiu kyu; mwpag;gl;ljhy;jhd; vj;jidNah g+f;fs; ,Ug;gpDk; mj;jidapYk; mzpfydhf> jkpou; kyu;g;gz;ghl;bd; kzpKbahfj; jhkiu jpfo;tjhf Rl;bf;fhl;lg;gLfpwJ.

Cultural significance

Hindu goddess **Lakshmi** holding & standing on a lotus.Vishnu holding the lotus, also sitting on it and wearing a lotus-bud crown. From ancient times the lotus has been a divine symbol in **Asian** traditions representing the **virtues** of **sexual purity** and **non-attachment**. **Hindus** revere it with the divinities **Vishnu** and **Lakshmi** often portrayed on a pink lotus in iconography. In the representation of Vishnu as **Padmanabha** (Lotus navel), the lotus issues from his navel with **Brahma** on it. Goddess **Sarasvati** is portrayed on a white-colored lotus.

Often used as an example of divine beauty, Vishnu is often described as the 'Lotus-Eyed One'. Its unfolding petals suggest the expansion of the soul. The growth of its pure beauty from the mud of its origin holds a benign spiritual promise. In **Hindu iconography,** other deities, like **Ganga** and **Ganesha** are often depicted with lotus flowers as their seats. The lotus plant is cited extensively within **Puranic** and **Vedic** literature, for example:

One who performs his duty without attachment, surrendering the results unto the Supreme Lord, is unaffected by sinful action, as the lotus is untouched by water.

-**Bhagavad Gita** 5.10:

3.3. MODERN ASPECT

Action:

Flower : Cooling, sedative, Astringent, Chologouge, Diuretic, Bitter, Refrigerant,

Haemostatic and Expectorant.

Leaves : Refrigerant, Haemostatic

Root : Demulcent

Seeds : Demulcent

Stamens:

Stamens are the male reproductive part in the flower. Sperm and stamens both are similar in morphological structure. Lotus stamens act an **Astringent**; in fact it is a more potent astringent than lotus seed (share sweke et.al)

Uses:

- It helps to treat conditions such as leucorrhea, diarrhea, frequent urination and **premature ejaculation**.
- It used to help lower blood pressure.
- In addition, lotus stamen (in extract form) can be applied to the skin to prevent skin burn and discolourati -The acupuncture and oriental medicine news source

Traditional uses:

- The leaves are boiled with *Mimosa pudica* in goat's milk to treat diarrhea.The leaf paste is applied to the body in fever and inflammatory skin conditions.
- Young leaves are taken with sugar to treat rectal prolapsed.
- The **stamens** are mixed with ghee and jaggery and used in treating hemorrhoids.
- The leaves and flowers are both useful in many varieties of *raktapitta,* or bleeding disorders.
- The flowers are sometimes prescribed to promote conception.
- The petals alleviate thirst and inflammations.
- The seed powder mixed with honey is given in cough.
- The roots are said to be health for teeth. Taken with ghee, milk, and gold it is a general tonic said to promote strength, virility, and intellect.

-Kapoor, Hand book of ayur medicinal plants

- The honey from bees which visit lotus flowers are reported to posseses the tonic properties and considered useful for affections of the eye.
- Saline extracts of stem, leaves, and flowers posses bacteriostatic action against Gram positive gram negative bacteria.

- Wealth of India vol-3

- Flowers, filaments and juice of the flower stalks are useful in diarrhea, cholera and in liver complaints.
- It is recommended also as cardiac tonic. Compound decoction is useful in bilious fevers. The root, flowers, stalk and leaves in the form of infusion are used in fever as refrigerant and diuretic .Syrup of flowers used in cough, menorrhagia and dysentery.

- Pistils are used with black pepper externally and internally as an antidote in snake poisoning and in scorpion-sting.
- In bleeding piles the filaments of lotus are given with honey and fresh butter or with sugar.
- In folk medicines, seeds are used in the treatment of tissue inflammation, cancer, skin diseases, leprosy, poison antidote and generally prescribed to children as diuretic and refrigerant.

-Dr. Nadkarni's materia medica

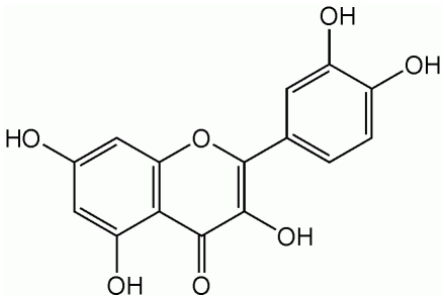
Phyto chemistry:

- Embryos of seed -isoquinoline -sedative -anti spasmodic

  Other alkaloids are, Dauricine, Nelumbine, Neferine, Roemerine, Isoliensinin, Aporphine, Lotusine, Nuciferine and Pronuciferine.

- The ether extract of the petals and **stamens** yielded **quercitin.** The aqueous extract of the leaves yielded **flavonoids, quercitin, isoquercitrin and leukodelphinidin.** The seeds contain between 2-3% oil comprised of **myristic, palmatic, oleic, and linoleic acid**. The alcoholic root extract have shown CNS-depressant and diuretic activity in rodents.(Journal of natural remedies)

QUERCITIN



Nutritional value of Lotus flower

Nutritional values	
Water	10.5%
Total CHO	66.6%

Protein	17.2 %
Fibre	2.6%
Fat	2.4 %
Ash	3.8%
Calcium	136
Sucrose	4.1%
Phosphorus	294
Reducing sugar	2.4%
Iron	2.3mg/100gm

Ascorbic acid present

Iron	0.199%
Chromium	0.0042%
Magnesium	9.2 %
Sodium	1%
Copper	0.0463%
Potassium	28.5 %
Zinc	0.084%
Calcium	22.1%
Manganese	0.356%

Njd; (mDghd kUe;J):

nra;iffs;:

- cs;soyhw;wp - Demulcent
- kykpsf;fp - Laxative
- Jtu;g;gp - Astringent
- mOfyfw;wp - Antiseptic
- Nfhioafw;wp - Expectorant
- Ngh\zfhup - Digestive
- grpj;jPj;J}z;b - Stomachic
- J}f;fKz;lhf;fp - Sedative

Fzk;:

“IapUk yPistpf;f yf;fpg;Gz; ntg;Gly;Neha;

iga nthopAk; grpAKWk;- itafj;jp

nyz;Zkpir ahkUe;jpw; Nfw;w tDghd

ez;Zkiyj; Njndhd;wp dhy;”.

-gjhu;j;j Fz rpe;jhkzp

cgNahfq;fs;:

Njd; xU rpwe;j Jiz kUe;jhFk;. mDghdg; nghUshtjd;wp mtpo;jg; nghUshfTk; ,Ue;J Njfj;ij ed;dpiyapy; itj;J> thj Kjypa Kf;Fw;wq;fisAk; Nghf;Ffpd;wJ.

“mDghd kha;g;gpd; mtpo;jKkha;j; Njhd;wp

fdkhd Njfepiy fhl;bg;- gpDNk

aurd; Kjy;Nth iuAkhl;L tpj;jhNy

gpurj; jpdhw;Nghk; gpzp”.

-Njud; nghUl;gz;G E}y;

mtpo;jk; gypf;f Ntz;Lkhapd; mDghdg;nghUs; Njit vd;gijAk;> mt;tDghdg; nghUl;fspy; NjDk; xd;W vd;gjidAk;

“mDghdj;jpdhNy atpo;jk; gypf;Fk;

,dpjhd Rf;F d;dypQ;rp – gpDNk

Nfhkak; ghy;Kiyg;ghy; Nfhnea;Njd; ntw;wpiyePu;

Mkpijah uha;e;Jnra yhk;”

-Njud; nghUl;gz;G E}y;

- Foe;ijfspd; ,UkYf;Fj; Njd; ,uz;L mTd;;];> vYkpr;ir gourk; rkmsT $l;b nfhLf;f jzpAk;.
- Njidg;ghdfk; nra;J te;jhy; fgg;gpzpfs; jPUk;>

“,wTsu; mKijia ,wTsjhf;Fk;” vd;w mbahy; mwpayhk;.

- Njid #Ls;s ghu;yp muprp fQ;rpAld; nfhLf;f kyge;jk;> nrupahik> ePu;f;Nfhit> ,Uky;> njhz;il tpuzk;> EiuaPuy; rk;ke;jkhd gpzpfs; jPUk;.

Nutrition:

Honey is a mixture of sugars and other compounds. With respect to carbohydrates, honey is mainly **fructose** (about 38.5%) and **glucose** (about 31.0%), making it similar to the synthetically produced **inverted sugar syrup**, which is approximately 48% fructose, 47% glucose, and 5% **sucrose**. Honey's remaining carbohydrates include **maltose**, sucrose, and other **complex carbohydrates**. As with all nutritive sweeteners, honey is mostly sugars and contains only trace amounts of **vitamins** or **minerals** Honey also contains tiny amounts of several compounds thought to function as **antioxidants**, including **chrysin**, **pinobanksin**, **vitamin C**, **catalase**, and **pinocembrin**. The specific composition of any batch of honey depends on the flowers available to the bees that produced the honey.

Typical honey analysis:

- **Fructose** **: 38.2%**
- **Glucose** **: 31.3%**
- **Maltose** **: 7.1%**
- **Sucrose** **: 1.3%**
- **Water** **: 17.2%**
- Higher **sugars** **: 1.5%**
- **Ash** **: 0.2%**

- Its **glycemic index** ranges from 31 to 78, depending on the variety.
- Honey has a **density** of about 1.36 kilograms per litre (36% denser than water).

Uses:

- Osmotic effect Honey is primarily a saturated mixture of two **monosaccharides**, with a low **water activity**; most of the water molecules are associated with the sugars and few remain available for microorganisms, so it is a poor environment for their growth. If water is mixed with honey, it loses its low water activity, and therefore no longer possesses this antimicrobial property.
- Topical honey has been used successfully in a comprehensive treatment of **diabetic ulcers** when the patient cannot use topical antibiotics.
- The **pH** of honey is commonly between 3.2 and 4.5. This relatively acidic pH level prevents the growth of many bacteria.
- Some studies suggest the topical use of honey may reduce odors, swelling, and scarring when used to treat wounds; it may also prevent the **dressing** from sticking to the healing wound.
- Honey has been shown to be an effective treatment for **conjunctivitis** in rats.
- Persons who have cough, pneumonia or some other conditions at the lung may take one tea spoon of honey with as much of almond oil twice a day and alternatively one tea spoon of honey with warm water twice a day.
- Asthma patients also get relief by taking two tea spoons of honey is a glass of boiling water.
- Copper in honey works to the good of liver disorders.
- In rheumatic and gout cares, it helps to reduce the uric acid.
- For athletic Nutrition in a rating of 1 to 10, honey ranks the highest at 9. Sulphur in honey purified blood.

-Articles on health Ayurveda 2010

3.4. SIDDHA ASPECT OF THE DISEASE:

rk;Nghf thjk;

(Erectile Dysfunction)

“rk;Nghf thjkJ ijayhu; rq;fkj;jpd;

tk;Nghf tPo;tjpy; gpwf;Fk;-**mk;Ge;**

jsU%u;r; rpf;Fk;ePu;j; jhfk; gyk;Ngha;

csUk;gpd; Nehahk; ciu”

-mfj;jpau; itj;jpa rpe;jhkzp 4000 ghly; 145

ngz;Nru;f;ifapd; NghJ Fwpjsu;jy;> %u;r;rpj;jy;> jhfk;> gyk;Fiwjy; Nghd;w FwpFzq;fs; fhzg;gLk;.

Rf;fpythjk;

(Premature Ejaculation)

“thAthjk; fhw;wpdpil te;jhy; mtatq;fs;

ghAq;fhy; typf;Fk; gz;ZFzk;-fhaj;jpd;

Rf;fpyf; fhye;jpuj;jpw; Jd;D Jupjkpd;Dk;

Gf;fpepwj; **jhJ nfl;Lg**;NghFk;”.

-mfj;jpau; itj;jpa rpe;jhkzp 4000 ghly; 144

Rf;fpyk; tpiue;J ntspahjy;> jhJnfly; Nghd;w FwpFzq;fs; fhzg;gLk;.

Nkl;\upa thjk;:

Mz;Fwpapd; td;ik Fiwe;JtpLk;.vupr;ry;>fdj;jy;>Nehjy;cz;lhFk;.mjpfupj;jhy; gP[k; tPq;Fk;. -Nuhf epu;za rhuk; (v)Nuhf epjhdk; gf;fk; 41

Rf;fpyj;ijalf;fpdhy;:

“Rf;fpye; jidalf;fpd; RuKldPu;f;fl;lhFk;

gf;fkhq; iffhy; re;J ghuNeha; topapwq;Fk;

kpf;fkhu; NehAz;lhFk; kpFj;jpLk; gpuNkfe;jhd;

jf;fNjhu; NghJkhfpd; jupj;jpLk; thAf; $Nw”.

-cly;jj;Jtk; gf;fk; 231

Rf;fpyk; ntspj;js;sg;gLtJk; Ntfepfo;Tfspy; xd;Nw mt;Ntfq;fs; jilg;gl;lhy; Neha;fs; cz;lhFk;. Rf;fpyj;jpid fl;Lg;gLj;jpdhy; Ruk;> ePu;f;;fl;L> iffhy;fs; Nehjy;>tpe;J mepr;irahff; frpe;J ePs;rPiy eidjy;> khu;gilg;G> khu;G Jbg;G ,it cz;lhFk;.

“Mz;kpfpy; Mzhk; ngz;kpfpy; ngz;zhk;

G+zpuz; nlhj;Jg; nghUe;jpy; mypahFe;

jhz;kpF khfpy; juzp KOjhSk;

ghit kpf;fpby; gha;e;;jJk; ,y;iyNa”

-jpU%yu; jpUke;jpuk; ghfk; 2

fytpapd; NghJ Mzpd; rf;jp ePbj;J epd;why; gpwf;Fk; Foe;ij cyifNa Msf;$ba Mw;wy; cs;stdhf ,Ug;ghd;. Mz; jho;T kdg;ghd;ik nfhz;L Jtz;L Nghthdhdhy; Rf;fpyk; ntspg;gLtJk; epd;WtpLk; vd jpU%yu; $Wfpwhu;.

“fhaj;jpNy %d;W ehspw; fye;jpl;Lf;

fhaj;Jl; ld;kd khFq; fyhtpe;J

Neaj;Nj epd;Nwhu;f;F ePq;fh tplhikapd;

khaj;Nj nry;Nthu; kdj;NjhlopANk”.

- jpU%yu; jpUke;jpuk; 1898

thjk; thOkplk;:

fhkf;nfhb> ce;jpapd; fPo;%yk;> euk;Gf;$l;lk;> Cd; Mfpa ,lq;fspy; fhzg;gLk;.

tspapd; ,aw;ifg;gz;G:

Cf;fKz;lhf;fy;> lk;nghwpfl;F td;ikiaf; nfhLj;jy;> gjpdhd;F Ntfq;fis ntspg;gLj;jy;.

tsp nra;njhopy;:

cWg;Gj;jsu;r;rp> cWg;Gfs; njhopy; Gupahky; kuk; Nghy; fplj;jy;.

tsp kpFFzk;:

Ik;nghwpfspd; td;ik Fd;wy;> cly; td;ik Fiwjy;

ehb eil:

thjgpj;jk;> gpj;jthjk;

-

Neha;ehly; Neha;Kjy; ehly; ghfk; 1

3.5. MODERN ASPECT OF THE DISEASE

Impotence (erectile dysfunction)

Introduction:

Erectile dysfunction is also known as impotence, is the inability to achieve or sustain an erection for satisfactory sexual activity. This is differ from other conditions that interfere with male sexual intercourse, such as lack of sexual desireness (decrease libido), and problems with ejaculation and orgasm (ejaculatory dysfunction).

Approximately 35% of men 40-70 years of age suffer from moderate to severe erectile dysfunction. 50 % of men over the age of 40, having erectile dysfunction, 10% of men below 40.

India is the impotence capital of the world.

Physiology of erection:

- An erection begins in the brain, physical or mental stimulation cause nerves in the brain to send chemical messages to nerves in the penis telling the blood vessels to relax so that can flow freely in to the penis.
- Once in the penis, high pressure traps the blood with in both corpora cavernosa. This causes the penis to expand and sustain an erection.
- Erection is reversed when the inflow of blood is stopped and opening outflow channel open, allowing the penis to become soft.

-Human physiology, Guyton

Molcular mechanism of erection:

- During sexual excitement, nitric oxide is released from the cavernous nerve (which control erection), nitric oxide activates an enzyme in smooth muscle called guanylyl cyclase.
- This activated enzyme in turn transforms GTP, an important energy source inside cells, in to cGMP.
- cGMP is a molecule that through a complex process causes smooth muscle relaxation,leading to dilatation of arteries and the rapid filling of the spongy erectile tissues.

Nerve supply:

- Parasympathetic supply- vasomotor supply $S_{2,3,4}$ (Nervi ergentes)

  It causes dilatation of helicine arteries during the erection of penis.
- Sympathetic supply - Vaso constrictor nerves of the penile vasculature.

  Sympathetic from L_1 segment reaches the penis through the branches of pudendal nerve.
- Somatic sensation -carried out by the dorsal nerve of the penis, they supply the skin and muscle acting on penis.

Neuro transmitters:

- The erectile mechanism is mainly driven by the acetyl choline-parasympathetic action, which produce the nitric oxide (erectile neurotransmitter) and c GMP (erectile dilator).
- On the other hand, the dopamine and nor epinephrine axis boosts libido and promotes the burning of testosterone, which expands the erectile tissues to an extreme state.
- Then, a large amount of nor-epinephrine becomes epinephrine (adrenaline) by conversion.
- That triggers the sympathetic ‘Fight or Flight’ command, where Fight means ejaculation and orgasm (if acetyl choline action is sufficient) and Flight the erection or engorgement withdrawal (if acetyl choline action is insufficient).

- ❖ Serotonin can block or reduce nor epinephrine-adrenaline conversion (adrenaline is the main enemy of erection or engorgement)
- ❖ In the foreplay and erectile states the stress hormone (adrenaline) can also block the incoming parasympathetic motoring communication from the brain to the targeted organ.
- ❖ Without stress hormone and with a high testosterone level, the parasympathetic nervous communications from the brain to the sex organs- the erection circuit will be frequently turned on.

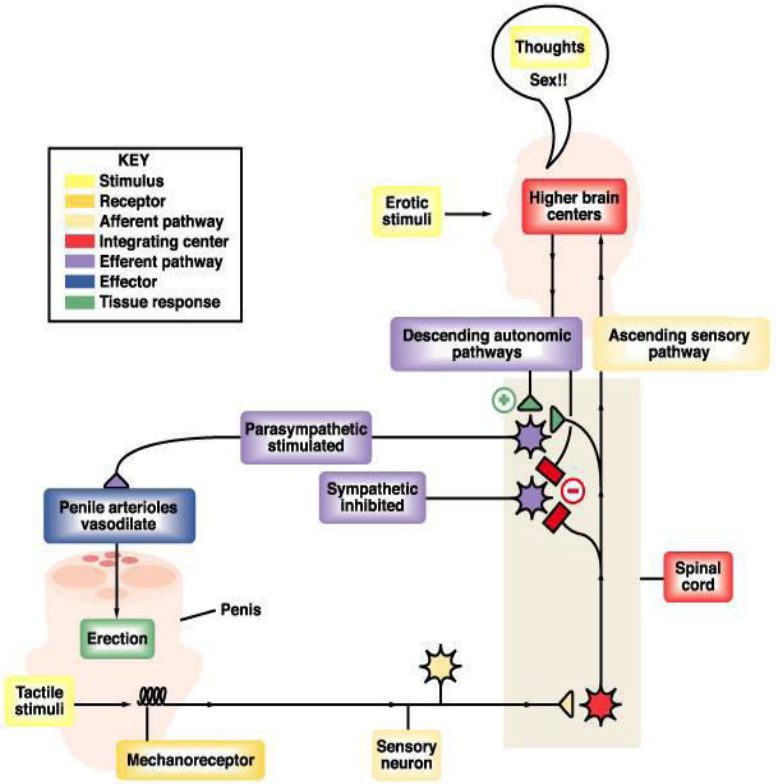


Figure: 3.5.1

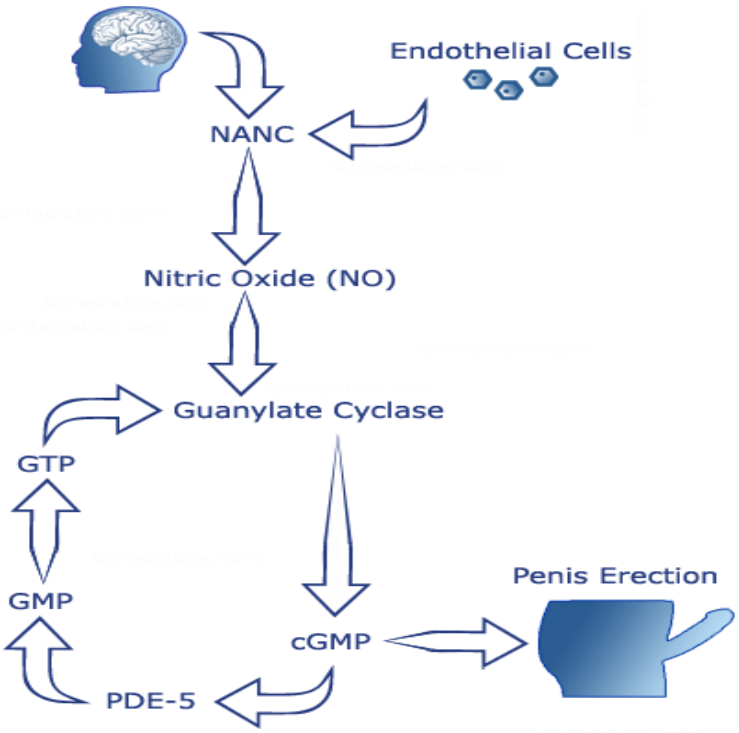


Figure: 3.5.2

Male sexual response cycle

Based on the literature support the normal male sexual response cycle can be functionally divided into five interrelated events that occur in a defined sequence: libido, erection, ejaculation, orgasm, and detumescence.

1. Libido or sexual desire:

Libido is defined as the biological need for sexual activity (the sex drive) and frequently is expressed as sex-seeking behaviour. Its intensity is variable between individuals as well as within an individual over a given time. Higher serum testosterone appears to be associated with greater sexual activity in healthy older but not younger men.

2. Erection:

Erection is the enlarged and rigid state of the sexually aroused penis sufficient enough for vaginal penetration. It results from multiple psychogenic and sensory stimuli arising from imaginative, visual, auditory, olfactory, gustatory, tactile, and genital reflexogenic sources.

3. Ejaculation:

Ejaculation is the act of ejecting semen. It is a reflex action that occurs as a result of sexual stimulation. It is made up of two sequential processes. The first process called emission is associated with deposition of seminal fluid into the posterior urethra while the second process is the true ejaculation, which is the expulsion of the seminal fluid from the posterior urethra through the penile meatus.

4. Orgasm:

This is the climax of sexual excitement. The entire period of emission and ejaculation is known as the male orgasm.

5. Detumescence: This is the subsidence of an erect penis after ejaculation.

Male sexual dysfunction-Impotence

Sex disorders of the male are classified into disorders of sexual function, sexual orientation, and sexual behaviour. In general, several factors must work in harmony to maintain normal sexual function. Such factors include neural activity, vascular events, intracavernosal nitric oxide system and androgens. Thus, malfunctioning of at least one of these could lead to sexual dysfunction of any kind. Sexual dysfunction in men refers to repeated inability to achieve normal sexual intercourse. It can also be viewed as disorders that interfere with a full sexual response cycle. These disorders make it difficult for a person to enjoy or to have sexual intercourse. While sexual dysfunction rarely threatens physical health, it can take a heavy psychological toll, bringing on depression, anxiety, and debilitating feelings of inadequacy.

Unfortunately, it is a problem often neglected by the health care team who strive more with the technical and more medically manageable aspects of the patient's illness. Sexual dysfunction is more prevalent in males than in females and thus, it is conventional to focus more on male sexual difficulties. It has been discovered that men between 17 and 96 years old could suffer sexual dysfunction as a result of psychological or physical health problems. Generally, a prevalence of about 10% occurs across all ages. Because sexual dysfunction is an inevitable process of aging, the prevalence is over 50% in men between 50 and 70 years of age. As men age, the absolute number of Leydig cells decreases by about 40%, and the vigour of pulsatile lutenizing hormone release is dampened. In association with these events,

free testosterone level also declines by approximately 1.2% per year. These have contributed in no small measure to prevalence of sexual dysfunction in the aged.

Sexual dysfunction takes different forms in men. A dysfunction can be life-long and always present, acquired, situational, or generalized, occurring despite the situation. Male sexual dysfunction can be categorized as disorders of desire, disorders of orgasm, erectile dysfunction, disorder of ejaculation and failure of detumescence.

A. Disorders of desire:

Disorders of desire can involve either a deficient or compulsive desire for sexual activity. Dysfunctions that can occur during the desire phase include:

(i) Hypoactive sexual desire

Defined as persistently or recurrently deficient (or absent) sexual fantasy and desire for sexual activity leading to marked distress or interpersonal difficulty. It results in a complete or almost complete lack of desire to have any type of sexual relation.

(ii) Compulsive sexual behaviours

Constitute a wide range of complex sexual behaviours that have strikingly repetitive, compelling, or driven qualities. They usually manifest as obsessive-compulsive sexuality (e.g. excessive masturbation and promiscuity), excessive sex-seeking in association with affective disorders (e.g. major depression or mood disorders), addictive sexuality (e.g. attachment to another person, object, or sensation for sexual gratification to the exclusion of everything else), and sexual impulsivity (failure to resist an impulse or temptation for sexual behaviour that is harmful to self or others such as exhibitionism, rape, or child molestation).

B. Erectile dysfunction (ED)

This is a problem with sexual arousal. ED can be defined as the difficulty in achieving or maintaining an erection sufficient for sexual activity or penetration, at least 50% of the time, for a period of six months. It results in significant psychological, social and physical morbidity, and annihilates his essence of masculinity.

C. Disorders of ejaculation

There exists a spectrum of disorders of ejaculation ranging from mild premature to severely retard or absent ejaculation. These include:

(i) **Premature ejaculation***:* which is the most common male sexual dysfunction and can be any of the following: a) persistent or recurrent ejaculation with minimum sexual stimulation that occurs before, upon, or shortly after penetration and before the person wishes it; b) marked distress or interpersonal difficulty; and c) the condition does not arise as a direct effect of substance abuse. Premature ejaculation and sexual desire disorders were the frequent reported problems in young adult males with adverse familial relationship**.**

(ii) Painful ejaculation*:* which results from side effect of tricyclic antidepressants is a persistent and recurrent pain in the genital organs during ejaculation or immediately afterwards**.**

(iii) Inhibited or retarded ejaculation: This is when ejaculation does not occur at all.

(iv) Retrograde ejaculation: This is when ejaculation is forced back into the bladder rather than through the urethra and out of the end of the penis at orgasm.

D. Disorders of orgasm

Male orgasmic disorder is defined as a persistent or recurrent delaying or absence of orgasm after a normal sexual excitement phase during sexual activity.

E. Failure of detumescence

It is a prolonged erection usually lasting for between 4 h or greater. It is painful and always unaccompanied by sexual desire despite the fact that it is often preceded by usual sexual stimuli. Diagnostic options for male sexual dysfunction include: patient's history which embodies medical history (evaluating historical events like chronic disease, pharmacological agents, endocrine disorders, surgeries and trauma), psychological history (assessing individual's upbringing relationships, early sexual experiences, inadequate sexual information and general psychological health), sexual history (to ascertain the time and manner of onset, its course, current status, and associated medical or psychological problems), physical examination (entails general and systemic evaluation, assessment of gonadal function, vascular competence, neurological integrity, and genital organ normalcy),

diagnosis testing (include blood tests, vascular assessment, sensory testing and nocturnal penile tumescence and rigidity testing).

Types of erectile dysfunction:

1. Arteriogenic
2. Neurogenic
3. Endocrinologic
4. Mixed
5. Psychogenic

Primary- Impotence since birth

Secondary- Impotence sets in after years of normal sex

Causes:

Psychological causes:

These factors are responsible for about 10%-20% of all cases.

It is often a secondary reaction to an underlying physical cause.

- Stress
- performance Anxiety
- Guilt
- Depression
- Low self esteem
- Fear of sexual failure

Physical causes:

- Aging (decrease In hormonal level with age)
- Chronic medical conditions (diabetes, hypertension)
- Vascular insufficiency (atherosclerosis, venous leakage)
- Penile disease (Peyronie's, priapism, phinosis, smooth muscle dysfunction)
- Pelvic surgery (to correct arterial or inflow disorder)
- Neurological disorders (Parkinson's disease, stroke, cerebral trauma, Alzhemier's spinal cord or nerve injury)

- Drugs (side effects -anti-hypertensives, central agents, psychiatric medications, antiulcer, antidepressants, and anti-androgens)
- Systemic diseases (cardiac, hepatic, renal, pulmonary, cancer, metabolic, post-organ transplant)
- Life style (chronic alcohol abuse, cigarette smoking)
- Androgen deficiencies (testosterone deficiency, hyperprolactinemia)

Chronic anxiety and sexual activity:

- It is an indicator that there are modulation disorders of serotonin and GABA on the autonomic nervous system.It usually leads to overpowered nervous function.this in turn leads to premature ejaculation and performance anxiety.
- Generally the serotonin and GABA modulate the nor adrenergic-sympathetic nervous function in two days
- By modulating the ANS-Autonomic nervous system via direct norepinephrine neurons of the hypothalamic locus coeruleus (LC).
- By modulating the neuro endocrine humoral outflow via the hypothalamic-pituitary-adrenal axis.
- The serotonin, GABA and endorphin nervous control can reduce seminal vesicles, prostate and penile nervous sensitivity.
- Also the GABA-erginic nerves control the non adrenergic firing in the LC while the serotonin-ergic nerves reduce the nonadrenergic sympathetic nervous function.
- Sexual stimulation or orgasm ignites conversion of dopamine-nor epinephrine in the hypothalamus and adrenal medulla, after that nor-epinephrine neurons of the locus coeruleus are activated. ProstoglandinE_2 is stimulated by the norepinephrine.
- Prostaglandin E_2 sensitizes the sympathetic nerves in the adrenal glands, seminal vesicles, testicles, penis and prostate for the norepinephrine release.
- Norepinephrine release, in turn, triggers the neurotransmitters prostaglandin E_1 and prostaglandin E_2 release.
- The release of Prostaglandins triggers the nervous erectile mechanism (with the release of Nitric oxide and cGMP) that leads to erection.
- However, high levels of Prostoglandin E_2 may over sensitize the sympathetic and somatic nerves located in the prostate, bulbo urethral glands and penis, which in turn

inflame the organ and will cause numerous symptoms,such as,fast ejaculation(even with in seconds) and precum leakage.

Diagnosing of impotence:

Patient history

- Is the patient suffering from erectile dysfunction or from loss of libido or disorder of ejaculation?
- Is ED is due to psychological or physical factors?
- Prior history of smoking,heart attacks,strokes
- Is the patient taking medications that can contribute to ED?

Physical examination

- Not response in touch stimuli-problem in nervous system
- Small testicles, Lack of facial hair, enlarged breast –hormone problem
- Reducing blood flow-Atherosclerosis can be diagnosed
- Bending of the penis with painful erection-Peyronie's disease

Laboratory tests:

- Total testosterone level

Total testosterone	
Men	270-1070 **ng/dL** (9-38 **nmol/L**)
Women	15-70 ng/dL (0.52-2.4 nmol/L)
Children	2-20 ng/dL or 0.07-0.7 nmol/L

Free testosterone	
Men	50-210 **pg/mL**

(174-729 **pmol/L**)

1.0-8.5 pg/mL

Women

(3.5-29.5 pmol/L)

- Complete blood counts
- Urinalysis
- Liver and kidney function test
- Lipid profile
- Blood glucose level
- Blood HbA_1C
- Other hormones-LH, FSH, Prolactin, Thyroid function test
- Prostate specific antigen

Imaging test:

- Duplex Ultra sound of penis and testicles
- Doppler scan
- Angiogram
- Penile biothesiometry
- Dynamic infusion cavernosometry
- Cavernosography
- Arteriography

Others

- Nocturnal penile tumescence
- Vasoactive injection
- Bulbocavernosus reflex

Current treatment strategy:

The first anti-impotence drug, alprostadil, was marketed in 1995 and is available as a local injection or an intraurethral pellet. The latter method of delivery was discovered after it was noted that drugs could be absorbed into the cavernosal bodies through the walls of the urethra. More recently oral therapies for the treatment of impotence have been marketed, starting with the accidental discovery of sildenafil citrate (Viagra).

In 1991, researchers discovered that chemical compounds belonging to the pyrazolopyrimidinone class were useful for treating cardiac conditions such as angina. In 1994, whilst trials for this were underway (with little success) it was noted that the drug also increased blood flow to the penis and therefore increased erections. Subsequently, in 1998, the FDA gave approval for sildenafil citrate as the first oral anti-impotence drug. With the latest addition, apomorphine (Uprima), there is now a race to produce a pill with a faster onset of erection, fewer side effects, available to all patients and with no restriction on the frequency of use.

- Making lifestyle improvements (for example quitting smoking and exercise more)
- Taking drugs (PDE5 inhibitors)
- Intra urethral suppositories
- Intra cavernosal injections
- Vaccum constrictive device
- Penile prostheses
- Psychotherapy

Herbal drugs:

Some herbal drugs are given as aphrodisiac, namely

Botanical name	**Active principles**
Argimone maxicana	- L-arginine
Sida cordifolia	- Phytosterols
Tribulus teresteres	- Protodiacin
Mucuna pruriens	- L-DOPA
Asparagus adcendens	- Asparagin
Withania somnifera	- Withaferin-A
Nut meg fruit	- Myristicin
Glycyrrhiza glabra	- Glabridin
Bacopa monnieri	- Bacoside-A
Albizzia lebbeck	- **Quercitin**, Betulinic acid
Yohimbe tree	- Yohimbine

3.6. LATERAL RESEARCH:

Anti-oxidant activity

- Antioxidant activity of ***Nelumbo nucifera*** **flowers** (Ushimaru et al.2006) in isolated perfused rat kidney.Results suggest flowers extract exhibits anti-oxidant activity in oxidatively stressed isolated perfused kidney.-Medicinal and Aromatic Plant Abstract (MAPA) -2009 August
- Anti oxidant principles of ***Nelumbo nucifera*** **stamens** (Jung et al.2003,Wu et al.,2003)was evaluated for their potential to scavenge stable 1,1-diaphenyl-2-picrylhydrazyl (DPPH) free radicals,inhibit total reactive oxygen species(ROS) generation,in kidney homogenates using 2,7-dichloro dihydrofluorescein diacetate(DCHF-DA) and scavenge authentic peroxy nitrates(ONOO).Amethonol extract of the stamens of Nelumbo nucifera showed strong anti-oxidant activity in the ONOO system,and marginal activity in the DPPH and total ROS system,so these were fractionated with several organic solvents. Seven known flavanoids are,

  1. Kaemferol-3-0-beta-D-glucuronopyranosyl methyllester
  2. Kaemferol-3-0-beta-D-glucopyranoside
  3. Kaemferol-3-0-beta-galactopyranoside
  4. Myricetin 3`5` -dimethylether 3-0-beta-D glucopyranoside
  5. Kaemferol-3-0-alpha-L-rhamnopyranosyl
  6. Kaemferol-3-0-beta-D-glucoronoopyranoside
  7. Beta-sitosterol glucopyranoside.

  -MAPA 2003-December page 791
- The major constituents are isolated from the lotus plant are alkaloids (liensinine, neferine, nuciferine, remrefidine and isoliensinine) and flavonoids ((+)-1(R)-coclaurine, (-)-1(S)-norcoclaurine and quercetin 3-O-b-D-glucuronide). Several previous reports suggested that seed could suppress cell cycle progression, cytokine genes expression and cell proliferation in human peripheral blood mononuclear cells. Recently, the leaf of N.nucifera showed the hypotensive effects that were mediated by vasodilatation via nitric oxide and betulinic acid isolated from rhizomes and used as anti-tumoral and melanoma specific cytotoxic agent. -IPCBEE Vol 5-2011
- A new phenolic dibenzylisoquinoline alkaloid-isoliensinine-isolated, a new base-neferine isolated from embryo (chem.abs.1965,63)

- A quarternary base-lotusine along with isoliensinine from embryo, structure of the former determined (chem.abs.1965,63)
- However, scientific evidence on antioxidant potential in hydroethanolic extract of white N.nucifera is still unknown. Therefore, our study has been focused to gain extensive knowledge regarding the power of antioxidants from white N.nucifera flowers and to tap their potential.
- Effects of Nelumbins semen on contractile dysfunction in Ischaemic and repurfused rat heart.Results suggest that Nelumbo semens have distinct anti-ischaemic effects through calcium antagonism.

-Journal of natural remedies-april 2004

- Effects of Nelumbins semen on contractile dysfunction in ischaemic and reperfused rat heart.Results suggest that N.semen has distinct anti-ischaemic effects through calcium antagonism.

-MAPA June 2007 page 250

- Effects of extracts and Neferine from the embryo of N.N seeds on the central nervous system. Results suggest, Neferine has several central effects and that Neferine may participate in the efficacy of the sedative effects.

-MAPA June 2009 page 378

- Assessment of analgesic activity of red and white lotus seed, Results suggest that white lotus seed higher dose group exhibited significant analgesic activity than other lotus seed treated groups.

-MAPA Feb-2010 page 46

- Procyanidins extracted from the lotus seedpod ameliorate scopolamine-induced memory impairment in mice. Results suggested that lotus seedpod extract may play a useful role in the treatment of cognitive impairment caused by Alzhemer's disease and aging.

-MAPA June 2010 page 41

- Anti-diabetic effect of ***Nelumbo nucifera*** **flowers**

  The powdered N.N sun dried flowers, as well as the aqueous and alcoholic extract of these, produced significant hypoglycaemia in fasting normal albino-rabbits. -MAPA Feb-1992 page 28
- Inhibitory effect in pulmonary fibrosis:

Isoliensinine bisbenzyl isoquinoline alkaloid was extracted from the seed embryo of N.N have inhibitory effect on bleomycin induced pulmonary fibrosis in mice - MAPA August 2005 page 442

- Lim et al. (2006) worked on the rat lens aldose reductase (RLAR) (a principal enzyme of polyol pathway associated with diabetes) inhibitory constituents of stamens of *Nelumbo nucifera* in rat lens.Methonol extract of the stamens exert an inhibitory effect on RLAR.

Antisteroidogenic effect

The petroleum ether extract of the seeds of Nelumbo nucifera and its fractions were administered orally to sexually immature female rats and mature male rats on alternate day for 15 days.The treatment caused a remarkable delay in sexual maturation in prepubertal female rats as evidenced from age of vaginal opening and first estrus (cornified smear) and a significant reduction in the sperm count and motility in mature male rats.In both the cases treatment resulted in accumulation of cholesterol and ascorbic acid and reduction in D5- 3b-hydroxysteroid dehydrogenase and Glucose-6-phosphate dehydrogenase activity in the ovary and testis of female and male rat respectively.These results indicate suppression of steroidogenesis in both ovary and testis.

-MAPA-August 1997 page 2114

Nelumbo nucifera Gaertn (Family: Nelumbonaceae), medicinally versatile and used as an important raw material of age-old traditional medical practices like *siddha* and folk medicine. Bioassays for antimicrobial activities were carried out using hydroethanolic extract of both white flowers of *Nelumbo nucifera Gaertn* plant.Tthe flower extracts was tested against five important bacterial strains and two fungal strains. Further, Minimum Inhibitory Concentration (MIC) was evaluated against *Escherichia coli* (gram negative) and *Staphylococcus aureus* (gram positive) organisms. The flower extract showed considerable activity against all tested bacteria and fungi strains. MIC for white flower extract against *Escherichia coli* and *Staphylococcus aureus* was found to be 430µg and 450µg respectively. The antibacterial and antifungal activities flower extract was selected chemical antibiotics suggesting that potential as alternatives to orthodox antibiotics in the treatment of infectious caused by these microorganisms (Brindha et.al 2010).

The stamens are used to"purify the heart, permeate the kidney, strengthening of **virility,** to blacken the hair, for haemoptysis and **spermatorrhoea".** They are also used to treat **premature ejaculation**, as **astringent** for **bleeding,** excessive **bleeding** from the uterus,

abdominal cramps, bloody discharges**,** metrorrhagia, non-expulsion of the amniotic sac, and as cooling agent during **cholera.** -U.K Net guide

In scientific research:

The roots of *Nelumbo nucifera* are planted in the soil of the pond or river bottom, while the leaves float on top of the water surface or are held well above it. The flowers are usually found on thick stems rising several centimeters above the leaves. The plant normally grows up to a height of about 150 cm and a horizontal spread of up to 3 meters, but some unverified reports place the height as high as over 5 meters. The leaves may be as large as 60 cm in diameter, while the showy flowers can be up to 20 cm in diameter.

Researchers report that the lotus has the remarkable ability to regulate the temperature of its flowers to within a narrow range just as humans and other warmblooded animals do. Dr. Roger S. Seymour and Dr. Paul Schultze-Motel, physiologists at the University of Adelaide in Australia, found that lotus flowers blooming in the Adelaide Botanic Gardens maintained a temperature of 30–35 °C (86–95 °F), even when the air temperature dropped to 10 °C (50 °F). They suspect the flowers may be doing this to attract coldblooded insect pollinators the study, published in the journal *Nature*, is the latest discovery in the esoteric field of heat-producing plants.

Speciality:

The Lotus flowers are sun-lovers and are generally intolerant of the colder weather. The petals of the Lotus flower close to control the plant's inner circulation of water, so it is not less affected by weather. Lotuses do not bloom during the cold of winter.Summer, or the season of Fire, is when the Lotus blossoms. In spring, and through the summer, the plant is vigorously growing, enjoying the warmth and humidity. The flowers open in response to sunlight, usually opening in the morning and closing in the afternoon.

cyu;e;j ntz;jhkiu kfue;jk;

Figure: 4.3

kfue;jj; J}s;

Figure: 4.4

4. MATERIALS AND METHODS

Drug selection:

In this dissertation the stamens of venthamarai (*Nelumbo nucifera)* was taken as a single drug for *Samboga vaatham* (Erectile dysfunction) from the literature of the preparation was collected from ***Gunapaddam,*** **First Part-*Mooligai Vaguppu*** (**Theran Porutpanbu Nool)** written by **K.S.Murugesa Mudaliyar,** Pag –no 404 & 405.

Collection of the drug:

Venthaamarai flowers were collected from Kumbakonam, Tamilnadu during the month of June 2011, and from Udayarpalayam tank, Ariyalur District, Tamilnadu during the month of November 2011.

Identification and Authentification of the drug:

The test drug *venthamarai* was identified and authenticated by Asst.Director (Pharmacognosy), Central Research Institute for *Siddha* and The Head of the department, P.G *Gunapadam* branch, GSMC, Arumbakkam, Chennai-106. Sample of the herb kept in PG *Gunapadam* department for future reference.

4.1. Preparation and Purification of the drug:

Venthaamarai flowers part were peeled out separately, and only stamens were collected, and then it shadow dried, pulverized and sieved to get a fine powder (*vasthirakayam)*. The purification process for the chooranam is depends on nature and active principles of the chooranam, because the trial drug contains Phenolic compounds which are easily denatured by heating. Also, due to the presence of high carbohydrate level it is become granule when it is exposed to the hot steam. So, this kind of the *chooranam* does not need to boil in the steam of milk. Every time the needed medicine for the trial was prepared in this same method. Because the life period of the *Chooranam* is only three months, the prepared *Chooranam* was used within the period.

Storage of the drug:

The test drug was stored in a clean, dry glass container.

The contents were inspected frequently to avoid moisture and Insects

Administration of the Drug:

Form of the medicine : *Chooranam*

Route of Administration : Enteral

Dose : 500 mg

Anubanam (Vehicle) : Honey

Time of Administration : once in a day; before food

Duration : 1-3 months

4.2. STANDARDIZATION OF DRUG

Standardization is the first step for the establishment of a consistent biological activity, a consistent chemical profile Standardized herbal products of consistent quality and containing well-defined constituents are required for reliable clinical trials and to provide consistent beneficial therapeutic effects.

Pharmacological properties of an herbal formulation depend on phytochemical constituents present therein. Development of authentic analytical methods which can reliably profile the phytochemical composition, including quantitative analyses of marker or bioactive compounds and other major constituents, without consistent quality of a phytochemical mixture, a consistent pharmacological effect is not expected (M.Mosihuzzaman et.al 2008).

4.2.1. QUALITATIVE PHYTO CHEMICAL ANALYSIS

Medicinal plants are of great importance to the health of individuals and communities. The medicinal value of these plants lies in some chemical substances that produce a definite physiological action on the human body and these chemical substances are phytochemicals. These are non-nutritive chemicals that have protective or disease preventive property. The most important of these phytochemicals are alkaloids, flavonoids, tannins and phenolic compounds (Hill, 1952).

Chemical tests were carried out using the aqueous extracts from Plants and or the powdered specimens, using standard procedures to identify the constituents as describe bySofowara (1993), Trease and Evans (1989) and Harborne (1973).

Table: 4.2.1

SL.NO	EXPERIMENT	OBSERVATION
I.	**Test for Tannins:** A plant sample dried powder 0.5 gm is boiled in 20 ml of water and filtered.The filterate 2 ml is taken and 3-5 drops of $Fecl_2$ (0.1%) is slowly added to it.	Forms a brownish-green or bluish- black colour.
II.	**Test for Phlobatannins:** An aqueous 2 ml of plant sample is boiled in a hot water bath with 1 ml of aqueous Hcl	A red precipitate is deposited
III.	**Test for Saponin:** A powdered 2 gm of plant sample is boiled with 20 ml of distilled water, then filtered, the filterate is added with fresh 5 ml of distilled water and shaken vigorously.	Permenant or persistant froth is not formed.The froth is not turned in to emulsion by adding three drops of olive oil.
IV.	**Test for Flavonoids:** An aqueous filterate of plant sample is mixed with 5 ml of dilute Ammonium solution and few drops of concentrated H_2SO_4 is slowly added through the sides of the test tube.	Yellow colour formed and disappears on standing.When 1% Alluminium solution is added in this mixture re-formation of yellow colour.
V.	**Test for steroids:** An ethonolic extract of plant sample 2ml is mixed with 2 ml H_2SO_4 and 0.5 gm Acetic anhydride.	The solution turns in to blue to green colour
VI.	**Test for Cardiac glycosides:** In 5 ml of plant Ethanolic extract, 2 ml of Glacial acetic acid, a drop of $Fecl_2$ and 1 ml of H_2SO_4 (slowly on the sides of the test tube) is added.	A brown ring indicates deoxy sugar of cardenolides/violet ring appears below brown ring/ in acetic acid layer a green ring is formed
VII.	**Test for Terpenoids:** In 5 ml of Ethanolic plant extract, 2 ml of chloroform and 3 ml of concentrated H_2SO_4 (slowly) is added.	A reddish brown interface layer is formed

VIII.	**Test for Carbohydrates:** An aqueous plant extract is boiled in a water bath with Benedict's solution.	A green or brick red or red precipitate shows the presence of reducing sugar
IX.	**Test for Alkaloids:** Alkaloids are identified by precipitate method	
	(a) Mayer's reagent: An aqueous plant extract of 2 ml is mixed with 2 ml of mayer's reagent	Forms whitish or yellowish cream colour precipitate
	(b) Wagner's reagent: An aqueous plant extract of 2 ml is mixed with 2 ml of wagner's reagent	Forms a brown or dark reddish precipitate
	(c) Dragendroff's reagent: An aqueous plant extract of 2 ml is mixed with 2 ml of Dragendroff's reagent.	Forms reddish brown precipitate
X.	**Test for Glycosides:** An aqueous plant extract of 2 ml is added with 1 ml of concentrated Hcl and boiled in a water bath for about 2 hours. The filtrate is separated and 3 ml of chloroform is added, then 10% of 1ml Ammonium solution is added.	Forms pink colour
XI.	**Test for Protein:** An aqueous extract /alcoholic extract of 2 ml is added with few drops of Biuret reagent and kept in hot water bath for 10 minutes.	Formation of light blue or Pale violet colour is absent
XII.	**Test for Phytosterols:** An ethanolic or a methonolic plant extract 2 ml is mixed with 2 ml of Acetic anhydride stirred well and heated for 2 minutes in hot water bath then allowed to cool.1 or 2 drops of H_2SO_4 is added with the mixture slowly through the sides of the wall .	Forms greenish blue layer on the upper surface
XIII.	**Test for Phenolic compounds:** About 2 ml of aqueous plant extract is mixed with	Formation of deep bluish green colour is absent

2 ml of $Fecl_3$ solution.

XVI.	**Test for Volatile oil:** An ethanolic plant extract of 2 ml is mixed with one or two drops of tincture in warm water bath in a screwed cap test tube.	Red colour is not appeared
XV.	**Test for Fixed oil:** One ml of ethanolic extract of plant sample is mixed with 1 ml of 1% copper sulphate solution and 5 drops of 10% sodium Hydroxide solution	Formation of a clear blue solution is absent

4.2.2. PHYSIO-CHEMICAL ANALYSIS OF TEST DRUG

சித்த மருத்துவ மைய ஆராய்ச்சி நிலையம், அரும்பாக்கம், சென்னை - 600 106
सिध्द केन्द्रीय अनुसंधान संस्थान, अरुम्बाक्कम, चेन्नई- 600106
Siddha Central Research Institute
Arignar Anna Govt. Hospital Campus, Arumbakkam, Chennai-600 106
(Central Council for Research in Siddha, Department of AYUSH,
Ministry of Health & Family Welfare, Govt. of India)
Phone: 044-2621 49 25,
Tele Fax: 044 26214809,
E.mail: crisiddha @ gmail.com
Web: www.crisiddha.tn.nic.in

Ash and acid insoluble ash:

To the ash add 1:5 Hcl: Distilled water 15 ml boil, cooled and then filtered using whatman filter paper (No.41) repeat 3 to 4 times till the yellow colour disappear or colourless, then remove the filter paper and add to the filter to the original dish and keep it in the muffle furnace at 600^{o} C and take constant weight and calculate the acid insoluble ash value.

$$\text{Acid insoluble ash (\%)} = \frac{\text{Weight of acid insoluble residue x 100}}{\text{Weight of the sample}}$$

Acid insoluble residue = Acid insoluble ash value – Empty weight of the dish

Loss on drying:

3gm of the drug is heated in a hot oven at 105^0 c to constant weight. The % of weight was calculated.

Loss on drying value at 105^0 c – 14.065 %w/w

Potential of hydrogen (pH):

The pH scale is logarithmic and runs from 0.0 to 14.0 with 7.0 being neutral. Readings less than 7.0 indicate acidic solutions, while higher readings indicate alkaline or base solutions.pH of *venthamarai magarantha chooranam* - 7.07

Thin layar chromatography (TLC):

Solvent system:

Toluene : Ethyl acetate (10:1).

TLC plate:

Aluminium plate precoated with silica gel $60F_{254}$ of 0.2 mm thickness (Merck).

Developing chamber:

Camag's twin through chamber.

Visualizing reagent : Vanillin-sulphuric acid reagent.

Extract Preparation:

4 g of the chooranam was soaked overnight in chloroform. Boiled on a water bath for 10 mins, filtered and concentrated to 10 ml.

Procedure:

The extract was applied on the TLC using capillary and developed in the solvent system. The developed TLC plate was air dried, dipped in vanillin-sulphuric acid reagent and heated in an oven at 105°C until the development of coloured spots.

Sl.No	Rf value	Colour of the spot
1	0.09	Purple
2	0.15	Purple
3	0.22	Purple
4	0.28	Purple
5	0.40	Purple
6	0.56	Purple
7	0.67	Violet
8	0.74	Violet
9	0.86	Purple

Table: 4.2.2

4.2.3. CHEMICAL ANALYSIS

Preparation of aqueous plant extract:

2gm of the sample is mixed with20 ml of distilled water. The solution is boiled for 10 minutes, cooled and then filtered. The filtrate is called **aqueous extract.** These extract is used for the following chemical tests.

Table: 4.2.3

SL NO	EXPERIMENT	OBSERVATION
I.	**Test for acid radicals:**	Absence of White Precipitate
1.(a)	**Test for Sulphate** 2 ml of the above prepared extract is taken in a test tube. To this add 2ml of 4% Ammonium oxalate solution.	
(b)	2ml of extract is added with 2ml of dilute hydrochloric acid until the effervescence ceases off. Then 2ml barium chloride solution is added	Absence of White Precipitate
2.	**Test for Chloride:** 2ml of extract is added with dilute nitric acid till the effervescence ceases. Then 2ml of silver nitrate solution is added.	Absence of white precipitate
3.	**Test for Phosphate**	Yellow Precipitate is

	2ml of the extract is treated with 2 ml of Ammonium molybdate solution and 2ml of concentrated nitric acid.	obtained.
4.	**Test for Carbonate:** 2ml of the extract is treated with 2ml of magnesium sulphate solution.	Absence of white precipitate
5.	**Test for Sulphide:** 1 gm of the substance is treated with 2ml of concentrated Hydrochloric acid	Absence of Rotten egg smelling
6.	**Test for Nitrate:** 1gm of the substance is heated with copper turnings and concentrated sulphuric acid and viewed the test tube vertically down.	Absence of reddish brown gas.
7.(a)	**Test for Fluoride and oxalate** 2ml of the extract is added with 2ml of dilute acetic acid and 2ml of calcium chloride solution and heated.	White precipitate is obtained
(b)	5 drops of clear solution is added with 2ml of dilute sulphuric acid and slightly warmed to this, 1 ml of dilute potassium permanganate solution is added.	Absence of KMNO4 solution discolourisation.
8.	**Test for Nitrite** 3 drops of the extract is placed on a filter paper. On that, 2 drops a Acetic Acid and 2 drops of Benzidine solution is placed.	Absence of yellowish red colour
9.	**Test for Borate** 2 pinches of the substance is made into paste by using Sulphuric acid and Alcohol (95%) and introduced into the blue flame.	Absence of Green tinged flame
II.	**TEST FOR BASIC RADICALS**	
10.	**Test for lead** 2 ml of the extract is added with 2 ml of Potassium iodide solution	Absence of Yellow precipitate
11.(a)	**Test for Copper**	Bluish green coloured

	One pinch of substance is made into paste with concentrated Hydrochloric acid in a watch glass and introduced into the non luminous part of the flame.	flame is obtained.
(b)	2ml of the extract is added with excess of Ammonia solution	Presence of deep blue
12.	**Test for Aluminium** To the 2 ml of extract. Sodium Hydroxide solution is added in drops to excess.	Absence of White precipitate.
13(a)	**Test for Iron** To the 2 ml of extract, 2 ml of Ammonium Thiocyanate solution is added.	Blood red colour is obtained
(b)	To the 2 ml of extract, 2 ml of Ammonium Thiocyanate solution and 2 ml of concentrated Nitric Acid is added.	Blood red colour is obtained.
14.	**Test for Zinc** To the 2 ml of extract Sodium Hydroxide solution is added in drops to excess.	Absence ofWhite precipitate
15.	**Test for Calcium** 2 ml of the extract is added with 2 ml of 4% Ammonium Oxalate solution.	White precipitate is obtained.
16.	**Test for Magnesium** 2ml of extract, Sodium Hydroxide solution is added in drops to excess.	Absence of White precipitate.
17.	**Test for Ammonium** 2 ml of extract few ml of Nessler's Reagent and excess of Sodium Hydroxide solution are added.	Reddish brown precipitate is obtained
18.	**Test for Potassium** A pinch of substance is treated with 2 ml of Sodium Nitrite solution and then treated with 2 ml of Cobal Nitrate in 30% glacial Acetic acid.	Presence of Yellow precipitate
19.	**Test for Sodium** 2 pinches of the substance is made into paste by using Hydrochloric acid and introduced into the blue flame.	Presence of Yellow colour flame
20.	**Test for Mercury**	Absence of yellow

	2 ml of the extract is treated with 2 ml of Sodium Hydroxide solution.	precipitate
21.	**Test for Arsenic** 2 ml of extract is treated with 2 ml of silver Nitrate solution	Absence of Yellow precipitate.
22.	**Test for Starch** 2ml of extract is treated with weak iodine solution	Absence of Blue colour.
23.	**Test of reducing Sugar** 5ml of Benedict's qualitative solution is taken in a test tube and allowed to boil for 2 minutes and added 10 drops of the extract and again boiled for 2 minutes. The colour changes are noted.	Green colour is obtained.
24.	**Test of the alkaloids** 2ml of the extract is treated with 2ml of potassium lodide solution	Red colour developed

Phyto chemical analysis result are discussed in table 4.2.1.

4.2.4. TOXICOLOGICAL STUDY:

Herbal medicines are generally regarded as safe based on their long-standing use in various cultures. However, there are case reports of serious adverse events after administration of herbal products. In a lot of cases, the toxicity has been traced to contaminants and adulteration. However, some of the plants used in herbal medicines can also be highly toxic. As a whole, herbal medicines can have a risk of adverse effects and drug–drug and drug–food interactions if not properly assessed. Assessment of the safety of herbal products, therefore, is the first priority in herbal research. There are various approaches to the evaluation of safety of herbal medicines.

Evaluation of the toxic effects of plant constituents of herbal formulation requires detailed phytochemical and pharmacological studies. It is, however, safe to assume that, based on human experiences in various cultures, the use of toxic plant ingredients has already been largely eliminated and recent reports of toxicity could largely be due to misidentification and overdosing of certain constituents

The experimental animals were maintained at normal room temperature with a humidity of ± 5%. All the animals were feed with pellet diet obtained and tap water ad libitum throughout the experimental period. The animals were acclimatized to the laboratory conditions before experimental procedures were started. The experimental protocol for *venthamarai magarantha Chooranam* (XIII/VELS/COL/05/CPCSEA/IAEC/23.09.11) was approved by the CPCSEA/IAEC of Vel's College of Pharmacy, Vel's University, Pallavaram, Chennai.

Acute toxicity study

The substance is administered orally to a group of experimental animals at one of the defined doses. The acute oral toxicity study was carried out as per the OECD guidelines-425. The substance is tested using a stepwise up and down procedure, Absence or presence of drug-related mortality of the animals dosed at one step to determine the next step, i.e.; − no further testing is needed. The method will enable a judgement with respect to classifying the test substance to one of a series of toxicity classes. Animals are observed individually after dosing at least once during the first 30 minutes, periodically during the first 24 hours, with special attention given during the first 4 hours, and daily thereafter, for a total of 14 days, except where they need to be removed from the study and humanely killed for animal welfare reasons or are found dead.

All observations are systematically recorded and Observations include changes in skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous systems, and somatomotor activity and behaviour pattern. Attention was directed to observations of tremors, convulsions, salivation, diarrhoea, lethargy, sleep and coma. One-tenth of the lethal dose was considered as therapeutic dose for further pharmacological study.

Animals

Female mice were fasted overnight and given single oral dose of *Venthamarai magarantha chooranam* suspended in 2% Carboxy Methyl Cellulose with water (Starting dose 500mg/kg and upto 5000mg /kg body wt).

The animals were fed with *Venthamarai magarantha chooranam* and then they were observed for 14 days to record signs of toxicity and death if any. Results are discussed in table 4.2.4.

4.2.5. PHARMACOLOGICAL STUDIES

Materials and methods adopted in this study

Drugs

The siddha drug *Venthamarai magarantha chooranam* was uniformly suspended in 2% Carboxy Methyl Cellulose in water to obtain 100mg/ml concentration as stock solution and Commercially available Sildenafil citrate (Pfizer pharma pvt Ltd) purchased from local market used in this study.

Evaluation of aphrodisiac activity

Animal selection

Male and female albino rats of average body weight of 190±7g were kept separately in individual polypropylene cages with stainless steel hopper in air-conditioned room (24°C) of the animal house under uniform animal husbandary conditions. The animals were fed basal diet (Sai meera foods, Bangalore) and water *ad libitum*. The animals were acclimatized to temperature and lighting (12 h light/dark) conditions of the animal house. Healthy and sexually experienced male albino rats that show brisk sexual activity selected for the study.

Experimental Design

Group-I Served as **Control** received only 2% CMC in saline

Group-II Served as **Standard** received Sildenafil citrate at the dose level of 4.5mg/kg

Group-III Served as **test** received *Venthamarai magarantha chooranam* 500mg/kg body wt.

Mating behaviour test

After drug administration to the animals according to the experimental design and objective, the male animals were brought to the laboratory and exposed to dim light at the stipulated time of testing daily (3-6 days) before the experiment. The female animals were artificially brought into oestrus by administering ethinyl oestradiol orally at the dose of 100µg/animal 48h prior to the pairing. The receptivity of the female animals was studied before the test by exposing them to male animals. The most receptive females were selected for the study. The experiment was conducted at 20:00 h in the same laboratory and under

light of same intensity. The receptive female animals were introduced into the cages of male animals in the ratio 1:1. An initial period of 15 minutes was considered as acclimatization period. After 15 minutes, the drug was administered the activity of male rat in each group was recorded individually for 60 minutes, the parameters of observed were**,**

Mount frequency, Intromission frequency, Mount latency, Intromission latency, Anogenital sniffing, Genital grooming.

Definitions of individual parameters observed

i. Mount frequency

Mounting is defined as the climbing of one animal by another usually from the posterior end with the intention of introducing one organ into another. Mount may also be operationally defined as the male assuming the copulatory position but failing to achieve intromission. Mount Frequency is therefore defined as the number of mounts without intromission from the time of introduction of the female until ejaculation.

ii. Intromission frequency

Intromission is the introduction of one organ or parts into another. e.g. the penis into the vagina.Intromission Frequency is therefore defined as the number of intromissions from the time of introduction of the female until ejaculation.

iii. Mount latency

Mount Latency is defined as the time interval between the introduction of the female and the first mount by the male.

iv. Intromission latency

Intromission Latency is the time interval from the time of introduction of the female to the first intromission by the male. This is usually characterized by pelvic thrusting, and springing dismounts.

v. Ejaculatory latency

Ejaculation is the act of ejecting semen brought about by a reflex action that occurs as the result of sexual stimulation. Ejaculatory Latency is defined as the time interval between the first intromission and ejaculation. This is usually characterized by longer, deeper pelvic thrusting and slow dismount followed by a period of inactivity or reduced activity.

vi. Post-ejaculatory interval

Post-ejaculatory interval is the time interval between ejaculation and the first intromission of the following series (Data not shown)

vii. Index of libido

Index of Libido is defined as the ratio of number mated to number paired expressed in percentage. This can be expressed mathematically as: % Index of Libido = Number mated x 100 Number paired (Data not shown).

Observation

In the present investigation, increase in mounting frequency and anogenital sniffing was noticed as compared to control. The attraction towards environment is more in control than drugs treated group. There is also increase in attraction towards female and genital grooming in treated rats, which is comparable with standard but was not statistically significant. An orientation activity reveals that the treatment of VMC causes increase in attraction of male towards female.

Several female proceptive and male precopulatory behaviour parameters were observed from the cage side when the VMC-treated male rats were introduced to the receptive female rats. The proceptive behaviour displayed by the female rats included ear-wiggling characterized by a rapid anteroposterior vibration of the ears, a short run where the female rats suddenly stops and present her posterior to the male rats (darting) and a short jump with stiff legs followed by immobility and presentation (hopping). The male rats, upon introduction, responded with immediate advances towards the females and displayed precopulatory behaviour such as chasing, anogenital sniffing which eventually culminated into mounting.

Lordosis was also displayed by the receptive female rats before, at the beginning and during the mounts. There was genital toileting after every mount that resulted in intromission.

Results are discussed in table 4.2.5.1.

Histopathological study:

At the end of the drug treatment and after blood collection the animals from each group was sacrificed with the help of diethyl ether euthanesia method and the abdomen was cut opened and the testis was carefully isolated and fixed in 10% formalin solution. The testis was embedded in paraffin and sectioned and stained with heamtoxylin and eosin and were examined microscopically for histopathological changes. -Kanitkar M et al.

Results are discussed in table 4.2.5.2

4.3. CLINICAL TRIAL

Aim

A systematic study of pharmaceutical products on human subjects (whether patients or non-patient volunteers) in order to discover or verify the clinical, pharmacological (including pharmacodynamics / pharmacokinetics), and or adverse effects, with the object of determining their safety and or efficacy.

The term impotence has traditionally been used to describe the inability of the male to attain and maintain adequate for sexual intercourse, and has been replaced by 'erectile dysfunction' since 1992. Male sexual dysfunction can be categorized as disorders of desire, disorders of orgasm, erectile dysfunction, ejaculation defect and failure of detumescence. The increasing incidence of male sexual dysfunction is necessitating more and rapid search into drugs with aphrodisiac potentials with negligible side effects. This study is intended to provide adequate information on the Clinical trial of *Venthamarai magarantha chooranam* with sex enhancing potentials.

Objectives:

- To evaluate the aphrodisiac effect of *venthamarai magarantha chooranam*
- To explore the efficacy of *venthamarai magarantha chooranam* in op patients with erectile dysfunction.

Design of the Study:

The Open clinical trial phase-2B

Study period was 2-3 months

Study Centre:

Govt.Siddha medical college hospital and Arignar Anna Government hospital of Indian Medicine and Homeopathy, Arumbakkam, Chennai – 106.

Study Participants:

Male patients in all races and ethnic groups were eligible for this trial. Treatment was administered on an inpatient basis. The patients will be selected from the In-patient department of Arignar Anna Government Hospital of Indian Medicine and Homeopathy, Chennai – 106.

Number of Subjects:

Number of participants will be 35-40.

Registration Process:

To register a patient, the following documents should be completed by the investigator.

- Copy of required laboratory tests
- Signed patient consent form
- Other appropriate forms (e.g., Trial profoma).

This Clinical trial is an ethical and scientific quality standard for designing, conducting and recording trials that involve the participation of human subjects. Compliance with this standard provides assurance to public that the rights, safety and well being of trial subjects are protected, consistent with the principles enshrined in the Declaration of Helsinki and ensures that clinical trial data are credible

Selection of patients

The patients were selected for clinical trail, those who had the following clinical features,

- Decreased erectile dysfunction
- Presence of nocturnal emission
- Premature ejaculation
- Decreased sexual desireness

Consent form

Patients were included in this clinical study only after getting the concern form accordanceof 'Helsinki". Voluntary written assent of a subject's willing to participate in this study and in its documentation. The confirmation is sought only after information about the trial including an explanation of its status as research, its objectives, potential benefits, risks and inconveniences, alternative treatment that may be available and of the subject's rights and responsibilities has been provided to the potential subject.

The patients were selected for clinical trials as per the following criterias, which are listed below

Inclution criteria

- Age-25-50
- Hormonal imbalance (testosterone)

- Psycological
- Premature ejaculation
- Decreased sexual desireness
- Nocturnal emission

Exclusion criteria

- Age above 50
- Cardiac diseases
- Diabetic mellitus
- Hypertension
- Spinal cord damage
- Substance abuse (alcohol)

Withdrawal criteria

- Irregular visit
- Incooprative patient
- Drug abuse
- Detoriation of vital signs
- Any adverse effects during the treatment period

Duration - 1-3 month (according to prognosis)

Investigation criteria:

- Complete blood count
- Lipid profile
- Blood glucose level
- Total testosterone level

Diagnosing of impotence:

Patient history

- Is the patient suffering from erectile dysfunction or from loss of libido or disorder of ejaculation?
- Is ED is due to psychological or physical factors?
- Prior history of smoking,heart attacks,strokes
- Is the patient taking medications that can contribute to ED?

Physical examination

- Not response in touch stimuli-problem in nervous system
- Small testicles, Lack of facial hair, enlarged breast –hormone problem
- Reducing blood flow-Atherosclerosis can be diagnosed
- Bending of the penis with painful erection-Peyronie's disease

Laboratory tests:

- Complete blood counts
- Blood glucose level
- Serum testosterone level

Testosterone level:

Testosterone level is chosen because it is the most costeffective way to screen. If the resultant testosterone level is abnormally low, the test should be repeated and followed-up with analyses of serum leutinizing hormone (LH), follicle stimulating hormone (FSH), free testosterone, and prolactin levels. Most of the testosterone in the blood is bound to a protein called **sex** hormone binding globulin (SHBG). Testosterone that is not bound ("free") can also be checked if a man or a woman is having sexual problems.

Two separate assessments may be performed as part of a testosterone test:

1. **Total testosterone**, which measures the entire amount of testosterone in the body, including both the amount bound to proteins that help transport the hormone through the bloodstream and free testosterone.
2. **Free testosterone**, which measures only the testosterone that's not attached to proteins.

No special preparations are needed for this test.Perform the test in the morning, when testosterone levels usually are highes.

Management: The aim of the *noineekkam* is based on

- To bring the three *thathus* in equilibrium

- Treatment of the disease
- *Paththiyam*
- *yogasanam*

“tpNurdj;jhy; thje; jhOk;” -rpj;j kUj;Jthq;fr; RUf;fk;

So before starting the treatment, *Agasthiyar kuzhambu* was given to all the patients, whom included in this study.

Drug and Dosage:

- The test drug *venthaamarai magarantha chooranam* was given to the patients at the dose level of **500 mg** once in a day with honey before food.
- The duration of the treatment varies according to the severity and response of the treatment.
- It had been given minimum of 1-3 months.

Dietery advice

Nuts:

- Walnuts
- Pine nuts

Fruits:

- Bananas
- Dates
- Figs
- Grapes

- Pomegranate
- Straw berry
- Mango
- Peach

Vegetables:

- Carrots
- Fennel
- Onions

- Garlic
- Cardamom
- Asafoetida and Pepper

Yogasanas:

Aasanas are streanthen the genital organs, those are following below.patient adviced to follow these aasanas.

- Sarvangasana
- Savasana
- Yogamuthra
- Aswini muthra
- Bathrasana

Criteria for assessment of response to therapy:

1) Marked Relief : 75%-90% relief in the presenting signs and symptoms marked normality pathological investigation.
2) Moderate Relief : 60%– 75% relief signs and symptoms, moderate normality of pathological investigation.
3) Mild Relief : 50%-60% relief of signs and symptoms no marked changes in pathological investigations.
4) Poor : Below 50% relief of signs and symptoms

Observation:

- The duration of the treatment ranged between 30-90 days.
- At the time of treatment, no adverse effects were observed.
- The drug was well accepted by all the patients.

Ethical Review:

The protocol and any amendments have been submitted to the Govt. Siddha Medical College, Chennai-106. Institutional Ethical Committee (IEC) for formal approval to conduct the study. All subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. This consent form was also submitted with the protocol for review

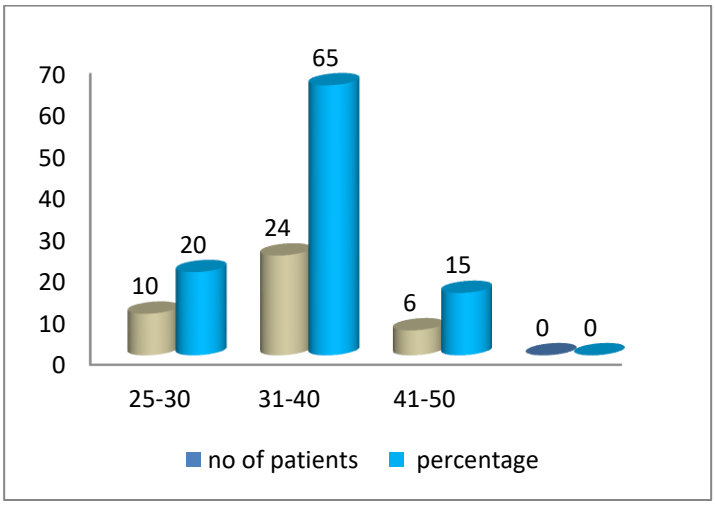
and it was approved by the IEC. The formal consent of a subject, using the IEC-approved consent form, has been obtained before that subject was admitted to any study procedure. This consent form was signed by the subject or legally acceptable surrogate, and the investigator-designated research professional obtaining the consent.

Statistical analysis:

The data were subjected to paired student‘t’ test to determine the significance of changes followed by comparisons to analyze the significance of difference within the before and after treatment. P values of <0.05 were taken as significant. Results are discussed in table 4.3.6.

Table:4.3.1 AGEWISE DISTRIBUTION

SL.NO	AGE	NO OFPATIENTS	PERCENTAGE (%)
1	25-30	10	25%
2	31-40	24	60%
3	41-50	6	15%



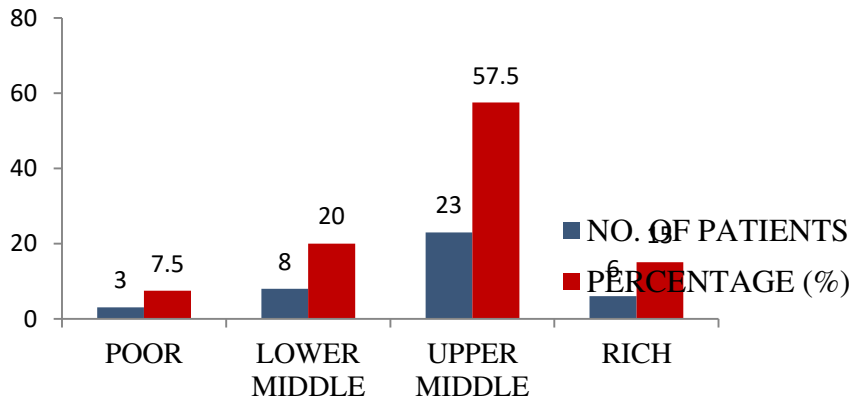
Inference

Among 40 patients,

- 10 patients belongs to the age group of 25-30 years
- 24 patients belongs to the age group of 31-40 years
- 6 patients belongs to the age group of 41-50 years

Table: 4.3.2 SOCIO-ECONOMIC STATUS

SL. NO	SOCIO – ECONOMIC STATUS	NO. OF PATIENTS	PERCENTAGE (%)
1	Poor	3	7.5
2	Lower middle	8	20
3	Upper middle	23	57.5
4	Rich	6	15
TOTAL		40	100



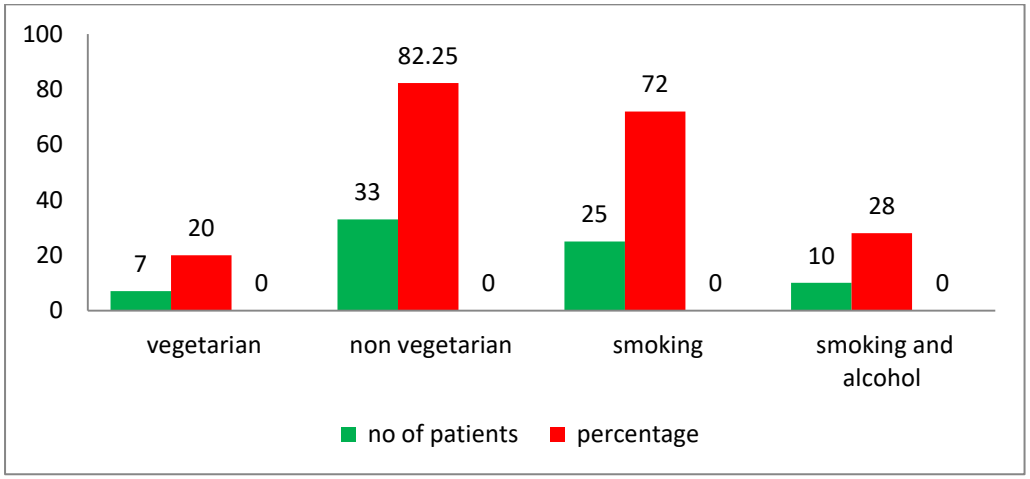
INFERENCE:

Among 40 patients,

- ❖ 3 patients were poor.
- ❖ 8 patients were lower-middle.
- ❖ 23 patients were upper middle.
- ❖ 6 patients were rich

Table: 4.3.3 PERSONAL HABITS

SL. NO	PERSONAL HABITS	NO. OF PATIENTS	PERCENTAGE (%)
1	Vegetarian	7	20
2	Non-vegetarian	33	82.25
3	Smoking	25	72
4	Alcohol&smoking	10	28



IMPROVEMENT IN SIGNS AND SYMPTOMS Table: 4.3.4

SL. NO	SIGNS AND SYMPTOMS	NO. OF PATIENTS			
		BT	AT	IMP.	IMPROVEMENT (%)
1	Erectile dysfunction	40	5	35	87.5
2	Decrease sexual desireness	21	3	18	86
3	Nocturnal emission	19	5	14	74
4	Premature ejaculation	28	5	23	82
5	Decrease erection duration	25	8	17	68
6	Early morning erection	18	5	13	72

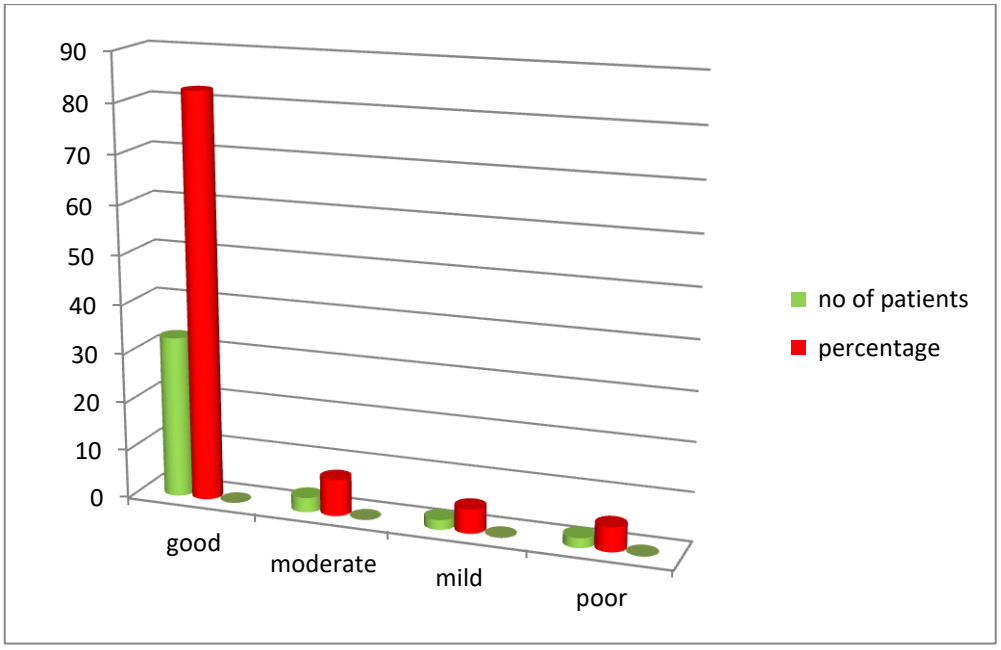
INFERENCE: Among 40 patients,

- ❖ 35 out of 40 patients were relieved from Erectile dysfunction.
- ❖ 18 out of 21 patients were relieved from Decrease sexual desireness.
- ❖ 14 out of 19patients were relieved from nocturnal emission.
- ❖ 20out of 28 patients were relieved from premature ejaculation.
- ❖ 23 out of 25 patients were relieved from decrease erection duration.
- ❖ 13 out of 18 patients were relieved from early morning erection.

GRADATION RESULT

Table: 4.3.5

SL. NO	LEVEL OF IMPROVEMENT	NO.OF PATIENTS	PERCENTAGE (%)
1	Good	33	82.5
2	Moderate	3	7.5
3	Mild	2	5
4	Poor	2	5
TOTAL		40	100



INFERENCE:

Among 40 patients,

- 33 patients were good.
- 3 patients were moderate
- 2 patients were mild.
- 2 patients were poor.

STATISTICAL ANALYSIS

DESCRIPTIVE STATISTICAL FOR IMPROVEMENT OF SIGNS & SYMPTOMS IN *"SAMBOGA VATHAM"*

PAIRED "t" TEST RESULT:

"p" value & statistical significance:

Table: 4.3.6

Treatment	Signs & symptoms	Mean	S.D	S.E.M
Before treatment	6	25.17	8.18	3.34
After treatment	6	20.00	8.15	3.33

From the table we calculated the descriptive statistic like Mean, S.D & S.E.M of Mean for the improvement score before and after treatment.

"t" Table: 4.3.7

t-Table	S.D	S.E.M	"t" Value	"p" Value
Pre vs Post	5	0.683	8.7831	0.0003

The two tailed "p" value equals 0.0003, by conventional criteria, this difference is considered to be extremly statistically significant.

From the above table we got a significant difference ($p < 0.05$). So we conclude that there is an improvement between before and after treatment.

5. RESULTS & DISCUSSION:

Various studies have been carried out in this trial drug *Venthamarai magarantha chooranam*. The study includes literary collections, Pharmacognostic study, physico and Phyto chemical analysis, toxicological study, pharmacological study and clinical study. *Venthamarai magarantha chooranam* was taken for the treatment of Impotence. The drug has been selected for the treatment of Impotence in reference with ***Theraiyar Porut panbu Nool*** written by **K.S.Murugesa Mudaliyar.**

Literary collections about the drug from various text books were done. It indicates the efficacy of the drug in the treatment of Impotence. **Botanical aspect** deals with the identification, description, cultivation and ethno medicinal importance of the plant. **Gunapadam aspect** expressed that the drug possess good Aphrodisiac property.

Literary collections about the drug from various text books give engross trust about its Aphrodisiac activity.

From the literatures, the trial drug has sweet and astringent taste, the potency of the drug is Cold and Bio- transformation of the drug is sweet. As per the siddha concept, this disease occurs due to the derangement of the vatha and pitha humour.

“thjk; Nkypl;lhy; kJuk; GspAg;G

NrjKwr; nra;Ak; rpiwak;” - fz;Zrhkpak;

The properties of sweet taste are decreases the vatha and pitha humour, increases the kabha humour. But the astringent taste increases vatha humour, and decreases the kabha and pitha humours. Sweet gives nutrition to semen and other thathus. Sweet and cold potency extends the life span and increase potency. Cold potency gives pleasure and fullfilment. By giving this drug it normalise the deranged humours, reduces the signs and symptoms and works as a kayakarpam.

Phyto chemical analysis:

Presence of phyto-chemical constituents of the test drug are Alkaloids, Terpenoids, Cardiacglycosides, Steroids, Flavonoids, Tannins, Phlebotannins, Glycosides, Phytosterols, Carbohydrates.

Table: 4.2.1

PHYTO CHEMICAL CONSTITUENTS	RESULTS
1.Tannins	**Present**
2.Phlebotannin	**Present**
3.Saponin	Absent
4.Flavonoids	**Present**
5.Steroids	**Present**
6.Cardiac glycosides	**Present**
7.Terpenoids	**Present**
8.Carbohydrates	**Present**
9.Alkaloids	**Present**
10.Glycosides	**Present**
11.Protein	Absent
12.Phenolic compounds	Absent
13.Phytosterols	**Present**
14.Fixed oil	Absent
15.Volatile oil	Absent

For the above results the presence of **Alkaloids** and **Terpenoids** were confirmed and are important to cure the chronic diseases and nervine disorders. The availability of Flavonoids in the trial drug clearly indicates the drug's potency against the degenerative changes and its anti-oxidant property. **Flavonoids** have vaso relaxant properties, which

may caused by increase in **NO production** in vascular bed and a decrease in its destruction.

The presence of **Steroids** and **Phytosterols** were confirmed ability to lower cholesterol reduce risk of heart disease and **enhancing sexual performance**. Phyto sterols work mostly with in the digestive system, blocking the absorption of cholesterol from the intestine.The availability of **Tannins** in the trial drug indicates its **neuro protective** property. The presence of **Cardiac glycosides** and **Phlobatannins** are essential in the treatment of Cardiac disorders and vascular complications.

By the available phytochemicals, the trial drug has the therapeutic potency of **vaso dilatation, enhancing libido** and **neuro protective** in the erectile dysfunction.

Physico chemical analysis

Table: 4.2.2

S.No	Parameter	I	II	Mean
1.	Loss on Drying at 105°C	13.986%,	14.144%,	14.065%
2.	Total Ash	5.275%,	5.823%,	5.549%
3.	Acid insoluble Ash	0.572%,	0.501%,	0.537%
4.	Water Soluble Extractive	13.789%,	14.205%,	13.997%
5.	Alcohol Soluble Extractive	9.814%,	10.041%,	9.928%
6.	pH	7.07		
7.	TLC	Enclosed		

By the above results, the trial drug has very low foreign matter and acid insoluble ash, indicates that trial drug will digest completely in human GI tract. The analytical parameters like total Ash value, Acid insoluble ash value, Loss on drying values are helping us to interpret the digestion and solubility capacity of the crude extract. As per the result the tested sample contains good percentage of solubility as well as digestive capacity.

Chemical analysis of test drug

Table: 4.2.3

Test for Chemicals	Observation	Inference
Ammonium	No appearance of brown colour	+
Sodium	No appearance of intense yellow colour	--
Magnesium	No formation of white precipitate	+
Aluminium	No characteristic changes	--
Potassium	No formation of yellow precipitate	--
Calcium	Formation of white precipitate	+
Ferrous iron	Appearance of blood red colour	+
Copper	Formation of blue precipitate	+
Zinc	No formation of white precipitate	+
Arsenic	No formation of brownish red precipitate	--
Mercury	Formation of yellow precipitate	--
Lead	No formation of yellow precipitate	--
Sulphate	No formation of white precipitate	--
Chloride	Formation of white precipitate	--
Phosphate	No formation of yellow precipitate	+
Carbonate	Formation of effervescence	--
Fluoride & Oxalate	No formation of cloudy appearance	+
Nitrate	No characteristic changes	--
Starch	No formation of blue colour	--
Reducing sugar	Mild colour changes	Trace
Alkaloids		

Meyer's method *Dragendroff' method*	Appearance of cream colour Appearance of orange precipitate	+ +
Amino acids	Formation of violet precipitate	+
Tannic acid	Formation of bluish black precipitate	+
Tannins	Formation of white precipitate	+
Unsaturated compounds	Get decolorized	+
Saponins	No froth formation	--
Sugar– *Bendict's method*	Mild colour change	+
Steroids – *Liberman Burchard test*	No formation of red colour	+
Protiens – *Biuret test*	Formation of violet colour	+
Flavanoids	No formation of pink colour	+
Phenols	No formation of deep sreen colour	+

From the preliminary chemical analysis of *Venthamarai poo magarantha chooranam* have an idea that the trial drug have Mg , Ca, Fe, Cu, Zn, Fluride, Oxalate, Phosphate, Ammonium, Alkaloids, Amino acids, Tannic acids, Tannins, Flavanoids, Phenols and Protiens.

Calcium ions are playing important role in the squeezing and relaxing of muscle, it is one of the micro nutrient which help to release hormones and other chemicals. It is sending and receiving nerve signals also. So Ca ions help to promote the nerve signals and release hormones, regulates squeezing and relaxing of muscle in erectile dysfunction. Also it keeps heart rate normally.

Mg ions have a role in oxidation of fattyacids, activation of amino acids and neurotransmission.It is the fourth most abundant mineral in the human body and essential to good health.

Zn and Amino acids are the important substance for vaso dilatation. So it may be increases the blood flow in the penis and increases the Libido, and can helpful in erectile dysfunction.

Cu ions are necessary for the formation of red blood cells and other components of the blood system. It regulates the body function such as neuro transmission.Copper also function to neutralize the free radicals that is which are unstable oxygen by products. It has anti-oxidant property which prevents aging.

Following above description, the major ions are performing an important role in the erectile disorders and promots erection. They decrease the symptoms and signs.

Toxicological study:

The toxicity and chronic toxicity studies results revealed the *Venthamarai magarantha chooranam* does not possess toxicity at a dose of 5000 mg / kg body weight. There were no behavioural changes / signs or mortality of animals observed during the experimental period. In the AOT study the trial drug given (*venthamarai magarantha chooranam* mixed with CMC) animals were survive after 48 hrs and showing good response in Alertness, Touch response, Gripping , Increased motor activity, and Normal respiration.

No	**Dose mg/kg**	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
1.	**500**	+	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-
2	**1000**	+	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-
3	**2000**	+	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-
4	**5000**	+	-	-	-	+	+	-	-	-	-	-	-	-	-	-	-	-	-	+	-

Table: 4.2.4 Dose finding experiment and its behavioral Signs of Toxicity

1.Alertness	6. Touch Response	11.Catatonia	16. Exophthalmos	
2. Aggressiveness	7. Decreased Motor Activity	12. Muscle relaxant	17. Diarrhoea	
3. Pile erection	8. Tremors	13.Hypnosis		18. Writhing
4. Grooming	9. Convulsions	14.Analgesia	19. Respiration	
5. Gripping	10. Muscle Spasm	15.Lacrimation	20. Mortality	

Pharmacological study:

VMC at 500mg/kg body weight, both MF and IF were increased (P<0.01) compared to the 2% CMC in saline-administered control and body weight also significantly increased. The MF of the *VMC* treated animals was remarkably altered and it was statistically significant. Administration of single dose of *VMC* at 500mg/kg body weight the EF increased significantly (P<0.01). There was vaginal plug in the female's vagina after ejaculation was observed.

Further administration of the *VMC* for 14days increased the EL whereas the PEI decreased. The changes in EL and PEI were statistically significant (P<0.01). The male sexual behaviour parameters, which included percentages of index of libido, mounted, intromitted, ejaculated and copulatory efficiency were higher in the *VMC*-treated animals compared to the 2% CMC in saline treated control animals. To understand the scientific reasons behind these traditional claims, an attempt was made to investigate the effects of *VMC* in this study. In this investigation, treatment of the male rats with the *VMC* enhanced the sexual behaviour of the male rats with 500mg/kg body weight producing better results. These sexual behaviours were preceded with proceptive and precopulatory behaviours in the animals. (For example, the ear wiggling, darting, hopping and lordosis by the receptive female rats in this study implied intense proceptivity and receptivity).

The pursuit of the female animals (the males running behind the female animals in close contact) suggested imminent copulation. Mount Frequency and Intromission Frequency are useful indices of vigour, libido and potency. While the number of mount (MF) reflects sexual motivation, increase in the number of intromission (IF) shows the efficiency of erection, penile orientation and the ease by which ejaculatory reflexes are activated. Therefore, the increase in MF and IF (P<0.01) following the administration of VMC at 500mg/kg body weight observation suggests enhanced libido. Such enhancement

of libido might have arisen from increase in the number of concentrations of several anterior pituitary hormones and serum testosterone, which in turn stimulated dopamine receptor synthesis and sexual behaviour.

This sexual behaviour may also be due to androgenic and gonadotropic activities of *VMC* in male rats. Furthermore, since intromission is not possible without adequate erection and coordinated activity of penile muscles, the increase in IF by the *VMC* in this study suggests that the mechanism of penile erection was activated. Therefore, *VMC* may increase potency by allowing or sustaining erection. The increase in ejaculation frequency by the *VMC* at 500mg/kg body weight is an indication of enhanced aphrodisiac effect. The presence of plug in the vagina of the female rats indicated that ejaculation occurred. This was further complemented by the genital toileting observed in the male rats.

Mount latency and intromission latency are indicators of sexual motivation. ML and IL are inversely proportional to sexual motivation. The decrease in the intromission latencies observed ($P>0.05$) at the dose of 500mg/kg body weight of the VMC in this study might imply stimulation of sexual motivation and arousability but it was not statistically significant when compared to control. Furthermore, the prolonged ejaculation latency by the *VMC* 500mg/kg body is an indication that copulatory performance in the animals was enhanced. It may also imply prolongation in the duration of coitus.In addition, the display of pelvic thrusting during intromission and ejaculation by the *VMC*-treated animals in this study further indicated that the male copulatory organ was in contact with the vaginal orifice, which might have activated or strengthened lordosis in the female rats. The post ejaculatory interval is considered an index of potency, libido and the rate of recovery from exhaustion after first series of mating. An increased post ejaculatory interval indicates that the male is sexually exhausted and the intensity of sexual behaviour will be reduced in subsequent mating.

Therefore, the significantly decreased post ejaculatory interval at 500 mg/kg body of *VMC* may be attributed to enhanced potency and libido or less exhaustion in the first series of mating or both, more so, since the values of PEI obtained in this study are close to the 90 min cut-off. In addition, the higher values of the male rat sexual behaviour parameters following treatment with the *VMC* when compared with the 2% CMC in saline-administered control animals are indications of significant and sustained increase in sexual activity.

As indicated in siddha literature, *VMC* may be effective as aphrodisiac through mechanisms such as vasodilation, generation of nitric oxide, elevation of androgens and gonadotropins. It may be inhibits the enzyme PDE-5 in the corpora cavernosa of the penis, there by prolonging the life of cGMP at that site,this causes relaxation of the smooth muscle of the corpora cavernosa permitting inflow of blood in to the sinuses resulting in better erection. It has also been documented that sexual behaviour and erection are dependent on androgen, which may act through central and peripheral mechanisms.

In conclusion, our results have revealed that the *VMC* at the dose of 500mg/kg body weight could be used as a stimulator of sexual behaviour in male rats and also indicates the profound increase in improvement of sperm health. This study thus supports the acclaimed aphrodisiac use. The data obtained revealed that the action of *VMC* was due to the influence on both sexual arousal and performance.

Table: 4.2.5.1 Effect of *Venthamarai Magarantha Chooranam* on Sexual Behaviour in Rats

Groups	**Parameters (Duration in Seconds)**					
	Mount frequency	**Intromission frequency**	**Mount latency**	**Intromission latency**	**Anogenital sniffing**	**Genital grooming**
Control	2.24±0.36	298.18±8.14	0.37±0.18	806.13±267.15	3.22±0.63	1.78±0.13
Standard (Sildenafil)	12.41±1.22**	115.19±7.52**	1.48±0.18**	174.99±95.15ns	15.02±1.38**	4.18±0.38**
VMC (500mg/kg)	7.85±0.96**	171.06±4.20**	1.63±0.25**	485.72±188.04ns	10.10±1.24**	2.92±0.50ns

Values are mean of 6 animals ± S.E.M. (Dunnett's test). $^{ns}P>0.05$; $^{**}P<0.01$ compared to control.

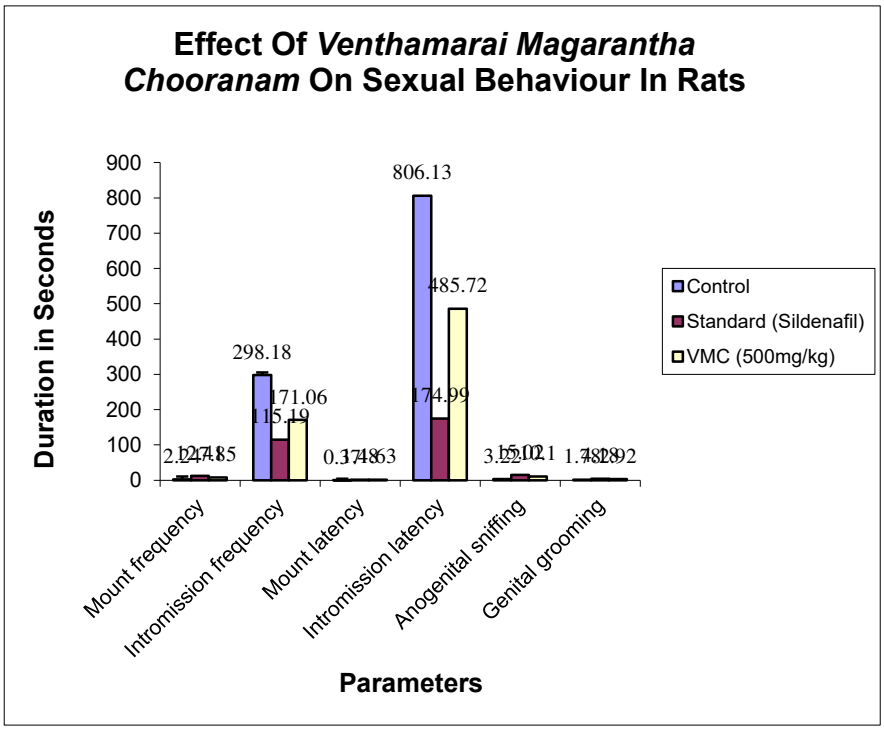
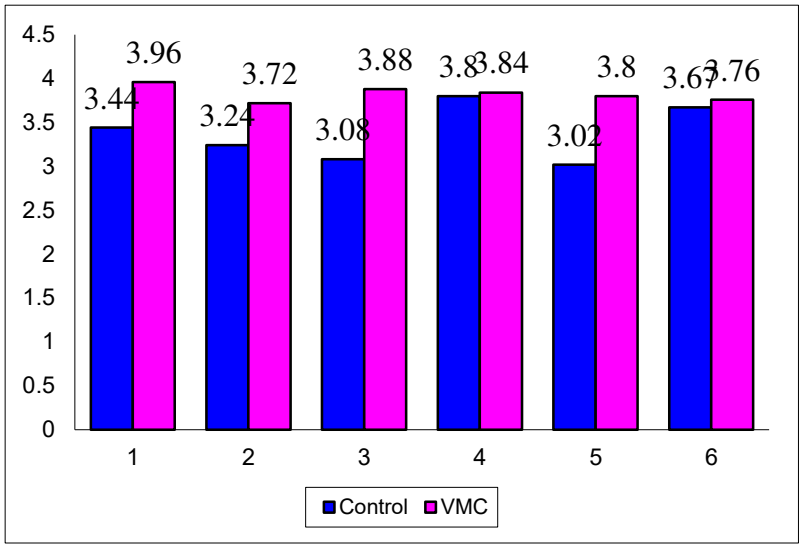


Table: 4.2.5.2 Effect of *VMC* on serum testosterone levels of rats in ng/ml.

Serum testosterone level (ng/ml)	
Control	**VMC 500mg/kg**
3.44	3.96**
3.24	3.72**
3.08	3.88**
3.80	3.84
3.02	3.80**
3.67	3.76*

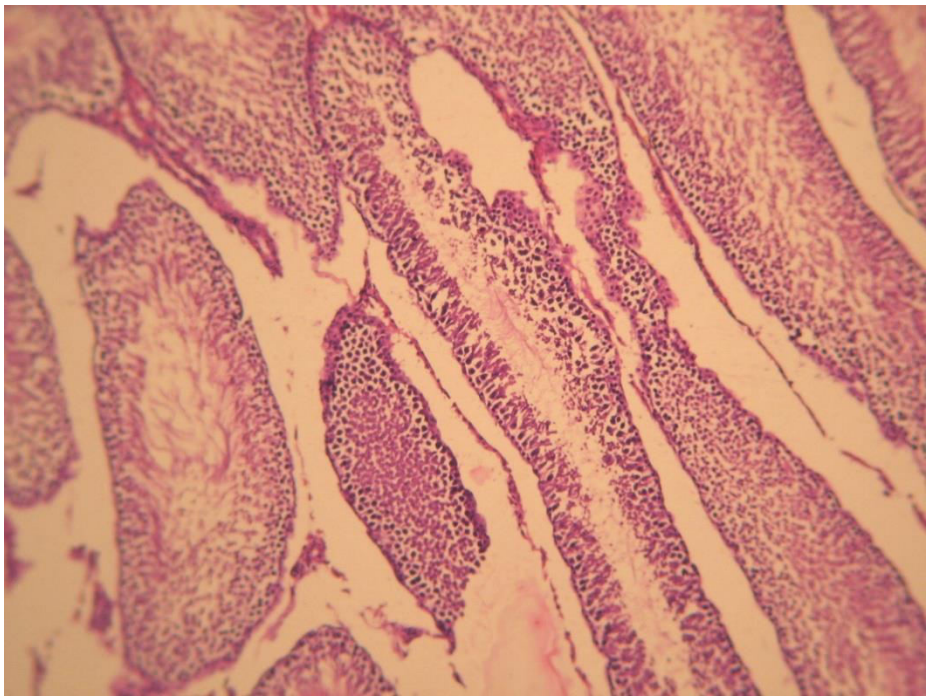


Histological study on Testis:

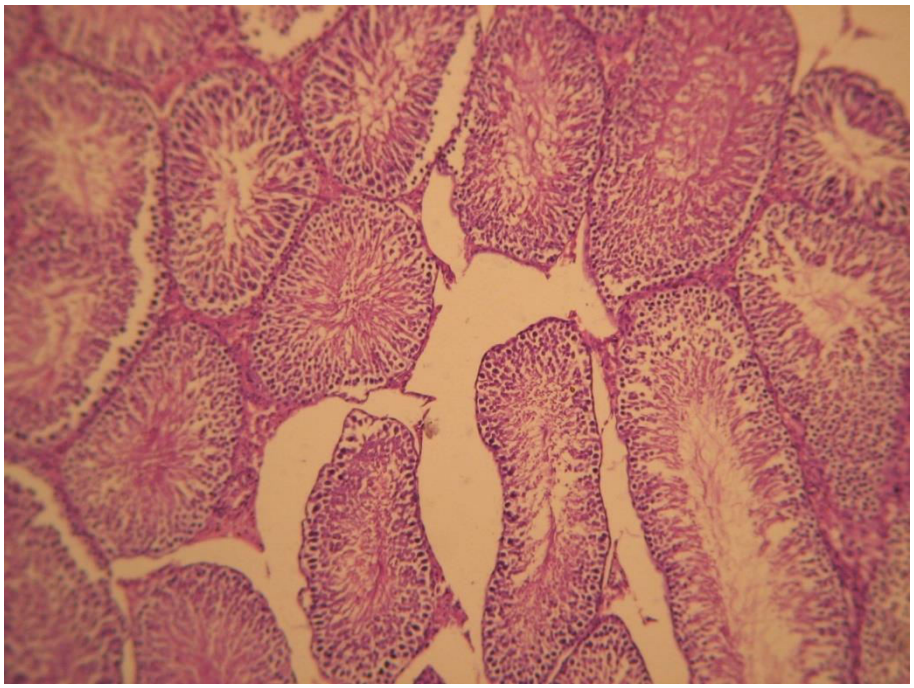
The testis section of control group animals showed normal histological texture. The diameter of seminiferous tubules varied within a range. The tubules having maximum diameter, were not abundant and well within range. The cuboidal germinal epithelium exhibited normal shape and size. Sertoli cells had many cytoplasmic processes, which were normal in size. Spermatozoa were embedded in the sertoli cells and showed normal cytoplasmic granulation. Leydigs cells had normal nuclear size. Luminal part of the tubule were normal in number with bundles of spermatozoa. Spermatozoa with long tail with small distinct head were more visible. The results shown no other significant changes were noted when compared with the control group.

Figure: 4.2.5.1

NORMAL GROUP HISTO PATHOLOGY OF TESTIS



VMC TREATED GROUP



Clinical study:

40 patients in male sex were selected. They were treated as out- patients in the Post graduate department of Gunapadam, Govt.Siddha medical college hospital and Govt. Arignar Anna hospital, Arumbakkam, Chennai- 106.Because of incooperation of patient unable to admit the patient in the IP ward.

Among 40 patients, 35 out of 40 patients were relieved from Erectile dysfunction,18 out of 21 patients were relieved from Decrease sexual desireness,14 out of 19patients were relieved from nocturnal emission,20out of 28 patients were relieved from premature ejaculation,23 out of 25 patients were relieved from decrease erection duration.

The results revealed that the drug possess 82.5% good relief, 7.5% moderate relief, 5% mild relief, 5% cases there was no improvement.

In this clinical study, the Open clinical Trial was conducted on 40 volunteer patients after getting the proper informed consent. Since, the treated disease ED is a phsycological, nervous and hormonal disorder. As per the obtained results 87.5% of cases (marked+moderate) were releaved that 82.5% improvement in the signs and symptoms and bio chemical parameters. With the obtained results the trial medicine has proven itself a promising drug of choice for the Erectile dysfunction patients.

Table: 4.3.4 Improvement in signs and symptoms:

SL. NO	SIGNS AND SYMPTOMS	NO. OF PATIENTS			
		BT	AT	IMP.	IMPROVEMENT (%)
1	Erectile dysfunction	40	5	35	87.5
2	Decrease sexual desireness	21	3	18	86
3	Nocturnal emission	19	5	14	74
4	Premature ejaculation	28	5	23	82
5	Decrease erection duration	25	8	17	68
6	Early morning erection	18	5	13	72

Stastical results:

Improvements of signs and symptoms by statistical analysis shows the two tailed "p" value equals 0.0003, by conventional criteria, this difference is considered to be very statistically significant. From the above results $p < 0.05$, it shows the improvement in the subjective parameters produced by *venthamarai magarantha chooranam* statistically significant.

P value and statistical significance:

The two-tailed P value equals 0.0005. By conventional criteria, this difference is considered to be extremely statistically significant.

Confidence interval:

The mean of Group One minus Group Two equals 5.17

95% confidence interval of this difference: From 3.49 to 6.85

Intermediate values used in calculations:

t = 7.8995, df = 5, standard error of difference = 0.654

Table: 4.3.6

Group	Mean	SD	SEM	No.
Group One	**25.17**	**8.18**	**3.34**	**6**
Group Two	**20.00**	**8.15**	**3.33**	**6**

6. CONCLUSION

The trial drug *Venthaamarai magarantha chooranam (Nelumbo nucifera,Gaertn)* is selected from the classical siddha text *Gunapadam- Mooligai vaguppu, Theran porut panbu nool*, for the evaluation of safety and efficacy in the management of Erectile dysfunction.

The trial drug was duely identified and authenticated by the botanist and *Gunapadam* experts.

Though the drug has the sweet taste, the cold potency and bio-transformation in to sweet, clearly indicates its activity on genital organs.

The presence of Ca and Zn ions indicates that they help in maintaining the vaso dilatation. The other components Tannins, Phlobatannins, Phenolic Compounds, Flavonoids, Alkaloids, Steroids, Phytosteroids and Cardiac Glycosides are also responsible for its Aphrodisiac property.

The acute oral toxicity results revealed that the *Venthaamarai magarantha chooranam* does not possess any toxicity even at a higher dose of 5000 mg / kg body weight. So, the drug was classified under class 5 in safety aspects. From this maximum tolerable dose level the therapeutic dose (1/10 of MTD) for the pharmacological study was determined.

Single dose (500 mg/kg body weight, oral) treatment with the siddha drug *venthamarai magarantha chooranam* produced remarkable aphrodisiac activity. Finally it can be concluded that *venthamarai magarantha chooranam* was found to possess remarkable ($P< 0.005$) in male rats.

The open clinical trial results reveal that 87.5% of patients were having 82.5% of improvement in the clinical futures and biochemical reports. The study validates the effectiveness of herb in improving as well as preventing the functionality of sexual organ as well as substantiates the hype that these drug have aphrodisiac activity and helpful in improving the sexual behavior and performance.

The drug is easily available and preparation is very simple. The trial medicine is cost effective. No adverse effects were produced during the entire course of treatment. Conclusively, that the drug "*Venthamarai magarantha Chooranam*" (*Nelumbo nucifera, Gatern*) gives a new hope in the field of Impotence treatment.

7.**SUMMARY**

"*Venthamarai magarantham*" were collected from Kumbakonam and purified then powdered and stored. This drug was subjected for various studies by the author.

Venthamarai magarantha Chooranam was selected by the author for this study to establish the Aphrodisiac activity.

To collect the information about the drug, various text books, literature were referred. From them, the author came to an idea about the drug and its efficacy on Impotence.

A brief description about botanical aspect of the *Venthamarai magarantha Chooranam* and its identifying characters and Phyto chemical datas were given.

The wide use of according to Gunapadam aspect as well as in various siddha literatures were discussed with much importance to that of preparation related to Aanmaikuraivu.

The Phyto chemical analysis of the drug shows that it contains Potassium, Calcium, Zinc, Magnesium, Iron, and Tannins, Phlobatannins, Phenolic Compounds, Flavonoids and Cardiac Glycosides. It is related in treatment of Erectiledysfunction.

The preclinical study showed that the drug has got safety and significant Aphrodisiac activity.

The patients were responding well from the beginning of the treatment and no adverse effects were reported.

The clinical result reveals that 87.5% of patients were having 82.5% of improvement in the clinical futures and biochemical reports.

This present study confirms that *Venthamarai magarantha Chooranam* has the remarkable Aphrodisiac activity and high therapeutical value against the clinical symptom of Erectiledysfunction.

PART-2

BRONCHO DILATOR ACTIVITY OF MARICHIYATHI MAATHTHIRAI

1. INTRODUCTION

The prevention and the cure of illness are the basic aims of all systems of medicine. The Siddha system supercedes these aims and aim for the "**Immortality of the body".** According to siddhars, **'Nature is man, Man is nature**' therefore both are essentially one.The universe consists of two essential entities,matter and energy which is siddhars call '*Siva'* and *'Shakthi'*.The two has to co-exist and are inseperable.The universe consists of five elements and these eliments should not be confused with the elements of modern chemistry.They are primordial elements.

They are`*Munn*' (solid) *'Neer' (*fluid), '*Thee'* (radiance),'*Vayu*' (gas),and *'Akasam'* (ether). Every thing in this world is created and evolved from this five elements be it animal, vegetable or mineral falls under these categories. From the five fundamental elements *Thirithosham or Mukkuttram* that is *Vatham, Pitham*, and *Kabam* is formed. When there is an equilibrium maintained, these entitis are called as Thathu and when there is a disturbance in the equilibrium, a disease is horn.

From the script of Thiruvalluvar, it is stated that,

kpfpDk; FiwapDk; Neha;nra;Ak; E}Nyhu;

tspKjyh vz;zpa %d;W. -jpUf;Fws;

Siddha medicines identifies this human body is a part of entire cosmos and when there is a difference or difficulty arises from the environmental it is reflected in the human body also. One important such disease is "*Suvasakasam"* which can be equated nearly as Bronchial asthma from its signs and symptoms.

Siddha medicines are being increasingly utilized to treat a wide variety of diseases, though the knowledge about their mode of action is relatively scanty. There is a growing interest regarding the pharmacological evaluation of various drugs used in traditional system of medicine. Allergies occur when a hypersensitive immune system reacts to a common or unusual substance. The number of individuals suffering with allergic illnesses

is increasing in the industrialized, as well as in large cities of developing countries. Allergies also have reached high prevalence and incidence in all over the world.

Most of the allergic diseases are due to allergens like airborne pollens (grass, trees, and weeds), house-dust, mites, animal dander, cockroaches, fungal spores, etc. Overproduction of histamine in body triggers the allergic and inflammatory responses. Drugs always exist in the nature to prevent the effect of histamine. Asthma is one of the common global health problems among the individual of all ages. About 5-10% populations were suffered due to asthma globally and the prevalence is increasing day by day mostly in children. Today numbers of synthetic antihistaminic drugs are available for symptomatic control of asthma along with their quit disturbing side effect. So the siddha medicines are the best alternative in treatment along with safety and security.

Among several respiratory diseases affecting man, Bronchial asthma is the most common disabling syndrome. Despite of the availability of a wide range of drugs, the relief offered by them is mainly symptomatic and short lived. Moreover these drugs produce side effect. Therefore, there is a dire need to identify effective and safe remedies to treat bronchial asthma. Several medicinal plants having Broncho dilator activity are being found to be effective in the treatment of bronchial asthma. The herbo mineral formulations described in siddha have been the basic of treatment of various human diseases.

The current accepted modern medicine or allopathy has gradually developed over the years by scientific and observational efforts of scientists.However, the basis of its development remains rooted in traditional medicine and therapies. Siddha herbal medicines are being used by nearly about 80% of the world population.Siddha system provides many such cost effective, simple herbo-mineral remedies with good results from time memorial.But not many scientific documentation on its pharmacological studies are existing.

So I have taken up a simple, cost effective drug ***'Marichiyathi maaththirai'*** for my dissertation work on Bronchial asthma. Hence, in the present study aimed at elaboration of the Anti-histaminic and Broncho dilator activity of ***Marichiyathi Maththirai*** in animal model and to explore the clinical efficacy and safety of the trial drug in patient with Bronchial asthma.

2. AIM AND OBJECTIVES

Aim

Some human health problems have taken different dimensions during the past five decades may due to environmental hazards. *Suvasakasam* is one of the diseases among them. Roughly 10% of population suffers from *Suvasakasam.* Today numbers of synthetic antihistaminic drugs are available for symptomatic control of asthma along with their quit disturbing side effect. The available treatment options for upper and lower respiratory tract allergic diseases have major limitations owing to low efficacy, associated adverse effects and compliance issues. Therefore the world is in search for suitable traditional remedies, which can serve mankind from dawn of civilization. In order to achieve this aim an attempt was made to establish the scientific validity for the bronchodilator and antihistaminic property of *Marichyathi Mathirai* (MM).

Objectives:

The main objective of the present study is to high light the efficacy of ***Marichiyathi maaththirai*** on ***Suvasakasam***, the following methodology was adopted to evaluate drugs in MM and its standardization studies.

- Identification of the drugs in the MM
- Preparation of *Marichchiyathi maththirai* as per classical literature
- Collection of materials from the relevant literature
- Phyto-chemical study of Test drug
- Physio chemical analysis of Test drug
- Evaluation of the toxicity of Test drug
- Evaluation of the Anti-histaminic of Test drug on isolated Guinea pig ileum
- Evaluation of Broncho dilator activity of test drug in experimental animal model
- Clinical efficacy of Test drug on Suvasakasam (Bronchial asthma)
- Statistical analysis

3. REVIEW OF LITERATURE

The literature support for my trial drug were collected from the Siddha text books, classical literatures of Siddha, Materia medica, Compendium of Medicinal Flora, Wealth of India, Chemical Abstracts, MAPA, Internet Journals and Search web sites.

3.1. Botanical aspect

kpsF

Botanical name **:** *Piper nigrum*

Family **:** Piperaceae

Part uses : Fruit

Taxonomical classification:

Kingdom : Plantae

Division : Angiosperms

Order : Piperales

Family : Piperaceae

Genus : Piper

Species : nigrum

Distribution:

The fruit, known as a peppercorn when dried, is approximately 5 millimetres (0.20 in) in diameter, dark red when fully mature, and, like all **drupes** contains a single **seed** Peppercorns, and the powdered pepper derived from grinding them, may be described simply as pepper.

Black peppers are native to **India** and are extensively cultivated there and elsewhere in **tropical** regions. Currently **Vietnam** is the world's largest producer and exporter of pepper, producing 34% of the world's *Piper nigrum* crop as of 2008.

3.2. Gunapadam aspect

kpsF- *Piper nigrum*

NtWngau;fs; :

kuPrk;>fwp> fhak;> fypid> Nfhsfk;> jpuq;fy;> kpupay;> rUk ge;jk;> FWkpsF> kiyahsp.

“khjkWf;fp khepj;jpiu Nghf;fp

Nghjkyj;ij Nghf;fpa rpw;gup

fhjk; guprpf;ff; fLq;fhu Nfhgj;jp

Ntjkpsfpd; tpsq;fpa ehkNk”.

-rl;il Kdp epfz;L-1200

Vernacular names:

Tamil	- Milagu
English	- Pepper
Telugu	- Miriyalu
Malayalum	- kurumilagu
Kannadam	- Menasu
Sanskrit	- Maricha
Hindhi	- Kali mirich
Persian	- Filfliaisiah

kpsfpd; ngUik:

“jPahfp naq;Fk; jpupAkij ahtj;J

Nkhahk nyg;gbA Kz;lhf;fhw;- ghahJ

Nghe;jpkpu;th jq;fpue;jp Gz;zPUk; kz;ztu;f;Fk;

fhe;jpnka;th jr;rYg;igf; fha;”.

-Njud; ntz;gh

gad;gLk; cWg;G : tpij> nfhb

Rit : ifg;G> fhu;g;G

jd;ik **:** ntg;gk**;**

gpupT : fhu;g;G

nra;iffs;;;;;:

fhwYz;lhf;fp ntg;gKz;lhf;fp

mfl;Ltha;tfw;wp tPf;fq;fiur;rp

Kiw ntg;gfw;wp thjklf;fp

jbg;Gz;lhf;fp er;rup

nghJFzk;:

“rPjRuk; ghz;L rpNyj;kq; fpuhzpFd;kk;

thjk; mUrpgpj;jk; kh%yk;- XJre;jp

ahr;kg]; khuk; mld;Nkfk; **fhrkpit**

ehrq; fwpkpsfpdhy;”;.

-

mfj;jpau; Fzthflk**;**

tof;F Kiwfs;:

- kpsfpid J}s; nra;J 260-350 fpuhk; mstpy; nfhLf;f grpiaj;J}z;Lk;.ntg;gj;ij cz;Lgz;zp kdntOr;rpia cz;lhf;Fk;.
- kpsifj;J}s; nra;J FitdhTld; Nru;j;J toq;f Kiwr;Ruk; ePq;Fk;.
- kpsFj;J}s; 50 fpuhk;> ePu; 700 kpyp tpl;L miukzp Neuk; fha;r;rp tbfl;b> mjpy; 30-60 kp.fp tPjk; jpdk; 2-3 Kiw nfhLj;J tu njhz;ilf;fk;ky;> njhz;ilg;Gz; ,it jPUk;.jtpu tapw;W Neha;fSk; jPUk;.
- kpsF> mgpdp>ngUq;fhak; ,it tiff;F 20 fpuhk; vLj;J nrt;itahf miuj;J 12 khj;jpiufs; nra;J> mjpy; xU kzpf;nfhU Kiw xU khj;jpiu nfhLj;J tu the;jpNgjp ePq;Fk;.
- Kf;fLfpy; ,JTk; xd;W.

- kpsFj;J}s; 10 fpuhk;> vUf;fk;Ntu; 18 fpuhk; vLj;J gidnty;yk; jFe;j msT Nru;j;jiuj;J jpidasT khj;jpiu nra;J> xU khj;jpiu jpdk; ,UNtis rhg;gpl;L tu> nfhUf;F Neha;FzkhFk;.
- kpsFj;J}s;> ntq;fhak;> cg;G ,itfisr; Nru;j;jiuj;J jiyapy; fhZk; GOntl;Lf;F g+r> kapu; Kisf;Fk;.
- kpsF>Rf;F>jpg;gpyp> ngUQ;rPufk;> ghiw cg;G ,itfs; Xu; msthfr; Nru;j;Jg;nghb nra;J 2-4 fpuhk; cztpw;F gpd; thapypl;L nkd;W tpOq;f> nrupg;igg; gpwg;gpj;J tapw;W NehiaAk; Nghf;Fk;.
- kpsF 51 fpuhk;> ngUq;fhak; 68 fpuhk;> Njd; 340 fpuhk; Nru;j;J Nyfpakhf;fp> fow;rpf;fha; msT jpdkpUNtis rhg;gpl;Ltu KjpNahUf;Fk; nkype;Njhu;f;Fk; cz;lhfpd;w %yNeha; jzpAk;.

-Fzghlk; %ypif tFg;G

3.3. Phyto chemical constituents:

- Dried ground pepper has been used since antiquity for both its flavour and as a medicine.
- The spiciness of black pepper is due to the chemical **piperine**. Pepper gets its spicy heat mostly from the **piperine** compound, which is found both in the outer fruit and in the seed.
- Black pepper contains between 4.6% and 9.7% **piperine** by mass, and white pepper slightly more than that Refined piperine, by weight, is about one percent as hot as the capsaicin in chili pepper
- The outer fruit layer, left on black pepper, also contains important odour - contributing terpenes including **pinene, sabinene, limonene, caryophyllene, and linalool**, which give citrusy, woody, and floral notes. These scents are mostly missing in white pepper, which is stripped of the fruit layer.

-Wealth of India volume-5

Black peppers (Piper nigrum),
Nutritional value per 100 g.
(Source: USDA National Nutrient data base)

Principle	Nutrient Value	Percentage of RDA
Energy	255 Kcal	13%
Carbohydrates	64.81 g	49%
Protein	10.95 g	19.5%
Total Fat	3.26 g	11%
Cholesterol	0 mg	0%
Dietary Fiber	26.5 g	69%
Vitamins		
Choline	11.3 mg	2%
Folic acid	10 mcg	2.5%
Niacin	1.142 mg	7%
Pyridoxine	0.340 mg	26%
Riboflavin	0.240 mg	18%
Thiamin	0.109 mg	9%
Vitamin A	299 IU	10%
Vitamin C	21 mg	35%
Vitamin E-γ	4.56 mg	30%
Vitamin K	163.7 mcg	136%
Electrolytes		
Sodium	44 mg	3%
Potassium	1259 mg	27%
Minerals		
Calcium	437 mg	44%

Copper	1.127 mg	122%
Iron	28.86 mg	360%
Magnesium	194 mg	48.5%
Manganese	5.625 mg	244.5%
Phosphorus	173 mg	25%
Zinc	1.42 mg	13%
Phyto-nutrients		
Carotene-β	156 mcg	--
Carotene-α	0 mcg	--
Crypto-xanthin-β	48 mcg	--
Lutein-zeaxanthin	205 mcg	--
Lycopene	6 mcg	--

jpg;gpyp

3.1. BOTANICAL ASPECT:

Botanical name*: Piper longum*

Family : Piperacea

Part used : Fruit

Taxonomical classification:

Kingdom : plantae

Division : Angiosperms

Order : Piperales

Family : Piperaceae

Genus : Piper

Species : Longum

Long pepper (*Piper longum*), (*Pippali*), sometimes called **Indian long pepper**, cultivated for its fruit, which is usually dried and used as a **spice**.

The fruits contain the **alkaloid piperine**, which contributes to their pungency.

3.2. GUNAPADAM ASPECT:

jpg;gpyp

NtWngau;fs;:

“jpg;gpypapd; Ngu;jidNa nrg;gf;NfS
jPl;rz jz;LyfkhF---khFk;
gg;gpypghshf;fp ahk; rgykhFk;
ngUj;j rTz;b rpakhKg Fy;ypakhFk;
tg;gpypahk; itanjf;f Nfhydhkk;
thjFd;kj; jpupNjh\ ehrdpwkhFk;

fg;gpypahq; **Nfhiojid** aWf;FQ; #jd;

fUjpaNjhu; jpg;gpypapd; ehkkNk".

-Nghfu; epfz;L 1200 701Mk;ghly;

fhkd;> FNlhup> NfhioaWf;fp> fid> nrsz;b> Nfhyfk;> fzk;> fypdp> ghzk;> gpg;gpyp> itNjfp> mk;G> MjpkUe;J>khfjp

tsupay;G:

,/J nfhb tif> njd;dpe;jpahtpYk; tq;fhsj;jpd; fPo;ghfq;fspYk; gapuhfpd;wJ. kpsfpid tpl fhuk;mjpfk;. ,U tif cz;L. muprpj;jpg;gpyp> fz;lj;jpg;gpyp vd;git MFk;.

gad;gLk;cWg;G: fha;> muprp

Rit **:** fhu;g;G

jd;ik : ntg;;gk;

gpupT **:** ,dpg;G

nra;iffs;;;:

ntg;gKz;lhf;fp> mfl;Ltha;tfw;wp;> NfhioaWf;fp

Vernacular names:

Tamil	-	Thippili
English	-	Long pepper
Telugu	-	Pippila
Sanskrit	-	Pippali
Malayalam	-	Thippili
Duk	-	Pipliyan
Kannadam	-	Hippili
Persian	-	Daraife-fil

nghJFzk;:

"fl;b najpu; epd;W fLNehnay; yhk;gzpAk;

jpl;b tpidafYk; N;jfnkj;j-Gl;bahk;

khkDf;F khkndd kw;wtu;f;F kw;wtdhq;

fhkndDe; jpg;gpypf;Fk; if". -Njud; Fzthflk;

"<is **apUk ypiug;Gg; Grg;gpzpfs;**

khs nthopahky; thl;LNk- ahSKiw

ghq;fh awpe;J nra;tPu; gz;bjj;ij gz;bjNu

Ntq;iftha;g; ghd;fiz nka;”.

-Njud; ntz;gh

<is> ,Uky;> ,iug;G> cg;gprk; Kjypait jPUk;.

tof;F Kiwfs;;:

- jpg;gpyp 70 fpuhk;> fuprhiy ,iy 1 gyk;> 350 kpyp ePu; Nru;j;J ePiur;Rz;l fha;r;rp epw;Fk; jpg;gpia nghbj;J rkd;vil ru;f;fiu Nru;j;J %tpuy; msT cl;nfhs;s ,Uky; jPUk;.
- jpg;gpyp > fk;khW ntw;wpiy rhW kw;Wk; Njd;Nru;j;J cl;nfhs;s Nfhio> ,Uky;. Ruk; jPUk;.
- jpg;gpyp #uzk; fhy;gyj;ij 350 kpyp gRtpd; ghypy; tpl;Lf; fha;r;rp rhg;gpl;L tu ,Uky;> %u;r;ir> Kg;gpzp jPUk;.
- jpg;gpyp #uzk;;:

  jpg;gpyp 350 fpuhk;> kpsF 175 fpuhk;>Rf;F 175 fpuhk;>rPufk; 70 fpuhk;> ngUQ;rPufk; 70 fpuhk; muj;ij 70 fpuhk;,tw;iw ,stWg;gha; tWj;Jg;nghbj;J rkd; msT ru;f;fiu Nru;j;J xU rpl;bif 40 ehs; rhg;gpl ,isg;G> <is> ,Uky; jPUk;. -Fzghlk; %ypif tFg;G

3.3. Phyto chemical constituents:

- **Pippali** contains less essential oil than its relatives (about 1%), which consists of sesquiterpene hydrocarbons and ethers (bisabolene, β-caryophyllene, β-caryophyllene oxide, each 10 to 20%; α-zingiberene, 5%), and, surprisingly, saturated aliphatic hydrocarbons: 18% pentadecane, 7% tridecane, 6% heptadecane.
- The fruits contain the **alkaloid piperine**, which contributes to their pungency Long pepper is known to contain **Piperlongumine**, a compound believed to have an anti-tumor effect.

Uses:

- **Long pepper** is useful in respiratory discomfort (including asthmatic condition) and cough.
- It is used in therapeutic cleansing of the body parts abole the clavicle level.

- It is useful in therapeutic vomiting and alleviates anorexia.
- Stimulates digestive fire making a person feel hungry and having tranquillizer (Pain killer) action.
- Increases sexual desire and a rejuvenator of the body
- **Long pepper** is useful in All skin diseases and Useful in all urinary disorders including Diabetes
- It removes unnecessary fat from the body and *u*seful in all infectious conditions
- In chronic fever **long pepper** powder should be taken with jaggery.
- Taking long pepper powder with castor oil and cow urine is very effective in management of neurralgic conditions specially the Sciatica.
- Thippili should be taken with honey to get rid of unwanted fat and maintain normal body weight.

-Ayurvedic herbal plants

khJis:

3.1. Botanical aspect:

Botanical name : *Punica granatum*

Family : Lythracea

Taxonomical classification:

Kingdom	-	Plantae
Division	-	Angiosperms
Class	-	Magnoliopsida
Sub class	-	Rosids
Order	-	Myrtales
Family	-	Lythracea
Genus	-	Punica
Species	-	Granatum
Synonym	-	*Punica malus* (Linnaeus 1958)

Vernacular names:

Tamil - Mathulai

English	-	Pomegranate
Telugu	-	Danimma
Malayalam	-	Mathlam
Kannadam	-	Dalimba
Sanskrit	-	Shukhdana
Arab	-	Rumaman
Persian	-	Gulman
Hindi	-	Anar
Duk	-	Darim

Distribution and discription:

The ***Punica granatum*** **leaves** are opposite or sub-opposite, glossy, narrow oblong, entire, 3–7 cm long and 2 cm broad. The **flowers** are bright red, 3 cm in diameter, with four to five petals (often more on cultivated plants). Some fruitless varieties are grown for the flowers alone.

The edible **fruit** is a **berry** and is between a **lemon** and a **grapefruit** in size, 5–12 cm in diameter with a rounded hexagonal shape, and has thick reddish skin. The exact number of seeds in a pomegranate can vary from 200 to about 1400 seeds, contrary to some beliefs that all pomegranates have exactly the same number of seeds. Each seed has a surrounding water-laden pulp—the edible **aril**—ranging in color from white to deep red or purple. The seeds are embedded in a white, spongy, **astringent** pulp.

Varieties:

Punica granatum *nana* is a dwarf variety of *Punica granatum* popularly planted as an **ornamental plant** in gardens and larger containers, and used as a **bonsai** specimen tree. It could well be a wild form with a distinct origin. The only other species in the genus ***Punica*** is the **Socotran pomegranate (*Punica protopunica*)**, which is **endemic** to the island of **Socotra**. It differs in having pink (not red) flowers and smaller, less sweet fruit

Uses:

Pomegranate aril juice provides about 16% of an adult's daily **vitamin C** requirement per 100 ml serving, and is a good source of vitamin B_5 (**pantothenic acid**), **potassium** and polyphenols, such as **tannins** and **flavonoids**.

Pomegranates are listed as high-fiber in some charts of nutritional value. That fiber, however, is entirely contained in the edible seeds which also supply unsaturated oils. People who choose to discard the seeds forfeit nutritional benefits conveyed by the seed fiber, oils and **micronutrients**.

The most abundant polyphenols in pomegranate juice are the hydrolyzable tannins called **ellagitannins** formed when **ellagic acid** binds with a **carbohydrate**. **Punicalagins** are tannins with **free-radical** scavenging properties in laboratory experiments and with potential human effects. Punicalagins are absorbed into the human body and may have dietary value as **antioxidants**, but conclusive proof of efficacy in humans has not yet been shown. During intestinal metabolism by bacteria, ellagitannins and punicalagins are converted to urolithins which have unknown biological activity in vivo.

Other **phytochemicals** include polyphenolic **catechins**, **gallocatechins**, and **anthocyanins**, such as **prodelphinidins**, **delphinidin**, **cyanidin**, and **pelargonidin**. The **ORAC** (antioxidant capacity) of pomegranate juice was measured at 2,860 units per 100 grams.

Many food and **dietary supplement** makers use pomegranate phenolic extracts as ingredients in their products instead of the juice. One of these extracts is **ellagic acid**, which may become bioavailable only after parent molecule **punicalagins** are metabolized. However, ingested ellagic acid from pomegranate juice does not accumulate in the blood in significant quantities and is rapidly excreted. Accordingly, ellagic acid from pomegranate juice does not appear to be biologically important **in vivo.**

Clinical trial rationale and activity

- **Metabolites** of pomegranate juice ellagitannins localize specifically in the prostate gland, colon, and intestinal tissues of mice, leading to clinical studies of pomegranate juice or fruit extracts for efficacy against several diseases.
- In 2011, 32 **clinical trials** were registered with the **National Institutes of Health** to examine effects of pomegranate extracts or juice consumption on a list of diseases; consumption of pomegranates and pomegranate juice appear to correlate with preventing such diseases like **Prostate cancer,** prostatic **hyperplasia, diabetes, lymphoma, rhinovirus** infection (completed, July 2008)**, common cold**

(completed, June, 2007)**, oxidative stress** in diabetic **hemodialysis, atherosclerosis, coronary artery disease, infant brain injury, hemodialysis** for **kidney** disease.

3.2. GUNAPADAM ASPECT

NtWngau;fs;:

jhbkk;> gPrGuk;> khJsq;fk;> khJsk;> khJSq;fk;> fOKs;

"khJisapd; Ngu;jidNa tOj;jf;NfS
kfj;jhd jhbkq; Fl;bkKkhFQ;
rhjisahQ; rbgQ;R thJ jk;kpy;
rjf;fhd uj;j gPrfKkhFk;
MjisahQ; Rf;fpNy\;lQ; Rfty;ygkhFe;
jpgj;jp ahNuhf ehrdpAkhFk;
g+jisapd; mUz epwg;G\;gpahFk;
Nguhd khJisapd;NgUkhNk".

-NghfKdptu; epfz;L 1200

gad;gLk; cWg;Gfs;:

g+> gpQ;R> gok;> tpij> gl;il> Ntu;

Rit:

goj;Njhy; : Jtu;g;G

gok; : ,dpg;G

jd;ik : jl;gk;

gpupT : fhu;g;G> ,dpg;G

nra;iffs;:

Jtu;g;gp : Astringent

GOf;nfhy;yp : anthelmintic

FUjpg;ngUf;flf;fp : Haemostatic

Mz;ikg;ngUf;fp : Aphrodisiac

grpj;jPj; J}z;b : Stomachic

Fspu;r;rpAz;lhf;fp : Coolant

nghJf;Fzk;:

“tha;ePUwy; frg;G the;jptpf;fz; ke;jkpff;

fha;ntg;g neQ;nruptp fhjilg;G –Nthah

kaf;fKe; jPu;e;JtpL khJsk;goj;jhw;

waf;fnkdj; NjnkhopNa rhw;W”.

-jd; te;jpup Foe;ijthflk; 170 gf;fk;

“the;jpgpj;j NjhlnkhL khwhf; fLg;giyQ;

Nru;e;Jepd;w %yuj;je; jPu;f;Fq;fhz;- khe;jspu;f;if

khNj! apuj;jG\;b ty;ygyd; cz;lhFk;

g+jyj;Js; khJisapd;g+”.

-mfj;jpau; Fzthflk;

,jdhy; FUjp the;jp> tapw;Wf;fLg;G> ntg;gk;> FUjp %yk; ,it jPUk;>FUjpiag; ngUf;Fk;>td;ikiaj;jUk;.

tof;FKiwfs;:

- khJisapd; goj;ij jpdKk; Grpj;J tu Mz;ik ngUf;F cz;lhFk;.
- G+ nkhf;if cyu;j;jp nghbj;J 130; kp.fpuhk; nfhLf;f ,Uky; ePq;Fk;.
- gpQ;irf; FbePupl;L rPjNgjp> mjprhuk; ,tw;wpw;F jUtJ ehl;L tof;fk;.
- gor;rhw;wpid fw;fz;L Nru;j;J kzg;ghF nra;J mUe;j Fspu;r;rpia cz;L gz;Zk;.
- gor;rhw;wpid ,isg;G NehapdDf;F juyhk;
- goj;Njhypid cyu;j;jp gy tpj fopr;rYf;F juyhk;

-Fzghlk; %ypif tFg;G.

“tha;ePUuy; frg;G the;jptpf;fz; ke;jkpff;

fha; ntg;g neQ;nruptp fhjilg;G –Nthah

kaf;fKe; jPu;e;J tpL khJsk; goj;jhw;

waf;f kdj; NjnkhopNa rhw;W”.

-jd;te;jpup Foe;ij thflk;

3.3. Phyto chemical constituents:

- Pomegranate aril juice provides about 16% of an adult's daily **vitamin C** requirement per 100 ml serving, and is a good source of vitamin B_5 (**pantothenic acid**), **potassium** and polyphenols, such as **tannins** and **flavonoids**.
- Pomegranates are listed as high-fiber in some charts of nutritional value. That fiber, however, is entirely contained in the edible seeds which also supply unsaturated oils.
- The most abundant polyphenols in pomegranate juice are the hydrolyzable tannins called **ellagitannins** formed when **ellagic acid** binds with a **carbohydrate**. **Punicalagins** are tannins with **free-radical** scavenging properties in laboratory experiments and with potential human effects. Punicalagins are absorbed into the human body and may have dietary value as **antioxidants**, but conclusive proof of efficacy in humans has not yet been shown. During intestinal metabolism by bacteria, ellagitannins and punicalagins are converted to urolithins which have unknown biological activity in vivo.
- Other **phytochemicals** include polyphenolic **catechins**, **gallocatechins**, and **anthocyanins**, such as **prodelphinidins**, **delphinidin**, **cyanidin**, and **pelargonidin**.

Uses:

- The pomegranate has extensively been used as a source of traditional remedies for thousands of years. The rind of the fruit and the bark of the pomegranate tree is used as a traditional remedy against diarrhea, dysentery and intestinal parasites. The seeds and juice are considered a tonic for the heart and throat,
- The astringent qualities of the flower juice, rind and tree bark are considered valuable for a variety of purposes, such as stopping nose bleeds and gum bleeds, toning skin, (after blending with mustard oil) firming-up sagging breasts and treating hemorrhoids.
- Pomegranate juice (of specific fruit strains) is also used as eyedrops as it is believed to slow the development of cataracts. -Hand book of medicinal plants

ntq;fhuk;:

3.1. Modern aspect

Chemical Name: **Sodium borate**

Hydratedsodiumborate $Na_2B_4O_7$ -$10H_2O$

Source:

It occurs as a natural deposit. Crude borax is found in masses by evaporation of water, on shores of dried up lakes in India and Tibet.It is also obtained from the mud of lakes surrounded by hills of Nepal. In this crude state it is known as sohagoor, when purified by dissolving it in water, straining through cloth, evaporating to dryness and crystallizing, it is called borax.

Chemical properties:

These are several borates of Sodium, Sodium tetra borate is used commonly in all purposes.

- Sodium tetra borate-$Na_2B_4O_7 10H_2O$ or anhydrous
- Sodium meta borate-$Na_2BO_4H_2O$
- Sodium per borate -$NaBO_2H_2O_3H_2O$
- Sodium penta borate-$Na_2B_{10}O_{16}10H_2O$

Specific gravity - 1.7

Characters:

It is composed of boric acid and soda. In the native state it exists as an impure saline incrustation of a dirty white colour. It exists as crystalline tough masses or in the form of translucent irregular masses. Exposed to the air it becomes opaque. The colour is grayish-white .on exposure it becomes opaque or dirty white.

Purification:

Borax is purified by being steeped for a night in kanji and dried in the sun.

Action:

Diuretic, Antacid, Astringent, Emmenogouge, Local sedative, Anti septic

Uses of borax:

External

Borax have the power of destroying micro-organisms and are thus disinfectant and **antiseptic**, and it is much more active in preventing than in inhibiting decomposition. The action is extremely local.

Internal

Borax checks the action of saliva on **starch**, but, if anything, they increase the action of the gastric juice and the pancreatic secretion. Large amounts, however, slightly retard digestion, and still larger are **gastro-intestinal irritants.**

-**Materia Medica Pharmacy, and Pharmacology and Therapeutics"**, by W. Hale White.

- They are largely used to keep wounds, ulcers, and sores sweet. The action is so local that they cannot be used to dress cavities.
- Borax has been given in epilepsy, and its **use i**s gaining ground. It is often prescribed with advantage in combination with bromides, but it is decidedly inferior to them, although in exceptional cases it may succeed when they have failed. As it is an antiseptic it has been given internally in typhoid **fever** and phthisis, but with doubtful benefit.
- Taken internally, it is said to relieve irritability of the bladder.
- In rare cases its use has caused either psoriasis, a papular eruption especially marked near the elbows, an erythematous rash, or eczema. Nausea, loss of appetite, vomiting, and diarrhoea may be produced.
- Borax is used internally in dose varying from 10-30 grains, in acidity of stomach, amennorrhoea, dysmenorrheal, menorrhagia, puerperal convulsions and to promote uterine pain during labour.

-Dr.Nadkarni's materia medica 176

Borax has four special centers of action,

- Mucous membranes - Aphthous inflammation
- Skin - Slight injuries suppurate
- Sexual organs in women - Stimulates menstruation
- Locally - Powerful antiseptic and disinfectant

-Physiological material medica W.H .Hul

3.2. Gunapadam Aspect

NtWngau;fs;;:

nghupfhuk;> fhuk;> cUf;fpdk;> cUf;Fkpj;jpud;> lq;fzk;> J}kj;ijalf;fp>

“fhup nghupf;fhup fLk;Ngjfkzp

NeupAUf;fpdk; Neu;e;j kzpfhuk;

thupa J}kj;ij alf;fpa rpw;gup

fhupare;jhdp fupj;jFNlhupNa”

-rl;il Kdpepfz;L 1200

“ntq;fhug; Ngu;jidNa tpsk;gf;NfS

NkjpdpNahu; jq;fSf;F cUf;fpdkhFQ;

rq;fhuk; NghyNt rj;njy;yhkhFk;

rj;jhdg; nghupfhupf; FNlhupahFk;

mq;fhup lq;fzKkh klq;fhj

J}kj;ij mlq;fg; gz;zp

nghq;fhup ruf;Ff;F kpj;JU Ntahd

nghupfhup jdf;fpire;j NgUkhNk”. -Nghf Kdptu; epfz;L 1200

fpilf;Fkplq;fs;:

mjpf msT fypNghu;dpahtpYk;> ,e;jpahtpYk>; jpngj;> Neghsk; Kjypa ,lq;fspYk; fpilf;fpwJ.

jd;ik:

nts;isaha; njsptha; rpy Nfhzq;fnshL $bajha; nfhQ;rk; kpDkpDg;gha; ,Uf;Fk;. ,J ePupy; fiuAk;. rhuhaj;jpy; fiuahJ.

Rit: ,dpg;Gld; $ba Jtu;g;Gr;Rit cilaJ.

tPupak;: ntg;gk; MFk;.

,jid **“ntq;fhuk; nta;njdpDk; Neha; jPu;f;Fk;”** vd;gjhy; mwpayhk;.

nra;iffs;:

cl;gpuNahfk;

Fspu;r;rpAz;lhf;fp - Refigerant

rpWePu; ngUf;fp - Diuretic

fw;fiur;rp - Lithontriptic

UJTz;lhf;fp - Emmenogogue

ntspg;gpuNahfk;

cly;Njw;wp - Alterative

Jtu;g;gp - Astringent

mOfyfw;wp - Antiseptic

nghJFzk;:

“nrhwpGilnaz; Fd;keik Nrhup aurk;

gwpfpufzp fy;Y}dk; gd;Ndha; - newpiaj;

jlq;fzq;f gq;fpUkp ru;g;gtplQ; re;ep

aplq;fzq;f yf;fpw;Ngh nkz;”;.

-gjhu;j;j Fzrpe;jhkzp

vz;tiff; Fd;kk;> jpdT> ,uj;j %yk;> xOf;Ff;fpufzp> mr;kup> ehstopiaj;jLf;fpd;w %j;jpu fpupr;ruq;fs;> **fghjpf;fk**;> re;epghjk; ,it jPUk;.

“ntq;fhuQ; Nrj;Jkj;ij NtWgz;Z NkfLF

jq;Frpy ePu;Kwpaj; jhd;thq;Fk;”.

fgj;ijAk;> ePu;g;gpzpiaAk; thq;Fk;.

Rj;jpKiw:

- gRtpd; rhzg;ghypy; ,jidf; fOtp cyu;j;j Rj;jpahFk;.
- vUik %j;jpuj;jpy; %d;W ehopif Cwitj;J vLf;f Rj;jpahFk;
- rl;bapypl;Lg;nghupj;J fhbapyhtJ gor;rhw;wpyhtJ miuj;J cyu;j;jp vLf;f Rj;jpahFk;.
- ePu; tw;Wk;gb nghupj;Jf; nfhz;lhy; Rj;jpahFk;
- gor;rhw;wpyhtJ muprp fOtpa ePupyhtJ miuj;J cyu;j;jpf;nfhz;lhy; Rj;jp.

cgNahfq;fs;:

- ntq;fhuj;ijg; nghupj;J nea;> my;yJ ntz;nzapy; fye;J jlt> cjL ntbg;G> tha; tpuzk;> ehg;Gz; ,itfs; MWk;. Njfk; FspUk;.
- **ntq;fhu kJ**: nghupj;j ntq;fhuk; 1 tuhfDld; Njd; 1 gyk; fye;J tha;g;Gz;>mf;fuk;> ,itfl;Fj; jlt Fzj;ijf; nfhLf;Fk;.
- ntq;fhuk; xU tuhfd; vLj;J 1/8 Mohf;F ePupy; fye;J Kiyf;fhk;G ntbg;G> Gz; ,itfSf;Fj; Jzpapy; eidj;J NkYf;Fg;Nghl FzKz;lhFk;.
- ntq;fhuk; 1 tuhfd; 1/8 Mohf;F gd;wp nea;apy; fye;J> typAld; $ba %yj;jpw;F Nghl FzKz;lhFk;.
- nghupj;j ntq;fhuj;ij ,sePupy; fye;J nfhLf;f ePu;f;fl;L FzkhFk;.
- fz;Neha;fspy; fz; fOt 4 cSe;njil ntq;fhuj;ij Xu; mTd;]; ePupy; fye;J cgNahfpf;f Ntz;Lk;.
- ntq;fhuj;ij 65 kp.fp tiu jha;g;ghypy; fye;J nfhLf;f Foe;ijfSf;F fhZk; typ ePq;Fk;.
- **ntq;fhuk; 2 ½ Fd;wpnail> kpsFj;J}s; 1 ½ Fd;wpnail ,uz;ilAk; 1 Njf;fuz;b Njdpy; fye;J jpdk; %d;W Ntis mUe;j fhrk;> Rthrfhrk; Kjypad jPUk;.** -Fzghlk; jhJ rPt tFg;G

gidnty;yk; -Palm jaggery

Vernacular names:

Sanskrit - Guda

Kannada - Bella

Telugu - Bellam

Malayalam - Karuppatti

Hindi - Gud

gad;fs;;:

gidnty;yj;jhy; Kf;Fw;wj;jhy; tUk; Neha;fs; jPUk;. Kg;gpzp> Ritapd;ik> Fd;kk; ,it ePq;Fk;.

“jq;Fgid nty;yj;jhy; thjgpj;jk; tPWfgQ; re;epNeha;

ty;yUrp Fd;kkW khy;”.

-mfj;jpau; Fzthflk;

Palm jaggery is made from the extract of Palm Trees in Southern India. These trees are also known as *Toddy palm trees or Palmyra trees* .

The palm jaggery obtained after processing is darker and richer in colour. It is slight salty to taste but much healthier of the two. Due to its cooling effects over human body, it is of high value. It does not have the bone meal content which is used for whitening processed sugar. The price of the palm jaggery is double that of sugar.

The first extract of the palm juice which is boiled at high temperatures, is being added with a little salt. The added salt then acts as a preservative. This also prevents the jaggery from becoming too sweet.

When it gets cooled, it is poured into a long cone made of palm leaves. The preservation of the final product is done by wrapping the cone with rice straws. At home, the consumers finely slice the cone, so that the jaggery is cut into disc shapes leaving a palm ribbon around its edges. Some families simply dry the extracted palm juice on mats. After it dries, the jaggery is being stored in an air-tight container which preserves it for

nearly one year. **Palm Jaggery is rich in calcium, iron and other useful vitamins and minerals.**

- One of the tastiest and healthy products. It is used in the preparation of sweet dishes.
- The medicinal properties are in it makes it a unique product that can be used by people of all ages.
- It may be used sufficiently by people who suffer from diabetes.
- It is used as a substitute of sugar in the preparation of coffee, tea, etc.
- Panakam or Juice is prepared by adding black pepper and palm jaggery, to a glass of water. Sometimes a pinch of cardamom (elaichi) is also added to get a good flavor and taste.
- In the South Kanara district region, most of the time it is given to women who give birth to a child. If the mixture of powdered palm jaggery and black jeera are given to such women, then impurities in the breast milk would disappear and baby gets the white and clean milk during breast feeding. Even in the case of milking cows, the same thing is repeated after it gives birth to a calf.
- The preventive action of jaggery on smoke-induced lung lesions suggest the potential of jaggery as protective agent for workers in dusty and smoky environments- paper presented by scientists of Industrial Toxicology Research Centre at a Workshop held in Lyon, France.
- Hence, it fights pollution too! No wonder Jaggery is regularly consumed by thousands of industrial workers / traffic policemen who are exposed to higher levels of pollution. It helps them breathe easier and counter pollution naturallyAccording to an experiment, Jaggery treated rats showed enhanced translocation of coal particles from lungs to tracheobronchial lymph nodes.-*Environ Health Perspect, 102(Suppl 6): 211-214 (1994)*

Nutritional values:

Palm jaggery (gur) is much more nutritious than crude cane sugar, containing

protein,	1.04%
fat,	0.19%
sucrose,	76.86%
glucose,	1.66%
total minerals,	3.15%
calcium,	0.861 %
phosphorus	0.052%
iron per 100 g	11.01 mg
copper per100 g.	0.767 mg

The fresh sap is reportedly a good source of vitamin B complex.

-Atchley, A. A. 1984. Nutritional values of Palm. *Principes* 28(3):138-143.

kpsF> jpg;gpyp> ntq;fhuk; NrUk; gpw kUe;Jfs;:

- fhr Fyhe;jf khj;jpiu - vz; tiff; **fhrk;** jPUk;
- RthrFNlhup khj;jpiu - vy;yh tif **Rthrfhrk;** jPUk;
- re;jpug;gpufhr khj;jpiu - ghupr thA> jkuf thA> **,Uky**; jPUk;
- re;jpNuhja khj;jpiu - rd;dp> Ruk; jPUk;
- gl;il khj;jpiu - mrPuzk>; tapw;Wg;nghUky; jPUk;
- Fsq;fyf;fpf; Fspif - ryf;Nfhit> fhkhiy>CJ fhkhiy jPUk;
  -tPukhKdptu; thflj;jpul;L
- kpsFj;ijyk; - jiy %o;f **raNuhfk;** jPUk;
  -jd;te;jpup ijyk; 500
- RthrFNlhup #uzk; - **<is> ,Uky;> Nfhio** ,it jPUk;
- jpg;gpyp #uzk; - **Rthr fhrk;> ,Uky;> <is** jPUk;
- ,Uky; khj;jpiu - **Rthr fhrk**; jPUk;
- fhr FNlhup khj;jpiu - **Rthr fhrk;> ,Uky;** ,it jPUk;
- rQ;rPtp khj;jpiu - nts;shl;Lg;ghypy; fye;J ju fgk; jPUk;

- Fq;Fkg;g+ khj;jpiu - **ryNjh\k;> rPjsk;> Ruk; jPUk**;
- ghy rQ;rPtp khj;jpiu - Ruk;> ,Uky; jPUk;
- jpg;gpyp Nyfpak; - <is> ,Uky;>fhrk; jPUk;
- jpg;gpyp fpUjk; - fhrk; jPUk;
- gQ;r NfhyfpUjk; - ,Uky;> ryNjh\k;> <is jPUk;
- fe;jff; fWg;G - Ruk;> fhkhiy> ghuprthjk; jPUk;

-fz;Zrhkp guk;giu itj;jpak;

khJsk; goXL NrUk; gpw kUe;Jfs;:

- fpuhzpfghlk; - mjprhuk;> fpuhzp> ,uj;jf;fopr;ry; jPUk;

-mfj;jpau; itj;jpa rpe;jhkzp 4000

- tr;rpufghlf;Fspif - mjprhuk; NghFk;.

-Cu;trp; ,urthj rpl;fh

- **fy;ahz fpUjk;** - **Rthr fhrk; jPUk**;
- khJis nea; - fz#L jPUk;.Foe;ij tsk; ngUk;

-rpfpr;rh uj;d jPgk;

- jpUNkdpahjpj; ijyk; - gPdprk;> kz;ilr;#iy jPUk;

-jd;te;jpup itj;jpak;

- khJisf;fpUjk; - rPjNgjp> c\;zNgjp jPUk;
- khJisj; ijyk; - ku;k];jhd jsu;r;rp jPUk;
- fuz;b fl;Lthjp - mjprhuk;>fpuhzp tiffs; jPUk;

-tPukhKdptu; thflj;jpul;L

- Gspahiuf; fpUjk; - fpuhzp> khu;G Neha; jPUk;
- mWfd;Ntu;f;fpUjk; - gpuNkfk;> #iy jPUk;

-fz;Zrhkp guk;giu itj;jpak;.

3.4. SIDDHA ASPECT OF THE DISEASE

Rthrfhrk;

NtWngau;fs;: ,Og;G Neha;> ,iug;gpUky;

,ay; :

- ,d;d tifnad;W Fwpg;gpl;Lf; $wKbahjgb xU fhuzKkpd;wp khu;ig ,Wf;fpaJ Nghd;w Ntjid
- %r;ir ntspaplTk;> cs;,Of;fTk; Kbahky; jpzwr;nra;jy;
- ntspahFk; %r;R kpFe;j rpukj;Jld; ntspahjy;

- Foy;> aho;> tPiz> Nghd;w thj;jpaq;fisg; Nghy; xyp
- ,Uky; fhzy;> Nfhio ntspahjy; ,y;iy

Neha; tUk; top:

- Iaj;ij kpFjpg;gLj;Jk; czT tiffshYk;
- Gy;> g+z;L> muprp>Nfo;tuF Kjypaitfspd; RizahYk;>
- jdf;F xt;thj ehw;wg; nghUl;fis Kfu;tjhYk; ,e;Neha; gpwf;Fk;

"fhy;ngUf; FzTnghUs; jz;zPu; khwy;
fUjpUky; kpfy;the;jp Fspu;e;j fhw;W
khy;nra;J ehs;NjhWk; tWj;Jq; fha;r;ry;
ke;jd Kapu;epiyap ybfs; jhf;fy;
Vy;rPj Ngjptpl ghz;L Giffs;
,yfpa ney; yhjpkzpr; RizAl; nry;yy;
Nky;topapw; rpytupD kpiug;ghk; NehA
NkTnkd Kdptuu;fs; tpsk;gpdhNu".

-ifnaOj;Jg;gpujp

Nehapd; Kw;FwpFzq;fs;:

gd;dhl;fs; Jd;gg;gl;ltu;fs; Neha;tUKd; ,jd; Fwpia mwpthu;fs;.tuf;$ba Nehapd; td;ikiaAk; mstpLthu;fs;. Mfhj czTk; Mfhj fhw;wpd; kzKk; gl;lTld; %f;fpy; ePu;gha;jy;> Jk;kYz;lhjy;> khu;G Nehjy;> khu;ig ,Wf;fpf; fl;baJ NghypUj;jy;> Ntjid>,aw;if %r;rhdJ jilg;gly;> tpyhg;gf;fk; typj;J %r;Rj;jpzwy;> tapWg;gy;> cly;tpau;j;jy; Nghd;w FwpFzq;fs; cz;lhFk;.

-rpj;j kUj;Jthq;fr; RUf;fk;

"khu;gpy; tpyhtpuz;by; kz;ZkpU neupapy;;
Nru;e;J typj;jy; jpzwy; - jhu;%r;R
cg;gy; tapw;wp; YUtJNt Kw;Fwpahr;
nrg;gpiug;G Neha;f;fpjidj; Nju;".

-A+fp itj;jpa rpe;jhkzp

nghJFwpFzq;fs;:

“td;ikaha;f; Nfhiofl;b ,Ukp tPOk;
khehfk; NghyNt thq;FQ; Rthrk;
jpz;ikaha;r; nrUkYz;lh kbf;f bf;FQ;
rPuz kpyhkNy tapW %Jk;
ed;ikaha; ehrpaJ jzy;Ngh yhFk;
eype;Jlk;G tw;wp tUq; FuYq; fk;Kk;
cz;ikah Az;zhf; fpY}Wq; Nfzp
Aoe;JNk Rthrfh rj;jp ndhg;Ng”.

-

a+fp itj;jpa rpe;jhkzp

,e;Nehapy; %f;fpypUe;J ntspahFk; fhw;W mdy; tPRk;.njhz;il fl;b %r;R vyp $r;rpLjy; Nghy; xypf;Fk;. khu;gpy; Nfhio fl;b ,UknyOk;.Neha; Kjpupd; ntspahFk; %r;R ey;y ghk;G rPWtJ Nghy; xypf;Fk;.czT nrupahJ> tapWg;Gk;. ,jid **,rpT ,Uky**; vd;Wk; $Wtu;.

“fl;bNa Nfhio ,UkNt tPo;e;J
fr;nrtp rPWjy; Nghy;
Kl;bNa %r;R td;ikaha;r; nrUkp
%f;foy; va;jpNa Alyk;
tw;wpNa nkype;Jz; zhtiu ePUk;
tul;rP uzkpF tpau;it
fl;bNghy; tapW %jpb ypiug;gh
kpUknyd; NwhJtu; fhNz”.

-

A+fp itj;jpa rpe;jhkzp

Neha; vz;:

1. tsp,iug;G
2. Ia,iug;G
3. Iatsp,iug;G
4. Kf;Fw;w ,iug;G
5. Nky;Nehf;F ,iug;G

- rpj;j kUj;Jthq;fr;RUf;fk; gf;fk; 117

Kf;Fw;w Kjypa NtWghLfs;:

tspAk; IaKk; Nru;e;j kpFjpNa fhuzk;.

cw;wpLk; Iaehb

Xq;fpNa Jbj;J epd;why;

gw;wpLk; kpUk yPis

gjwpNa ,iug;Gz;lhf;fp

nkj;jNt Nfhio thA kpFe;jpLk;

-A+fp itj;jparpe;jhkzp

ehbeil:

“fgj;jpidad;wp fhrRthrk; fhzhJ”

-Neha;ehly;

Neha;Kjy;ehly; ghfk;-1 gf;fk;216

Ia ehb kpFjpahYk;> tsp Ia njhe;jj;jhYk;> thAthy; J}z;lg;gl;l gpj;jkpFjpahYk;> Ia gpj;j njhe;jj;jhYk; ,iug;G Neha; cz;lhFk;.

vr;rpy;:

- Nfhio my;yJ rspahdJ Eiuj;Jk;>mstpy; kpFe;Jk;> gStw;Wk; ,Ug;gpd; tspf;Fw;wj;jpdhy; te;jJ vdyhk;.
- fWj;Jf;nfl;bg;gl;L> Gyhy; kzj;Jld; fbdkhfTk;> ntSj;jr; rPo; fye;jJ NghYk; kQ;rs; epwj;JlDk; fhzpd; Iaf;Fw;wj;jpdhy; te;jJ vdyhk;.

-Neha;ehly; Neha;Kjy;ehly; jpul;L-ghfk;1 gf;fk;115

ePu;f;Fwp:

“mwntspu;g;gpYk; rspiag; Nghy; tpopdJ

kwtd; mjp nfhjpg;ghy; tUtdNk”

ePu; kpfTk; ntSj;jhYk;> mjpy; rspiag; Nghy; tpOe;jhYk; me;j ePu; Iaj;jpd; kpFe;j nfhjpg;ghy; tUfpd;w ePuhFk;.

“tpe;Jitg; Nghd;w ePu; tpoy; fg NehiaAk;

ge;jpj;j re;epghjj;ijAe; jUk;”

vd;gjdhy; ,e;jpupaj;ijg; Nghd;w ePuhdJ> td;ikAs;s fg NehiaAk; (Nfhio Neha;fshfpa rak;> Rthrk;> fhrk; Kjypait) cWjpAs;s rd;dp NehiaAk; jUk;.

nea;f;Fwp:

“Kj;njhj;J epw;fpd; nkhoptnjd; fgNk.”

vz;nza;j;Jsp tpl;lJ tpl;lthNw rpwpJk; guthky; Kj;Jg;Nghy; epw;Fkhdhy; me;ePu; Ia Nehiaf; fhl;LtjhFk;.

epwf;Fwp:

“epykpF fgNk Mfpd;

epiwEiu Nghd;wpUf;Fk;

,yFkk; %j;jpuj;jpy;

vz;nza;;ia tpl;Lg;ghu;f;fpy;

rhw;wpd fgj;jp Df;Fr;

ry;yilf; fz;Nghw; fhZk;

Ntw;nwhU Jspaha; epd;why;

tpUjhFQ; rhj;jpae;jhd;

Mw;wpNa nky;yg; gutpd;

mJ Rf rhj;jpae; jhd;.”

-Neha;ehly;

Neha;Kjy; ehly; ghfk; 1

Nrj;JkNfhg ePu; epwk;:

“tsKiw nts;isahfp tw;wp ePu;FWfp epd;why;

njspTwr; Nrj;Jkj;jpd; nra;if nad;Wiwf;Fk;

Fspu;ikapdhNy nts;isahfpa Fzkhnkd;Wk;

,sF gr;rpuj;je;jd;dh ypWfpd njd;WQ; nrhy;Ny.”

-Neha;ehly; Neha; Kjy; ehly; ghfk; 1

ePu; ntz;ik epwk; nghUe;jp mstpYk; Fiwe;jpUe;jhy; mJ Nrj;Jkj;jhYz;lhd FzkhFk;.

rPjkpFjp nea;f;Fwp;:;

“ty;yey; nyz;nza; Jspah thu;; neha;Kjy;ehlyj;jjpy; nefpohjhfpy;

nrhy;yUq; Fspu;ik kPwpj; Njh\Kw; nwa;J nkd;Wk;.”

ePupy; tpl;l vz;nza;j;JspahdJ nefpohky; mg;gbNaapUe;jhy;>rPjkpFjpahy; cz;lhdnjd;W mwpayhk;.

3.6. MODERN ASPECT OF THE DISEASE:

Bronchial asthma

Difinition:

- Asthma is an inflammatory disease of the small airways,
- It is characterized by episodic, reversible bronchial obstruction due to hyper-responsiveness of tracheobronchial tree to a multiplicity of intrinsic and extrinsic stimuli manifested
- Clinically by paroxysms of polyphonic wheeze, dyspnoea, and cough which may be relieved spontaneously or as a result of therapy.

Asthma is best described by its technical name:

- Reversible Obstructive Airway Disease (ROAD). In otherwords, asthma is a condition in which the airways of the lungs become either narrowed or completely blocked, impeding normal breathing.
- However, in asthma, this obstruction of the lungs is reversible, either spontaneously or with medication. Quickly reviewing the structure of the lung: air reaches the lung by passing through the windpipe (trachea) which divides into two largetubes (bronchi), one for each lung.

- Each bronchi further divides into many little tubes (bronchioles), which eventually lead to tiny airsacs (alveoli), in which oxygen from the air is transferred to the bloodstream, and carbon dioxide from the bloodstream is transferred to the air.
- Asthma involves only the airways (bronchi and bronchioles), and not the air sacs. The airways are cleaned by trapping stray particles in a thin layer of mucus which covers the surface of the airways.
- This mucus is produced by glands inside the lung, and is constantly being renewed.The mucus is then either coughed up or swept up to the windpipe (trachea) by cilia, tiny hairs on the lining of the airways. Once the mucus reaches throat, it can again be coughed up. Do not reswallow.
- Although everyone's airways have the potential for constricting in response to allergens or irritants, the asthmatic's airways are oversensitive, or hyperreactive.

Common asthma triggers include:

- Animals (pet hair or dander)
- Dust
- Changes in weather (most often cold weather)
- Chemicals in the air or in food
- Exercise
- Mold
- Pollen
- Respiratory infections, such as the common cold
- Strong emotions (stress)
- Tobacco smoke
- Drugs - Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) provoke asthma in some patients.

Many people with asthma have a personal or family history of allergies, such as hay fever (allergic rhinitis) or eczema. Others have no history of allergies.

Epidemiology

As of 2009, 300 million people worldwide were affected by asthma leading to approximately 250,000 deaths per year. It is estimated that asthma has a7-10% prevalence

worldwide. As of 1998, there was a great disparity in the prevalence of asthma across the world, with a trend toward more developed and westernized countries having higher rates of asthma, with as high as a 20 to 60-fold difference. Westernization however does not explain the entire difference in asthma prevalence between countries, and the disparities may also be affected by differences in genetic, social and environmental risk factors. Mortality however is most common in low to middle income countries, while symptoms were most prevalent (as much as 20%) in the United Kingdom, Australia, New Zealand, and Republic of Ireland; they were lowest (as low as 2–3%) in Eastern Europe, Indonesia, Greece, Uzbekistan, India, and Ethiopia.

Asthma affects approximately 7% of the population of the United States and 5% of people in the United Kingdom. Asthma causes 4,210 deaths per year in the United States. In 2005 in the United States asthma affected more than 22 million people including 6 million children. It accounted for nearly 1/2 million hospitalizations that same year. More boys have asthma than girls, but more women have it than men. In England, an estimated 261,400 people were newly diagnosed with asthma in 2005; 5.7 million people had an asthma diagnosis and were prescribed 32.6 million asthma-related prescriptions.

History:

Asthma was first recognized in ancient Egypt and treatment was inhalation of frankensense. Officially, it recognized as a specific respiratory problem separate from others was first recognized and named by **Hippocrates** circa 450 BC. During the 1930s–50s, asthma was considered as being one of the 'holy seven' **psychosomatic illnesses**. Its **aetiology** was considered to be psychological, with treatment often based on psychoanalysis and other **'talking cures'.** As these psychoanalysts interpreted the asthmatic wheeze as the suppressed cry of the child for its mother, so they considered that the treatment of depression was especially important for individuals with asthma. Among the first paper in modern medicine are one that was published in 1873 and this paper tried to explain the **pathophysiology** of the disease. And one of the first papers discussing treatment of asthma was released 1872; the author concluded in his paper that asthma can be cured by rubbing the chest with **chloroform liniment.**

Among the first times researchers referred to **medical treatment** was in 1880, when Dr. J. B. Berkart used **IV therapy** to administer doses of a drug called pilocarpin. In 1886, F.H. Bosworth FH suspected a connection between asthma and **hay fever. Epinephrine** was first referred to in the treatment of asthma in 1905, and for acute asthma in 1910.

Disease pattern

- Episodic - acute exacerbations interspersed with symptom-free periods
- Chronic - daily airway obstruction which may be mild, moderate or severe may or may not superimposed acute exacerbations
- Life-threatening- slow-onset or fast-onset(fatal within 2 hour)

Mortality

- Fatal asthma 1-7% asthmatics
- Increasing death rate,abuse of inhaled BronchoDilators
- Risks for death: previous life-threatening asthma, severe disease, recent hospitalization or emergency room treatment, non-compliant and confusion of re treatment, under- treatment with Corticosteroids, discontinued treatment, severe airway hyper reactivity.

Types:

Extrinsic asthma (Atopic asthma, early onset asthma)

- Onset is in childhood.
- Identified by skin sensitivity test
- Asthmatic inflammatory reaction is characterized by a cellular infiltrate rich in Eosinophils.

Intrinsic asthma (Non-atopic asthma, late onset Asthma)

- It can begin at any age
- Especially in late adulthood
- There was no role of allergens in the production of the disease.

Pathophysiology:

- chronic airway inflammation as evidenced by cellular infiltration of airway by activated eosinophils,mastcells,macrophages and T-lymphocytes
-
- Released mediators from the above cells cause bronchial smooth muscle contraction
- Denudation and desquamation of the epithelium forming mucous plugs that obstruct the airway
- Airway remodeling as evidenced by
  - Smooth muscle hypertrophy and hyperplasia
  - Goblet cell and sub-mucosal gland hypertrophy leading to mucous hypersecretion
  - Collagen deposition causing thickening of lamina reticularis
  - Cellular infiltration, oedema and possible airway wall thickening.

Clinical features:

Symptoms

Most people with asthma have attacks separated by symptom-free periods. Some people have long-term shortness of breath with episodes of increased shortness of breath.

Either wheezing or a cough may be the main symptom. Asthma attacks can last for minutes to days, and can become dangerous if the airflow is severely restricted.

Symptoms include:

- Cough with or without sputum (phlegm) production
- Pulling in of the skin between the ribs when breathing (intercostal retractions)
- Shortness of breath that gets worse with exercise or activity
- Wheezing, which:
  - Comes in episodes with symptom-free periods in between
  - May be worse at night or in early morning
  - May go away on its own
  - Gets better when using drugs that open the airways (bronchodilators)
  - Gets worse when breathing in cold air
  - Gets worse with exercise

- Gets worse with heartburn (reflux)
- Usually begins suddenly

Emergency symptoms:

- Bluish color to the lips and face
- Decreased level of alertness, such as severe drowsiness or confusion, during an asthma attack
- Extreme difficulty breathing
- Rapid pulse
- Severe anxiety due to shortness of breath
- Sweating

Other symptoms that may occur with this disease:

- Abnormal breathing pattern --breathing out takes more than twice as long as breathing in
- Breathing temporarily stops
- Chest pain
- Tightness in the chest

Status asthmaticus:

It is a medical emergency, patient is hypoxic and cyanosed due to severe bronchospasm.It is characterized by Tachycardia (pulse rate > 120), Tachypnoea (respiratory rate > 30/minute), sweating, pulsus paradoxus (> 10 abnormal,> 20 profound obstruction), altered level of consciousness, and an inspiration-expiration ratio of 1:3 or 1:4.

Life threatening Features:

- Patient cannot speak

- Central cyanosis
- Exhaustion,confusion,altered consciousness
- Bradycardia
- Silent chest
- Unrecordable peak flow
- Severe hypoxaemia(< 8 kPa)

Diagnosis:

Clinical diagnosis

- **Episodic asthma**: Paroxysms of wheeze, dyspnoea and cough, asymptomatic between attacks.
- **Acute severe asthma**: Upright position, use accessory respiratory muscles, can't complete sentences in one breath, tachypnea > 25/min, tachycardia > 110/min, PEF < 50% of pred or best, pulsus paradoxus, chest hyperresonant, prolonged expiration, breath sounds decreased, inspiratory and expiratory rhonchi, cough.
- **Life-threatening features**: PEF < 33% of pred or best, silent chest, cyanosis, bradycardia, hypotension, feeble respiratory effort, exhaustion, confusion, coma, PaO2 < 60, PCO2 normal or increased, acidosis (low pH or high [H+]).
- **Chronic asthma**: Dyspnea on exertion, wheeze, chest tightness and cough on daily basis, usually at night and early morning; intercurrent acute severe asthma (exacerbations) and productive cough (mucoid sputum), recurrent respiratoryinfection, expiratory rhonchi throughout and accentuated on forced expiration.

Physiological diagnosis

- Demonstration of variable airflow obstruction with reversibility by means of FEV1 and PEF measurement (spirometer and peak flow meter).

  1. FEV1 < 80% of pred – PEF < 80% of pred.

  2. Reversibility: A good bronchodilator response is a 12% and 200ml improvement in FEV1 20 min after inhalation of 200ug salbutamol (2 puffs).

3. Diurnal peak flow variation: Normal variation: Morning PEF 15% lowers than evening PEF. With asthmathis variation is > 15% (morning dipping).

4. Provocation studies:

(a) **Exercise:** A 15% drop in FEV1 post exercise indicates exercise induced asthma.

(b) **Metacholine challenge**: A 20% reduction in FEV1 at Metacholine concentrations < 8mg/ml indicates bronchial hyperreactivity. This is expressed as a PC20 value of eg 0.5mg/ml (= a 20% reduction in FEV1 at 0.5mg/ml Metacholine).

Immunological diagnosis

- Skin pricks wheal and flare response.
- IgE
- Eosinophil cationic protein (ECP).
- Peripheral blood and sputum eosinophilia
- Chest X Ray may be normal between attacks, Rule out other causes of wheezing.

Differential diagnosis:

- Chronic bronchitis
- Emphysema
- Cystic fibrosis
- Mechanical airway obstruction
- Foreign body aspiration
- Endobronchial tumour
- Cardiac failure
- Pulmonary embolism
- Pulmonary eosinophililia
- Carcinoid syndrome
- Allergic bronchopulmonary aspergillosis

3.6. LATERAL RESEARCH:

- The purified alkaloid piperdine was observed only in *Piper nigrum* but not in *Piper longum (*Lim *et al* 2009) idientified the alkaloids like pelliterine, piperidine, piperine and pellitorine in *Piper nigrum* and *Piper betle* and that was the first report on (E)-1-[3'4'-(methylenedioxy) cinnamoyl] pierdine 2 from Piper nigrum as a natural product.
- Catechin is a well-known flavonoid found in many food plants and often utilized by naturo-paths for the symptomatic treatment of several gastrointestinal, respiratory and vascular diseases. The Aim was to explore the biological basis for the medicinal use of this flavonoid by investigating whether catechin exhibits any pharmacological activity on smooth muscle preparations. Found that catechin dose-dependently relaxes both spontaneous and high K^+ (80 mM)-induced contraction in rabbit jejunum, showing specificity for the latter by causing a right-ward shift in the Ca^{2+} dose-response curve. Similar results were observed with verapamil, a standard Ca^{2+} channel blocker (CCB). Catechin also inhibited high K^+-induced contraction in intact smooth muscle preparations from rat stomach fundus, guinea-pig ileum and guinea-pig trachea. In rat aorta, catechin inhibit phenylephrine (PE, 1 uM) and K^+-induced contractions in a similar fashion. In PE-contracted, endothelium-intact aorta, this vasodilator effect was partially blocked by Ncùnitro-L-arginine methyl ester and atropine, indicating activity at cholinergic receptors and possibly a CCB effect at higher doses of catechin. In guinea-pig atria catechin was found inactive. These data suggest that catechin may possess Ca^{2+} antagonist activity - in addition to an endothelium-dependent relaxant component in blood vessels - thus providing a pharmacological basis for the efficacy of catechin in hyperexcitability disorders of gastrointestinal, respiratory and vascular smooth muscle.
- As an **anti-bacterial** compound, boric acid can also be used as an **acne** treatment. Boric acid can be used to treat **yeast** and **fungal infections** such as **candidiasis** (vaginal yeast infections) by inserting a vaginal **pessary** containing 600 mg of boric acid daily for 14 days or for yeast infection of the male pubic region (jock-itch or strong genital odor) by applying the powder to the skin all over the pubic region for several days to a week.

3. MATERIALS AND METHODS

Materials:

Marichchiyathi maaththirai has been selected from the classical siddha literature, “Anuboga Vaithya Theva Ragasium”.Incredients of the test drug are Pepper,Long pepper,Pomegranate fruit skin,Borax and Palm jaggery.

4.1.1. Collection of the drugs:

Pepper:

250 gram of the raw drug were collected from the Tampcol raw drug store at Chennai.The adulteration particles were cleaned well.And treated in shade drying.

Long pepper:

250 gram of the drug was collected from the Tampcol raw drug store at Chennai. Adulteration particles were cleaned well and treated in shade drying.

Pomegranate fruit skin:

Pomegranate fruits were collected from fruit stall, Thiruvanmiyur.peeled out the skin and treated the skin at shade drying (skin weight 500 gm).

Borax:

250 gram Borax was collected from the Tampcol raw drug store at Chennai.

Palm jaggery:

1 kg of Palm jaggery collected from raw drug store, Aminjikkarai, Chennai.

All materials were identified and confirmed by the Head of the Gunapadam department, GSMC, Chennai.

4.1. Preparation of the drug:

Purification of the raw materials:

- All the herbal raw drugs were cleaned to remove the impurities.

- Pepper was dipped in butter milk for one and1/2 hour,after that it was removed from butter milk,washed it thouroughly in water.After drying the water,it was fried well in a pan and spread in a plate.
- Long pepper was purified by lemon juice, it was dipped in lemon juice for 3 hours, and it was treated in shade drying.
- Vengaram was fried till the water content was evaporated, and then it was grinding with lemon juice, then it was dried.
- Mathulai pasha thol was treated in shade drying.

After purification process, each material should be complete dried and was powdered separately by grinding method.Those powder was sieved by white cloth (*Vasthirakayam).* Palm jaggery also powdered well. All material powder was stored in air tight container separately.

Preparation of Pills:

Purified Pepper (*Piper nigrum)* - ¼ part

Purified Long pepper (*Piper longum)* - ¼ part

Purified Borax (sodium bi borate) - half of the ¼ part

Pomegranate fruit skin *(Punica granatum*) - ½ part

Palm jaggary - 2 parts

Borax powder and pomegranate skin powder were put in a *kalvam* and mixed thouroughly for 10 minutes. After that pepper and long pepper powder also mixed for 10 minutes. Grinding should be done evenly. Palm jaggery was added with those material, and grinding for ½ anhour .Then it turn in to paste form.after that it remove from *kalvam* and put in a clean, dry vessel.The product was weighed by electronic weighing machine.

Wear a glouse in hand and rolling the pills. Each pill was 130 mg in weight. Pills are treated in shade dry for 2 days. After drying pills were stored in the air tight container.

Administration of the drug:

Form of the Drug : Maaththirai (tablet)

Route : Enternal (oral)

Dose : 1 maththirai (130 mg, 3 times a day)

Time of administration : After food (chewing type)

Vehicle : Water

kpsF (*Piper nigrum)*

Figure: 4.1

jpg;gpyp (*Piper longum)*

Figure: 4.2

khJis *(Punica granatum)*

Figure: 4.3

ntq;fhuk; (Borax)

Figure: 4.4

gidnty;yk; (PALM JAGGERY)

Figure: 4.5

kupr;rpahjpkhj;jpiu

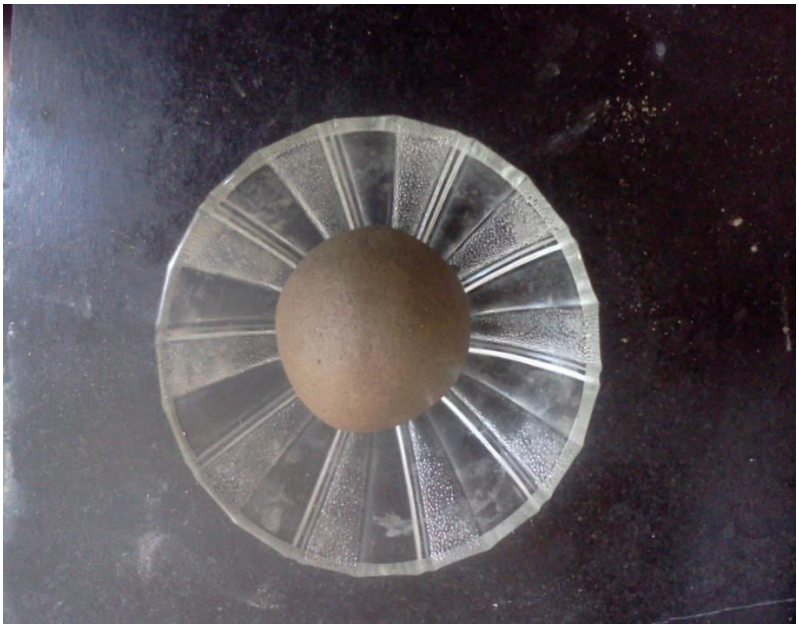


Figure: 4.6

Figure: 4.7

4.2. STANDARDIZATION OF TEST DRUG:

4.2.1. PHYTO CHEMICAL ANALYSIS OF TEST DRUG:

Medicinal plants are of great importance to the health of individuals and communities. The medicinal value of these plants lies in some chemical substances that produce a definite physiological action on the human body and these chemical substances are phytochemicals. These are non-nutritive chemicals that have protective or disease preventive property. The most important of these phytochemicals are alkaloids, flavonoids, tannins and phenolic compounds (Hill, 1952)

Table: 4.2.1

SL.No	EXPERIMENT	OBSERVATION
I.	**Test for Tannins:** A plant sample dried powder 0.5 gm is boiled in 20 ml of water and filtered.The filterate 2 ml is taken and 3-5 drops of $Fecl_2$ (0.1%) is slowly added to it.	Forms a brownish-green or bluish- black colour.
II.	**Test for Phlobatannins:** An aqueous 2 ml of plant sample is boiled in a hot water bath with 1 ml of aqueous Hcl	Absent of red precipitate
III.	**Test for Saponin:** A powdered 2 gm of plant sample is boiled with 20 ml of distilled water, then filtered,the filterate is added with fresh 5 ml of distilled water and shaken vigorously.	Permenant or persistant froth is not formed.The froth is not turned in to emulsion by adding three drops of olive oil.
IV.	**Test for Flavonoids:** An aqueous filterate of plant sample is mixed with 5 ml of dilute Ammonium solution and few drops of concentrated H_2SO_4 is slowly added through the sides of the test tube.	Yellow colour formed and disappears on standing.When 1% Alluminium solution is added in this mixture re-formation of yellow colour.
V.	**Test for steroids:** An ethonolic extract of plant sample 2ml is mixed with 2 ml H_2SO_4 and 0.5 gm Acetic anhydride.	The solution turns in to blue to green colour

VI.	**Test for Cardiac glycosides:** In 5 ml of plant Ethanolic extract, 2 ml of Glacial acetic acid, a drop of $Fecl_2$ and 1 ml of H_2SO_4 (slowly on the sides of the test tube) is added.	A brown ring indicates deoxy sugar of cardenolides/violet ring appears below brown ring/ in acetic acid layer a green ring is formed
VII.	**Test for Terpenoids:** In 5 ml of Ethanolic plant extract, 2 ml of chloroform and 3 ml of concentrated H_2SO_4 (slowly) is added.	A reddish brown interface layer is formed
VIII.	**Test for Carbohydrates:** An aqueous plant extract is boiled in a water bath with Benedict's solution.	A green or brick red or red precipitate shows the presence of reducing sugar
IX.	**Test for Alkaloids:** Alkaloids are identified by precipitate method	
	(d) Mayer's reagent: An aqueous plant extract of 2 ml is mixed with 2 ml of mayer's reagent	Forms whitish or yellowish cream colour precipitate
	(e) Wagner's reagent: An aqueous plant extract of 2 ml is mixed with 2 ml of wagner's reagent	Forms a brown or dark reddish precipitate
	(f) Dragendroff's reagent: An aqueous plant extract of 2 ml is mixed with 2 ml of Dragendroff's reagent.	Forms reddish brown precipitate
X.	**Test for Glycosides:** An aqueous plant extract of 2 ml is added with 1 ml of concentrated Hcl and boiled in a water bath for about 2 hours. The filtrate is separated and 3 ml of chloroform is added, then 10% of 1ml Ammonium solution is added.	Forms pink colour
XI.	**Test for Protein:** An aqueous extract /alcoholic extract of 2 ml is added with few drops of Biuret reagent	Formation of light blue or Pale violet colour is absent

	and kept in hot water bath for 10 minutes.	
XII.	**Test for Phytosterols:** An ethanolic or a methonolic plant extract 2 ml is mixed with 2 ml of Acetic anhydride stirred well and heated for 2 minutes in hot water bath then allowed to cool.1 or 2 drops of H_2SO_4 is added with the mixture slowly through the sides of the wall .	Forms greenish blue layer on the upper surface
XIII.	**Test for Phenolic compounds:** About 2 ml of aqueous plant extract is mixed with 2 ml of $Fecl_3$ solution.	Formation of deep bluish green colour is absent
XVI.	**Test for Volatile oil:** An ethanolic plant extract of 2 ml is mixed with one or two drops of tincture in warm water bath in a screwed cap test tube.	Red colour is not appeared
XV.	**Test for Fixed oil:** One ml of ethanolic extract of plant sample is mixed with 1 ml of 1% copper sulphate solution and 5 drops of 10% sodium Hydroxide solution	Formation of a clear blue solution is absent

Results are provided in table 4.2.1

4.2.2. CHEMICAL ANALYSIS

Preparation of extract of test drug:

2 gm of *Marichiathi maaththirai* is added with 5 gm of Sodium carbonate and taken in a 100 ml clean beaker and added with 20 ml of distilled water. The solution is boiled well for 10 minutes, then it is cooled and then filtered in a 100 ml volumetric flask. The filtrate is called sodium carbonate extract.

Then the following tests for the presence of acid radicals, basic radicals and miscellaneous were done.

Table: 4.2.2

SL NO	EXPERIMENT	OBSERVATION
I.	**Test for acid radicals:**	Presence of White Precipitate
1.(a)	**Test for Sulphate** 2 ml of the above prepared extract is taken in a test tube. To this add 2ml of 4% Ammonium oxalate solution.	
(b)	2ml of extract is added with 2ml of dilute hydrochloric acid until the effervescence ceases off. Then 2ml barium chloride solution is added	Absence of White Precipitate
2.	**Test for Chloride:** 2ml of extract is added with dilute nitric acid till the effervescence ceases. Then 2ml of silver nitrate solution is added.	Absence of white precipitate
3.	**Test for Phosphate** 2ml of the extract is treated with 2 ml of Ammonium molybdate solution and 2ml of concentrated nitric acid.	Yellow Precipitate is obtained.
4.	**Test for Carbonate:** 2ml of the extract is treated with 2ml of magnesium sulphate solution.	White precipitate is obtained.

5.	**Test for Sulphide:** 1 gm of the substance is treated with 2ml of concentrated Hydrochloric acid	Absence of Rotten egg smelling
6.	**Test for Nitrate:** 1gm of the substance is heated with copper turnings and concentrated sulphuric acid and viewed the test tube vertically down.	Absence of reddish brown gas.
7.(a)	**Test for Fluoride and oxalate** 2ml of the extract is added with 2ml of dilute acetic acid and 2ml of calcium chloride solution and heated.	Presence of white precipitate
(b)	5 drops of clear solution is added with 2ml of dilute sulphuric acid and slightly warmed to this, 1 ml of dilute potassium permanganate solution is added.	Absence of KMNO4 solution discolourisation.
8.	**Test for Nitrite** 3 drops of the extract is placed on a filter paper. On that, 2 drops a Acetic Acid and 2 drops of Benzidine solution is placed.	Absence of yellowish red colour
9.	**Test for Borate** 2 pinches of the substance is made into paste by using Sulphuric acid and Alcohol (95%) and introduced into the blue flame.	Absence of Green tinged flame
II.	**Test for basic radicals**	
10.	**Test for lead**	
	2 ml of the extract is added with 2 ml of Potassium iodide solution	Absence of Yellow precipitate
11.(a)	**Test for Copper** One pinch of substance is made into paste with concentrated Hydrochloric acid in a watch glass and introduced into the non luminous part of the flame.	Bluish green coloured flame is obtained.
(b)	2ml of the extract is added with excess of Ammonia solution	Absence of deep blue

12.	**Test for Aluminium** To the 2 ml of extract. Sodium Hydroxide solution is added in drops to excess.	Absence of White precipitate.
13(a)	**Test for Iron** To the 2 ml of extract, 2 ml of Ammonium Thiocyanate solution is added.	Presence of Blood red colour
(b)	To the 2 ml of extract, 2 ml of Ammonium Thiocyanate solution and 2 ml of concentrated Nitric Acid is added.	Blood red colour is obtained.
14.	**Test for Zinc** To the 2 ml of extract Sodium Hydroxide solution is added in drops to excess.	Absence White precipitate
15.	**Test for Calcium** 2 ml of the extract is added with 2 ml of 4% Ammonium Oxalate solution.	Presence of White precipitate.
16.	**Test for Magnesium** 2ml of extract, Sodium Hydroxide solution is added in drops to excess.	Presence of White precipitate.
17.	**Test for Ammonium** 2 ml of extract few ml of Nessler's Reagent and excess of Sodium Hydroxide solution are added.	Reddish brown precipitate is obtained
18.	**Test for Potassium** A pinch of substance is treated with 2 ml of Sodium Nitrite solution and then treated with 2 ml of Cobal Nitrate in 30% glacial Acetic acid.	Presence of Yellow precipitate
19.	**Test for Sodium** 2 pinches of the substance is made into paste by using Hydrochloric acid and introduced into the blue flame.	Presence of Yellow colour flame
20.	**Test for Mercury** 2 ml of the extract is treated with 2 ml of Sodium Hydroxide solution.	Absence of yellow precipitate
21.	**Test for Arsenic** 2 ml of extract is treated with 2 ml of silver	Absence of Yellow precipitate.

	Nitrate solution	
22.	**Test for Starch** 2ml of extract is treated with weak iodine solution	Absence of Blue colour
23.	**Test of reducing Sugar** 5ml of Benedict's qualitative solution is taken in a test tube and allowed to boil for 2 minutes and added 10 drops of the extract and again boiled for 2 minutes. The colour changes are noted.	Green colour is obtained.
24.	**Test of the alkaloids** 2ml of the extract is treated with 2ml of potassium lodide solution	Red colour developed

Results are discussed in table 4.2.1

4.2.3. PHYSIO-CHEMICAL ANALYSIS OF TEST DRUG:

Elemental analysis of *marichiyathi maaththirai*

FTIR

- **Fourier Transform Infrared Spectroscopy** (FTIR) is an analytical technique used to identify mainly organic materials.
- Itis useful in identifying the functional groups like -OH, -CN, -CO, -CH, -NH2, etc.
- Especially capable of identifying the chemical bonds of organic materials
- Identifies water, phosphates, sulphates, nitrates, nitrites, and ammonium ions

The interpretation of infrared spectra involves the correlation of absorption bands in the spectrum of an unknown compound with the known absorption frequencies for types of bonds. This table will help users become more familiar with the process. Significant for the identification of the source of an absorption band are intensity (weak, medium or strong), shape (broad or sharp), and position (cm-1) in the spectrum. The result of FTIR is discussed in graph 4.2.3.1.

ICP-OES:

Inductively coupled plasma atomic emission spectroscopy (ICP-AES), also referred to as inductively coupled plasma optical emission spectrometry (ICP-OES), is an analytical technique used for the detection of trace metals.

It is a type of emission spectroscopy that uses the inductively coupled plasma to produce excited atoms and ions that emit electromagnetic radiation at wavelengths characteristic of a particular element. The intensity of this emission is indicative of the concentration of the element within the sample.

SEM:

The Scanning Electron Microscope (SEM) is a microscope that was electrons rather than light to form an image. There are many advantages to using the SEM instead of a light microscope.

The SEM has a large depth of field, which allows a large amount of the sample to be in focus at one time.

The SEM also produces images of high resolution, which means that closely spaced features can be examined at a high magnification. Preparation of the samples is relatively easy since most SEM one require the sample to be conductive.

The combination of higher magnification, larger depth of focus, greater resolution, and easy of sample observation marks the SEM one of the most heavily used instruments in research areas today. The results are provided in the figure 4.2.3.2.

4.2.4. TOXICOLOGICAL STUDIES

We should consider all available information on the test substance prior to conducting the study. Such information will include the identity and chemical structure of the test substance, its physical chemical properties and the results of any other *in vitro* or *in vivo* toxicity tests on the substance, toxicological data on structurally related substances or similar mixtures, and the anticipated uses of the substance. This information is useful to determine the relevance of the test for the protection of human health and the

environment, and will help in the selection of an appropriate starting dose. The method permits estimation of an LD50 with a confidence interval and the results allow a substance to be ranked and classified according to the Globally Harmonised System for the classification of drugs which cause acute toxicity.

The experimental animals were maintained at normal room temperature with a humidity of ± 5%. All the animals were feed with pellet diet obtained and tap water ad libitum throughout the experimental period. The animals were acclimatized to the laboratory conditions before experimental procedures were started. The experimental protocol for *marichiyathi maththirai* (XIII/VELS/COL/07/CPCSEA/IAEC/23.09.11) was approved by the CPCSEA/IAEC of Vel‘s College of Pharmacy, Vel‘s University, Pallavaram, Chennai.

4.2.4.1. Acute toxicity study:

Healthy nulliparous and non-pregnant adult albino Swiss mice (20- 35g) of female sex were housed in polyethylene-walled cages and subjected to acute toxicity studies as per guidelines (425) suggested by the OECD 2001. The animals were kept on a 12 h light: 12 h dark regime (lights on from 7:00 h to 19:00 h) at 23 °C prior to the experiments. The animals had free access to water and standard diet. Mice were deprived of food but not water 3 and 12 h prior to administration of the test substances respectively.

Groups of albino Swiss mice were given single oral doses of 2000 mg/kg b.w. of Marichyathi Mathirai. The control group received distilled water at the same volume. Observations were made systematically and all rats were observed at the first, second, fourth and sixth hours and once daily. The number of survivors was noted after 24 h and these were then maintained for a further 14 days with a once daily observation.14 days for clinical signs of toxicity such as changes in rate and depth of breathing, color of body surfaces, frequency and nature of movement, marked involuntary contraction or seizures, contraction of voluntary muscle, and loss of reflex, etc.

The survival rats were weighed daily and observed further for clinical signs of toxicity for up to 14 days. After the experimental period, as the conclusion of experiment, all surviving animals were fasted and anesthetized with anesthetic ether and the gross

morphology of internal organs such as heart, lungs, livers, kidneys, spleen, adrenals, sex organs, brain were examined.The result is discussed in table 4.2.4.1.

4.2.4.2. Sub-acute toxicological studies:

A 28-day study with a 14-day recovery period was conducted. The study design met the criteria outlined in OECD Guideline 407 ("Repeated Dose 28-Day Oral Toxicity Study in Rodents") and was conducted as a limit test. Groups of 4-5-week-old Wistar rats were given by gavage 0 (vehicle control) or 250, 500 and 1000mg/kg bw/day of Marichyathi Mathirai in 2% Carboxy methyl cellulose for 28 days. Half of the animals were followed for a 14-day recovery period. The animals were housed 2 per cage and were given rodent diet and tap water ad libitum.

Body weights were recorded on the day of arrival, day of randomization, prior to treatment, on days 7, 14, 21, and 28 of post dosing, and on days 7 and 14 of the recovery period. The rats were observed twice daily for any adverse clinical signs or mortality during the treatment and recovery periods. Feed consumption (g/day) was recorded weekly throughout the entire study and water intake (g/day) was recorded daily during different weeks of the treatment period and of the recovery period. Prior to termination, fasting blood samples were taken from the retro orbital vein for hematological and clinical chemistry evaluations.

Main Observations made in this study

Clinical signs

All the rats were observed at least twice daily with the purpose of recording any symptoms of ill-health or behavioural changes. These observations were also performed on week-ends. The observations included but were not limited to changes in skin and fur, in the eyes and mucous membranes, in the respiratory, circulatory, central nervous and autonomous systems, somatomotor activity and behaviour.

Body weight

The bodyweight of each rat was recorded one week before the start of treatment, daily during the course of the same and on the day of sacrifice. The rats selected for the recovery period were weighed twice a week and on the day of sacrifice. The mean weights for the different groups and sexes were calculated from the individual weights.

Food intake

Prior to the beginning of treatment, and afterwards once a week, the food intake of each cage was recorded and the mean weekly intake per rat was calculated.

Water intake

Water intake was checked by visual observation during the Study. In addition, the water consumption in each cage was measured daily for a period of 5 days, during the 3rd week of treatment and, subsequently, during the 2nd week of the recovery period.

Ophthalmoscopy

Before treatment started, the eyes of all animals were examined. These examinations included the cornea, the conjunctiva, the sclera, the iris and fundus. The observations were made with the aid of an indirect ophthalmoscope. Before the end of the treatment and before the end of the recovery period, additional examinations of the eyes of the animals from the Control and high dose groups were made.

Laboratory Studies

During the 4th week of treatment, samples of blood were withdrawn from the retro orbital sinus of rats from each group, under light ether anaesthesia after fasting for 16 hours. The blood samples were taken from each animal approximately between 7:30 and 10:00 hours in order to reduce biological variation caused by circadian rhythms. In addition, samples of the urine produced during 16 hours by rats were taken. To this end the rats were deprived of food for this period of time.

Haematology

The following determinations were performed:

Haemoglobin g/100 mL, Haematocrit %, Mean corpuscular volume (MCV) fL, Mean corpuscular haemoglobin (MCH) pg, Mean corpuscular haemoglobin concentration

(MCHC) g/100 mL, Reticulocyte count %, Total leukocyte count $10^3/\mu L$, Differential leukocyte count$10^3/\mu L$ includes Neutrophils, Lymphocytes, Eosinophils, Basophils, Monocytes, and Platelet count $10^3/\mu L$.

Biochemistry

The following blood chemistry determinations were carried out:

Glucose mg/100 mL, Urea mg/100 mL, Creatinine mg/100 mL, Total bilirubin mg/100 mL, Aspartate aminotransferase (AST/GOT) U/L, Alanine aminotransferase (ALT/GPT) U/L, Alkaline phosphatase U/L, Total cholesterol mg/100 mL, Sodium mmol/L, Potassium mmol/L, Chloride mmol/L, Calcium mg/100 mL, Total protein g/100 mL Albumin g/100 mL.

Analysis of urine

The following determinations were made:

Colour, Volume, Macroscopic observation, Specific gravity, pH, Proteins, Glucose, Bilirubin, Ketones, Urobilinogen, Haemoglobin

The results are presented using the following scale:

0 = negative, + = small quantity of the parameter analyzed, ++ = moderate quantity of the parameter analyzed, +++ = large quantity of the parameter analyzed. The urinary sediment was examined for the detection of Pus cells, RBCs, Epithelial cells, Crystals, Casts and Others.

Terminal Studies

On completion of the 4 weeks of treatment, two rats from each group were sacrificed by ether inhalation. The remaining rats were sacrificed at the end of the recovery period. A full autopsy was performed on all animals, which included examination of the external surface of the body, all orifices, cranial, thoracic and abdominal cavities and their contents. As the number of animals exceeded the number that could be sacrificed in one day, the autopsies were carried out at the end of the treatment period. However, each rat continued to receive the test substance until the day prior to its sacrifice.

After the blood collection, internal organs such as heart, lungs, livers, kidneys, spleen, stomach and brain, eyes, sex organs, uterus and epididymis were removed from all rats for detection of gross lesions. After routine processing, the paraffin sections of each tissue were cut at 5μm thickness and stained with haematoxylin and eosin for a microscopic examination.

Organ weights

After the macroscopic examination the following organs were weighed after separating the superficial fat like Brain, Heart, Spleen, Kidneys, Testes and epididymides, Liver, Lungs, Ovaries, Uterus, Pancreas, Spleen, Stomach, Testes and epididymides and Uterus (corpus and cervix). Organ weights were recorded. The results are provided in tables 4.2.4.2 to 4.2.2.10.

Statistical analysis:

The results are presented as means + SEM. Statistical significance was determined by one-way analysis of variance (ANOVA) and Dunnet't' test for significant difference. *P* values less than 0.05 were considered significant.

4.2.5. PHARMACOLOGICAL ACTIVITY

Broncho dilator and anti histaminic activity of *marichiyathi maththirai*

Materials and methods

Drugs:

Histamine dihydrochloride (Hi-media) was dissolved in distilled water and desired concentrations were prepared. The test drug *Marichyathi mathirai* concentration was 100microgram per ml prepared by dissolving with saline and then the volume was adjusted to 10 ml with normal saline for making the concentration of 100 μg/ml.in distilled water.

Drugs and Stock solution

Histamine dihydrochloride (Hi-media) was freshly prepared in normal saline (NaCl, 8.5 g/l), Carboxy methyl cellulose (2%) (Loba chemie Pvt. Ltd) was diluted with distilled water and desired concentrations were prepared. Physiological saline was widely

recommended, as it is known to be compatible with human tissue, and isotonicity with body fluid.Tyrode solution, Hisatmine (Sigma-Aldrich Chemie GMbH, Germany), Salbutamol (Loba Chemie Pvt. Ltd., India), Dexchlorpheniramine (Loba Chemie Pvt. Ltd., India). All other chemicals used were of analytical grade. All the prototypes were dissolved in minimum quantity and then the volume was adjusted to 10 ml with normal saline for making the concentration of 50 and 100µg/ml. The *Marichyathi Mathirai* was mixed uniformly in saline solution to achieve 1mg/ml as main stock solution and used in this study.

Animal

Male albino guinea pig weighing 350– 400g and Mice of either sex weighing 25-30g was kept in fasting condition 18 hours prior to commencement of experiment and given water ad libitum. The Institutional Animal Ethics Committee approved the experimental protocol and the conditions in the animal house approved by Committee for Supervision on Experiments on Animals. The study was conducted in accordance with IAEC guidelines. Animals were housed under standard laboratory conditions of temperature (25 ± 2°C) and 12/12 hr light/dark cycle and for antihistaminic study the guinea pigs were sacrificed by a blow to the head and exsanguinated as per CPCSEA recommended guidelines.

Invitro antihistaminic activity of *marichyathi mathirai* on isolated guinea pig ileum

Experimental Procedure

Guinea pig was sacrificed and a segment from ileum (2 cm) was dissected from the terminal ileum and mounted in an organ bath containing Tyrode solution (10 ml) between two stainless steel hooks under 0.5 to 1 g initial tension. The lower hook was fixed at the bottom of the organ bath and upper one was connected to an isotonic transducer. The Tyrode solution composition (pH 7.4) was NaCl-8.0, KCl-0.2, $CaCl_2$-0.2, $MgCl_2$-0.1, $NaHCO_3$ .1.0, NaH_2PO_4-0.05, and Glucose-10.0 gms/liter.

It was continuously aerated and maintained at 37 ± 0.5ºC The equilibrium period was 60 min and the bath solution was refreshed every 15 min. After equilibrium period, a

dose response curve for histamine in variant molar concentrations, by maintaining 45 min time cycle was taken separately.Results are provided in the table 4.2.5.1.

In Vivo Broncho dilator activity of *Marichiyathi maththirai* in Guinea pig

Experimental Procedure

Experimental bronchial asthma was induced in guinea pigs by exposing them to histamine. Overnight fasted guinea pigs of either sex (350-450) were selected and randomly divided in to five groups each consisting of six animals. Group 1 was treated as control, Test group animals received of Marichyathi Mathirai at the dose (500 mg/kg). All the doses were given orally. Prior to drug treatment each guinea pigs were exposed to an atomised fine mist of 2% w/v histamine dihydrochloride aerosol (dissolved in normal saline) using a nebulizer in the histamine chamber. Guinea pigs exposed to histamine aerosol showed progressive signs of difficulty in breathing leading to convulsions, asphyxia and death. The time until signs of convulsion appeared is called pre-convulsion time (PCT) and was determined from the time of exposure to onset of convulsions.

As soon as pre convulsion time was noted, animals were removed from the chamber and placed in fresh air to recover. The percentage protection offered by treatment was calculated by using the following formula:

Percentage protection = $(1 - T_1/T_2) \times 100$

Where; T_1 = the mean of PCT of control group animals.

T_2 = the mean of PCT of test group animals.

Statistical Analysis

Ileum contractions induced by agonist were assumed as 100% and reductions induced by test drug calculated. Percentage of ileum contraction was expressed as mean ± SEM. Results were analyzed using one-way analysis of variance (ANOVA). Probability value less than 0.05 were considered as significant.Results are discussed in table 4.2.5.2.

GUINEAPIG

Figure: 4.2.5.1

HISTAMINE AEROSAL CHAMBER

Figure: 4.2.5.2

4.3. CLINICAL ASSESSMENT

This study is an initial step, to once again prove that siddha medicine still continues to shine in limelight in the new millennium and definitely it will be very useful if further research is made.

Siddha medicines are being increasingly utilized to treat a wide variety of diseases, though the knowledge about their mode of action is relatively scanty. There is a growing interest regarding the pharmacological evaluation of various drugs used in traditional system of medicine. Allergies occur when a hypersensitive immune system reacts to a common or unusual substance. The number of individuals suffering with allergic illnesses is increasing in the industrialized, as well as in large cities of developing countries. Allergies also have reached high prevalence and incidence in all over the world.

Objectives:

- To evaluate the Broncho dilator and anti-histaminic activity of *marichiyathi maththirai.*
- To explore the efficacy of *marichiyathi maththirai* in op patients with bronchial asthma.

Design of the Study:

- The Open clinical trial phase-2B
- Study period was 2-3 months

Study Centre:

Govt.Siddha medical college hospital and Aringar anna government hospital of Indian Medicine and Homeopathy, Arumbakkam, Chennai – 106.

Study Participants:

Both men and women and members of all races and ethnic groups were eligible for this trial. Treatment was being administered on an *inpatient/outpatient* basis. The patients were selected from the In-patient and Out-patient department of Govt Siddha medical college hospital and Arignar Anna Government Hospital of Indian Medicine and Homeopathy, Chennai – 106.

Number of Subjects:

Number of participants will be 40-50.

Registration Process:

To register a patient, the following documents should be completed by the investigator.

- Copy of required laboratory tests
- Signed patient consent form
- Other appropriate forms (e.g., Trial profoma).

This Clinical trial is an ethical and scientific quality standard for designing, conducting and recording trials that involve the participation of human subjects. Compliance with this standard provides assurance to public that the rights, safety and well being of trial subjects are protected, consistent with the principles enshrined in the Declaration of Helsinki and ensures that clinical trial data are credible

Selection of patients

The Clinical trial is usually focus on asthma control as measured by pulmonary function test (FEV_1, FVC, PEFR, FVR), symptom scores and medication requirement. After taking the short history of patient, all the selected cases were carefully examined and records were maintained. To arrive at the diagnosis along with the history taking and the following investigations were done. The patients were selected for clinical trials as per the following criterias, which are listed below

- Recurrent wheezing
- Coughing
- Trouble in breathing
- Chest tightness
- Symptoms that occurs or worsen at night
- Symptoms that are triggered by cold air,exercise or exposure to dust,smoke and pollens
- Family history also taken.

Consent form

Patients were included in this clinical study only after getting the concern form accordance of 'Helsinki'. Voluntary written assent of a subject's willing to participate in this study and in its documentation. The confirmation is sought only after information about the trial including an explanation of its status as research, its objectives, potential benefits, risks and inconveniences, alternative treatment that may be available and of the subject's rights and responsibilities has been provided to the potential subject.

The patients were selected for clinical trials as per the following criterias, which are listed below

Inclusion criteria:

- Co operative patient
- Cough with expectoration
- Expiratory wheeze
- Tightness of the chest
- Positive allergic history
- History of previous attack

Exclusion criteria:

- Infectious disease patient
- Pulmonary tuberculosis
- Malignancy
- Renal diseases
- Cardio vascular diseases

Withdrawal criteria:

- Exacerbations of symptoms
- Unacceptable adverse events
- Patient decided to withdraw from the study
- Irregular visit
- Irregular Medications
- Alcohol intake

Investigations criteria:

Blood: TC, DC, ESR, Hb, blood sugar PP.

Stool: Routine examination

Urine: Routine examination

Chest: X-ray

Sputum for AFB

ECG to exclude cardiac disease

Peak flow meter reading

Spirometry reading

PEAK FLOW METER

Figure: 4.3.1

SPIROMETRY

Figure: 4.3.2

Peak flow meter:

A peak flow meter is a small device, that patient blow into. It measures the fastest rate of air (airflow) that they can blow out of the lungs. It records airflow in litres per minute (l/min). There are different brands of peak flow meter. They all do the same job.

Measuring method:

Step 1: Before each use, make sure the sliding marker or arrow on the Peak Flow Meter is at the bottom of the numbered scale (zero or the lowest number on the scale).

Step 2: Stand up straight. Take a deep breath (as deep as we can). Put the mouthpiece of the peak flow meter into the mouth. Close lips tightly around the mouthpiece. Be sure to keep the tongue away from the mouthpiece. In one breath, blow out as hard and as quickly as possible. Blow a "fast hard blast" rather than "slowly blowing" until emptied out nearly all of the air from the lungs.

Step 3: The force of the air coming out of the lungs causes the marker to move along the numbered scale. Note the number on a piece of paper.

Step 4: Repeat the entire routine three times.

Step 5: Record the highest of the three ratings. Do not calculate an average. This is very important. Can't breathe out too much when using the peak flow meter but can breathe out too little. Record the highest reading.

Spirometry:

The spirometry test is performed using a device called a **spirometer,** which comes in several different varieties. Most spirometers display the graphs, called spirograms.

Procedure

The basic forced volume vital capacity (FVC) test varies slightly depending on the equipment used. Generally, the patient is asked to take the deepest breath they can, and then exhale into the sensor as hard as possible, for as long as possible, preferably at least 6

seconds. It is sometimes directly followed by a rapid inhalation (inspiration), in particular when assessing possible **upper airway obstruction.** Sometimes, the test will be preceded by a period of quiet breathing in and out from the sensor (tidal volume), or the rapid breath in (forced inspiratory part) will come before the forced exhalation.

During the test, soft nose clips may be used to prevent air escaping through the nose. Filter mouthpieces may be used to prevent the spread of microorganisms.

Limitations of test

This scheme is highly dependent on patient cooperation and effort, and is normally repeated at least three times to ensure reproducibility. Since results are dependent on patient cooperation, FVC can only be underestimated, never overestimated. FEV_1 may sometimes be overestimated in people with some diseases — a softer blow can reduce the spasm or collapse of lung tissue to elevate the measure.

Due to the patient cooperation required, spirometry can only be used on children old enough to comprehend and follow the instructions given (6 years old or more), and only on patients who are able to understand and follow instructions — thus, this test is not suitable for patients who are unconscious, heavily sedated, or have limitations that would interfere with vigorous respiratory efforts. Other types of lung function tests are available for infants and unconscious persons.

Another major limitation is the fact that many intermittent or mild asthmatics have normal spirometry between acute exacerbations, limiting spirometry's usefulness as a diagnostic. It is more useful as a monitoring tool, a sudden decrease in FEV1 or other spirometric measure in the same patient can signal worsening control, even if the raw value is still normal. Patients are encouraged to record their personal best measures.

Drug and dosage:

Drug	: Marichchiyathi Maaththirai
Route	: Enternal
Dose	: 1 tablet (130 mg) Tid (After food)

Vehicle : Water

Dietery advice:

Therapeutic foods or **nutrients** that help controlling asthma are: Omega-3 and omega-6 **fatty acids**, foods high in flavonoids and beta carotene, Vitamin B12, Vitamin B6 (Vitamin B6 deficiency is common in asthmatics), high amounts of **vitamin B12 supplements** (1,500 mcg per day) have been found to reduce the tendency for asthmatics to react to sulfites, Selenium, **Vitamin E, Vitamin C,** and Magnesium (magnesium can prevent spasms of the bronchial passages).

Medical advice:

- Patients are advised to avoid known offending allergen which is identified either by experience or by skin sensitivity test.
- Take light meals at night and try to sleep early
- Drink plenty of water
- Try to avoid dust, cigarette smoke and smoky surroundings.
- Avoid cold water bath.Avoid cold, deep fried food.
- Avoid keeping pets such as dogs, cats.
- Avoid alcohol, lime and bananas.
- Advice to do breathing exercise

Criteria for assessment of response to therapy:

1. Marked Relief : 75%-90% relief in the presenting signs and symptoms marked normality pathological investigation.
2. Moderate Relief : 60%– 75% relief signs and symptoms, moderate normality of pathological investigation.
3. Mild Relief : 50%-60% relief of signs and symptoms no marked changes in pathological investigations.
4. Poor : Below 50% relief of signs and symptoms

Observation:

- ❖ The duration of the treatment ranged between 45-90 days.
- ❖ At the time of treatment, no adverse effects were observed.
- ❖ The drug was well accepted by all the patients.

Ethical Review:

The protocol and any amendments have been submitted to the Govt. Siddha Medical College, Chennai-106. Institutional Ethical Committee (IEC) for formal approval to conduct the study. All subjects for this study will be provided a consent form describing this study and providing sufficient information for subjects to make an informed decision about their participation in this study. This consent form was also submitted with the protocol for review and it was approved by the IEC. The formal consent of a subject, using the IEC-approved consent form, has been obtained before that subject was admitted to any study procedure. This consent form was signed by the subject or legally acceptable surrogate, and the investigator-designated research professional obtaining the consent.

Statistical analysis:

The data were subjected to paired student‘t’ test to determine the significance of changes followed by comparisons to analyze the significance of difference within the before and after treatment. P values of <0.05 were taken as significant.Results are discussed in table 4.3.6.

Table: 4.3.1 PERSONAL HABITS

Habits	No of patients	Percentage (%)
Vegetarian	8	14.5%
Non- vegetarian	47	86%
Smoking	28	51%
Alcohol & Smoking	18	33%

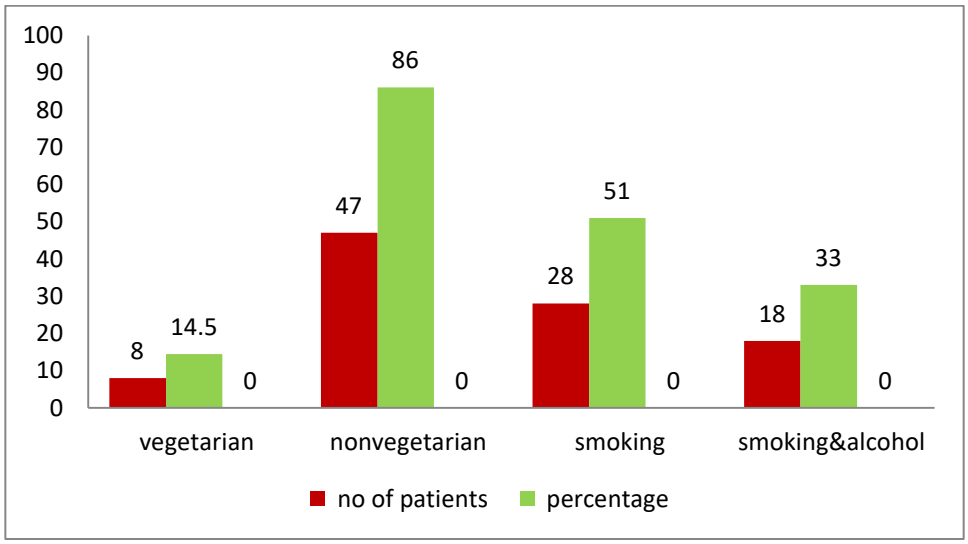
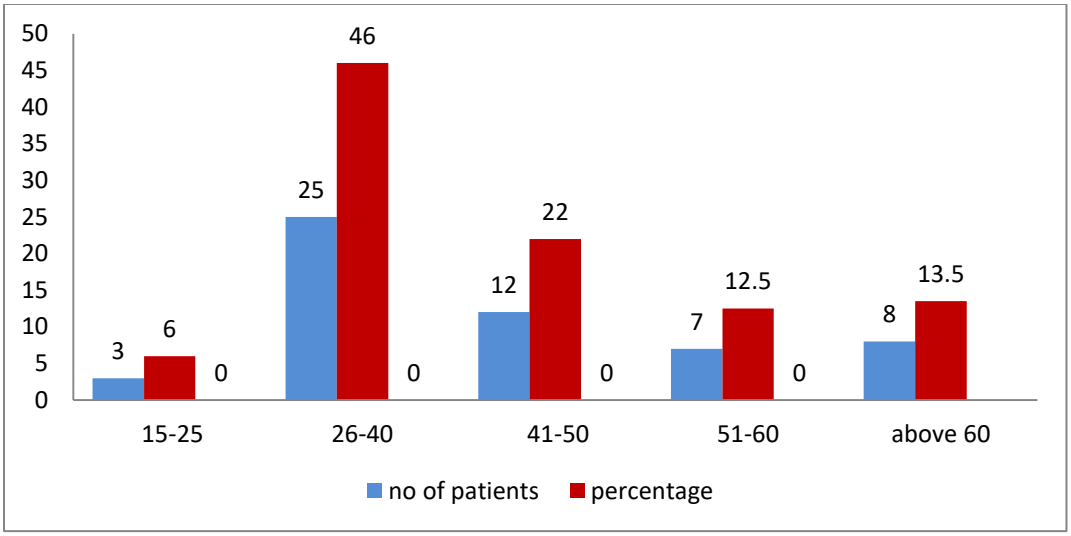


Table: 4.3.2 AGE DISTRIBUTION

SL. NO	AGE	NO OF PATIENTS	PERCENTAGE(%)
1	15-25	3	6%
2	26-40	25	46%
3	41-50	12	22%
4	51-60	7	12.5%
5	Above60	8	13.5%

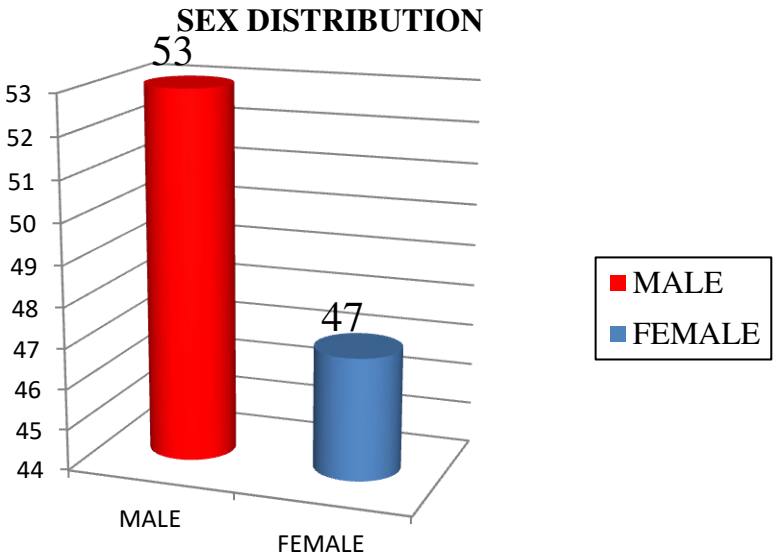


Inference: Among 55 patients,

- ❖ 3 patients belongs to the age group of 15-25 years
- ❖ 25 patients belongs to the age group of 26-40 years
- ❖ 12 patients belongs to the age group of 41-50 years
- ❖ 7 patients belongs to the age group of 51-60 years
- ❖ 8 patients belongs to the age group of above 60 years

Table: 4.3.3 SEX DISTRIBUTION

SL. NO	SEX	NO. OF PATIENTS	PERCENTAGE
1	Male	29	53
2	Female	26	47
TOTAL		55	100



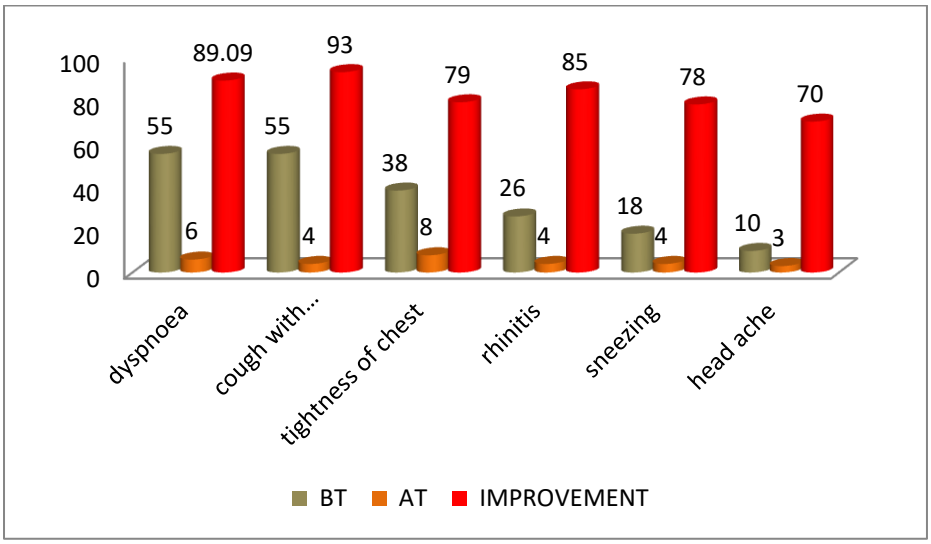
Inference:

Among 55 patients,

- 29 patients were male
- 26 patients were female

Table:4.3.4 **IMPROVEMENT IN SIGNS & SYMPTOMS**

S. No.	SIGNS AND SYMPTOMS	NO. OF PATIENTS			
		BT	AT	IMP.	IMPROVEMENT (%)
1	Dyspnoea	55	6	49	89.09
2	Cough with Expectoration	55	4	51	92.72
3	Tightness of chest	38	8	30	79
4	Rhinitis	26	4	22	85
5	Sneezing	18	4	14	78
6	Head ache	10	3	7	70



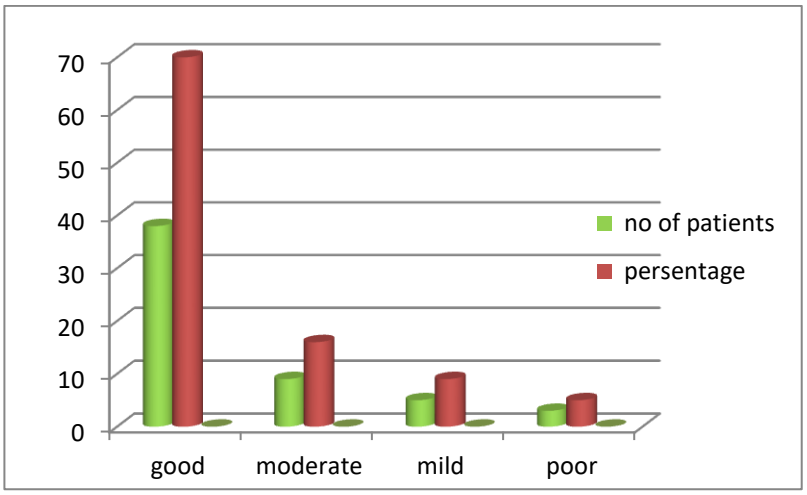
Inference:

Among 55 patients

- 49 out of 55 patients were relieved from Dyspnoea.
- 51 out of 55 patients were relieved from cough with expectoration.
- 30 out of 38 patients were relieved from Tightness of chest.
- 22out of 26 patients were relieved from Rhinitis.
- 14 out of 18 patients were relieved from Sneezing.
- 7 out of 10 patients were relieved fromHead ache.

Table:4.3.5 GRADATION OF RESULT

Relief	No of patients	Results (Percentage)
Good	38	70%
Moderate	9	16%
Mild	5	9%
Poor	3	5%



INFERENCE:

Among 55 patients,

- ❖ 38 patients were good.
- ❖ 9 patients were moderate
- ❖ 5 patients were mild.
- ❖ 3 patients were poor.

STATISTICAL ANALYSIS:

"p" value & statistical significance:

Table: 4.3.6

Treatment	Signs & symptoms	Mean	S.D	S.E.M
Before treatment	6	28.83	18.28	7.46
After treatment	6	22.83	17.30	7.06

From the table we calculated the descriptive statistic like Mean, S.D & S.E.M of Mean for the improvement score before and after treatment.

"t" Table:

t-Table	S.D	S.E.M	"t" Value	"p" Value
Pre vs Post	5	5.395	5.4367	0.0003

The two tailed "p" value equals 0.0003, by conventional criteria, this difference is considered to very statistically significant.

4. RESULTS & DISCUSSION

Various studies have been carried out in this trial drug *Marichiyathi maaththirai.* The study includes literary collections, physico and Phyto chemical analysis, pharmacological study, toxicological study and clinical study. *MM* was taken for the treatment of Bronchial asthma. The drug has been selected for the treatment of Bronchial asthma in reference with ***Anubava vaithya deva ragasium*** written by J.Seetharama prasath.

Literary collections about the drug from various text books were done. It indicates the efficacy of the drug in the treatment of Bronchial asthma. **Botanical aspect** deals with the identification, description, cultivation and ethno medicinal importance of the raw drugs. **Gunapadam aspect** expressed that the drug possess good Broncho dilator property.

Literary collections about the drug from various text books give engross hope about its Broncho dilator activity.

From the literatures, pepper and long pepper have pungent taste, Pomegranate has astringent and Borax has sweet and astringent tastes. The potency of all drugs is Hot and Bio-transformation of the compound drug is pungent.

The trial drug has Pungent and sweet taste.The potency of the drug is Hot and Bio transformation of the drug is pungent. As per the siddha concept,

“fgj;jpdhyd;wp fhrRthrk; fhzhJ”

–Njiuau; gpzpKjw; fhuzk;-ntz;gh

Eraippirumal occurs due to the derangement of the kabha humour.

“fhue; Jtu;frg;Gf; fhl;LQ; Ritnay;yhk;

rhug; gupfhuQ; rhw;W”

-fz;Zrhkpak;

The properties of pungent taste are decreases the kabha humour, increases the vatha and pitha humour. It relieves throat congestion. Properties of hot potency are decreasing the kabha, neutralize the vatha humour and regulate the digestion. By giving this drug it normalise the deranged humours and reduces the signs and symptoms.

Phyto chemical analysis:

Presence of phyto-chemical constituents of test drug are Alkaloids, Terpenoids, Carbohydrates, Steroids, Flavonoids, Tannins, Glycosides, Phytosterols, Cardiac glycosides.

Table: 4.2.1

SL.NO	PHYTOCHEMICAL CONSTITUENTS	RESULT
1.	Alkaloids	Presents
2.	Flavonoids	Presents
3.	Steroids	Presents
4.	Phlobatannins	Presents
5.	Glycosides	Presents
6.	Carbohydrates	Presents
7.	Aminoacids	Presents
8.	Triterpenoids	Presents
9.	Cardiac glycosides	Presents

From the above results, the presence of **Alkaloids** and **Terpenoids** were confirmed and are important to cure the chronic diseases and nervine disorders. Alkaloids are the substances which has anti allergic and anti asthmatic activities.The presence of **Cardiac glycosides** and **Phlobatannins** are essential in the treatment of Cardiac disorders and vascular complications. They have an anti inflammatory activity which helps in chronic disorders.

The availability of **Flavonoids** and Phenolic compounds in the trial drug clearly indicates the drug's potency against the degenerative changes and aging process by the anti-oxidant property. Flavonoids also having anti-inflammatory activities.It also help to relieve from inflammation and degeneration of lungs in BA.

Presence **Aminoacids** were confirmed that the broncho dilator property of the test drug. Presence of **Steroids** in this test drug was confirmed and important to cure the chronic inflammatory diseases like BA. By the available phytochemicals, the trial drug has the therapeutic potency against the chronic inflammatory disorders like Bronchial asthma and its complications.

Chemical analysis:

The bio-chemical analysis of Marichiyathi maaththirai showed the following chemicals,

Acid radical: Fluride, Oxalate, Phosphate, Borate, Carbonate, Pottassium, Magnesium, Sodium, Ammonium

Basic radical: Iron, calcium, copper

Reducing sugar and Alkaloids also present.

The Mg ions are playing the important role in the Respiratory system. The Mg is the one of the principle cations of soft tissues .Even in acute asthma the Magnisium ions are responsible for broncho dilator and anti cholinergic action.

Presence of ferrous ion in the drug increased Hb concentration in the blood, enhancing the arterial oxygen level higher than the co_2. The ferrous ion in the MM maintains the normal arterial PAO_2 (12 KPa).The drug prevents hypoxaemia and enhances gas exchange effectively.They will promote the normal ventilation of the lungs and reduces the dyspnoea.

Presence of Calcium ions were confirmed that keeping the normal heart beat.Calcium is very much important in relaxing of muscles and help to prevent the chet congestion.

The availability of ammonium was clearly indicates that this drug is the best expectorant action in chloride form and caused by irritative action on the bronchial mucosa.This causes production of excess respiratory tract fluid which presumably is easier to cough up. Presence of borate also indicates that this drug has strong broncho dilator activity.

Copper is necessary for the formation of RBC and other components of the blood system.Cu ions also functions to neutralize the free radicals which are unstable oxygen by products that are formed as a result of normal body processes or exposure to environmental pollutants and can cause severe damage to cells. Presence of Cu indicates the anti oxidant property of the drug, which helps to prevent the degeneration.

-Ambika shanmugam, Fundamentals of BioChemistry, page no.554, 569 and 577.

Flavanoids, Tannic acids Tannins and Phenols containing plants are having Anti-oxidant and Expectorant properties. –**Javanmwas ardi J et al.**

From above description, conclude that the test drug have important role in respiratory disorders like BA.

Physio chemical analysis:

FTIR absorptions:

Frequency,cm^{-1}	Bond	Functional group
3433	- N-H stretch	1^0,2^0 amines,amides
2923,2853	- O-H stretch	Carboxylic acids
2384	- C=O stretch	carbonyls(general)
2127	- -C=C- stretch	alkenes
1633	- N-H bend	1^0 amines
1446	- C-C stretch (in-ring)	aromatics
1257	- C-N stretch	aromatic amines
1164	- C-N stretch	aliphatic amine
1110	- C-N stretch	aliphatic amines
1084	- C-O stretch	alcohols, carboxylic acids, esters, ethers
900	- C-H “oop”	aromatics
666	- C-Br stretch	alkyl halides

Physio chemical analysis:

Total ash value - 9.73% w/w

Acid insoluble ash - 0.88% w/w

Water soluble ash - 5.4% w/w

Moisture content - 8.55% w/w

Crude fibre content - 29.70% w/w

pH - 7.1-7.5

SEM particle size in micron- 100-200µ

This level is indicates the absorption is very good.

Physico chemical analysis:

Table: 4.2.3.1.

Colour Charecters of Herbo Mineral:

S.No	Sample	Colour-Under ordinary light	Colour-Under UV light
1	Powdered material	Brown	Brown

Table : 4.2.3.2.

S.No.	Parameters	Values obtained (%w/w)	Heavy Metals	Result
1	Total ash value	9.76	Lead	BDL
2	Acid insoluble ash	0.94	Cadmium	BDL
3	Water soluble ash	5.6	Mercury	3ppm
4	Moisture content	8.75	Arsenic	BDL
5	ForeignOrganic Matter	0.86	Iron	0.5ppm

BDL – Below Detective Level; PPM – Parts Per Million.

The colour of the sample is same in both the ordinary light and UV light, which proves that there is no radio active compounds present in that. The total ash value is 9.76% (w/w), acid-insoluble ash value is 0.94% (w/w) and most of the total ash is soluble in acid. So acid-insoluble ash value is very low denoting that it fully gets digested in our alimentary without producing any illeffects. Meanwhile, the water-soluble ash value is 5.6% (w/w) and the foreign organic matter is also very low and this proves that it paves no way for the growth of micro organisms.So this study helps to standardize the preparatory method of this herbo mineral formulation.

By the heavy metal analysis result, there is no detection of the heavy metal in test drug.

The analytical parameters like total Ash value, Acid insoluble ash value, Loss on drying values are helping us to interpret the digestion and solubility capacity of the crude extract. As per the result the tested sample contains good percentage of solubility as well as digestive capacity.

Toxicological study:

Acute and sub acute toxicity

The oral toxicity study has been done as per the OECD guidelines 425.According to literature, MM that causes no adverse effect at a dose exceeding 5 g/kg will be considered as 'practically non-toxic'. No adverse clinical signs were reported with the exception of one treated rat, which showed mild lethargy with decreased motor activity on the first day of the post treated observational period. Pathological examination revealed these deaths to be gavage errors rather than inherent toxicity of MM. Hence, 0.25, 0.5 and 1g/kg of *Marichyathi Mathirai* are selected for further sub-acute study.

In sub acute study, no statistically significant differences were observed in body weight, feed consumption, water intake, urine analysis, pathological examinations, organ weights, or histopathology between control and treated rats. Hematological parameters were similar between control and treated rats, with the exception of slight but statistically significant increases in WBC content in treated at the end of the 2-week recovery period. These small changes were considered not to be related to the test compound and of no biological importance. Clinical chemistry values remained within normal ranges after 28 days of treatment. Na, K, and Cl ions were slightly elevated in treated animals; however, the differences were small and not considered biologically important. Based on these findings,

the no observed adverse effect level in this oral sub acute study was the tested dose of up to 1000 mg/kg bw/day of *Marichyathi Mathirai.*

A significant decrease in serum AST & ALT levels showed beneficial effects to the respective organs rather than adverse effects. Serum urea and creatinine were examined as indicators for kidney function tests while lipid metabolism profiles were mainly represented by serum cholesterol and triacylglycerol. Based on the results obtained after analysing serum urea, creatinine, total cholesterol and triacylglycerol, it has demonstrated that repeated administration of *Marichyathi Mathirai* had no direct adverse effect on kidney function and also lipid metabolism in normal young rats. In general, liver damage can be divided into direct destruction of hepatocytes or impairment of bile flow.

In the early stage of liver damage, cytoplasmic enzymes in hepatocytes may leak from cells into blood whose membrane permeability has been increased. Liver damage often leads to fat accumulation in hepatocytes. According to literature proof, the increase in liver mass in short term experiments cannot usually be attributed to pathologic or regenerative changes but appears to be due to a combination of hypertrophy and hyperplasia. Enhancement of the activity of enzymes, which degrade drugs or other lipophilic substrate, is the alteration most frequently encountered. Relative liver weight in normal young rats that showed increment when continuously fed with *Marichyathi Mathirai* was abolished during recovery period.

Hence, the effect of *MM* on rat liver is reversible. The doses examined throughout this study were several times higher than those used in other pharmacological or clinical studies of *MM*. As compared with the control group, the body weight and internal organ weights of treated rats showed no significant changes. Moreover, gross examinations of the internal organs revealed no pathological abnormalities relative to the control.

These results suggest that the *MM* is practically not toxic after an acute exposure. In the sub-acute toxicity study at the dose of 1,000 mg/kg/day the mild abnormalities in glomeruli, tubules were observed. At higher doses, lethargy, lack of touch response was observed. These however abated after 24 hr. However, further investigation such as histological and morphological experiments need to be carried out to confirm the chronic effect *of MM*. In sub-acute toxicity study rats treated with 250, 500 and 1000 mg/kg doses of *MM* had a progressive weight in body and organ gained.

The increase in weight was not significantly different from that of the control. The progressive increase in body weight and organ weight at doses used in rats during 28 days of administration of *MM* may indicate the improvement in the nutritional state of the animal. However there was no correlation between relative weight of the organs and the various doses of the *MM* administered. Furthermore, gross examination of internal organs of all the rats revealed no detectable abnormalities. In conclusion, this study presents strong evidence of the nontoxic effect of the *MM*. These results showed that the use of *MM* is safe and explained the extensive utilization of the traditional medicine.

Table: 4.2.4.1 Dose finding experiment and its behavioral Signs of Toxicity

No	**Dose mg/kg**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**
1.	**500**	-	-	-	-	+	+	+	-	-	-	-	-	+	-	-	-	-	-	+	-
2	**1000**	-	-	-	-	+	+	+	-	-	-	-	-	+	-	-	-	-	-	+	-
3	**2000**	-	-	-	-	+	+	+	-	-	-	-	-	+	-	-	-	-	-	+	-
4	**5000**	-	-	-	-	+	+	+	-	-	-	-	-	+	-	-	-	-	-	+	-

1. Alertness 2. Aggressiveness 3. Pile erection 4. Grooming 5. Gripping 6. Touch Response 7. Decreased Motor Activity 8. Tremors 9. Convulsions 10. Muscle Spasm 11. Catatonia 12. Muscle relaxant 13. Hypnosis 14. Analgesia 15.Lacrimation 16. Exophthalmos 17. Diarrhoea 18. Writhing 19. Respiration 20. Mortality

Table: 4.2.4.2 Body wt (g) of albino rats exposed to *Marichyathi Mathirai* for 28days.

Dose (mg/kg/day)	Days				
	1	**7**	**14**	**21**	**28**

Control	128±6.2	130±5.0	134±5.3	137±4.6**	141±5.01**
250	132±5.8	136±5.2	140±5.8*	144±4.9**	148±6.3**
500	127±5.0	128±5.1	132±6.2*	136±4.1**	142±5.0**
1000	130±4.9	135±5.6	141±5.1*	145±6.0**	149±5.4**

Values are mean of 6 animals ± SEM (Dunnett's test). *P<0.05; N=6.

Table: 4.2.4.3 Food (g/day) intake of albino rats exposed to *Marichyathi Mathirai* for 28days.

Dose (mg/kg/day)	**Days (gms/rats)**				
	1	**7**	**14**	**21**	**28**
Control	40.10±2.10	42.11±2.3	40.10±2.5	40.22±2.2	41.14±2.21
250	38.02±1.9	40.20±2.1	42.17±1.8	41.28±2.6	46.60±2.20**
500	41.27±2.7	40.51±2.6	40.42±2.0	45.16±2.1*	44.52±2.18*
1000	40.20±2.2	42.17±2.8	43.05±1.8	42.14±2.4	42.20±1.15

Values are mean of 6 animals ± SEM (Dunnett's test). *P<0.05; **P<0.01; N=6.

Table: 4.2.4.4 Water (ml/day) intake of albino rats exposed to *Marichyathi Mathirai* for 28days.

Dose (mg/kg/day)	Days (ml/Group)				
	1	**7**	**14**	**21**	**28**
Control	40.6±1.7	41.8±2.5	42.2±2.9	40.9±2.0	42.2±2.5
250	40.8±2.1	40.4±2.0	42.3±2.4	43.2±2.1	42.4±1.8
500	41.2±3.0	41.5±2.1	42.5±2.5	42.6±2.0	43.6±2.5
1000	40.3±2.2	41.3±2.5	43.1±2.1	42.4±2.2	42.2±2.5

Values are mean of 6 animals ± SEM (Dunnett's test). $^{ns}P>0.05$; N=6.

Table: 4.2.4.5 Hematological parameters after 28days treatment with the *Marichyathi Mathirai*

Parameter	**Control**	**250mg/kg**	**500 mg/kg**	**1000 mg/kg**
RBC (mm^3)	5.27±0.29	5.36±0.24	5.12±0.22	4.98±0.30
HB (%)	14.16±0.24	14.10±0.31	14.46±0.20	14.81±0.35
Leukocyte ($x10^3/mm^3$)	4.3±0.5	5.2±0.5*	5.4±0.6**	5.7±0.5**
Platelets/ul	1.43±0.12	1.62±0.15	1.70±0.18	1.54±0.21

MCV (gl)	84.10±4.2	85.11±5.1	86.12±4.67	86.48±5.00
N	47.34±4.49	44.10±4.46	46.15±4.12	45.88±4.62
L	44.28±3.5	45.00±4.04	44.54±2.49	44.56±4.13
M	3.12 ± 3.00	3.60 ± 3.00	3.17 ± 2.48	3.31 ± 2.11
E	2.27 ± 0.18	2.18 ± 0.20	2.19 ± 0.18	1.22 ± 0.15
B	1.25 ± 0.20	1.25 ± 0.31	1.34 ± 0.25	0.32 ± 0.22
ESR (mm)	1±00	1±00	1±00	1±00
PCV	44.15±2.5	45.64±2.6	44.28±2.4	44.10±2.11
MCH pg	30.25±1.5	30.10±1.2	30.42±1.6	30.31±1.2
MCHC g/dl	35.40±0.5	37.42±0.5	35.55±0.5	34.64±0.6

Values are mean of 6 animals ± SEM (Dunnett's test). *P<0.05; **P<0.01. N=6.

Table: 4.2.4.6 Effect of 28days treatment with *Marichyathi Mathirai* on biochemical parameters-LFT

Dose (mg/kg)	**Control**	**250mg/kg**	**500 mg/kg**	**1000 mg/kg**
Total Bilirubin(mg/dL)	0.60±0.24	0.61±0.18	0.60±0.15	0.61±0.22
ALP (IU/L)	62.10±4.4	63.22±4.6	62.14±5.0	63.11 ±4.7
AST (IU/L)	91.50±6.5	90.44±7.15	86.72±6.2	87.06±6.13
ALT (IU/L)	89.15±5.2	90.16±5.4	92.4±5.6	90.1±5.90

Protein (g/dl)	5.2±0.5	5.4±0.5	5.1±0.4	4.99±0.5
Albumin (g/dl)	4.6±0.4	4.1±0.4	4.3±0.3	4.16±0.4

Values are mean of 6 animals ± SEM (Dunnett's test). ^{Ns}P>0.05 *vs. control group* N=6.

Table: 4.2.4.7 Effect of 28days treatment with *Marichyathi Mathirai* on RFT

Dose (mg/kg)	**Control**	**250mg/kg**	**500 mg/kg**	**1000 mg/kg**
Urea (mg/dl)	36.02±4.5	38.59±4.0	38.00±5.4	40.11±5.3
Creatinine (mg/dl)	0.97±0.20	1.10±0.24	1.18±0.38	1.22±0.4
Uric acid (mg/dl)	5.36±1.2	5.4±1.0	5.3±1.15	4.86±1.20
Sodium	140±2.1	141±2.4	144±2.3	147.1±2.2
Potassium	7.18±0.62	7.3±0.6	8.86±0.4	9.18±0.4*
Chloride	100.04±1.8	104.5±2.2	106.5±3.4	109.2±3.6*

Values are mean of 6 animals ± SEM (Dunnett's test). *P<0.05 *vs control group* N=6.

Table: 4.2.4.8 Effect of 28days treatment with *Marichyathi Mathirai* on Lipid Profile

Dose (mg/kg)	**Control**	**250mg/kg**	**500 mg/kg**	**1000 mg/kg**
Cholesterol (mg/dl)	74.2±4.3	73.8±3.7	74.12±4.0	75.50±5.1
HDL (mg/dL)	14.12±2.62	14.40±2.42	14.3±2.67	14.2±2.32
LDL (mg/dL)	35.18±2.15	34.3±2.30	33.44±2.51	34.28±2.17
VLDL (mg/dl)	20.16±2.15	21.10±2.30	21.12±2.32	20.20±2.32
Triglyceride (mg/dl)	90.55 ± 20.80	87.52 ± 20.61	89.46 ±25.15	90.44 ± 24.90

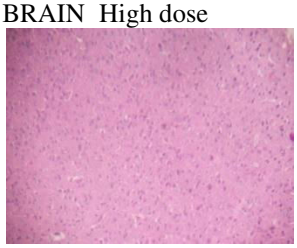
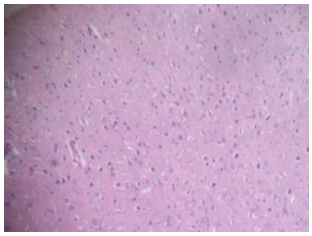
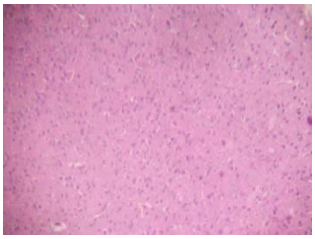
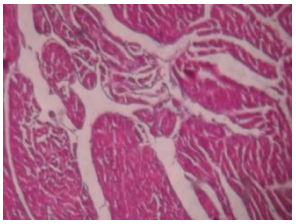
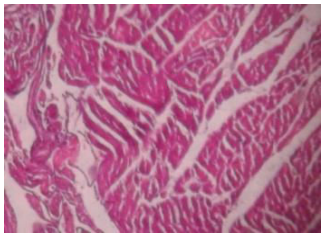
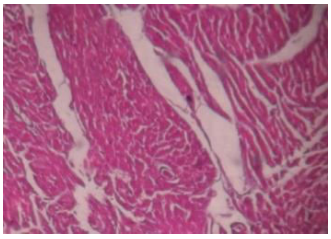
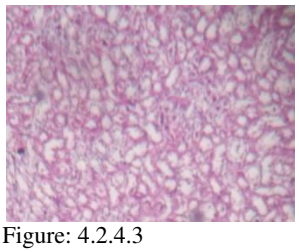
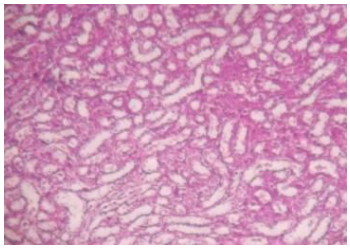
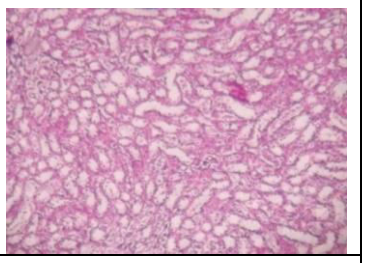
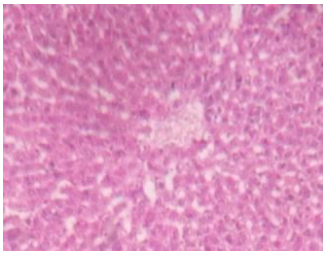
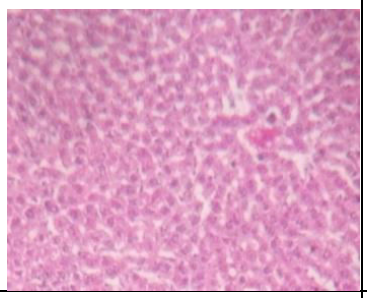
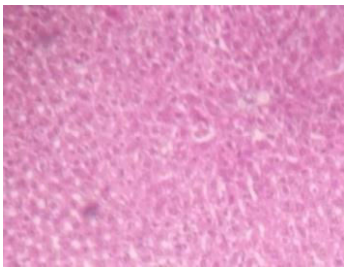
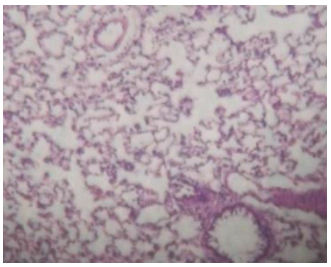
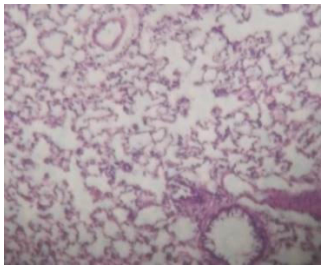
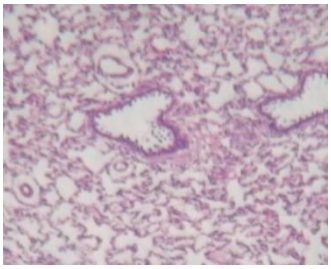
Glucose (mg/dl)	107±8.2	104±8.6	105±7.4	109±8.82

Values are mean of 6 animals ± SEM (Dunnett's test). $^{Ns}P>0.05$ *vs control group* N=6.

Table: 4.2.4.9 Effect of 28days treatment with *Marichyathi Mathirai* on Urinary Parameters

Parameters	**Control**	**250mg/kg**	**500 mg/kg**	**1000 mg/kg**
Colour	Yellow	Yellow	Yellow	Yellow
Transparency	Clear	Slightly turbid	Slightly turbid	Slightly turbid
Specific gravity	1.010	1.010	1.010	1.010
PH	7.6	>8.1	>7.8	>8.0
Protein	Nil	Nil	1+	1+
Glucose	Nil	Nil	Nil	Nil
Bilirubin	-ve	-ve	+ve	+ve
Ketones	-ve	-ve	-ve	+ve
Blood	Absent	Absent	Absent	Absent
Urobilinogen	Normal	Abnormal	Abnormal	Abnormal
Pus cells	Nil	0-cells/HPF	Nil	Nil
RBCs	Nil	Nil	0-1cells/HPF	Nil
Epithelial cells	Nil	Nil	0-1cells/HPF	0-1cells/HPF
Crystals	Nil	Nil	Nil	Nil
Casts	Nil	Nil	Nil	Nil
Others	Bacteria seen	Bacteria seen	Bacteria seen	Bacteria seen

Sub acute toxicological study slides

BRAIN High dose  Figure: 4.2.4.1	Low dose 	Mid dose 
HEART  Figure: 4.2.4.2		
KIDNEY  Figure: 4.2.4.3		
LIVER  Figure: 4.2.4.4		
LUNGS  Figure: 4.2.4.5		

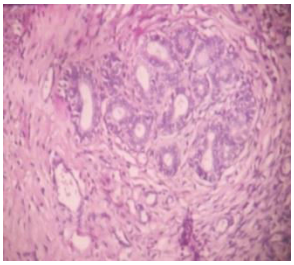
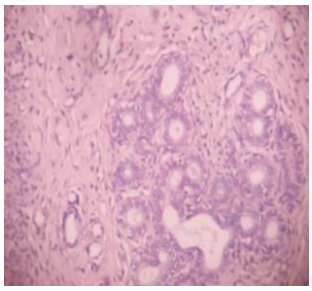
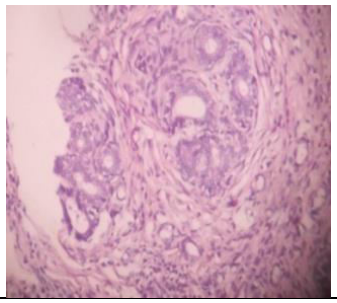
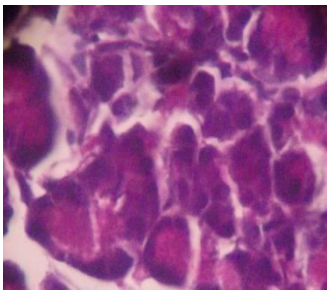
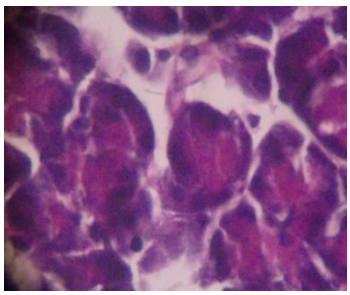
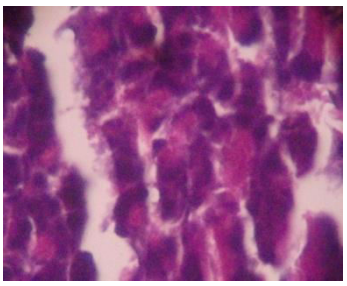
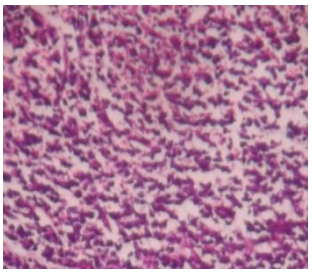
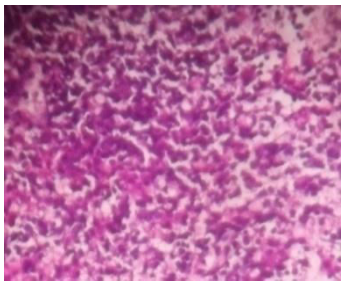
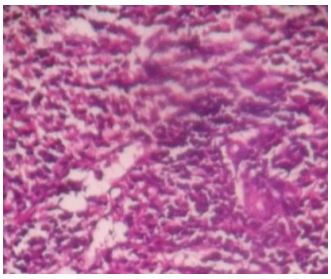
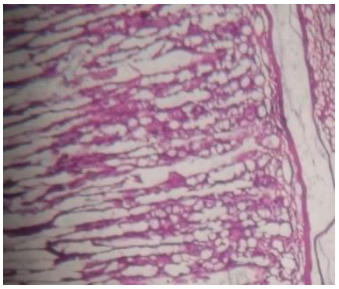
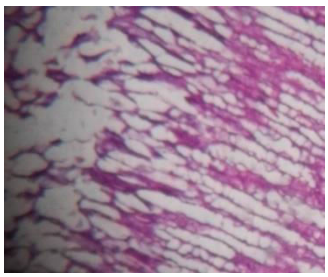
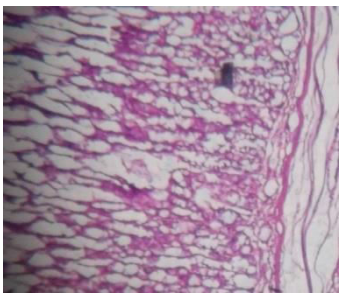
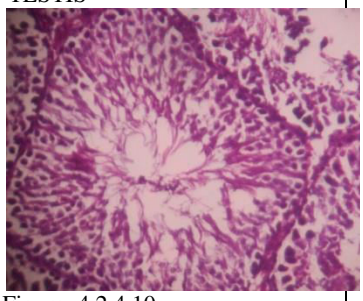
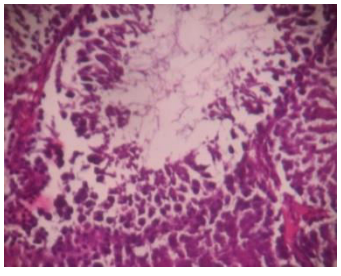
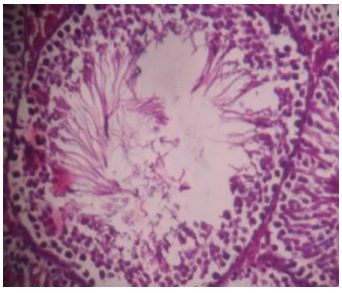
OVARY  Figure: 4.2.4.6		
PANCREAS  Figure: 4.2.4.7		
SPLEEN  Figure: 4.2.4.8		
STOMACH  Figure: 4.2.4.9		
TESTIS  Figure: 4.2.4.10		

Table: 4.2.4.10 Effect of 28days oral administration of a *Marichyathi Mathirai* on organ weight

Dose (mg/kg)	**Control**	**250mg/kg**	**500 mg/kg**	**1000 mg/kg**
Liver (g)	4.71±0.48	4.16±0.45	4.21±0.38	4.30±0.32
Heart (g)	0.61 ±0.04	0.60±0.4	0.62±0.05	0.62±0.04
Lung (g)	0.73±0.05	0.70±0.04	0.74±0.05	0.72±0.4
Spleen (g)	0.64±0.05	0 .66±0.05	0.64 ±0.04	0.65±0.05
Ovary (g)	0.05±0.02	0.05±0.04	0.04±0.02	0.05±0.04
Testis (g)	1.06±0.04	1.08±0.05	1.02±0.03	1.04±0.04
Brain (g)	1.32±0.18	1.15±0.20	1.12±0.20	1.20±0.22
Kidney (g)	0.61±0.04	0.60±0.04	0.62±0.05	0.60±0.05
Stomach (g)	1.35±0.05	1.22±0.04	1.31±0.05	1.29±0.04

Values are mean of 6 animals ± SEM (Dunnett's test). ^{Ns}P>0.05 *vs control* N=6.

Statistical analysis:

The results are presented as means + SEM. Statistical significance was determined by one-way analysis of variance (ANOVA) and Dunnett's test for significant difference. *P* values less than 0.05 were considered significant.

Pharmacological study:

Greater than 50 different mediators have been implicated in BA, among these histamine is the major targeting mediator in treatment of asthma. The biologically active siddha drug Marichyathi mathirai exerted antagonistic effect on histamine induced contraction (P<0.01).

Hence, Marichyathi mathirai affirm the antihistaminic effect in presence of agonist like histamine which justify the antagonistic claim. Further studies may help to establish the antihistaminic activity in other tissues and also to identify the active principle responsible for the action.

In conclusion, the test drug marichyathi mathirai was found to be more effective in their antagonism against histamine at 100µg/ml when compared with that of the standard antagonistic drug chlorpheneramine.From the present findings, it is manifest that the marichyathi mathirai had shown marked antihistaminic activity in isolated tissue of guinea pig ileum. Hence this may help to design further in vivo studies to check their antihistaminic effect or bronchodilator activity.

In vivo study of Marichyathi Mathirai have been also shown the significant increase in pre-convulsion time due to pre-treatment at the dose of 250 and 500 m/kg of body weight of guinea pigs, when the guinea pigs were exposed to histamine. The results of Marichyathi Mathirai suggested that it is effective in reducing the symptoms of bronchial asthma and also improve the lung function parameters of asthmatic subjects.

In the present study, guinea pigs were used because of the extreme sensitivity of their airways to the primary mediators of bronchoconstriction, including histamine and leukotrienes and their ability to be sensitized to foreign proteins. Although there are various model of asthma, guinea pig airways react to histamine, acetylcholine, leukotrienes and other bronchoconstrictors in a manner similar to that seen in humans. Another similarity between the guinea pig model and asthmatic patients is that enhanced bronchoconstriction occurs in both species following sensitization, in response to β-adrenergic antagonists.

Thus, the guinea pig model resembles the human allergic pathology in several aspects, especially in terms of mediator release. Histamine antagonists can be conveniently recognized and assayed by their ability to protect guinea pigs against lethal effects of histamine-induced bronchospasm.

In conclusion, the test drug *marichyathi mathirai* was found to be more effective in their antagonism against histamine at 100µg/ml when compared with that of the standard antagonistic drug chlorphemaramine. From the present findings, it is manifest that the *marichyathi mathirai* had shown marked antihistaminic activity in isolated tissue of guinea pig ileum. And also it is suggested that *Marichyathi Mathirai* significantly protected the Guinea pigs against histamine-induced bronchospasm. The guinea pigs exposed to histamine

aerosol showed signs of progressive dyspnoea leading to convulsions. The two doses of *Marichyathi Mathirai* significantly prolonged the latent period of convulsions (PCT) as compared to control following the exposure of histamine aerosol. Over all our investigation suggest that the siddha drug *Marichyathi Mathirai* possess significant antihistaminic and bronchodilator activity.

Statistical Analysis

Ileum contractions induced by agonist were assumed as 100% and reductions induced by test drug calculated. Percentage of ileum contraction was expressed as mean ± SEM. Results were analyzed using one-way analysis of variance (ANOVA). Probability value less than 0.05 were considered as significant. For bronchodilator activity, the data were expressed as Mean ± SEM. Differences between groups were analysed by one way analysis of variance (ANOVA) followed by Dunnet "t" test. Differences were considered significant when $P< 0.05$ and very significant when $P< 0.01$.

Table 4.2.5.1: Effect of Marichyathi mathirai on isolated rat ileum preparation (Histamine)

Values are expressed in mean±SEM, *p< 0.05; **p< 0.01 compared with histamine alone (45mm as 100%); n=3.

Sr. No	Log dose Histamine (100 µg/ml)	Percent of maximum response	
		Histamine alone	Histamine+Marichyathi mathirai (1mg/ml)
1	0.20	7.15±0.7	7.10±1.41
2	0.28	14.16±0.947	10.12±1.862
3	0.36	26.66±2.12	18.60±0.746
4	0.66	47.42±2.58	36.80±1.832*
5	1.2	92.80±3.76	68.21±3.872**

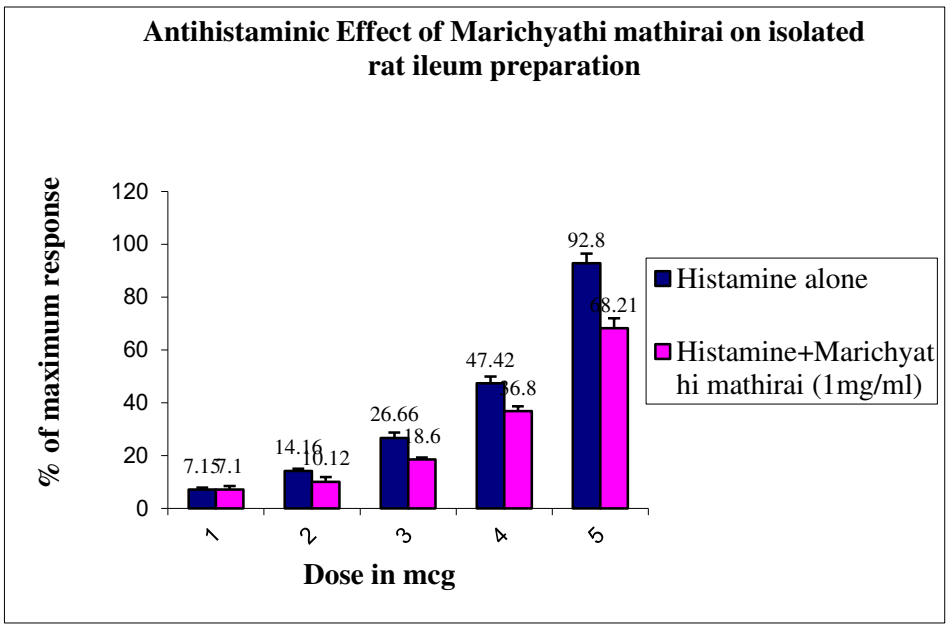
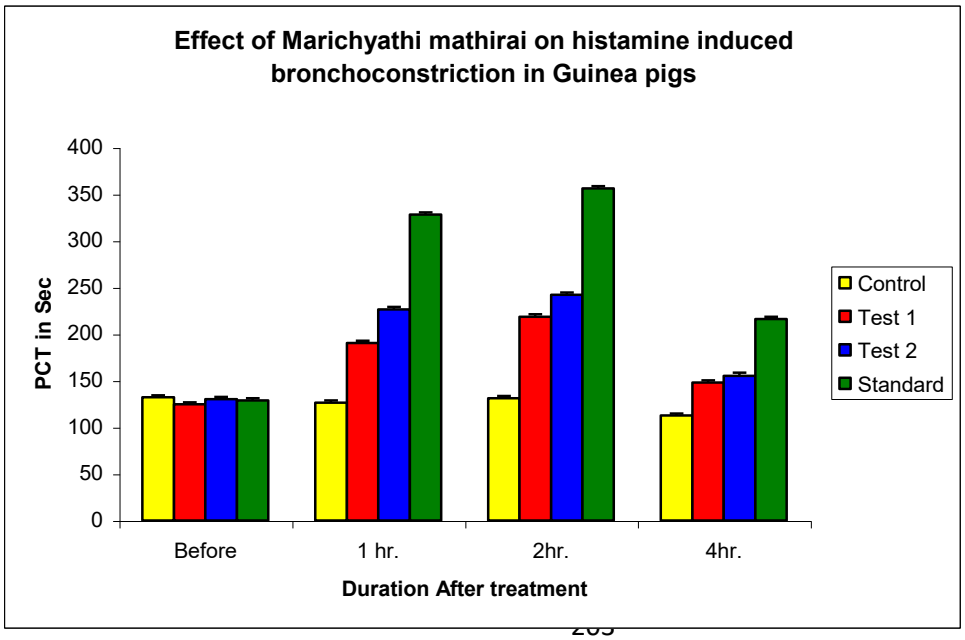


Table: 4.2.5.2 Effect of Marichyathi mathirai on histamine induced bronchoconstriction in Guinea pigs.

Groups	Treatment and Dose	Pre-convulsion time in Seconds			
		Before	1 hr.	2hr.	4hr.
Control	Normal Saline	132.1±2.28	126.5±2.53	131.29±2.79	112.7±2.33
Test 1	Marichyathi mathirai *250mg/kg*	124.5±2.18	190.3±2.15**	218.6±2.62**	148.1±2.18**
Test 2	Marichyathi mathirai *500mg/kg*	130.2±2.56	226.4±2.16**	242.0±2.56**	155.3±2.98**
Standard	Salbutamol 5mg/kg	128.6±2.12	328.1±2.88**	356.1±3.42**	216.0±2.34**

Values are in mean ± SEM; Statistical analysis done by using One-way ANOVA followed by Dunnet 't'-Test.

**p<0.01, compared to control; n=5; control = histamine (0.2%, aerosol).



Clinical study:

55 patients of both sexes were selected. Among the 55 patients, 45 patients were treated as out- patients in the Post graduate department of Gunapadam, Govt.Siddha medical college hospital and Govt. Arignar Anna hospital, Arumbakkam, Chennai- 106. 10 patients were treated as in - patients. The results revealed that the drug possess 70% good relief, 16% moderate relief, 9% mild relief, 5% cases there was no improvement.

In this clinical study, the Open clinical Trial was conducted on 55 volunteer patients after getting the proper informed consent. Since, the treated disease BA is a chronic, inflammatory disease, complete reverse to normally, is not possible. So the aim is to maintain the life style of the patients without any big modifications.As per the obtained results 70% of cases (marked+moderate) were releaved that 75% improvement in the signs and symptoms and bio chemical parameters. With the obtained results the trial medicine has proven itself a promising drug of choice for the Asthma patients.

Improvement in clinical features:

Table 4.3

S. No.	SIGNS AND SYMPTOMS	NO. OF PATIENTS			
		BT	AT	IMP.	IMPROVEMENT (%)
1	Dyspnoea	55	6	49	89.09
2	Cough with Expectoration	55	4	51	92.72
3	Tightness of chest	38	8	30	79
4	Rhinitis	26	4	22	85
5	Sneezing	18	4	14	78
6	Head ache	10	3	7	70

The two-tailed P equals 0.0003, By conventional criteria; this difference is considered to be **statistically significant.**

Statistical analysis:

P Value and statistical significance:

The two-tailed P Value equals 0.0003,

By conventional criteria, this difference is considered to be extremely statistical.

Confidence interval:

The mean of Group One minus Group Two equals 6.00

95% confidence interval of this difference: From 4.24 to 7.76
t = 8.7831 df = 5 standard error of difference = 0.683

Table: 4.3.6

Treatment	Signs & symptoms	Mean	S.D	S.E.M
Before treatment	6	28.83	18.28	7.46
After treatment	6	22.83	17.30	7.06

From the above table we got a significant difference ($p < 0.05$). So we conclude that there is an improvement between before and after treatment.

5. CONCLUSION

The test drug *Marichiyathi Mathirai* is selected from the text *Anubava vaithya deva ragasium*, page no.482 for the evaluation of safety, efficacy and the theraupeutical potential of the drug in the BA patients.

All the drugs were purchased from Tampcol raw drug store and duly authenticated, then subjected to preparation.

From the acute toxicity study was performed as per OECD guideline-425, it was concluded that the test drug *Marichiyathi Mathirai* class 5 safety drug, wich has no lethal effect upto 5g/kg body weight after oral administration in mice.

MM did not produce any oral acute or sub acute toxicity in both female and male rats. Over all results suggest that *Marichiyathi Mathirai* is relatively safe in rats. These results showed that the use of *Marichiyathi Mathirai* is safe and explained the exploitation of the drug as traditional medicine.

After evaluvate the safety the drug, the Broncho dilator and anti-histaminic property of *MM* is elaborated. Hence it can be concluded that this drug may have the action like PGE, and may inhibits the the tone of tracheal and bronchial muscles and thus has a broncho dilator action. It is possible that the broncho dilator activity of the *MM* may involve, mainly, inhibition of prostaglandin synthesis but encumbrance of the metabolism of other algesic agents or barricade of their receptors.

After the above evaluation the drug *Marichiyathi Maththirai* is subjected to open clinical trial. The open clinical trial results reveal that 70% of patients were having 75% of improvement and 16% have 60% of improvement in the clinical futures and biochemical reports.

From the above pre-clinical and clinical observation, the author concluds that the drug *Marichiyathi Maththirai* is endow with the new hope in the treatment part of Bronchial asthma which is cost effective and has easiest preparation method.

7. SUMMARY

Marichiyathi Maththirai was selected by the author for this study to elaborate the broncho dilator and anti-histaminic activity. Collect the assorted information about the drug from the Variety of text books and literature. From them, the author came to an inspiration about the drug and its efficacy on Bronchial asthma.

The Phyto chemical analysis of the drug shows that it contains Calcium, Iron, and Tannins, Alkaloids, Steroids, Phlobatannins, Phenolic Compounds, Flavonoids and Cardiac Glycosides. It is related to the treatment aspect of BA.

The preclinical study showed that the drug has got safety and significant Broncho dilator and Anti-histaminic activity.

The patients were relieved well from the signs and symptoms gradually and no adverse effects were reported.

The clinical result reveals that 70% of patients were having 75% of improvement in the clinical futures and biochemical reports.

This present study confirms that the *Marichiyathi Maaththirai* has a remarkable Broncho dilator and Anti-histaminic activity and high therapeutical value against the disease of Bronchial asthma.This must be implicated in the future studies to explorate the accurate target activity such as anti-tuberculosis and to explore the active compounds for the standardization.

BIBILIOGRAPHY

1. Agaththiyar paripooranam-400 pg no:145,147
2. Aganaanuru
3. Agathiyar vauthya sindhamani -4000 , 44,60,89,103, 110,117,141, 144,145 183,
4. Agaththiyar gunavagadam
5. Agaththiyar paripooranam -400 page: 107
6. Anuboga vaithiya Navaneetham. Part -2
7. Anuboga vaithiya Navaneetham. Part -4 P.No: 54. Hakkim P Mohammed abdullah saibu.
8. Anuboga vaithiya Navaneetham. Part -5
9. Boga munivar nigandu-1200 page no-850,911,919
10. Bogar karukkidai nigandu-500 page; 39,40
11. Dhanvanthiri kuzhanthai vaagadam – P.No 170 – 174. Thamarai Nulagam Vadapalani. Chennai – 26.
12. Gunapadam Mooligai Vaguppu (Murugesa Mudhaliyar)– Indian Medicine and homeopathy Dept. – Chennai-106.p.no-404-406
13. Gunapadam Thathu – Seeva Vaguppu (Part (2 & 3) Dr.R .Thiyagarajan. L.I.M. Indian Medicine and Homeopathy Dept. Chennai-106. P.No:
14. Indian Material Medica – Vol -2, P.No: 1096. Dr. K.M. Nadkarni, “Popular Prakasham. Pvt. Ltd. Asiatic Publishing House. Bombay.
15. Ingurunooru vezhappaththu oadal
16. Kabilar kurinjippattu
17. Kannusamiyam ennum vaithya sekeram
18. Kannusamy Parambarai Vaidhiyam P.No: (89, 102, 110, 123, 131, 133, 134, 159, 160, 170, 235,237, 244, 253, 254, 255, 297, 442, 448) Rathina Nayagar & Sons, Thirumazhl Aachagam Chennai -79.
19. Karuvoorar pala thirattu page 68
20. Kazhaga tamil agarathii pgno: 422
21. Marunthu sei iyalum kalaium
22. Maruthuva Aagarathi. P.No: 125, 298, 815,
23. Mega nivaarana bothini pg no;77 Hakkim .p. mohammed abdullah saibu
24. Mooligai marmam.
25. Nakkeerar thirumurugatruppadai
26. Noi nadal noi muthal nadal paagam1noiyilla neri page no 25

27. Patharththa guna sinthamani
28. Paththuppattu
29. Pirana rakshamirtha sindhu-12 th part page 30
30. Roga nirnaya saram ennum roaga nithanam
31. Sarebenthirar pitha roga sigichai page No: 1168,156
32. Sarebenthirar vauthya muraigal pg no: 23
33. Sattai muni nigandu -1200 pg no:143
34. Serebenthirar vaithya rathnavali 2 part page no 69
35. Siddha maruththuvanga surukkam
36. Siddha Maruthuva Noi Nada Noi Mudhal Naadal Thirattu, Part - I 1998, Part –II. Govt of Tamil Nadu.
37. Siddha Maruthuvam – Fr. Kuppusami Mudhaliar. P.No:
38. Siddha Maruthuvanga Churukkam, Dr. K.S. Uthamarayan.
39. Siddha vathya thirattu
40. Sikcha rathana Deepam – P.No: 119,103,173,204,206,209. Kannusamy Pillai, Thirumazhi Aachagam Chennai- 79.
41. T.V. Sambasivampillai agarathi Inidan medicine and Homeopathy Durai. Vol – V. PNo: 3105, 3156, 3294.
42. Thanvanthiri thylam 500 page 97
43. Thanvanthiri vaithiyam page 386,395,402,406
44. Theraiyar gunavagam
45. Theraiyar Vagadam Indian medicine & Homeopathy thurai. Chennai -106. P.No: 92.
46. Theraiyar yamaga venba
47. Thirumanthiram-462 290 T.R. Magadevapandither
48. Thirumoolar thirumanthiram part 2
49. Thirumoolar karukkidai vaithiyam
50. Udal thathuvam pg no- 337
51. Yugi vaithiya Chinthamani- 800 P.No: 95
52. Compendium Indian Medicinal Plants – P.No: 569. A Compendium of 500 Specierrs, Vol – 3 Rastosi & Mehrutra, PID, New Delhi – 1993.
53. Davidson’s Principles and Practice of Medicine. 20th Edition by Nicholos A. Boon. International Editor John A.A. Hunter.
54. Fundamental of Bio-Chemistry for Medical student. P.No: 459.

55. Hutchinson's Clinical Methods. 402, 11-12, 79, P.No: 230, 285, 286, 222, 261.
56. Illustrated Indian Medicinal Plants Vol – 4, P.No: 57. Kitikar and Basu, Satguru Publication, Delhi.
57. LD CRC Hand book of Ayur medicinal plants
58. Manual of Practical Medicine. P.No: 485, 497. Dr. R. Alagappan.
59. Medical Physiology. Prof. Guyton. MD.
60. Pathologic basic of Disease. Dr. Robins.
61. Practical Medicine – Prof. P.J. Mehta's P.No: 211, 182, 193, 277, 256, 212, 284, 236-239.
62. Text Book of Bio-Chemistry by SathyaNarayanah P.No: 449 to 455.
63. Text Book of Medical bio-Chemistry - S. Ramakrishnan. P.No: 245.
64. Text Book of Medicine. Prof. K.V. Krishnadas.
65. Text Book of Medicine. Prof. P.C. Das. P.No: 382, 383, 396.
66. The Wealth of India – Volume -2 (218). A. Krishnamoorthi, Chief Editor, Publications Information directorate, CSIR, New Delhi – 1100112.
67. 1, Ojewole JAO. Studies on the Pharmacology of echitamine, an alkaloid from the stem bark of Alstonia boonei L (Apocynaceae). Int J Crude Drugs Res 1984:22:121-43.
68. Azuzu IU, Ananga AO.P harmacological screening of the aqueous extract of Alstonia boonei stem bark. Fitoterapia 1991; 62:411-7.
69. B. K. Toone, M. Wheeler, M. Nanjee, P. Fenwick and R. Grant, Sex hormones, sexual activity and plasma anticonvulsant levels in male epileptics. J. Neurol. Neurosurg. Psychiatry, 46:824–826 (1983).
70. Bridha et.al JPRHC- April 2010 2 voume 147-155
71. C. Guyton and J. E. Hall, Textbook of Medical Physiology (Tenth Edition). Harcourt International Edition, W. B. Saunder Company, Philadelphia. (2000) pp. 279-281.
72. Carro-Juarez M, Cervantes E, Cerevantes-Mendez M. Aphrodisiac properties of *Montanoa tomentosa* aqueous crude extract in male rats. J. Pharmacol. Biochem and Behavior 2004; 78: 129-134.
73. E. O. Laumann, A. Paik and R. C. Rosen, Sexual dysfunction in the United States: Prevalence and predictors. J. Am. Med. Assoc., 281: 537-544 (1999).
74. F. E. Govier, D. Asase, T. R. Hefty, R. D. McClure, T. R. Pritchett and R. M. Weissman, Timing of penile color flow duplex ultrasonography using a triple drug mixture. J. Urol., 153:1472–1475 (1995).

75. F. M. Joe, Erectile Dysfunction: Sexual response in men. Arch. Sexual Behav, 14: 33-39 (1990).
76. F. R. Kandeel, V. K. T. Koussa, and R. S. Swerdloff, Male sexual function and its disorders: Physiology, Pathophysiology, Clinical Investigation and, Treatment. Endocr. Rev, 22(3): 342-388 (2001).
77. G. Wagner, Erection: physiology and endocrinology. In: Wagner, G. and Green, R. (eds) Impotence: Physiological, Psychological, Surgical Diagnosis and Treatment. Plenum Press, NY, (1981) pp. 25–36.
78. H. A. Feldman, I. Goldstein, D. G. Hatzichristou, R. J. Krane, and J. B. McKinlay, Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. J Urol., 151:54–61 (1994).
79. H. S. Kaplan, Erotic obsession: relationship to hypoactive sexual desire disorder and paraphilia. Am. J. Psychiatry, 153(Suppl 7): 30–41 (1996).
80. Harborne, Jeffrey B., and Herbert Baxter, eds. *Phytochemical Dictionary: A Handbook of Bioactive Compounds from Plants.* Bristol: Taylor & Francis, 1995.
81. International conference bioscience, bio chemistry and bio informatics.
82. Journal of natural remedies april 2004
83. Kar N, Chandra G. Comprehensive Textbook of Sexual Medicine, 1st edition, Jaypee Brothers Medical Publishers, New Delhi, 2005, pp. 280-285, 309-313.
84. Kothari P. common sexual problems, 3rd edition, UBS publishers, New Delhi, 2001, pp. 1-6, 155, 203, 204, 221.
85. Kulkarni SK, Reddy DS. Pharmacotherapy of Male Erectile Dysfunction with Sildenafil. Ind. J. Pharmacol. 1998; 30: 367-378.
86. Kutchan, Toni M. "Alkaloid Biosynthesis: The Basis for Metabolic Engineering of Medicinal Plants." *Plant Cell* 7 (1995): 1095-1070.
87. M,Mosihuzzamam et al.IUPAC pure and applied article
88. M. Monga, The aging penis: erectile dysfunction. Geriatr. Nephol. Urol. 9(1): 27-37 (1999).
89. M. S. Rendell, J. Rajfer and P. A. Wicker, Sildenafil for treatment of erectile dysfunction in men with diabetes. JAMA, 282: 421-426 (1999).
90. M. T. Yakubu, M. A. Akanji and A. T. Oladiji, Aphrodisiac potentials of aqueous extract of Fadogia agrestis (Schweinf. Ex Hiern) stem in male albino rats. Asian J. Androl., 7(4): 399-404 (2005).

91. Mann, John, R. Stephen Davidson, John B. Hobbs, Derek V. Banthrope, and Jeffrey B. Harborne. *Natural Products: Their Chemistry and Biological Significance.* Essex: Longman Group, 1994.
92. Medicinal and aromatic plant abstract August 1997, Feb 1992, dec 2003, August 2005, December 2003, June 2007, August 2005. August 2009,feb 201o
93. P. C. Walsh and J. D. Wilson, Impotence and infertility in men. In: Braunwald E, Isselbacher KJ, Petersdorf RS, Wilson JD, Martin JB, Fauci AS (eds) Harrison's Principals of Internal Medicine, ed 11. McGraw-Hill Book Co., NY, (1987) pp 217– 220.
94. P. H. Salmon, Psychosexual dysfunction in chronic renal failure: An overview. Proc. EDTNA, 12: 209-212 (1983).
95. R. C. Kolodny, W. H. Masters and V. E. Johnson, Sexual anatomy and physiology. In: Textbook of Sexual Medicine. Little, Brown and Co., Boston, MA. (1979) pp. 1– 28.
96. R. C. Rosen and A. K. Ashton, Prosexual Drugs: Empirical Status of New Aprhodisiacs. Arch. Sexual Behav, 22: 521-543 (1993).
97. R. J. Bosch, F. Bernard, S. R. Aboseif, C. G. Steif, T. F. Lue and E. A. Tanagho, Penile detumescence: characterization of three phases. J. Urol., 146: 867 (1991).
98. S. M. Petak, and J. B. Perez, American Association of Clinical Endocrinologist: Medical Guidelines for Clinical Practice for the evaluation and treatment of male sexual dysfunction. A couple's problem. Endocrinol. Pract, 9(1): 78-95 (2003).
99. S. Tajuddin, A. Latif and I. A. Qasmi, Effect of 50% ethanolic extract of Syzygium aromaticum (L) Merr. & Perry. (Clove) on sexual behaviour of normal male rats. BMC Complemen. Altern. Med., 4: 17-24 (2004).
100. Subramoniam A, MadhavachandranV, Rajasejharan S, Pushpangadan P. Aphrodisiac property of *Trichopus zeylanicus* extract in male mice. J. Ethnopharmacol.1997; 57: 21-27.
101. www.U.k net guide.com
102. W. D. Ratnasooriya and M. G. Dharmasiri, Effects of Terminalia catappa seeds on sexual behaviour and fertility of male rats. Asian J. Androl., 2: 213-219 (2000).
103. Wink, Michael, ed. *Biochemistry of Plant* Secondary Metabolism. Sheffield, UK, and Boca Raton, FL: Sheffield Academic Press and CRC Press, 1999
104. Jung HA, Kim JE, Chung HY, Choi JS. Faculty of Food Science and Biotechnology, Pukyong National University, Busan 608-737, Korea.