PRECLINICAL EVALUATION OF THE POSSIBLE MECHANISMS OF ANTI –HYPERTENSIVE, DIURETIC AND ANTI-OXIDANT ACTIVITIES OF *"MUNTHIRIKAI CHOORANAM"* IN RODENTS

The dissertation Submitted by

Dr. M.SUMITHRA

Reg no: 321412109

Under the Guidance of

Dr. V.VELPANDIAN, M.D(S).,Ph D

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

OCTOBER 2017

GOVT.SIDDHA MEDICAL COLLEGE, ARUMBAKKAM,

CHENNAI-106

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"Preclinical Evaluation of the Possible Mechanisms of Anti-Hypertensive, Diuretic, Anti-oxidant Activities of *"Munthirikai Chooranam*" in Rodents** is a bonafide and genuine research work carried out by me under the guidance of **Dr.V.Velpandian M.D(S).,Ph.D** Post Graduate Department of *Gunapadam*, Govt.Siddha Medical College, Arumbakkam, Chennai-106 and the dissertation has not formed the basis for the award of any Degree, Diploma, Fellowship or other similar title.

Date: **Signature of the Candidate**

Place: **M.Sumithra**

GOVT. SIDDHA MEDICAL COLLEGE, ARUMBAKKAM,

CHENNAI-106

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled "**Preclinical Evaluation of the Possible Mechanisms of Anti-Hypertensive, Diuretic, Anti-oxidant Activities of "*Munthirikai Chooranam*" in Rodents** is submitted to the Tamilnadu Dr.M.G.R.Medical University in partial fulfillment of the requirements for the award of degree of M.D (Siddha) is the bonafide and genuine research work done by M.Sumithra Under my supervision and guidance and the dissertation has not formed the basis for the award of any Degree, Diploma, Associateship, Fellowship or other similar title.

Date: **Signature of the Guide**

Place:

ENDORSEMENT BY THE HOD

PRINCIPAL /HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled **"Preclinical Evaluation Of The Possible Mechanisms of Anti-Hypertensive, Diuretic, Anti-Oxidant activities of "*Munthirikai Chooranam*" in Rodents** is a bonafide work carried out by **M.Sumithra** under the guidance of **Dr.V.Velpandian M.D(S).,Ph.D** Post Graduate Department of *Gunapadam*, Govt Siddha Medical College, Chennai-106.

Signature of the HOD **Signature of the Principal**

ACKNOWLEDGEMENT

This dissertation one of the milestones in the journey of my professional carrier as it is the key program in acquiring my MD(S) degree. Thus I came across this task which kept on track and been seen through to completion with the support and encouragement of numerous people including my teaching staff, family numbers, my friends and various institutions. So I take great pleasure in thanking all the people who made this dissertation study a valuable and successful one, which I owe to treasure it.

I express my sincere thanks to our Principal **Prof**. **Dr.K.Kanagavalli, M.D(S)**, Govt. Siddha Medical College, Chennai for her permission to perform this study and also for her valuable ideas and support throughout the course of the study.

It is a genuine pleasure to express my deep sense of thanks and gratitude to my mentor and guide **Dr.V.Velpandian M.D(S), Ph.D**., Head of the Dept of PG *Gunapadam*, Govt Siddha College, Chennai. His dedication and keen interest above all his overwhelming attitude to help his students had been solely and mainly responsible for completing my work. His timely advice, meticulous scrutiny, scholarly advice and scientific approach have helped me to a very great extent to accomplish this dissertation work.

I wish to express my profound gratitude to **Prof Dr.V.Banumathi M.D(S)**, Director of National Institute of Siddha, Tambaram Sanatorium, Chennai for her valuable ideas to this dissertation and encouragement me for the completion of this dissertation.

I wish to express my thanks to co-guide **Dr.K.Nalina Saraswathi M.D(S)**, Asst. Lecturer, Department of PG *Gunapadam* for his valuable ideas and suggestions to my study.

I acknowledge my thanks to **Dr.K.RajammaDevi Sorubarani M.D(S) Dr.L.Lakshman Raj M.D(S)** for their support and guidance.

I cordially register my humble thanks **to Dr. P. Muralidharan M.pharm, Ph.D**., HOD, Department of Pharmacology, C.L Baid Metha College of Pharmacy, Dhuraipakkam, Chennai, for helping in the preclinical study. It was under their direct supervision that the work contained in the dissertation was performed.

I acknowledge my thanks to **Dr. Murugesan Ph.D**., SAIF, IITM, Chennai. Prof **Dr.R.Rajesh M.Phil, Ph.D.,** Biogenix Research Centre, Trivandrum. **Dr. B. Janarthanan Ph.D.,** Poonga Biotech Research Centre, Chennai. **R.Shakila** Research Officer (Chemisrty) CRI, Arumbakkam, Chennai. **Prof Mr. Selvaraj M.Sc,M.Phil,** HOD, Department of Bio-Chemistry, Govt. Siddha Medical College, Chennai.

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

I would like to thank **Vice Chancellor**, **The Tamilnadu Dr.MGR Medical University** for giving permission to carry out my dissertation work and to the **Additional Chief Secretary** and **Commissioner of Indian Medicine and Homeopathy Department,** Arumbakkam, Chennai-106, for giving consent to do the dissertation.

I am also thankful to **all my college staff** for their kind co-operation for my study. I should express my gratefulness to **all my Classmates and PG Gunapadam students** for lending their helping hands whenever needed during the course of the study.

Last but not least , I would like to pay high regards to all my family members, **Father Mr.T.Manoharan, Mother Mrs.R.Chandra Kumari** for their sincere encouragement and inspiration throughout my research work and lifting me uphill this phase of life. I owe everything to them. Besides this several people have knowingly and unknowingly helped me in the successful completion of this project.

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ABBREVIATIONS

2K1C	Two kidney one clip
ACE inhibitors	Angiotensin converting enzyme
ALT	Alanine amino transferase
ANOVA	Analysis of variance
ARBs	Angiotensin receptor blockers
AST	Aspartate aminotransferase
Bp	Blood pressure
BUN	Blood urea nitrogen
CCBs	Calcium channel blockers
CCF	Congestive cardiac failure
CMC	Corboxymethylcellulose
CVD	Cardiovascular disease
DMSO	Dimethyl sulfoxide
DOCA	Deoxycorticosterone acetate
DPPH	2,2-diphenyl-1-picrylhydrazyl
ECG	Electro cardio gram
EDTA	Ethylenediaminetetraacetic acid
ET	Endothelin
FTIR	Fourier Transform Infra-Red Spectroscopy
GFR	Glomerular filtration rate
GOT	Glutamate oxaloacetate transaminase
GPT	Glutamate pyruvate transaminase
Hb	Haemoglobin
HDL	High density lipoprotein
IAEC	Institutional animal ethical committee
ICPOES	Inductively coupled plasma optic emission spectroscopy

IHD	Ischemic heart disease
JNC	Joint national committee on prevention, detection , evaluation and treatment of high Blood pressure
LD	Lethal dose
LDL	Low density lipoprotein
MI	Mayocardial infarction
NO	Nitric oxide
NSAIDs	Non steroidal anti inflammatory drugs
OECD	Organization for economic co-operative development
PCV	Packed cell volume
PVD	Peripheral vascular disease
RBC	Red blood corpuscles
SBP	Systolic blood pressure
SEM	Scanning electron microscope
SEM	Standard error meaning
SHR	Spontaneously hypertensive rats
SLE	Systemic lupus erythematus
MC	Munthirikai chooranam
TGR(m Ren2)	Transgenic rats over expressing the mouse Ren2
TIA	Transient ischemic attack
TLC/HPTLC	Thin layer chromatography/High performance thin layer chromatography
TSH	Thyroid stimulating hormone
UV	Ultra violet
WBC	White blood corpuscles
WHD	World Hypertension Day
WHL	World Hypertension League
WHO	World health organization

1. INTRODUCTION

Hypertension is one of the most common life style disorder. It is a one of the most preventable causes of premature morbidity and mortality in worldwide [1]. This disease being closely associated with diet, it is conceivable that food is conductive to preventing and enhancing such diseases as an adjunct to drug therapy. Therefore we tried to develop a novel food protein with anti-hypertensive activity for the dietetics of hypertension.

Primary hypertension is remarkably common in the population and the prevalence is strongly influenced by age and life style factors. According to research surveys based on Medline, web of science and Scopus databases, 25% rural and 33% urban Indians are hypertensive [2]. It is estimated that the number of people living with hypertension will be increased as more than 1.56 billion by the year 2025[3].

Systemic hypertension is the persistent rise of basal blood pressure above the arbitrary level of 140/90 mmHg recorded on 3 or more successive occasions. Blood pressure is quantified as diastolic and systolic pressure measured in millimetres of Mercury (mm hg). The diastolic pressure represents the pressure during ventricular relaxation in diastole, where as the systolic pressure represents the peak pressure due to ventricular contractions during systole.

Primary hypertension is remarkably common in the population and the prevalence is strongly influenced by age and life style factors. Systolic pressure elevation is the more dominant feature of hypertension in older patients and diastolic pressure more commonly elevated in younger patients. Many diseases fall under the category of “Silent killers”, including Hypertension is one among them. Cardiovascular and cerebro vascular diseases are the major risk factors seen in patients of Hypertension[4].

In worldwide raised blood pressure is estimated to cause 7.5 million deaths, about 12.8% of the total of all deaths. Globally the overall prevalence of raised blood pressure in adults aged 25 and over was around 40% in 2008. In India high blood pressure is a major public health problem and its prevalence is rapidly increasing among both urban and rural populations. In fact, hypertension is the most prevalent chronic

disease in India. 2012 studies show that for every known person with hypertension there are two persons with either undiagnosed hypertension or prehypertension.

The morbidity of prolonged hypertension damages the blood vessels of heart results in atherosclerosis, stroke, kidney disease, diabetes mellitus, metabolic syndrome, preeclampsia, erectile dysfunction and retinopathy. Anti hypertensive act by influencing the BP regulatory systems, the autonomic nervous system, rennin-angiotensin system, calcium channels.

World hypertension day (WHD) –MAY 17th (Healthy heart beat - Healthy blood pressure)[5].

The purpose of world hypertension day is to promote public awareness of hypertension and to encourage the citizens of all the countries to prevent and control this silent killer, in the modern epidemic.WHD has been recommended by World hypertension league (WHL) that blood pressure should be less than 140/90 mmHg for general population[6].

A number of safe and effective medication are available for treatment of high blood pressure, Current treatment strategies for hypertensive includes,

1. Diuretics
    - ✓ Thiazides -hydrocholorothiazide, chlorthalidone, indapamide
    - ✓ Loop diuretics - Frusemide, bumetanide, torsemide
    - ✓ K^+ Sparing diuretics - Spironolactone, amiloride, triamterene.
2. Drugs acting on renin angiotensin system
    - ✓ Angiotensin converting enzyme inhibitors

      -Captopril, enalapril, lisinopril, ramipril.
    - ✓ Angiotensin II receptor antagonists - Losartan, valsartan.
    - ✓ Renin inhibitor - Aliskiren.
3. Sympatholytics
    - ✓ Centrally acting drugs - Guanfacine, Clonidine, Guanabenz, Methyldopa.
    - ✓ Ganglion blockers -Trimethaphan,

- ✓ Adrenergic neuron blockers -Guanethidine, reserpine.
- ✓ Adrenergic receptor blockers-

  α-blockers -Prazosin, phenoxybenzamine

  β-blockers -Propranolol, atenolol.

  Mixed α and β blockers-Labetalol,carvedilol
- ✓ Ca^{++} channel blockers - Nifedipine, nicardipine, amlodipine, verapamil

5. Vasodilators

- ✓ Arteriolar dilators-Hydralazine, minoxidil
- ✓ Arteriolar and venular dilators-Sodium nitroprusside

Though such drugs showing better results in treating hypertension some serious adverse effects such as drowsiness, parotid gland swelling and pain, constipation, fluid retention, impotence, tremors, sweating, tachycardia, palpitation, hypotension always seen towards the usage of those drugs[7]. In order to negotiate those adverse effects observed for the usage of modern medicines there is an emergence need for the medical world to treat the highly prevalence disease hypertension.

Herbals and herbo-mineral formulations are always fame because of its therapeutic source without causing adverse effects. Now the people among the world is awakened about the clinical importance in use of herbal medicines. At the same time even herbal medicines are considered as effective as well as good without causing any harmful effects, due to various changes in our environment here is a need to confirm the safe use of herbal drugs. Siddha system is an immemorial system with several admirable properties. It's not only cures disease but also helps in the prevention of disease, thereby increasing the longevity of life.

Hypertension described in modern medicine correlates with that of "*Kuruthi azhal noi*" as mentioned in Siddha literature. It is also known as "*Raktha pitham*". "Prevention is better than cure" which is the main target of Siddha system. Siddha medicines were formulated by using the theory of "*Arusuvaikal*" and it includes the material ingredients such as plant, animal products, metals and minerals. According to Siddha system the herbo-mineral preparations are having more potent therapeutic value.

In Siddha medical system, So many compounds were formulated by the great siddhars for the management of "*Kuruthi Azhal Noi*".

In Siddha system there is a slogan which is "**உணவே மருந்து மருந்தே உணவு**" which indicates that the role of food habits plays a major role in the management of diseases for better cure. Each food has some characteristic property functioning in role of treating diseases especially lifestyle disease like hypertension.

"*Munthirikai chooranam*" is a herbo-mineral formulation was indicated in Siddha text "*Aathma Ratchamirtha Vaithiya Saara Sangiragam*" for the treatment of *Ratha Pitham*, Peripheral neuritis, Vertigo [8]. The Siddha term "*Ratha Pitham"* which is described for the condition of pathology of Hypertension. Even though the herbal and herbo-minerals are safe, proper scientific validation is needed to ensure its safety and efficacy for better clinical use. Since there are no scientific backgrounds regarding the anti-hypertensive activity of this novel Siddha formulation "*Munthirikai Chooranam*".

Hence the author is interested in doing the Preclinical Evaluation Of "*Munthirikai Chooranam"* For Its Anti-Hypertensive, Diuretics, Anti-Oxidant Activities. In addition to that going to create finger prints through physico-chemical and bio chemical characterization to standardize this drug "*Munthirikai chooranam*" in a scientific way.

2. AIM AND OBJECTIVES

AIM

The aim of this treatise is to Evaluate the Anti-hypertensive, Diuretic and Anti -oxidant Activity of ***Munthirikai Chooranam*** and going to create the fingerprints to standardize this medicine with reference to the authentic drugs.

OBJECTIVES:

The key objectives of the study are:

- Collection of various Siddha and modern literature relevant to the study.
- Preparing the drug according to Siddha classical text.
- Subjecting the drug into physico-chemical standardization.
- Analyzing the drug chemically for detection of acid and basic radicals.
- Focusing the drug for analytical assessment through sophisticated analytical modern techniques like FTIR, ICPOES, SEM, XRD
- Studying the toxicity profile of *Munthirikai chooranam* according to OECD guidelines.
- Evaluation the pharmacological study of the test drug ***Munthirikai Chooranam*** through the following activities,
- Anti-hypertensive, Diuretic Activities in wistar albino rats
- Anti Oxidant Of - Through DPPH assay
- Evaluation of anti-microbial load for this formulation.
- Analyzing all the above study results to evaluate the benefits of ***Munthirikai Chooranam***

3. REVIEW OF LITERATURE

3.1 Drug Review

3.1.1 Gunapadam aspect[9]

Munthirikai pazham (*Vitis vinifera)*

Alternative names

Aravaram, Kodimunthiri, Kodimunthirikai, Munthirikai, Thrakshai, Madhurasam, Koothirikai Thirakam, Paloththamai.

Vernacular names

English **:** Grapes, Common grape-vine, winegrape, Europeangrape.

Telugu **:** Draksha

Sanskrit **:** Draksha

Hindi **:** Munakha

Malayalam **:** Draksha

Part used : Leaves, Fruit

Suvai **:** *Inippu*

Thanmai **:** *Thatpam*

Pirivu **:** *Inippu*

Action

- Refrigerant
- Nutritive
- Demulcent
- Diuretic
- Tonic
- Laxative
- Astringent

Uses : It gives strength for cardiac musculature.

Thipilli moolam (*Root of Piper longum*)

Alternative name

Ambinadi,Kiranthiver,Kiranthikam,Thanman,Thanmoolam,Thippilikattai,Thaesavaram, Nathikaranthai,Narukuvaeru,Narukkuthippili,Kandaththippili,Modiver.

Vernacular names

English **:** Long - pepper - Root

Telugu **:** Pippili-mulam

Sanskrit **:** Pipalee-moola

Hindi **:** Felfelai-maya

Malayalam **:** Kattu-thippili

Part used **:** Root

Properties

Suvai **:** *Inippu*

Thanmai **:** *Thatpam*

Pirivu **:** *Inippu*

General character

தாகபித்தஞ் சோகந் தணியாச் சுரமிருமல்
மேகங் குரற்கம்மல் மெய்க்கடுப்பும்- ஏகுங்காண்
திப்பிலிமூ லங்கண்டத் திப்பிலிய தாம்நறுக்குத்
திப்பிலியென் றேயொருக்காற் செப்பு.

-அகத்தியர் குணவாகடம்

Actions

- Stomachic

Uses

- It is used in the treatment of cough, diarrhoea.

Thiri kadugu

***Chukku* (*Zingiber officinale*)**

Alternative names

Arukkan, Sundi, Sondi, Vidamoodiya Amirtham, Verkombu.

Vernacular name

English : Dried Ginger

Telugu : Sondi

Malayalam : Chukku

Sanskrit : Nagaram

Hindi : Sonth

Part used : Tuber

Properties

Suvai : *Karppu*

Thanmai : *Veppam*

Pirivu : *Karppu*

General character

சூலைமந்தம் நெஞ்செரிப்பு தோடமேப் பம்மழலை
மூலம் இரைப்பிருமல் மூக்குநீர் -வாலகப
தோடமதி சாரந் தொடர்வாத குன்மநீர்த்
தோடம்ஆ மம்போக்குஞ் சுக்கு.

-அகத்தியர் குணவாகடம்

Actions

- Carminative
- Stimulant
- Stomachic

Uses : It is used in the treatment of Ulcer, Cough, Cold and Anaemia.

Milagu (*Piper nigrum)*

Alternative names

Kari, Kaayam, Maasam, Kurumilagu, Malayalam

Vernacular name

English **:** Black Pepper

Telugu **:** Miriyalu

Malayalam **:** Kurumulakku

Sanskrit **:** Marucha

Hindi **:** Kallirmirch

Part used **:** Seed, Climber

Properties

Suvai **:** *Kaippu, Karppu*

Thanmai **:** *Veppam*

Pirivu **:** *Karppu*

General character

தீயாகி யெங்கும் திரியுமதை யாவத்து
மோயாம லெப்புடியு முண்டாக்காற்-பாயாது
போந்திமிர்வா தங்கிரந்தி புண்ணீரும் மண்ணவர்க்கும்
காந்திமெய்வா தச்சலுப்பைக் காய்.

தேரன் வெண்பா

Actions

- Stimulant
- Acrid
- Anti-dote

Uses: It is used in the treatment of Ulcer, Cough, Cold, Anaemia and Hemiplegia.

Thippili *(Piper nigrum)*

Alternative names

Aarkathi, Kaman, Saram, Aathi marunthu, Vaitheki.

Vernacular name

English **:** Long pepper

Telugu **:** Pippilu

Malayalam **:** Thipili

Sanskrit **:** Papal

Part used **:** Seed, Fruit

Properties

Suvai **:** *Inippu*

Thanmai **:** *Thatppam*

Pirivu **:** *Inippu*

General character

கட்டி யெதிர்நின்று கடுநோயெல் லாம்பணியும்
திட்டி வினையகலும் தேகமெத்த - புட்டியாம்
மாமனுக்கு மாமனென மற்றவர்க்கு மற்றவனாங்
காமமெனுந் திப்பிலிக்கும் கை.

-தேரன் வெண்பா

Actions

- Carminative
- Stimulant
- Stomachic

Uses

It is used in the treatment of Ulcer, Cough, Cold, Anaemia, ENT diseases, Headache.

Sengkazhunir (*Nymphaea alba)*

Alternative names

Urpalam, Kuvalai, Kuvalaiyam, Kazhunir.

Vernacular names

English **:** Water lily

Telugu **:** Nirucancha

Malayalam **:** Chenkazhuneer

Part used **:** Whole plant

Properties

Taste **:** Sweet

Character **:** coolant

Division **:** Sweet

Actions

- ❖ Anti-pitta
- ❖ Refrigerant

General character

"உடற்குக் குளிர்ச்சியதா முள்ளுழலை மாற்றும்
அடற்கப வரோசகத்தை யாற்றுங் - கடற்குள்
எழுநீர்க் குமிழியிகழு முலையாய்
கழுநீர்மல ரெனவே காண்".

-அகத்தியர் குணவாகடம்

Uses

- ❖ Infusion- used to treat thirst and dry powder along with sugar it cures the loss of taste sensation.

Vetiver (Vetiveria zizanioides)

Alternative names :*Vetiver,Vizhal ver,Viranam,Kuru ver*

Vernacular name

English **:** Cuscus grass

Telugu : Vattiveri

Malayalam : Veti-veru

Sanskrit : Usheera veeranam

Hindi : Balah

Part used : Ver

Properties

Suvai : *Inippu*

Thanmai : *Thatppam*

Pirivu : *Inippu*

General character

பித்தவி தாகம் சசிகா மிலங்கறைப் பித்தமனற்
றத்திடு குட்டஞ் சிரநோய் களமடி தாதுநட்ட
மத்தம னற்புண் டனப்புண்வன் மூர்ச்சை வரிவிழிநோய்
வித்திர மேகத்தின் கட்டியும் போம் வெட்டி வேரினுக்கே.

- அகத்தியர் குணவாகடம்.

Actions

- Tonic
- Diuretic
- Febrifuge
- Stimulant

Uses

It is used in the treatment of Hypertension, Jaundice, Eye diseases, Fever

Chandanam (Santalum album)

Vernacular names

Eng name : Sandalwood

San name : Chandanam

Tel name : Gandeapu-chkka

Mal name : Chandana

Hindi name : Chandan

Part used : Sandalwood, Sandal oil

Properties

Suvai **:** Bitter, Mild Astringent

Thanmai **:** Coolant, Hot

Pirivu **:** Sweet, Acrid

Action

- Alternative
- Diuretic
- Diaphoretic
- Stimulant
- Disinfectant
- Astringent
- Cooling

General character

"கோதில் சந்தனஞ் சீதோஷ்ணங் கொண்டிருக்கும்
வாதபித்தம் ஐயம்மனப் பிரமை - ஓதுசுரம்
மேகம்தனித் தாகம்வெப்பு சொறியும் போக்கும்
ஆகந்தனக் குறுதி யாம்".

- **அகத்தியர் குணவாகடம்**

Uses

Decoction of sandal wood powder used to treat in Fever, Tachycardia and decreases the pulse rate.

Also used to treat in various Skin diseases and Diarrhoea.

Vilamichu (Plectranthus vettiveroides)

Vernacular name

Eng name : White Cuscus grass

Mal.name : Iru veli

Sans.name : Hroeveram

Part used : Ver

Properties

Suvai **:** *Kaiippu*

Thanmai **:** *Seetham*

Pirivu **:** *Inippu*

General character

"மேகம்விழியெரிச்சல்வீறிரத்தபித்தமொடு
தாகமதமூர்ச்சைபித்தந்தன்மயக்கம்- சோகஞ்
சிரநோய்இவையேகுஞ்செய்யவிலாமிச்சுக்
கெரிசுரமும்இல்லையிசை".

- **குணபாடம் மூலிகை வகுப்பு**

Actions

- Refrigerant
- Anti-pitta

Uses

It is used in the treatment of Hypertension, Diabetes, Anaemia, Head ache.

Atimaduram (Glycyrrhiza glabra)

Alternative names : *Athingam, atti madhugam, Kundri ver.*

Vernacular names

Eng name : Jequitity, Indian or Jamaica liquorice

Tel name : Ati-madhukam, yeati-madhukam

Mal name : Ati-madhuram, iratti-madhurarr

San name : Yesti-madhukam

Hindi name : Jathi-madh, mulath

Part used : Root

Properties

Suvai **:** Sweet

Thanmai **:** Hot

Pirivu **:** Sweet

Actions

- Emollient
- Demulcent
- Expectorant
- Tonic
- Laxative

General character

"கத்தியரி முப்பிணி யால்வருபுண் தாகங்
கண்ணோய் உன்மாதம் விக்கல்வலி வெண்குட்டம்
பித்த மெலும்புருக்கி கிரிச்சரம் ஆவர்த்த
பித்தமத மூர்ச்சை விடபாகம் வெப்பந்
தத்திவரு வாதசோணிதங் காமாலை
சருவ விடங் காமியநோய் தாதுநட்டங்
குத்திருமல் ஆசியங்கம் இதழ்நோய் இந்து
குயப்புணும் போம் மதூகமெனக் கூறுங் காலே".

- குணபாடம் மூலிகை வகுப்பு

Uses

The root of Indian liquorice is chewed for cough.

It is also indicated for Jaundice, Arthritis, Eye diseases, Skin diseases, Leucoderma and Migraine.

Muthakkasu (Cyperus rotandus)

Other name : *Muthakkasu*

Vernacular names

Eng name : Nut grass

San name : Mutha

Tel name : Tungamusta

Hindi name : Mutha

Mal name : Muththana

Part used: Root tuber

Action

- Astringent
- Stimulant
- Tonic
- Diuretic
- Diaphoretic
- Demulcent

General character

"சீத சுரந்தீர்க்குஞ் செம்புனல்பித் தம்போக்கும்
வாத சுரந்தணிக்கும் வையகத்தில்-வேதைசெய்ய
வந்தபிணியெல்லாம் வாட்டுமுத் தக்காசு
கொந்துலவும் வார்குழலே! கூறு"

"அதிசாரம் பித்தம் அனற்றாகம் ஐயங்
குதிவாதஞ் சோபங் கொடிய - முதிர்வாந்தி
யாரைத் தொடர்ந்தாலும் அகவ்வவர்க்கெ லாங்குளத்துக்
கோரைக் கிழங்கைக் கொடு".

- குணபாடம் மூலிகை வகுப்பு

Uses

The decoction of nut grass is potentially used for fever.

It along with ginger is effectively used to treat dysentery.

The paste of fresh nut grass is used as an external application for skin rashes.

It is also an antidote for Indian hemp, opium poisons.

Vilva poo (*Aegle marmelos)*

Alternative names

Kushavi, Koovilam, Koovilai, Sivathurumam, Maaluram.

Vernacular name

Eng name : Bael(tree) Holy fruit tree

Tel. name : Bilvamu

Mal.name : Kuvalam

Sans.name : Bilva

Hindi name : Bel

Part used : Leaves, Flower, Fruit, Young fruit, Root, Bark, Root bark.

Properties

Suvai **:** *Thuvarppu, Kaippu*

Thanmai **:** *Thatppam*

Pirivu **:** *Karppu*

General character

பல்லவம்பூ பிஞ்சின் பழநிரியம்சம் முறையே
வல்லவம் மேகமந்த மாகுன்மம் - செல்லுகின்ற
நோக்கமருள் விந்துநட்ட நூறு மடுத்தவர்கட்
காக்கமருள் வில்லுவத்தி லாம்.

- அகத்தியர் குணவாகடம்

Actions

- ❖ Aphrodisiac
- ❖ Febrifuge
- ❖ Stomachic
- ❖ Astringent

Uses

Its juice is used to make drink and squashes, especially in summer season because of its sweet and pleasant nature and also used for increase appetite.

Its extract oil is used to cure respiratory problems.

Yelarisi (Eletaria cardamom)

Vernacular names

Eng name **:** Cardamomum seeds

Tel name **:** Elakulu

Mal name **:** Elettari

Hindi name **:** Elachi

San name **:** Ela

Other names: Angi, Korangam, Thudi

Part used **:** Seed

Taste : Acrid

Character : Hot

Division : Acrid

Action: Carminative, Stimulant, Stomachic, Aromatic.

General character

"தொண்டைவாய்கவுள் தாலுகுதங்களில்
தோன்றும் நோயதிசாரம் பன்மேகத்தால்
உண்டை போல்எழுங்கட்டி கிரிச்சரம்
உழலை வாந்தி சிலந்திவிஷஞ்சுரம்
பண்டைவெக்கைவிதாக நோய்காசமும்
பாழுஞ்சோமப்பிணிவிந்துநட்டமும்
அண்டை யீளைவன்பித்தம் இவைக்கெல்லாம்
ஆல்மாங்கமழ் ஏலமருந்தே".

-பதார்த்த குண சிந்தாமணி

Uses

Useful in various stomach problems and safely used as carminative in convalescence after diarrhoea. Decoction of cardamoms together with their pericarp and jaggery to relieve giddiness caused by biliousness.

Kothumalli (Coriandrum sativum)

Alternative names: *Urrul arisi, Dhaniya*

Vernacular name

Eng name **:** Coriander seeds

Tel. name **:** Kotimiri

Mal.name **:** Kotta-malli

Sans.name **:** Kustumbari

Kan name **:** Kottamari-bija

Hindi name **:** Dhanya

Part used : Leaves, Seeds.

Properties

Suvai **:** *Kaarppu,*

Thanmai **:** *Seetha veppam*

Pirivu **:** *Karppu*

General character

கொத்துமல்லி வெப்பம் குளிர்காய்ச்சல் பித்தமந்தஞ்
சர்த்திவிக்கல் தாகமொடு தாதுநட்டம் - கத்தியெழும்
வாத விகார்மடர் வன்கர்த்த பிவிரணம்
பூதலத்தில் லாதகற்றும் போற்று.

- அகத்தியர் குணவாகடம்

Actions

- Stomachic
- Carminative
- Diuretic

Uses

The seed extracts are used in cleansing of eye. It is also used in the treatment of chronic ulcers, giddiness.The spinach of coriandrum sativum is used in the treatment of ageusia, fever and it is aphrodisiac in nature.

Thiripala

Kadukai (Terminalia chebula)

Alternative names

Anthan, Abhayan,Amutham, Devi,Divya, Rohini, Abaranam, Aritaki, Varikkai, Jeevanathi.

Vernacular name

English : Chebulic Myrobalan

Telugu : Karak-kaya

Malayalam: Katukkai

Sanskrit : Pathya

Kannadam: Anile-Kayi

Hindi : Pilen Hara

Part used : Leaves, Seeds.

Suvai **:** *Kaarppu,*

Thanmai **:** *Seetha veppam*

Pirivu **:** *Karppu*

General character

கடுக்காயுந் தாயுங் கருதிலொன்றென் றாலும்
கடுக்காய்த் தாய்க்கதிகங் காண்நீ- கடுக்காய்நோய்
ஓட்டி யுடற்றேற்றும் உற்றவன்னை யோசுவைகள்
ஊட்டியுடற் றேற்று முவந்து.

- அகத்தியர் குணவாகடம்

Actions

- ❖ Stomachic
- ❖ Carminative
- ❖ Diuretic
- ❖ Stimulant

Uses

The extracts of *Terminalia chebula* are used in the treatment of polyuria, haemorrhoids, dysentery. *Kadukkai* pills are used in the treatment of ulcers, respiratory diseases, anaemia, dropsy, liver diseases, asthma, ascites and leucorrhoea.

Nelli vatral (Phyllanthus emblica)

Alternate names

Aamalagam, Aalagam, Aambal, Amarigam, Thaththari, Thathiri,Korangam.

Vernacular names

Eng name : Indian gooseberry

San name : Amalaki

Tel name : Usirika

Hindi name : Amlika

Mal name : Nellikay

Kan name : Nellikai

Part used : Leaf, Flower, Bark, Root, Seed

Taste : Sour, Acrid, Sweet

Character **:** Coolant

Division **:** Sweet

Action **:** Astringent, Refrigerant, Laxative, Diuretic

General character

"நல்லநெல்லி முள்ளியது நாக்குக் குருசிதரும்
அல்லல்விரி பித்தம் அகற்றுமதை-மெல்லத்
தலைமு ழுகக்கண்குளிருந்தா வுபித்தவாந்தி
இலையிழிமே கங்களும் போம்எண்".

- தேரையர் குணவாகடம்

Uses

The dried fruit of amla is indicated for blood related disorders, mennorrhagia, psychotic disorder, nausea, vomiting.

- ❖ Decoction of dried fruit is used for nausea, vomiting, giddiness.
- ❖ Also indicated for the treatment of diarrhoea, dysentery, and leucorrhoea.

Thandrikkai (Terminalia bellerica)

Alternative names

Amutham, Coolithurumam, Thabamari, Erikatbalam , Boothavasakam, Veebethekam

Vernacular name:

Eng name **:** Beleric Myrobalans

Tel. name **:** Thandra-kaya

Mal.name **:** Thanni-kai

Sans.name **:** Vebeethaki

Kan name **:** Tanri-kayi

Hindi name **:** Bhairah

Part used : Leaves, Seeds, Fruit.

Properties

Suvai **:** *Thuvarppu*

Thanmai **:** *Veppam*

Pirivu **:** *Inippu*

General character

"சிலந்திவிடம் காமியப்புண் சீழான மேகங்
கலந்துவரும் வாதபித்தங் காலோ- டலர்ந்துடலில்
ஊன்றிக்காய் வெப்ப முதிர்பித் துங்கரக்குந்
தான்றிக்காய் கையிலெடுத் தால்."

- குணபாடம் மூலிகை வகுப்பு

Actions

- Astringent
- Expectorant
- Laxative
- Tonic

Uses: It is used in the treatment of Hypertension, cough, leucorrhoea, asthma.

Ner pori (Oryza sativa)

Alternative names: *Thorai, Vai, Virihi, Sennel, Sali, Vari*

Vernacular name

Eng name **:** Paddy (The husked rice)

Tel. name **:** Vari

Mal.name **:** Nella

Sans.name **:** Vrihi

Kan name **:** Bhatha

Hindi name **:** Chaval

Part used **:** rice

Properties

Suvai **:** *Inippu*

Thanmai **:** *Thatppam*

Pirivu **:** *Inippu*

General character

நெற்பொறியைத் தின்றால் நெடுந்தாகம் வாந்திமந்தம்
மற்பித்த வாதமத மூர்ச்சை-பற்பலவாம்
பேதி யருசியிவை பேருலகை விட்டொழியுமஞ்
சாதி மடமயிலே சாற்று.

-அகத்தியர் குணவாகடம்

Actions

- Nutrient
- Refrigerant
- Demulcent

Uses

It is used in the treatment of leucorrhoea, fever, ascites, diarrhoea, ageusia. Decoction of nerpori is used in the treatment of giddiness, ulcers .

Pericham pazham *(Phonex dactilifera)*

Vernacular name

Eng name **:** Date palm

Tel. name **:** Karjuramu

Mal.name **:** Tenech-cha,Perich-cha

Sans.name **:** Kharjjuram

Kan name **:** Kharjura

Hindi name **:** Kajur

Part used : Seeds, Fruit.

Properties

Suvai **:** *Inippu*

Thanmai **:** *Veppam*

Pirivu **:** *Karppu*

General character

வாயிலுண்டா மூற்றடலை மாற்றும் பசியில்லை
யாயிலுண்டா லுண்டா மதுமேக-நோயுள்
பெருநீர் மறுக்குமினும் பெண்களைக் கூடில்
தருணநீர்மை சூரக்காய் தான்.

- அகத்தியர் குணவாகடம்.

Actions

- Tonic
- Aphrodisiac
- Nutritive
- Expectorant
- Laxative
- Diuretic
- Stomachic

Uses

It is used in the treatment of cardiac diseases, scabies, tinea, Hanson's disease cough, diabetes, anaemia, dropsy and hypertension .

Patchai karpooram *(Borneo camphor)*[10]

Borneo camphor is one of the twenty five types of Karasaara.

Vernacular name: *Imavalugam, Athaliuppu, Kelithipachchai, Sasi, Chandran,, Somanuppu, Seethalam, Pachchai Karpooram, Mathi, Paarmagan Saari,Maruvaali, Pooram ,Vintham,Iravikanji And Pachchai Ganasaram.*

It is soluble in atmospheric air. It has pleasant odour, cooling agent. It is considered that there are three types of Borneo camphor.

1. Esan 2.Veeram 3.Poothachirayan.

General Properties of *Esan* camphor

This is effective in kapha fever, pitha, giddiness and diseases of the nose and polydipsia. It is white in colour and sour in taste.

"ஈசனென்னும் பூரவெண்மை யென்பரது காரமுமாம்
பேசரிய சீதமுஷ்ணம் பித்தமயல்-வீசுகின்ற
பீநசமுட் டாகமிவை பேர்த்துவிடுங் காந்தியுண்
டான ததுவசிய மாம்."

General Properties of *Veeman* camphor

This is demulcent and a tonic. It is effective in glossitis, polydipsia and vomiting.

"வீமனெனுங் கர்ப்பூரம் மேக வழுக்கு வெண்மை
சேம முறுங்குளிர்ச்சி தின்றக்கா-னாமருவு
நோயகலுந் தாகமறும் நுண்பே தியுமாகுந்
தூய மதிமுகத்தாய் சொல்."

General properties of *Poothasirayan* camphor

This is effective in controlling of cough, *vatha, pitha, kapha dosas,* three humours, itching and ulcers. If it is added as an adjuvant with the medicines intended for women, it will give best result.

General properties and uses of Borneo camphor : The borneo camphor is effective in eight types of Gastric ulcers, *Vatha* disease , joint pains and *Kapha.*

"அட்டகுன்மஞ் சூலை யணுகாது வாதமொடு
துட்டமே கப்பிணியுந் தோற்றாதே-மட்டலருங்
கூந்தலுடை மாதே கொடியகபம் போகுஞ்
சார்பச்சைக் கர்ப்பூரத் தால்."

This has astringent and salty taste. It's potency is cold and has expectorant tonic and demulcent properties.

Dosage: 8 mg to 162 mg.

Karkandu* (*Saccharum officinarum)

Alternative names

Punarpoosam, ikku, vaei

Vernacular names

Eng name **:** sugar cane, noble cane

Tel name **:** cheruku, kanupula-cheruku

Mal name **:** karinpa

Kan name **:** khabbu

Sans name **:** Ikshu, Rasalah

Hind name : Ukh-ganna

Part used : Juice, Sugar, Root

Suvai : *Inippu*

Thanmai : *Seetham*

Pirivu : *Inippu*

General properties

ஈறின் தடிப்பு மிருமலும்பல் வாந்திகளுஞ்
சீறுகப முட்டினமுஞ் சேராதே - தேறியநற
சொற்கண் டிளங்குயில்கள் சூழ மடவனமே
கற்கண் டெனவுரைக்குங் கால் .

-அகத்தியர் குணவாகடம்

Actions

- Demulcent
- Antiseptic
- Laxative
- Diuretic

Uses: It is used in the treatment of diabetes, leucorrhea, male infertility.

Lavanga pathiri (*Cinnamomum tamla)*

Alternative names: *Talisapathiri, Tamalapathiri*

Vernacular name

Eng name : Cassia cinnamon, Indian cassia lignea

Tel. name : Adavi-lavangapatri, Talisapatri

Mal.name : Paccila

Sans.name : Tamalapatram

Kan name : Kadu lavanga patte

Hindi name : Tejpatt

Part used : Leaves

Properties

***Suvai* :** *Karppu*

***Thanmai* :** *Veppam*

Pirivu **:** *Karppu*

General character

மேகசுரம் சீதசுரம் வெட்டைசுவா சங்காசம்
தாகபித்தம் வாந்திசர் வாசியநோய்-மேகத்தின்
கட்டியோடு தாதுநட்டங் கைப்பருசி போக்கிவிடும்
இட்டஇல வங்கத் திலை.

-அகத்தியர் குணவாகடம்.

Actions

- Stimulant
- Carminative
- Stomachic
- Diaphoretic

Uses: It is used in the treatment of Cough, Thirst, Vomiting and Asthma.

Chiru nagappu (*Mesua nagassarium)*

Alternative names :

Nagam, Nagaputpam, Naakaesaram, Kaesaram.

Vernacular name:

Eng name : Ceylon lorn wood

Tel. name : Naga-kesara

Mal.name : Nakappuvu

Sans.name : Naga-kesara

Kan name : Naga-kesara

Hindi name : Nag-kesar

Part used : Leaves, Bud, Seeds, Fruit, Bark.

Properties:

Suvai **:** *Siru kaippu, thuvarppu*

Thanmai **:** *Thatppam*

Pirivu **:** *Karppu*

General character:

சிறுநாகப் பூவினது செய்கைதனைச் சொல்வோம்
குறியாகும் மேகத்தைக் கொல்லும்-நெறிவிட்டுத்
தீதாய்ச் செல்வாயுவையுந் தீர்க்குமிரு மற்போக்கும்
கோதாய் இதையறிந்து கொள்.

- குணபாடம் மூலிகை வகுப்பு

Actions:

- ❖ Astringent
- ❖ Carminative
- ❖ Aromatic
- ❖ Acrid
- ❖ Purgative

Uses: It is used in the treatment of Leucorrhoea, Cough, Diarrhoea.

Koogai neeru ***(****Marantu arundinacea****)***

Alternative names: *Arrow root kizhangu, Kuva-maa kizhangu, Kookaik kizhangu*

Vernacular name:

Eng name **:** East Indian Arrow root

Tel. name **:** Ararut-gaddalu

Mal.name **:** Kuva,kuva-kizhanna

Kan name **:** Koove-Gedde

Hindi name **:** Tikhar

Part used **:** Kizhangu

Properties:

Suvai **:** *Inippu*

Thanmai **:** *Thatppam*

Pirivu **:** *Inippu*

General character:

மேனியிடும் வாய்க்கு மிருதுவாம் ஆக்கியுண்ணத்
தானிருமல் வெப்பதிக தாகமிவை-ஏனிருக்கும்
அம்பே றிளங்கிழங்கி தியாவர்க்கு மாமணப்பூங்
கொம்பேகூ கைக்கிழங்கைக் கூறு.

- அகத்தியர் குணவாகடம்

Actions:

- ❖ Refrigerent
- ❖ Demulcent
- ❖ Nutrient

Uses: It is used in the treatment of Cough, Fever, Thirst.

3.1.2 BOTANICAL ASPECT OF THE INGREDIENTS

Vitis vinifera

Taxonomical classification:

Kingdom : Plantae

Order : Vitales

Family : Vitaceae

Genus : *Vitis*

Species : *vinifera*

Distribution:

Cultivated throughout India.

Description:

A large, deciduous tendril climber, tendrils leaf-opposed, often bifid; leaves simple; flowers small green in leaf-opposed, panicles cymes; fruits bluish black; seeds 2-4 with a discoidal tubercle on the back.

Part used : ripe fruits (dried), leaves, stems, flowers.

Chemical constituents: Grapes contain a large amount of sugar (15 to 25%), with roughly equal amounts of glucose and fructose and only a trace of sucrose. Vitamin C content is low (around 3 mg/100g). The fruits contain tartaric acid and malic acid in similar concentrations (around0.5g/100g). The red and black grape pigments are anthocyanins.

Properties and uses: The fruits are sweet, refrigerant, laxative, cardio tonic, antispasmodic, aphrodisiac, rejuvenating, digestive, nervine tonic expectorant and tonic. They are useful in vitiated conditions of *pitha* and *kapha*, burning sensation, constipation, amentia, haemoptysis, anaemia, haemorrhages, fever, leprosy, skin diseases, dyspepsia, cough, asthma, bronchitis, jaundice and general debility.

The leaves are astringent anodyne, diuretic and depurative and are useful in scabies, cephalalgia, skin diseases, syphilis, haemorrhoids, splenomegaly and vomiting.

The ash of the stems is good for arthralgia, haemorrhoids and orchitis. The flowers are expectorant, emmenagogue and haematinic [11].

Zingiber officinale

Taxonomical classification:

Kingdom : Plantae

Order : Zingiberales

Family : Zingiberaceae

Genus : *Zingiber*

Species : *officinale*

Distribution: Cultivated throughout India, run wild in some places in the Westernghats.

Description: A slender, perennial rhizomatous herb; leaves linear, sessile, glabrous; flowers yellowish green in oblong, fruits oblong capsules. The rhizomes are white to yellowish brown in colour, irregularly branched.

Part used: rhizomes (raw as well as dry)

Chemical constituents: Ginger contains gingerols, a-curumene, citral, D-camphene, geraniol, zingiberenes, zingerone, phellandrene etc.

Properties and uses:

The raw ginger is acrid, thermogenic, carminative, laxative and digestive. It is useful in anorexia, vitiated conditions of vata and kapha, dyspepsia and inflammations.

Dry ginger is acrid, thermogenic, appetiser, laxative, stomachic, stimulant, and rubefacient, anodyne, aphrodisiac and carminative .It is useful in dropsy, otalgia, asthma, cough, diarrhoea, anorexia, nausea, vomiting and dyspepsia[11a].

Piper nigrum

Taxonomical classification:

Kingdom : Plantae

Order : Piperales

Family : Piperaceae

Genus : *Piper*

Species : *nigrum*

Distribution:

Throughout India, in evergreen forests up to 1,500 m and also widely cultivated.

Description:

A stout glabrous climbing perennial, rooting at the nodes; leaves simple, alternate; flowers minute in spikes, usually dioecious; fruits ovoid. Seed berries.

Part used : fruits

Chemical constituents: Piperine – 5 -10 % present both in white and black pepper and contains Piperethine,PiperoleinA&B,feruperine,Dihydroferuperine,Citronellol, Cryptone,Piperonal, Camphene, B-Caryophyllene, B-alanine, Pipecolic.

Properties and uses: The fruits are acrid, bitter, carminative, aphrodisiac, anti periodic, deobstruant, stimulant and stomachic. They are useful in arthritis, asthma, fever, cough, catarrh, dysentery, flatulence, hiccough, haemorrhoids and dyspepsia [12].

Piper longum

Taxonomical classification

Kingdom : Plantae

Order : Piperales

Family : Piperaceae

Genus : Piper

Species : *longum*

Distribution: Throughout India, in evergreen forests, often cultivated.

Description:

A slender aromatic climber, rooting at the nodes; leaves alternate; flowers in solitary spikes; fruits berries, small, red when ripe.The mature spikes collected and dried form the commercial form of pippali.Roots are known as pippalimulam.

Part used: roots,dried spikes.

Chemical constituents: It contains volatile oil, Resin, Piperin, piperlongumine, Brachyamide A & B, Brachystine, sterols, Glycosides.

Properties and uses:

The roots are bitter, thermogenic, tonic, diuretic, purgative, expectorant, anthelmintic, stomachic, digestive and emmenagogue. They are useful in vitiated conditions of vata, gout, dyspepsia, stomachalgia and splenopathy.

The dried spikes are acrid, stomachic, aphrodisiac, carminative, expectorant, tonic, laxative and antiseptic. They are useful in anorexia, dyspepsia, asthma, flatulent colic, epilepsy and fever [12a].

Nymphaea alba

Taxonomical classification

Kingdom : Plantae

Order : Nymphaeales

Family : Nymphaeaceae

Genus : *Nymphaea*

Species : *alba*

Distribution:

A native of Europe and north Africa, found in the lakes of Kashmir and in high altitude below 1,800 m.

Description: A perennial aquatic herb with black rhizomes. Leaves entire, orbicular, cordate. Flower floating, solitary,10-13 cm diam. Fruit a spongy berry, ripening under water. Seeds punctuate, triate, minute, buried in pulp.

Part used : Seeds, Flower, Rhizome.

Chemical constituents: The plant contains nupharine, nymphaein and the cardiac glycoside, nymphalin. The presence of β-sitosterol, gallic acid and myricitrin.

Therapeutical uses:

A decoction of flower is valued as a cardiac tonic in palpitation of heart. effective in combating thirst, diarrhea, burning sensation of the body, fainting, vomiting and internal hemorrhage. Decoction of rhizomes is given in diarrhoea, alcoholic extract has a mild sedative and spasmolytic action. Seeds are used in diabetes[14].

Vetiveria zizanioides

Taxonomical classification:

Kingdom : Plantae

Order : Poales

Family : Poaceae

Genus : *Chrysopogon*

Species : *zizanioides*

Distribution: Throughout India, in the plains and lower hills upto 1,200 m.

Description:

A densely tufted perennial grass, with aromatic roots and rhizomes; leaves narrow, linear, erect, sheaths compressed, ligules reduced to a scarious rim,midrib slender, lateral nerve close, spikelets grey, green or purplish in a panicle of numerous slender racemes,sessile spikelets.

Part used: Roots

Chemical constituents: Allokhusiol, Benzoicacid, Cyclocapacamphene, Epikhusinol, Eugenol, Isovalencic, Isovalencenol, Khusinol, Vanillin, Vertiselinenol, Vetivenic acid, Vetiverol, Zizaene, Zizanol etc.

Properties and uses:

The roots are bitter, sweet, acrid, refrigerant, aromatic, depurative, haematinic, expectorant, constipating, febrifuge, antispasmodic and tonic. They are useful in vitiated conditions of pitta and vata, burning sensation, ulcers, skin diseases, anaemia, nausea, dyspepsia, hiccough, fever, cough, asthma, cardiac debility, hysteria, amenorrhoea, helminthiasis, spasmodic affections and general debility[11b].

Santalum album

Taxonomical classification:

Kingdom : Plantae

Order : Santalales

Family : Santalaceae

Genus : *Santalum*

Species : *album*

Distribution :

It is commonly found in comparatively dry regions of peninsular India from Vindhya mountains southwards, especially in Mysore and Tamilnadu, ascending to an altitude of 1200 m. it has also been found in dry districts of Gujarat, Konkan, Deccan, Rajasthan, parts of Uttar Pradesh, Madhya pradhesh and Orissa.

Description :

A small medium sized, ever green semi parasitic tree, with slender branches, sometimes reaching up to 18 m in height and2.4 m in girth. Bark reddish or grey or nearly black, rough with deep vertical cracks on old trees; leaves glabrous ,thin, elliptic-ovate or ovate-lanceolate,1.5-8 cm.x1.6-3.2 cm., some times larger; flowers straw – coloured, brownish purple, reddish purple or violet, unscented, in terminal ,axillary paniculate cymes; drupe globose or 3 cm diam., purple-black, with hard, ribbed endocarp; seeds globose or obovoid.

Parts used: Heart Wood and oil

Chemical Constituents:

Sandalwood oil contains α and β santalol, α and β-santalenes, santenol, teresantalol, nor-tricycloeka santalal, exo-norbicycloeka santalal, isovaleraldehyde, santanone, teresantalic acid, trans-β-santalol, epi-cis-β-santalol, β-santalol, epi-β-santalane, cis-lanceol, cis-nuciferol, tropan alkaloids, santalbic acid, palmitc acid, oleicacid, betulaic acid, glucose, fructose, sucrose, betulinic acid and L-allohy droxyproline (leaves, fruit and seeds); urs-12-en-3β-yl.palmitate and β-sitosterol (bark).

Principles constituents of sandal wood:

Santalol (up to 90%), fusanol, santene, santalic acid, terestanol, borneol, santalone and others.

Properties and uses

The heart wood and essential oil yielded from it are bitter, sweet, acrid, cooling, blood purifier, intellect promoting, diuretic, expectorant, aromatic, deodorant, disinfectant, depurative, aphrodisiac, haemostatic, anodyne, cardiactonic, debility and spermatorrhea. It is useful in vitiated conditions of pitta, burning sensation, cephalgia, skin diseases, leprosy, foul odour due to hyperhidrosis, cardiac debility, loss of memory, cystitis, menorrhagia, intermittent fever and general debility[11c].

Plectranthus vettiveroides

Taxonomical classification

Kingdom : Plantae

Class : Magnoliopsida

Order : Lamiales

Family : Lamiaceae

Genus : *Plectranthus*

Species : *vettiveroides (barbatus)*

Synonyms:

Plectranthus barbatus, Plectranthus forskholi, Coleus forskholi

Distribution:

Found wild in dry and barren hills of subtropical Himalayas including Kumaon and Nepal ascending to 2700 m and in the decan peninsula, Gujarat, Bihar; cultivated in Baroda and Maharastra.

Description:

A perinneal plant, branched, aromatic herb,about30-60 cm height with thick root; stem-stout, villous with long hairs, ascending leaves, narrowed into petioles, ovate or abtuse, cerate villous or hispid, flowers borne in recemes, stout; upper calyx lip rounded ovate or abtuse; corolla pale blue; fruits nutlets.

Part used : aerial part of the root.

Chemical constituents:

Allylroyleanone,barbatusin,3-β-hydroxy-3-deoxy-barbatusin,coleons E and F, Cyclobarbatusin, plectrin, plectrinon A and B, barbatusol, 20-deoxocarnosol, coleol, coleonol D,E and F, coleonone, coleosol, deoxycoleonol, β-bisabolene, bornylacetate, camphene, α-copaene, β-cymene, 3decanone, β-elemene, cariocal,6-α-hydroxy carnosol.

Therapeutic uses:

Aerial part-spasmolytic, root-hypotensive, spasmolytic and given to children in constipation; decoction as tonic and in the treatment of worms; grounded root internally used to treat eczema and skin disease. forskohlii isolated from the root, is a bronchodilator, cardiac tonic in the treatment of congestive heart failure,glaucoma therapy, anti-hypertensive, remedy for metastatic conditions and thrombosis[14a].

Glycyrrhiza glabra

Taxonomical classification

Kingdom : Plantae

Class : Magnoliopsida

Order : Fabales

Family : Fabaceae

Genus : *Glycyrrhiza*

Species : *glabra*

Distribution:

Cultivated in Punjab and the subhimalayas tract.

Description:

A tall perennial under shrub about 1m high, leaves compound,l eaflet 4-7 pairs; flowers violet in racemes; pods, oblong to linear, flantened. The liquorice of commerce in the dried underground stems and roots.

Its outer surface is pale, chocolate brown in colour, flexible, fibrous and internally has a light yellow colour. It has a characteristic pleasant sweet taste.

Part used: Roots.

Chemical constituents:

Glycyrrhizin, glycyrrhetic acid, glycyrrhetinic acid, 24-hydroxy glycyrrhetic acid, mixture of potassium and calcium salts of glycyrrhizin (glycyrrhizic) acid, glabrin A and B, glycyrrhetol, glabrolide, isoglabrolide, formononetin, glabrone, neoliquiritin, hispaglabridin A and B; heriniarin, umbellifrone; licoagrodin, glabrol, onocerin, β-amyrin, stigmasterol, β-sitosterol, glabroisoflavanone A and B, glabrocoumarin, glychionide A and B and flavanoides[15].

Properties and uses:

The roots are sweet; refrigerant, emetic, tonic, diuretic, demulcent, mild laxative, aphrodisiac, expectorant, emmanagogue, alexipharmic, alterant and intellect promoting. They are useful in hyperdipsia, cough, bronchitis, vitiated in conditions of vatha, gastralgia, cephalalgia, fever, skin diseases, opthalmopathy.

An extract of the root is good for treating gastric ulcers. A decoction of the root is a good wash for falling and graying of hair. Externally the root is applied for cuts and wounds [13].

Cyperus rotandus

Taxonomical classification:

Kingdom : Plantae

Class : Liliopsida

Order : Poales

Family : Cyperaceae

Genus : *Cyperus*

Species : *rotandus*

Description:

It is a perennial, stolaniferous, rhizomatus, halophytic sedge. Rhizome many slender. Tuber-white, succulent when young, hard and black when mature; stem-leafy at base arising from a tuber. Leaf above dark green, with reddish brown sheaths, clustered at the base of stem. Inflorescence 3-9 spreading rays bearing tassels of few, large spikelet; spikelet 20-40 flowered, red brown to almost black. Fruit shape is oblong ovate.

Chemical Constituents: α-cyperone, β-selinene, cyperene, patchoulenone, sugeonol, kobusone, and isokobusone, that may scientifically explain the folk- and alternative-medicine uses. A sesquiterpene, rotundone, so called because it was originally extracted from the tuber of this plant.

Part used: Tubers

Medicinal Uses: The root is pungent, acrid, cooling, astringent, appetizer, stomachic, anthelmintic and useful in treatment of leprosy, thirst, fever, blood diseases, biliousness, dysentery, pruritis, pain, vomiting, epilepsy, ophthalmic, erysipelas etc[13a].

Aegle marmelos

Taxonomical classification

Kingdom : Plantae

Order : Spanidales

Family : Rutaceae

Genus : *Aegle*

Species : *marmelos*

Distribution:

Cultivated throughout in India,in dry forests.

Description:

A medium sized armed deciduous tree upto 8.0 m high with straight,sharp,axillary thorns and yellowish brown shallowly furrowed corky

bark;leaves trifoliate,aromatic, alternate;flowers greenish white,sweet scented,in axillary panicles;fruits globose;seeds numerous oblong,compressed.

Part used: Roots, leaves, fruits

Chemical constituents: Main chemical components are marmelosin, alloimperatorin, marmelide, tannic acid, marmin, umbelliferone, isoimperatorin, marmesin; a number of essential oils, fatty acids, beta-sitosterol.

Properties and uses: The roots are sweet, astringent, bitter and febrifuge.They are useful in diarrhoea, dysentery, dyspepsia, stomachalgia,vitiated conditions of vata, seminal weakness,vomiting and gastric irritability in infants.

The leaves are astringent, laxative, febrifuge and expectorant and are useful in ophthalmia, deafness, inflammations, diabetes And asthmatic complaints.

The unripe fruits are bitter, acrid, sour, astringent, digestive and stomachic and are useful in diarrhoea, dysentery and stomachalgia.

The ripe fruits are astringent, sweet, aromatic, cooling, febrifuge and tonic and also good for the heart and brain and in dyspepsia[13b].

Elettaria cardamomum

Taxonomical classification

Kingdom : Plantae

Order : Zingiberales

Family : Zingiberaceae

Genus : *Elettaria*

Species : *cardamomum*

Description:

Stem perennial, erect, joined,6-9 feet, enveloped in the sheaths of leaves; leaves lanceolate, acuminate, sub-sessile, entire,1-2 feet long; sheaths slightly villous; scapes several, flexuose, joined, branched1-2 feet long; flowers alternate, short stalked, solitary at each point of the receme; calyx funnel shaped, 3-toothed, inely striated, corolla tube

as long as the calyx; limb doubled exterior portion of 3 oblong, concave, nearly equal division; inner lip obovate, longer then the exterior division, curled at the marings.

apex 3- lobed, marked in the centre with purple white stripes; capsule oval, somewhat 3-sided,3- celled,3-valved;seeds numerous, angular; flowers pale-greenish white.

Part used: Seeds

Chemical constituents:

α-pinene, β-pinene, sabinene, myecene, a-phyllandrene, limonene;1,8-cineole,y-terpinene, p-cymene, terpinolene, linalool, linalyl acetate, terpinen-4-oil, α-terterpineol, α-terpineol acetate, citronellol, nerol, geraniol, methyl eugenol and trans-nerolidol.

Medicinal uses:

As cordial and stimulant the seeds are frequently used medicinally,but more frequently as corrective in conjunction with other medicines. A volatile is produced from them by distillation, which has a strong aromatic taste, soluble in alcohol. It loses its odour and taste by being kept too long. The natives chew the fruit with betle, and use it in decoction for bowel-complaints and to check vomiting in infusion it is given in cough.

Coriandrum sativum

Taxonomical classification

Kingdom : Plantae

Order : Apiales

Family : Apiaceae

Genus : *Coriandrum*

Species : *sativum*

Distribution: Cutivated throughout India.

Description:

A glabrous, aromatic, herbaceous annual 30-90 cm in height; leaves decompounds, lower ones long-petioled and upper ones short petioled; flower small, white or pinkish purple in compound terminal umbels; fruits yellowish brown, globular and ribbed, separating into two halves each containing a seed.

Part used: leaves, fruits

Chemical constituents:

It contains essential oil, tannins, terpenoids,reducing sugars,alkaloids, phenolics, flavonoids, fatty acids,sterols and glycosides.It also contained high nutritional values including proteins,oils,carbohydrates,fibers and vitamins.

Properties and uses:

The leaves are acrid, astringent, aromatic, analgesic, anti-inflammatory, and styptic and are useful in halitosis, pharyngopathy, epistaxis, chronic conjunctivitis, hiccough, inflammations and jaundice.

The fruits are aromatic, bitter, sweet, acrid, astringent, anti inflammatory, diuretic, antipyretic, stimulant, expectorant and are useful in vitiated conditions of pitta, cough, bronchitis, vomiting, anorexia, diarrhoea, dysentery, dropsy, intermittent fever, gout and giddiness[13c].

Terminalia chebula

Taxonomical classification

Kingdom : Plantae

Order : Myrtales

Family : Combretaceae

Genus : *Terminalia*

Species : *chebula*

Distribution: Throughout India, in deciduous forests on dry slopes upto 900 m,especially in Bengal,Tamilnadu,West coast and Western ghats.

Description:

A moderate sized to large deciduous tree with a cylindrical bole,rounded crown and spreading branches; leaves ovate, elliptic, glabrous to tawny-villous beneath with a pair of large glands at the top of the petiole;flowers yellowish white in terminal simple spikes;fruits glabrous,shining,ellipsoidal, ovoid drupes, yellow to orange brown in colour;seeds hard,pale yellow.

Part used: mature and immature fruits

Properties and uses: The fruits are astringent, sweet, acrid, bitter, sour, thermogenic, anodyne, anti-inflammatory, vulnerary, stomachic, laxative, purgative, carminative, digestive, cardiotonic, diuretic, antiseptic, aphrodisiac and tonic. They are useful in vitiated condition of tridosa, wounds, ulcers, inflammation, anorexia, helmenthiasis, haemorrhoids, jaundice, hiccough, cough, renal calculi, epilepsy, skin disease, cardiac disorder, neuropathy and genral debility [11d].

Indian gooseberry

Taxonomical classification

Kingdom : Plantae

Class : Magnoliopsida

Order : Malpighiales

Family : Phyllanthaceae

Genus : *Phyllanthus*

Species : *emblica*

Distribution:

A native of India, Wild or cultivated throughout tropical India from the foot of the Himalayas. It grows in Kurinji and Marutam tinai.

Description:

A large handsome deciduous tree with greenish-grey or red bark: peeling of scales and long stripes. Leaves pinnate distichously close set, linear -oblong; Feathery

small leaves are fine and delicate. The tree has a peculiarity of shedding its twigs along with the leaves attached; flowers are very small, greenish densely fascicled along the branchlets, yellowish; males on slender pedicels, females sub sessile; the flowering period is from March to May.

Parts used: Fruits, seeds, flowers, leaves, barks, roots

Chemical constituents: It contains Ascorbic acid, Tannins, Phyllemblic acid, Emblicol, Gallic and Ellagic acid.

Medicinal uses:

Astringent, carminative, stomachic and tonic. Seeds used in eye problems. Flowers refrigent; leaves juices applied externally to ulcers; infusion mixed with fenugreek seeds useful in chronic dysentery; bark and root astringent [12d].

Terminalia bellirica

Taxonomical classification

Kingdom : Plantae

Order : Myrtales

Family : Combretaceae

Genus : *Terminalia*

Species : *bellirica*

Distribution: throughout India, in deciduous forests upto an elevation of 900 m.

Description:

A large deciduous buttressed tree,20-30 m in height with thick brownish grey bark having shallow longitudinal fissures; leaves simple, alternate, long-petioled, crowded about the extremities of the branches, brodly elliptic, margine entire, main nerves 6-8 pairs, midrib prominent on both surfaces; flowers pale greenish yellow with an offensive odour; fruits ovoid grey drupes.

Part used: bark, fruits

Chemical constituents:

Its principal constituents are β-sitosterol, gallic acid, ellagic acid,ethyl gallate, galloyl glucose, chebulic acid, glucose, galactose, fructose and raminose.

Properties and uses: The bark is mildly diuretic and is useful in anaemia and leucoderma.The fruits are astringent, acrid, sweet, thermogenic, antiinflammatory, anodyne, styptic, narcotic, digestive, anthelmintic, expectorant, antipyretic, antiemetic and rejuvenating. They are useful in vitiated conditions of kapha and vata, cough, bronchitis, insomnia, dropsy, dyspepsia, vomiting, skin diseases, leprosy, fever and general debility.

The mature and dry fruit is constipating and is useful in diarrhoea and dysentery. The oil obtained from the seeds is trichogenous and is useful in dyspepsia, skin diseases, leucoderma and greyness of hair[11e].

Oryza sativa

Taxonomical classification :

Kingdom : Plantae

Order : Poales

Family : Poaceae

Genus : *Oryza*

Species : *sativa*

Distribution: Cultivated throughout in India.

Description:

An annual or perennial grass with tuft of fibrous roots and swollen nodes; leaves simple with sheathing bases, long and narrow, slightly pubescent with spiny hairs on the margins; flowers spikelet's in terminal compound panicles, lemma punctate or granulate without wing on the back, lemma and palea surrounding the kernel, golden yellow, reddish purple, brown or smoky black becoming straw-coloured on ripening, grains narrowly oblong, free within the lemma and palea.

Part used: Roots, grains

Chemical constituents: It contains majority of the tocotrienols and tocopherols (77 and 73% respectively) and oryzanols (91 %) remain integral to the oil bodies, one steroid-based antioxidant, ϒ-oryzanol.

Properties and uses: The roots are cooling, diuretic and febrifuge; and are useful in burning sensation, dipsia, bilious fever, strangury and diabetes.

The grains are sweet, acrid, oleaginous, aphrodisiac, diuretic, carminative, anti dysenteric and tonic. They are useful in vitiated conditions of pitta, pneumonosis especially pulmonary consumption, diarrhoea and colonopathy [12e].

Phonex dactilifera

Taxonomical classification

Kingdom : Plantae

Order : Arecales

Family : Arecaceae

Genus : *Phoenix*

Species : *dactylifera*

Distribution: A native of North America, Egypt, and Arabia; Now cultivated in Sindh Punjab.

Description:

A tall palm up to 36 m in height, the trunk covered over by persistent petiole bases, the base surrounded by a dense mass of root suckers; leaves pinnate up to 5 m long, lower pinnae modified into spines; flowers in long spadices, unisexual, fruits oblong berries reddish or yellowish brown when ripe, pulp fleshy, sweet; seeds cylindric, hard with a longitudinal furrow in front.

Part used: Leaves, flowers, fruits, seeds

Chemical constituents: It contains important phyto chemicals including carotenoids, phenolics and flavanoids.

Properties and uses:

The leaves are aphrodisiac and are reported to be good for hepatopathy. Flowers are bitter, purgative, expectorant, hepatic and febrifuge.

Fruits are sweet, cooling, aphrodisiac, tonic and diuretic. They are useful in nephropathy, pectoral diseases, bronchitis, cough, burning sensation and gastropathy.

A paste made out of the seeds is good for the opacity of the cornea, cephalalgia inflammations and wounds.The toddy is aphrodisiac, digestive, appetising, intoxicating and tonic. It is useful in bronchitis and vitiated conditions of vata and kapha[12f].

Saccharum officinarum

Taxonomical classification :

Kingdom : Plantae

Order : Poales

Family : Poaceae

Genus : *Saccharum*

Species : *officinarum*

Distribution: Cultivated throughout in India.

Description:

A tall perennial grass, upto 6 m high with stems of varying thickness and colour; leaves 1.5 m long,60 cm broad, erect or drooping, varying in colour from light to dark green; in florescence large, pyramidal, spikelets usually surrounded by long silky hair from their base, glumes two, glabrous on the back, grains oblong to sub globose.

Part used : Roots, Stems.

Properties and uses: The roots are cooling and diuretic and are useful in uropathy.

The stems (sugarcane) are sweet, cooling, emollient, laxative, cardio tonic, diuretic, galactogogue, aphrodisiac, expectorant, haemostatic and tonic. They are useful

in fatigue, leprosy, gastropathy, cardiac debility, haematemisis, cough, bronchitis, anaemia, erysipelas, ulcers of the skin and mucus membrane, emaciation and general debility[11f].

Cinnamomum tamala

Taxonomical classification

Kingdom : Plantae

Family : Lauraceae

Genus : *Cinnamomum*

Species : *tamala*

Distribution: Himalayas in areas of 900-2,400 m elevation

Description:

A moderate sized evergreen tree 7.5m in height with dark brown or blackish; leaves simple, opposite; ovate-lanceolate or ovate-oblong; flowers pale yellowish in axillary and terminal, lax puberulous panicles; fruits ovoid, fleshy, black drupe, supported by enlarged perianth tube.

Part used: Leaves

Chemical constituents:

The leaves yield an essential oil, which contains eugenol and phellandrene. The essential oil from the bark contains aldehyde.

Properties and uses:

The leaves are bitter, sweet, aromatic, and thermogenic, anthelmintic, diuretic, stimulant, carminative and tonic. They are useful in cardiac disorders, inflammations, helminthiasis, dyspepsia, vitiated conditions of vata, diarrhoea and splenopathy[13d].

Mesua nagassarium

Taxonomical classification

Kingdom : Plantae

Order : Malpighiales

Family : Clusiaceae

Genus : *Mesua*

Species : *ferrea*

Distribution: Throughout India, in evergreen forests up to 1,500 m.

Description: A medium sized to large handsome, glabrous, evergreen tree,18-30 m in height and reddish brown bark which peels off in thin flakes; leaves simple, opposite, thick, covered with waxy bloom underneath, acute or acuminate nerves; flowers white, fragrant, axillary or terminal, stamens very numerous, golden yellow, much shorter than the petals; fruits ovoid with a conical point surrounded by the enlarged sepals; seeds 1-4,angular,dark brown, smooth.

Part used: Flowers, oil

Chemical constituents: It contains mensuol, sitosterol, fatty acids, cyclohaxodine, mesuanic acid α- and β AMYRIN.

Properties and uses:

The flowers are astringent, bitter, acrid, anodyne, digestive, carminative, anthelmintic, diuretic, expectorant, stomachic, aphrodisiac and cardio tonic. They are useful in vitiated conditions of pitta and vata, asthma, cough, vomiting, scabies, leprosy, pruritus, ulcers fever and cardiac debility[12g].

Maranta arundinacea

Taxonomical classification :

Kingdom: Plantae

Order: Zingiberales

Family: Marantaceae

Genus: *Maranta*

Species: *arundinacea*

Distribution: Cultivated throughout India

Description:

A erect slender branched herb,90-180 cm high with fleshy cylindrical obovoid rhizome covered with pale scales leaving scars on falling; leaves ovate-oblong to ovate-lanceolate, base rounded; flowers white in clusters on diverging inflorescence branches, fertile stamen with appendage, ovary one-celled, one-ovuled.

Part used : underground rhizome.

Chemical constituents:

Maranta arundinacea tubers contain about 25-30% neutral starch, fiber, fat, albumen, sugar and gum. They are dried and powdered to get a white-starchy powder known as Arrowroot. This plant is different from Indian Arrowroot.

Properties and uses:

Starch obtained from rhizome is astringent, sweet, refrigerant, tonic, aphrodisiac, emollient, expectorant and febrifuge. It is useful in dysentery, diarrhoea, dyspepsia, bronchitis, cough and also as a nourishing food for infants, invalid and convalescents. It is the main ingredient in biscuits, cakes, puddings, jellies and face powders [12h].

3.2 DISEASE REVIEW

3.2.1 SIDDHA ASPECT

RAKTHA AZHUTHAM

Definition: It refers to the functional divergence in seneer thathu (blood), produced as a results of increased azhal (bio energy fire) eventully leading to consequent functional dearrangements in other udal thathus.

Vernacular names:

"இரத்தவ முக்கத்தியர் பெயரு ரைத்திடிற்
இரத்தாதிக்கம் யழுத்தம் இரத்தக் கொதிப்பு
நந்திடும் நாடி இறுக்கமும் நவில்வீர்
பத்திடுங் காரணம் பகரக் கேண்மோ"

-நோய்நாடல்நோய்முதல்நாடல்திரட்டு[16]

Raktha soodu, raktha azhutham, raktha miguthi, raktha perukkam, rakthathikkam, narambirukkam and naadi irukkam.

Types of *Raktha Azhutham:*

- ***Vali kuruthi azhal noai***
- ***Azhal kuruthi azhal noi***
- ***Iyya kuruthi azhal noai***
- ***Vali thee kuruthi azhal noai***
- ***Vali iyya kuruthi azhal noai***
- ***Iyya vali kuruthi azhal noai***
- ***Iyya azhal kuruthi azhal noai***
- ***Mukkutra kuruthi azhal noai***

Clinical features:

- Initially it begins with reccurent cough.
- Vomiting, Indigestion, fever will be a associated symptoms
- Head ache most commonly seen in occipital region.

- Dizziness, palpitation, easy fatigability, weakness.
- Dysponea, chest pain, pallor
- Perspiration, vertigo, syncope.
- Epistaxis, heamaturia, blurring of vision.
- Bloody vomiting will be common
- Sometimes bleeding will be seen in eyes, ears, nose, skin etc..

Clinical features:

- Head ache most commonly seen in occipital region, dizziness, palpitation, easy fatigability, weakness.
- Dyspnoea, chest pain, pallor, perspiration, vertigo, syncope.
- Epistaxis, heamaturia, blurring of vision.

Kuruthi azhal noi is high in urban population and more common in men than women. In females the prevalence is closely related to age. This is increased presumeably related to the menopause.

The *Elavenil* (early summer),*Muthuvenil* (late summer) aggrevate the disease.

Paalai (arid-tract) and *Neithal* (coastal-tract) reported compared to other areas.

3.2.2 MODERN ASPECT OF THE DISEASE

HYPERTENSION

The history of hypertension starts with the understanding of the cardio vascular system with the work of physician William Harvey who described the circulation of blood in his book “De motu cordis”. Then the English clergyman Stephen Hales is generally credited as being the first person to measure arterial pressure, direct intra-arterial pressure in the horse in 1733. Hypertension was described as a disease by Thomas young and Richard in 1836. In 1884 the first report of elevated blood pressure in a person without evidence of kidney disease was recorded. Eventually in 1896 the invention cuff-based sphygmomanometer done by Scipione Riva-Rocci. Then the blood pressure was measured in the clinics, Nikolai Korotkoff improved this technique by describing the Korotkoff sounds. These sounds are heard when the artery was auscultated with a stethoscope while the sphygmomanometer cuff was deflated.

Now in modern medicine hypertension is classified into two types essential and secondary hypertension. The concept of essential hypertension was introduced in1925 by the physiologist Otto frank, which has idiopathic origin. In 1928 the term malignant hypertension was coined by physicians from the mayo clinic. The essential hypertension may be the result of a combination of poor life style choices and genetics. Secondary hypertension that starts as a result of another disease especially kidney disease or disease associated with endocrine system[17].

Definition:

Systemic hypertension is the persistent rise of basal blood pressure above the level of 140/90 mm of Hg recorded on three or more successive occasions [18].

Classification of hypertension [19]

Etiological classification:

- Essential hypertension or idiopathic hypertension
- Secondary hypertension or symptomatic hypertension

Benign hypertension

- BP is more than 140/90 mmhg but less than 200/140 mmhg
- Progresses slowly

Malignant hypertension

- BP rises rapidly
- BP > 200/140 mmhg
- Shows retinal changes

White coat Hypertension

Commonly known as white coat syndrome or masked hypertension, is a phenomenon in which patients exhibit a blood pressure level above the normal range, in a clinical setting, though they don't having exhibit other it in other settings. It is believed that the phenomenon is due to anxiety that those afflicted experience during a clinica visit [20].

Pathophysiology of Hypertension

Blood pressure is determined by the balance between cardiac output and vascular resistance rise in either of these variables, in the absence of a compensatory decrease in the other, increases mean BP, which is the driving pressure.

Table no:1 Classification of blood pressure for adult(JNC7)[21]

Category	Systolic mmHg	Diastolic mmHg
Normal	90-119	60-79
High normal (pre-hypertension)	120-139	80-89
Stage I Hypertension	140-159	90-99
Stage II (Hypertension)	160-179	100-109
Stage III (Hypertensive emergency)	≥ 180	≥ 110
Isolated Hypertension	≥ 140	< 90

Factors that affect cardiac output include the following

- Barorecptors
- Extracellular volume
- Effective circulating volume- Arterial natriuretic hormones, mineralocorticoids, angiotensin
- Sympathetic nervous syndrome

Factors that affect vascular resistance include the following:

- Pressors :angiotensinII,calcium(intracellular),catecholamines,vasopressin
- Depressors :Artial natriuretic hormones, endothelial relaxing factors, kinins, prostaglandin, prostaglandin E_2, prostaglandin I_2

Changes in the electrolyte homeostasis particularly in sodium, calcium and potassium concentrations, affect some of these factors.

Under normal conditions, the amount of sodium excreted in the urine matches the amount of ingested, resulting in near constancy of extracellular volume. Retention of sodium results in increased extracellular volume, which is associated with elevation of Bp. By means of various physical and hormonal mechanisms, this elevation triggers changes in both the glomerular filtration rate (GFR) and the tubular reabsorption of sodium,resulting in excretion of excess sodium and restoration of sodium balance.

Increase in the intracellular calcium concentration,due to changes in plasma calcium concentration,increases vascular contractility. In addition, calcium stimulates release of rennin, synthesis of epinephrine and sympathetic nervous system activity. Increased potassium intake suppresses the production and release of rennin and induces natriuresis, decreasing the Bp.

Table no: 2 Common causes of hypertension by age

Infants	**Children 1-6 yrs**	**Children 7-12**
Thrombosis of renal artery or vein	Renal artery stenosis	Renal parenchymal disease
Congenital renal anomalies	Renal parenchymal disease	Renovascular abnormalities
Coarctation of aorta	Wilms tumor Neuroblastoma	Endocrine causes
Bronchopulmonary dysplasia	Coarctation of aorta	Essential hypertension

Predisposing factors for essential hypertension

- Family history
- Genetic factor-homozygos or the dominant gene is usually seen to be severly affected than the heterozygous.
- Age-commonly 45 years. But varies from 25 to 55 years.
- Sex-commonly seen in males
- Structural changes in arterioles: Thickening of the arteriolar wall and narrowing of the lumen leads to resistance in the blood flow.
- Salt intake: If the salt intake is more than the average, hypertension may result.
- Race - common in American Negroes and Japanese

- Influence of the sympathetic nervous system: Excessive sympathetic nervous activities may result in hypertension. It has an important role in young hypertensives who usually exhibit tachycardia and high output.
- Neurogenic hypertension-lesion of the carotid sinus and aortic baroreceptor may lead to hypertension.
- Psychic factor-it act via neural pathway
- Rennin Angiotensin system-renin is secrered from the juxta glomerular cells surrounding the afferent arteriole from various stimuli,e.g diminished renal perfusion, diminished blood volume, diminished cataecholamines, increased sympathetic activity, arteriolar stretching, hypokalaemia, etc.renin acts on angiotensinogen or rennin substrate to convert it to Angiotensin I. This is acted upon by Angiotensin II. This is a potent vasoconstrictor and stimulates aldosterone release from adrenal gland. Though the system has an important bearing on regulating blood pressure yet possibly it has no primary role in the pathogenesis of essential hypertension.
- Defect in natriuresis: In presence of elevated blood pressure, high serum Na+ or blood volume individual have increased natriuresis. In hypertensives this Na+ excretion ability is diminished, so this results in increased blood volume and high BP.
- In essential hypertension intracellular Na and Ca are elevated
- Miscellanious: Excessive intake of alcohol, smoking, steroids and NSAIDs, low potassium intake, exercise, polycythemia etc.

Causes for secondary hypertension

- Renal causes-acute nephritic syndrome, Chronic nephritis, Poly cystic kidney, Hydronephrosis, Chronic pyelonephritis, Renal artery stenosis, Rennin secreting tumour, Renal embolism.
- Endocrine causes-thyrotoxicosis and myxoedema, acromegaly, Cushing's syndrome, Cohn's syndrome, phaeochromacytoma.
- Metabolic causes- diabetes mellitus, chronic gout, toxaemias of pregnancy, atherosclerosis.
- Drugs- contraceptive pills, anabolic steroids, liquorice.
- Collagenosis and miscellaneous disease- SLE, polyarteritisnodosa scleroderma, dermatomyositis, pseudoxanthoma elasticum.

- Congenital- coarctation of aorta.
- Psychogenic
- Neurological- encephalitis, brain tumour, cerebro vascular accident, diencephalic Syndrome.
- Blood disease- Polycythemia
- Renovascular hypertension-particularly in renal artery stenosis.
- Miscellaneous- Pregnancy, Cyclosporine, NSAIDs.[22]

Clinical features:

- Pulsating head ache often occipital and occurs particularly in the morning.
- Easy fatiguability
- Insomnia
- Dizziness
- Lack of concentration
- Loss of memory
- Occational palpitation
- Breathlessness

Symptoms of associated disease may also present e.g. Cerebral Arteriosclerosis, Retinal Arteriosclerosis, Coronary Arteriosclerosis, Renal arteriosclerosis and Arteriosclerosis of limb of vessel [23].

Complication:

Cardiac hypertensive heart disease Left Ventricular Hypertrophy develops in 10-30% of chronic cases. It may produce myocardial ischemia, ventricular arrhythmia, CCF and sudden death LV diastolic dysfunction may also develop with CCF.

Cerebral

Cerebro vascular complications are more closely to systolic rather than diastolic blood pressure.

- Cerebral hemorrhages
- Cerebral thrombosis
- Lacunars infract

- Hypertensive encephalopathy-this condition is acute cerebral ischemia from Hypertensive spasm, Cerebral edema and minor degree of hemorrhages or thrombosis.
- TIA-transient ischemic attack
- Subarachnoid hemorrhages.
- Dementia-both vascular and Alzheimer's type

Retinal

- Dimness of vision
- Thickening of arteries with Narrowing of lumen, Hemorrhages and Exudates.
- Papilloedema.
- Detachment of Retina, Vitreous Hemorrhages.

Renal

Patients with hypertensive nephropathy should have BP at 130/85mmHg or less if protenuria is present. Hypertension accelerates all forms of renal disease mostly diabetic nephropathy.

- Nephrosclerosis
- Uraemia
- Renal infarct

Aortic dissection

- The major cause of it is hypertension.

Atherosclerotic complications Many patients of hypertension die out of these complication but the relationship is much less close than other complications.

- Cerebral arteriosclerosis
- Retinal arteriosclerosis
- Coronary arteriosclerosis
- Renal arteriosclerosis

Pregnancy induced hypertension

Gestational hypertension also referred to pregnancy induced hypertension (PIH) it is a condition of high blood pressure more than 140/90mmHg on two separate occasions, more than 6 hours apart, without the presence of protein in the urine during pregnancy. It is diagnosed after 20 weeks of gestation. Gestational hypertension can leads to serious condition called pre-eclampsia [24].

Hypertensive crisis

In some situations in an hypertensive patients rapid reduction of blood pressure is required. These situations are included under the category of hypertensive crisis. These situations are divided into two.

Hypertensive urgency

There is no evidence of end organ damage resulting from the elevated blood pressure.In these cases, oral medications are used to lower the BP gradually over 24 to 48 hours.

Hypertensive emergency (Malignant hypertension)

There is evidence of direct damage to one or more organs.The most affected organs include the brain, kidney, heart and lungs, producing symptoms which may include confusion, drowsiness, chest pain and breathlessness.In hypertensive emergency,the blood pressure must be reduced more rapidly to stop ongoing organ damage.

Clinical features include

- Headache
- Confusion
- Visual loss
- Focal Neuralogic features
- Somnolence
- Coma
- Fundus shows Hemorrhages, Exudates and Papilloedema.

Mode of termination

- Acute left ventricular failure(60%)
- Cerebral hemorrhages (35%)
- Uraemia rare(5%)

Investigations

Patients undergo a limited number of investigations

Investigation of all patient

- Urinanalysis for Blood, Protein and Glucose
- Blood, Urea, Electrolytes and creatinine
- Lipid profile
- Blood glucose
- Serum total and high-density lipoprotein(HDL) Cholesterol
- 12-lead ECG(left ventricular Hypertrophy, Coronary artery disease)
- Endocrine: Serum Sodium, Potassium, Calcium and TSH[25]

Investigation of selected patient

- Chest X-ray: To be detect Cardiomegaly, Heart failure, Coarctation of aorta
- Ambulatory BP recording: To assess borderline hypertension
- Echocardiogram: To detect or quantify left ventricular hypertrophy
- Renal Ultrasound: To detect possible renal disease
- Renal Aangiograpy: To detect or confirm presence of renal artery stenosis
- Urinary Catecholamines: To detect possible Pheochromacytoma
- Urinary Cortisol and Dexamethasone suppression test: To detect possible Cushing's Syndrome.
- Plasma Rennin Activity and aldosterone: To detect possible primary aldosteronism[26].

DRUG REVIEW –TREATMENT FOR HYPERTENSION IN *SIDDHA* ASPECT

In siddha system the treatment for *raktha pittha* is based on the normalizing the altered hypertension.

Vanthi* and *kazhichal maruthuvam

- *Vellai ennai*-15-30 ml at early morning
- *Meganatha thylam*-8-30ml at early morning
- *Kowshikar kuzhambu*-125-500 mg with ghee at early morning
- *Thiratchai kudineer*-40-80ml twice a day
- *Nerunjil kudineer*-40-80ml twice a day
- *Thamaraga kudineer*-40-80ml twice a day

The choices of medicine, doses and duration may be altered according to the condition of the patients and severity of the disease.

Chooranam

- *Seenthil chooranam*-1-2g twice a day with ghee(5ml)
- *Elathy chooranam1*-2g twice a day with warm water(50ml)
- *Parangipattai chooranam*:1-2 g twice a day with hot water(50ml)
- *Seeraha chooranam*-1-2 g twice a day with hotwater(50ml)
- *Thrachathy chooranam*-1-2g twice a day with honey(5ml)
- *Venthamarai chooranam*-1-2g twice a day with hotwater(50ml)
- *Marutham pattai chooranam*-1-2 g twice a day with hotwater(50ml)
- *Amukkara chooranam*1-2g twice a day with milk(50ml)

Nei

- *Brahmi nei*10-15ml twice a day with milk(50ml)
- *Madhulai nei* 10-15ml twice a day with milk(50ml)
- *Thaneer vitan nei* 10-15ml twice a day with milk(50ml)

Manappagu

- *Thurunchi manappagu*15ml twice a day with luke warm water (50ml)
- *Nannari manappagu*15ml twice a day with luke warm water (50ml)
- *Madhulai manappagu* 10-15 ml twice a day with luke warm water(50ml)

Ilagam

*Vilvathy ilagam*5-10g twice a day

Madhulai manappagu 3g twice a day

Karpam

- *Bavana kadukkai*(500mg) 1 before and after food twice day

Parpam

- *Silasathu parpam*300-600mgtwice a day with hot water(50ml)
- *Kungiliya parpam*100-300mg twice a day tender coconut water(50ml)
- *Sangu parpam*100-300mg twice a day with ghee(5ml)
- *Muthu parpam*65-130mg twice a day with ghee(5ml)
- *Siringi parpam*65-130mgtwice a day with brahmi nei(10ml)

Chendooram

- *Vediannabethi chenduram100*-200mg twice a day with honey(5ml)
- *Aya chenduram*65-130mg twice a day with honey(5ml)

In higher levels if palpitation and dysponea present than use

- *Pavala parpam* 100-200mg twice a day with ghee(5ml)
- *Muthu parpam*30-60mg twice a day with honey(5ml)
- *Naga parpam*65-130mg twice a day with honey(5ml)

External medicines

Oil bath may be adviced twice a week with any of the following medicated oil

- *Kaiyan thylam*
- *Seeraha thylam*
- *Lahusandhanathy thylam*
- *Arakku thylam*
- *Thirippala thyalm*

Pathiyam(diet)

Diet to be added

- Rice kanji-double boiled rice, *savarisi kanji, pori kanji, barley kanji, manakkathai,kuruvai rice.*
- Vegetables-*athi, avarai, kathari, vazhai, vendai, murungai, sundai, mullongi, pagal, sambal poosani, thoothuvalai, pirandai.*

- Greens-*puliyarai, manathakkali, ponnangani, kaiyan, sukkan, vasalai keerai, pasalai keerai.*
- Pulses-*ulunthu, pasipayaru*
- Dairy products-cow's butter milk
- Non-vegetrarian diet-*ayrai meen*(loach), *velladu*(capea hircus)

Diet to be avoided

- Intake of excessive salt,oil,fried food
- Excessive hot,sour and salt tastes,
- *Sarkkarai valli kizhangu* (Ipomoea batatas), *Seppankizhangu* (Colacasiaesculanta), *Kothavarai* (Cyamopsis tetragonoloba), *Kollu* (Macrotylorum uvifiorum), *Verkadalai* (Arachis hypogea), *Kaaramani* (Vigna ungiculata), *Pataani* (Pisum sativum), *Motchai*(lablab purpureus)[27].

Other advices

- Avoid smoking and alcohol intake
- Dietary management
- Regular physical activity(brisk walking) at least 30 min/day
- Weight reduction, maintain normal body weight
- Relief of stress.
- Rejuvenation therapy

Karpa marunthugal

Pothu karpam

- *Kattrazhai karpam* for 4 days
- *Ponnangani karpam* for 4 days

Sirappu karpam

- *Kadukkai karpam1*-2gms with hotwater at evening for 48 days
- *Panai ver kudinner* 60ml twice a day for 48 days
- *Vilva karpam* for 48 days
- *Elumitchai pazha karpam* for 48 days
- *Orilai thamarai karpam* with ghee for 48 days.

Karpayogam

- *Pranayamam*
- *Singasanam*
- *Sarvangasanam*
- *Puyangasanam.*

TREATMENT FOR HYPERTENSION IN MODERN ASPECT[28]

Anti-hypertensive drugs act by influencing the Blood pressure regulatory systems viz, the autonomic nervous system, Rennin Angoitensin System. Calcium channels or sodium and water balance in plasma volume.

Classification of anti-hypertensive drugs

Diuretics lowers the blood pressure by increasing urination.the anti hypertensive action of diuretics is mild BP falls by 15-20mmHg over 2-4 weeks. It enhance the excretion of sodium and water resulting in decreased plasma volume of CO and reduce BP.

- Thiazides(Hydrochlorothiazide,Chlorothiazide,Indapamide)
- Loop diuretics(Fruosemide,Bumetanide,Torsemide)
- K^+ (Spiranolactone,Amiloride,Trimterene)

Drugs acts on Rennin Angiotensin System

- Angiotensin converting enzyme inhibitors(ACE inhibitors) (Captopril, Enalapril, Lisinopril, Ramipril, Perindopril)
- Angiotensin II receptor antagonists (Losartan, Candesartan, Valsartan, Eprosartan, Irbesartan,Olmesartan)
- Rennin inhibitor(Aliskien)
- ACE inhibitors are presently the first line anti hypertensives.ACE inhibitors are useful in the treatment hypertension of all grades due to all causes. They are specially indicated as Anti-hypertensives in hypertension with left ventricular hypertrophy.
- Angiotensin II is powerful vasoconstrictor.ARBs are used in the treatment of hypertension in similar indications as that of ACE inhibitors as alternatives of ACE inhibitors, they can also be considered as the first line drug in hypertension.

- Rennin inhibitors blocks the effects of rennin there by reducing blood pressure. Use of several drugs like ACE inhibitors, ARBs and diuretics tend to bring about a compensatory rise in the plasma rennin levels. Because aliskiren blocks the effects of rennin,its action is synergistic with these drugs.

Sympatholytics

- Centrally acting drugs(Clodine,Methyldopa,Guanfacine)
- Ganglion blockers(Trimethaphan)
- Adrenergic receptor blockers(Guanethidine,Reserpine)
- Adrenergic receptor blockers
- α-blockers (Prazosin, Terazosin, Doxazosin, Phenoxybenzamine, Phentolamine)
- β-blockers (Propranolol, Atenolol, metoprolol)
- α and β blockers(Labetalo,Carvedilol).

Sympatholytics drugs may be used to interfere with sympathetic activity at different levels including centrally,at the ganglia,neurons and receptors.

Ganglion blockers block both sympathetic and parasympathetic ganglia resulting in decreased sympathetic tone and a fall in BP.

Adrenergic receptor blockers depletes the stores of nor adrenaline in the adrenergic neurons blockers its release.

α-blockers are used in the treatment of hypertension due to Pheochromacytoma. They block the α1 receptors in the arterioles and venules and thereby dilate both arteriole and venules. Peripheral vascular resistance is decreased leading to fall in BP with only mild tachycardia.β-blockers are mild anti-hypertensives. Blockade of β1receptors results in decreased myocardial contractility and cardiac output. Thus they reduce BP due to a fall in the cardiac output [29].

Table no: 3 Classification of Anti-Hypertensive Drugs

S.NO	TYPES OF DRUG	NAME OF THE DRUG
1.	ACE inhibitors	Captopril Enalapril Lisinopril Ramirpril
2.	Angiotensin antagonist	Losartan
3.	Calcium channel blockers	Nifidepine Felodipine Amlodipine Verapamil Diltiazem
4.	Diuretics	Hydrochlorothiazide Frusemide Indapamide Spironolactone Triamterene Amiloride
5.	β-adrenergic blockers	Propranolol Atenolol Metaprolol
6.	α-adrenergic blockers	Prazocin Terazocin Phentolamine
7.	Central sympatholytics	Clonidine Methyldopa
8.	Vasodilators (i)Arteriolar (ii)Arteriolar and venular	Hydralazine Minoxidil Diazoxide Sodium nitroprusside Pinacidil

Ca+ channel blockers

CCBs are another important group of anti-hypertensive. They are particularly used in elderly patients.CCBs may be used as mono therapy or in moderate to severe Hypertension along with other hypertensives (Nifedipine, Nicardipine, Nimodipine, Amlodipine, Felodipine, Verpamil).

Vasodilators

- ❖ Arteriolar dilators (Hydralazine,Minoxidil,Diazoxide)
- ❖ Arteriolar and venular dilators(sodium nitroprusside)

Vasodilators relax the vascular smooth muscle thus reducing BP due to decresed peripheral vascular resistance. Nitroprusside is the drug of choice in hypertensive emergencies. It is used in situations where short-term reduction of myocardial work load is required as serve heart failure and myocardial infarction.

Adverse effects of anti-hypertensive drugs

- ❖ Angiotensin receptor blockers cause Hypotensin and Hyperkalaemia.
- ❖ Sympatholytics like Methyldopa cause dryness of mouth and nose, depression, vertigo, extra-pyramidal signs, raised prolactin levels, postural hypertension.
- ❖ Vasodilators like Hydralazine cause headache, dizziness, flushing, palpitation, nausea, anorexia, hypotension and saltandwater retension.
- ❖ Sodium nitroprusside cause palpitation, sweating, weakness, nausea, vomiting and hypotension[30].

3.3 PHARMACOLOGY REVIEW

PHARMACOLOGICAL STUDY OF ANTIHYPERTENSIVE ACTIVITY IN ANIMAL MODELS

Hypertension Models

In-Vitro Model

- Endothelin receptor antagonism inporcine isolated hearts
- Monocrotaline induced pulmonary hypertension

Endothelin Receptor model

Endothelins(ET) have been implicated in the pathophysiology of cardiovascular diseases.In this model isolated porcine coronary artery is used since the smooth musculature of artery is considered to contain the ETA receptors.ET results in potent long lasting contractions of isolated blood vessel strips. An increase of blood pressure in vitro studies has been elicited by Endothelin peptides.

Monocrotaline-induced pulmonary hypertension

- Monocrotaline is a hepatotoxic pneumotoxic agent used in Rats pulmonary hypertension. It is a pyrolizidine alkaloid derived from crotalaria spectabilis and single injection leads to progressive pulmonary hypertensionfollowed by right ventricular hypertrophy and cardiac failure. Ultrastructural changes such as degeneration and fragmentation of endothelial cells and mascularization of pulmonary arteries, arterioles are also observed. Monocrotaline administration of rats can results in severe right ventricular hypertrophy accompanied by rats and pleural effusion.

IN-VIVO MODELS

RAT MODELS

I. Reno-vascular induced

- ❖ Two-kidney one clip method(Goldblatt hypertension,2K1C)
- ❖ Chronic renal hypertension in rats(1-kidney-1-clip method)
- ❖ Chronic renal hypertension in rats(Two kidney two clip method)

II. Neurogenic induced

- ❖ Blood pressure in pithed rats

III. Diet induced

- ❖ Fructose induced
- ❖ Increased salt induced

IV. Endocrine induced

- ❖ DOCA-salt rats

V. Psychogenic

- ❖ Air-jet stimulation induced hypertension

VI. Genetically induced

- Salt-sensitive Dahl rats
- Spontaneously hypertensive rats

DOG MODEL OF HYPERTENSION

- Chronic renal hypertension
- Neurogenic hypertension

MONKEY MODEL OF HYPERTENSION

- Renin inhibition in monkeys

TRANSGENIC MODEL OF HYPERTENSION

- Transgenic rats overexpressing the mouse Ren-2 gene[TGR(mRen 2)27]

Two kidney one clip (Goldblatt hypertension2k1c)

Sprague dawley rats used for this model

Ischemia of the kidney causes elevation of blood pressure by activation of rennin angiotensin system. In rats clamping the renal artery for 4hrs can activates peripheral RAAS and sympathetic nervous system and induce renal hypertension. After reopening the vessel, accumulated rennin is released into circulation leading to acute hypertension. Renin is secreted by the kidneys when sympathetic activity is increased. Renin converts Angiotensin to Angiotensin I, AngiotensinII is a potent vasoconstrictor and increase blood pressure. Angiotensin II also causes release of aldosterone leading to salt and water retention result in increased blood volume and hypertension. This model is used to evaluate anti-hypertensive activities drugs.

Chronic renal hypertension (one kidney one clip method)

The one kidney one clip method is the technique has been described several animal species.ne the most effective modifications in rats in which one kidney is removed. Constriction of one kidney is done on one side and the contralateral kidney is removed. There is an increase in blood pressure within few hours. Since there is no other kidney, there is no pressure, dieresis and natriuresis, so there is rapid salt and water retention. Plasma rennin activity is usually normal. Hypertension soon becames volume dependent.

Blood pressure in pithed rats

Male wistar rats (250-350 gms) are used in this model

The pithed rat model is divided for neurogenic reflex control that may modulate the primary drug effect. It is frequently used to evaluate drug action on the cardiovascular system.

Salt-sensitive Dahl rats

The kidneys have the ability to excrete easily the daily salt load without allowing a marked rise in extracellular volume. Chronic ingestion of excess salt produces hypertension in rats, which mimics human hypertension. The salt-sensitive dahl develop severe and fatal hypertension when fed high salt diets. This is the model of genetic hypertension, with the extra feature of Salt sensitivity.

Fructose induced hypertension in rats

Feeding a high fructose diet induces hypertension and insulin resistance in Sprague dawley rats.Fructose feeding also causes insulin resistance,hyperinsulinemia and hypertriglyceridemia in normal rats.Fructose feeding induces hypertension in normal or high salt feed animals and it is associated with an increased expression of the Angiotensin II type I receptor in adipose tissue.AT 1 receptor play a role in the pathophysiology of metabolic and hemodynamic abnormalities induced b fructose feeding.

DOCA-salt rats

Mineralocorticoids induces hypertension by causing in plasma and exracellular volume. The administration of deoxycorticosterone acetate(DOCA) ,a mineralocorticoid in combination with high salt diet and unilateral nephrectomy induces hypertension. There is increased DOCA induced reabsorption of salt and water leading to increased blood volume and hence increased blood pressure[31].

Spontaneously hypertensive rats

By breeding strain of spontaneous hypertensive wistar rats with a female having slightly raised blood pressure, Okamoto and Aoki obtained a strain of rats spontaneous hypertension,the SHR. Spontaneous Hypertension was devopled by meticulous genetic

in breeding that uniformly resulted in 100% of progeny having naturally occurring hypertension. Several researchers reported the spontaneous hypertension is an excellent model of experimental hypertension as well as model for complications of hypertension[32].

Transgenic rats overexpressing the mouse Ren2 gene[TGR(mRen2)27]

The ability to specifically introduce genetic constructs and thereby breed transgenic animal has opened new possibilities for hypertension research. Recently a transgenic rat has been obtained after introduction of the entire mouse Ren 2d gene. The introduction and over expression of mouse Ren2d in this rat leads to severe, lethal in the homozygous rat.

Method for the measurement of blood pressure in rats

- Tail-cuff method in rats
- Indwelling catheter for measurement of blood pressure in conscious rats.

Tail cuff method for measuring Bp

The indirect tail cuff method allows the measurement of BP without any surgical procedure. The principle used in this method is that the pulse obliterate when the cuff is inflated till above suspected systolic blood pressure. The pulse reappears as the pressure in the cuff is slowly released and it falls below the systolic blood pressure. The method is analogous to sphygmonometry in humans.

The indirect tail cuff method is widelyused to evaluate the influence ofantihypertensive drugs in spontaneouslyand experimentally induced hypertensive rats.

Indwelling catheter method

This method allows directly measurement of blood pressure in conscious rat. The influence of anesthesia on the cardiovascular regulation is eliminated by this method.

7 cm long cannulae are prepared by cutting pe 10 and pe 20tubing respectively. A style wire is inserted into the pe10 tubing is also slipped over the style wire. The tube ends are heated in a current of hot air and fused together. Using ridges the style wire is left inside the cannula and the cannula is heated in a jet of hot air. When the

polyethelene at the point of heating becomes soft,the cannula is pressed slightly and the ridges are formed.

Dog models of hypertension

- ❖ Chronic renal hypertension
- ❖ Neurogenic hypertension

Chronic renal hypertension

Partial constriction of renal arteries in dogs produces hypertension. This method is modified and is now known as the wrapping technique.A sheet of cellophane is placed around the kidney and held in place by silk sutures tied loosely around the renal hilus. Both kidneys are wrapped or one kidney is wrapped and other is removed. A fibro collagenous shell is formed around the kidney in 3-5 days because of reaction of the tissue to the foreign material. This shell compresses renal vascular pressure. This expands the extracellular volumeleading to increased peripheral resistance and hence increased blood pressure.

Neurogenic hypertension

Baroreceptors situated in the carotid sinus and aortic arch play an important part in the regulation blood pressure stimulation of baroreceptor causes inhibition of vasomotor center leading to vasodilatation, bradycardia and decrease in blood pressure. Sectioning of the baroreceptor nerves leads to persistant raise in blood pressure. Thus this produce acute neurogenic hypertension induced in dogs.

Renin inhibition method in monkey

Blood pressure is mainly regulated by the rennin Angiotensin system and can be influenced by the inhibition of rennin. Renin inhibitors developed for have a high specifically for primate rennin and cause only weak inhibition of rennin sub primate species. It suggests that most commonly laboratory animals such as dog are not suitable for in-vivo evaluvation of rennin inhibitor. Marmosets (callithrix jacchus) of 300-400gare fedpellet diet supplemented with fruits. These animals were used for rennin inhibition method [33].

ANIMAL MODEL FOR THE DISSERTATION

SPONTANEOUSLY HYPERTENSIVE RATS:

Systolic blood pressure (SBP) and heart rate measurement of SH rats was carried out using tail-cuff method plethysmography (LE 5001 Pressure Meter). A mean of six measurements was obtained for each animal. For blood pressure measurement, the animals were warmed up to 42°C for 5 min in a confinement cage. The animals were first submitted to a period of adaptation for 15 days before the experiments and only SHR with an SBP > 170 mmHg were selected for this study. During the final week of the treatment, the rats were allowed to acclimatize to the experimental conditions of noninvasive SBP measurements by allowing them to stand in rat restrainers for 30 min every day. SBP measurements were recorded 24 h after the last treatment dose. At least 8-10 recordings were taken for each rat and the mean of the lowest 4 values within less than 10 mmHg difference was taken as the mean SBP.

3.4 PHARMACEUTICAL REVIEW

CHOORANAM

Definition

Chooranam is a fine powder of drugs. The "*Chooranam*" may be applied to the powders of a single drug or a mixture of two or more drugs, which are powdered separately prior to their being mixed to homogeneity[34].

Method of preparation

Equipment required

1. The drug enumerated in the recipe in clean and well dried state.
2. A mortar and pestle.
3. A fine sieve or fine cloth of close mesh.

Process of preparation

The drugs which are to be used in the preparations should be taken from recently collected material. Drugs which are aged by prolonged storages or changed in colour, taste and scent and those that are insects infested or attacked by fungi should be positively rejected.

However drugs like Embelia fruits, Senna, Long Pepper, Jaggery and cows ghee are preferred from fairly aged stock, provided they are not infested with pests, deteriorated or spoiled or developed racidity.

In general the aromatic drugs are slightly fried in order to enhance their aroma and milling properties. Any extraneous material, organic or inorganic, should be removed from the drugs by close inspection.

The chooranam should be so fine to be called amorphous and should never be damp. The fineness of the sieve should be no 100 mesh or still finer.

Purification of the prepared chooranam

"தானென்ற சூரணத்தின் சுத்திக்கேளு
தப்பாதே சரக்கெல்லாஞ் சூரணித்து
நானென்ற வாவின் பாலாற் பிசைந்து
நலமான சட்டியிலே பாலைவிட்டு
வானென்ற சுத்தசலம் பாதிவிட்டு
வளமாக மேற்சீலை கோடு கட்டிப்
பானென்ற சூரணத்தைப் பிட்டுபோல் வைது
பதறாதே வெந்தெடுக்கச் சித்தியமே"

- அகஸ்தியர்வைத்தியஇரத்தினச்சுருக்கம்[35]

The prepared *chooranam* is mixed with the milk in a pot half quantity milk and half a quantity water is taken. The mouth of the pot is covered with a thin cloth material. Above this cloth the mixed chooranam is placed. The pot is placed over the stove and heated.

"ஆமப்பா ரவியுலர்த்திப் பொடிதான் செய்து
அப்பனே சமனாய்ச் சர்க்கரையைச்சேர்த்து
நாமப்பா கொண்டு வர தோஷம் போச்சு
நன்றாக்ச் சுத்தி செய்யாச் சூரணந்தான்
தாமப்பாரோகத்தைவெல்லாதப்பா
தளமான வியதி யெல்லாம் பாரிக்கும் பார்
வேமப்பா சுத்தி செய்து கொண்டாயனால்
வெகுசுறுக்காய் தீருமா வியாதி கேளு"

-அகஸ்தியர்வைத்தியஇரத்தினச்சுருக்கம்

Then the chooranam is placed in the sunlight and powdered. Equal amount of sugar is added and taken internally. All type of diseases get cured. If the drug is taken without purification the disease does not cure. If taken after purification the disease cures easily.

Storage

The prepared chooranam should be allowed to cool by spreading and mixing, prior to packing. They should be stored in tightly stoppered glass, polythene or tin containers, or in polythene or cellophane bags and sealed. These bags should in turn be enclosed in cardboard boxes.

The chooranam to facilitate easy handling and to assure exact dosage administration, could be pressed into tablets, could be packed in bottles or tubes made either of glass or plastic or packed in strip of metal foil or plastic sheets.

In industry the tablets are made, counted and packed by electronic devices.

Then chooranam is said to retain its potency for 3 months and then gradually deteriorate. However if properly packed and stored they keep good for a year. (Formulary of Siddha Medicines, 1993)

According to AYUSH guidelines shelf life of chooranam is one year. [36]

Table no: 4 ANALYTICAL SPECIFICATIONS OF CURNA/CHOORNAM

Sl.No	TESTS
1.	Description
	Macroscopic, Microscopic
2.	Loss on drying at 105˚ C
3.	Total – ash
4.	Acid – insoluble ash
5.	Water-soluble extractive
6.	Alcohol – soluble extractive
7.	Particle size (80-100 mesh for Churna; 40-60 mesh for churna)
8.	Identifications,TLC/HPTLC-withmarker(whereverpossible)
9.	Test for heavy/Toxic metals
	Lead
	Cadmium
	Mercury
	Arsenic
10.	Microbial contamination
	Total bacterial count
	Total fungal count
11.	Test for specific Pathogen
	E. coli
	Salmonella spp.
	S.aureus
	Pseudomonas aeruginosa
12.	Pesticide residue
	Organochlorine pesticides
	Organophosphorus pesticides
	Pyrethroids
	Test for Aflatoxins (B1,B2,G1,G2)

3.5 Lateral Research

***Vitis vinifera*:**

Grape Seed Procyanidins in Pre- and Mild Hypertension: A Registry Study

Diuretic activity:

The methonolic extract of grape seeds treated rats show high diuretic at a dose of 500 mg/kg by increasing total amount of urine levels of Na+,K+ and Cl- in urine as compared to control but effect was less than furosemide[37].

Antioxidant activity of Vitis vinifera:

The acetone, ethyl acetate, methanol and mixtures of different solvents, such as ethyl acetate(EtOAc)andwater extract of vitis vinifera showed antioxidant activity through a β-carotene-linoleate model system and linoleic acid peroxidation method.

In conclusion our studies identified some varieties of grapes with high antioxidant activities and showed that their high antioxidant potential may be due to their phenolic and flavonoid contents[38].

Zingiber officinale

Antioxidant activity

The ginger extract possessed antioxidant activity while evaluating using DPPH assay[39].

Antihypertensive activity[40]:

Zingiber officinale showed antihypertensive activity while experimentally induced hypertension in rats.

Phyllanthus emblica

Antioxidant activity[41]:

Emblica officinalis (EO) reduces oxidative stress, prevents development and progression of hypertension as well as cardiac and renal hypertrophy in DOCA/HS-induced hypertension via modulation of activated eNOS, endogenous antioxidants, serum NO and electrolyte levels.

Antihypertensive activity[42]:

This plant Exerts Antihypertensive Effect in a Rat Model of DOCA-Salt-Induced Hypertension

Piper longum:

Antihypertensive activity[43]:

Piperine lowering the blood pressure so it exerts antihypertensive activity.

Antioxidant activity[44]:

Choloroform extract of *Piper longum* (PC) showed the highest in vitro antioxidant activity.

***Aegle marmelos*:**

Antioxidant activity[45]:

Results of the present study reveal that the AM is a potential source of antioxidants which are responsible for the antioxidant activity. The stability to heat and pH of the different extracts of AM leaves extracts with strong antioxidant activity indicates its scope for utilization in food and biological systems.

Diuretic activity[46]:

Diuretic activity of the plant *Aegle marmelos* was confirmed experimentally in rats.

***Nymphaea alba*:**

The ethanolic and aqueos have exhibited significant antioxidant activity in DPPH, Nitric oxide and Hydroxyl radical induced invitro assay methods. The results indicate that both the extracts firmly possess strong antioxidant effects. Comparatively the ethanolic flower extract showed more antioxidant activity than the aqueous extracts. The results obtained from the present study indicate that the Nymphaea alba flower extract can be a potential source of natural antioxidant[47].

Antioxidant activity of cyperus rotundus[48]:

The hydroalcoholic extract of *C. Rotundus* expressed its antioxidant potential while evaluated pharmacologically using In vitro model free radical scavenging assay.

Phoenix dactilifera

Antioxidant activity[49]:

Variety of dates such as Khalas and Ajwa exhibited their antioxidant potentials in aqueous and alcoholic extract through DPPH assay.

Cinnomomum tamala

Antioxidant activity[50]:

One research study concluded that synaptosomes from diabetic rats are susceptible to oxidative damage and the positive effects of bay leaf in vitro, could be attributed to the presence of antioxidant phytochemicals.

Diuretic activity[51]:

The aqueous and ethanolic extracts of *Cinnamomum tamala* leaves were investigated for its diuretic activity tested in albino rats. Results revealed that both the alcoholic and aqueous extracts showed significant diuretic activity at a dose of 500mg/kg body weight by increasing the total volume of urine and concentrations of Potassium and Sodium salts in urine as compared to the standard drug Frusemide.

Terminalia bellerica

Antioxidant activity[52]:

The free radical scavenging activity and antioxidant potential of acetone extract/fractions of its fruit was investigated using in vitro assays, including scavenging ability against 2,2'-diphenyl-2-picrylhydrazyl (DPPH), beta-carotene bleaching inhibition, reducing power and chelating ability on Fe2+ ions. It was found that ethyl acetate fraction was more effective than crude acetone extract in all antioxidant assays, except chelating power which was highest in water fraction. Maximum antioxidant activities (expressed as EC50 values) observed were 14.56 microg/ml, 27.81 microg/ml and 67.8 microg/ml in DPPH, beta-carotene bleaching and reducing power assays, respectively. The antioxidant potential was compared with known antioxidant (butylated hydroxyl toluene) and correlated with total phenolic and flavonoid content in crude extract and

fractions. Fractions rich in polyphenolic content were more effective than the crude extract.

Diuretic activity[53]:

The study aim to evaluate potency and efficacy of *Terminalia belerica* fruit pulp aqueous extract (TBFPAE) in Wistar albino rats as a diuretic. TBFPAE possesses diuretic effect with a significant Potassium-sparing effect comparable to frusemide in the dose of 9, 18, and 36 mg/kg in Wistar albino rats comparable to frusemide.

Sandal

Safety assessment of sandal wood oil (Santalum album L.S)

Over 100 constituents of sandal wood oil have been identified with major constituents being alpha-santalol. Sandal wood oil was mutagenic in spore Rec assay and was found to have Anti-carcinogenic, Anti-viral and anti-bacterial activity [54].

4. MATERIALS AND METHODS

4.1 Drug selection:

In this research work, the "***Munthirikai Choornam",*** a poly herbal formulation, has been selected to evaluate **Hypertension**, mentioned in "***Aathma Ratchamirtha Vaithiya Saara Sangiragam" p.no:206.***

Ingredients:

- ***Munthirikai pazham (****Vitis vinifera)*
- ***Thipilli moolam*** (*Root of piper longum*)
- ***Thiri kadugu***
  - ***Chukku*** (zingiber officinale)
  - ***Milagu (****Piper nigrum)*
  - ***Thippili*** *(Piper longum)*
- ***Sengkazhunir (****Nymphaea alba)*
- ***Vetiver (****Vetiveria zizanioides)*
- ***Chandanam (****Santalum album)*
- ***Vilamichu (****Plectranthus vettiveroides)*
- ***Atimaduram (****Glycyrrhiza glabra)*
- ***Muthakkasu (****Cyperus rotandus)*
- ***Vilva poo (****Aegle marmelos)*
- ***Yelarisi (****Eletaria cardamom)*
- ***Kothumalli (****Coriandrum sativum)*
- ***Thiripala***
  - ***Kadukai (****Terminalia chebula)*
  - ***Nellikkai*** *(Phyllanthus emblica)*
  - ***Thandrikkai (****Terminalia bellarica)*
- ***Ner pori (****Oryza sativa)*
- ***Pericham pazham*** *(Phonex dactilifera)*
- ***Patchai karpooram*** *(Borneo camphor)*
- ***Karkandu (****Rock candy)*
- ***Lavanga pathiri (****Cinnamomum tamla)*
- ***Chiru nagappu (****Mesua nagassarium)*
- ***Koogai neeru (****Marantu arundinacea****)***

Source of Collection

The drug was purchased from authorized country Raw Drug Store in Chennai.

Identification and Authentication of the drug

The collected raw materials and plants were identified and authenticated by Botanist and faculties of *Gunapadam* department, Government Siddha Medical College, Arumbakkam, Chennai, and Tamilnadu. A specimen sample of each raw material has been kept in the department for future reference.

(Reg. No: GSMC/PGGM/072-095/2014-17)

Purification of the ingredients

All the drugs mentioned here were purified as per the Siddha literature. [55]

- The outer skin of Sandal woods, Turmeric, Tree turmeric were peeled off.
- The adventious roots of Nut grass were removed and dried.
- The roots of Cuscus grass cut into small pieces and dried in sunlight.
- Chukku was immersed by using limewater then it was dried in sunlight, finally the outer layer of skin were peeled off.
- Dried fruit of Indian gooseberry was boiled with milk and the seeds were removed.
- The root of Indian liquorice was cleaned with water and cut into small pieces and then dried.
- Nerpori-cleaned the dust particles
- Kadukkai-roasted in pan, inner seed was removed.
- Korai-kizhangu were washed in the running tap water to remove the soil and impurities.
- Thippili-Immersed in lemon juice and dried.
- Thippilli moolam-Nodes were removed and dried.
- Milagu-It was immersed in sour buttermilk for75minutes and dried.
- Dried fruits of *Nelli* (*Phyllanthus emblica*) were first dusted with a clean cloth and then purified by gently removing the outer skin.

Preparation of *Munthirikai Chooranam*

Procedure: The ingredients after purification were ground separately to powder. The powder was sieved through a white cloth (***Gunapadam Thathu JeevaVagupu*)** .All these powdered ingredients were mixed thoroughly in a stone mortar. The prepared test drug was stored in a clean, air tight glass container. The contents were inspected frequently to avoid moisture and insects. It was labelled as ***"Munthirikai Chooranam'' (MC).***

Purification of the *Chooranam*: steaming process (*Pittaviyalmurai*)

The ***MC*** was purified by *pittaviyal* method (steam cooking in milk) as per Siddha classical literature. A mud pot was taken and it was half filled by mixture of milk with equal quantity of water. The mouth of the pot was sealed by a cloth. This *Chooranam* was placed over the cloth and tied firmly around the mouth of mud pot by another pot. The gap between mud pots was tied with a wet cloth to avoid evopration. The mud pot was kept on fire and boiled until the cow's milk reduced in the lower pot. The same drug was later dried and powdered then sieved again. It was used for the further study [56] .

Storage of the drug

The prepared test drug was stored in a clean, air tight glass container. The contents were inspected frequently to avoid moisture and insects.

Administration of the drug

Form of medicine **:** *Chooranam*

Root of administration **:** Enteral

Dosage **:** 2 Gram twice a day- after food

Vehicle **:** Milk

4.2 STANDARDISATION OF THE DRUG

Standardisation of the drug brings the validation to be used as a medicine by subjecting the drug to many analysis and determining its quality and effectiveness. Standardization includes many studies such as its organoleptic properties, physical characteristics and

phytochemical properties and also to assess the active principles and elements present in the drug. Thus standardization brings the efficacy and potency of the drug.

4.2.1 Organoleptic character

The organoleptic characters of the sample drug were evaluated.1gm of the test drug was taken and the colour, texture, particle size and other morphology were viewed by naked eye under sunlight. Then the result is tabulated in Table no:9

4.2.2 Physicochemical Analysis

Physicochemical studies of the trial drug have been done according to the WHO guidelines [57].

Determination of Ash Values

Total Ash

3g of the test drug was accurately weighed and incinerated in a crucible dish at a temperature not exceeding 450^{o}C until it was free from carbon. It was then cooled and weighed. The % W/w of ash with reference to the air-dried powder was calculated.

Water Soluble Ash

The total ash was obtained as the above method for preparation of total ash. The ash was boiled with 25ml of water for 5minutes. The insoluble ashes were collected using filter paper. It was then washed with hot water and transferred to the silica crucible. It was then ignited for 15minutes at temperature not exceeding 450^{o}C. For determination of weight of the water soluble ash the silica crucible and residue were weighed until constant weight was attained. The weight of the water soluble ash was determined by subtracting the weight of insoluble ash from the weight of total ash.

Acid insoluble Ash

The total ash was obtained as the above method for preparation of total ash. The ash was boiled for 5minutes with 25ml 10% Hcl. The insoluble ashes were collected using filter paper and washed with hot water. It was then transferred to the silica crucible and ignited for 15minutes at temperature not exceeding 450^{o}C. The silica crucible and residue were weighed until constant weight is attained.

Determination of Extractive Value

Alcohol Soluble Extractive Value

3g of test drug powder was weighed and macerated with 100ml of ethanol in a closed container for 24 hours. The resulting solution was shaken continuously for 6 hours.It was then allowed to stand and soak for 18 hours. The solution was filtered and evaporated of the filtrate in a flat bottomed shallow dish and dried at 105^{o}C. Then the content was cooled and weighed.

Water soluble Extractive value

3g of test drug powder was weighed and macerated with chloroform and water, respectively, at 80^{o}C for 24 hours. The resulting solution was shaken continuously for 6 hours and allowed to stand and soak for 24hours then filtered. The solution from both chloroform and water respectively was filtered and evaporated of the filtrate in a flat bottomed shallow dish. It was dried at 105^{o}C then cooled and weighed.

Loss on Drying

The powdered drug was taken and dried in the oven at 100- 105°C to constant weight. The result was noted.

Physical characterization

Solubility

A little of the sample was shaken well with distilled water and then little of the sample was shaken well with con Hcl and Con $H2SO_4$. Sparingly soluble character indicates the presence of Silicate.

pH value

Potentiometrically pH value was determined by a glass electrode and a suitable pH meter.

Action on heat

A small amount of the sample was taken in a dry test tube and heated gently. If there was a strong white fumes evolving it indicates the presence of Carbonate.

Flame test

A small amount of the sample was made into a paste with con.Hcl in a watch glass. It was then introduced into non-luminous part of the Bunsen flame. Appearance of bluish green flame indicates the presence of Copper.

Ash Test

A filter paper was soaked into a mixture of sample and cobalt nitrate solution. It was then introduced into the Bunsen flame and ignited. Appearance of yellow colour flame indicates the presence of Sodium.

All the results were noted and tabulated in Table no:10

4.2.3 Phytochemical Analysis

The Phytochemical screening of the extract gives general idea regarding the nature of chemical constituents present in the crude drug. The phytochemical tests were done as the method illustrated in [58].

Test for Alkaloids

A small portion of solvent free extracts was stirred separately with few drops of dilute hydrochloric acid and filtered & tested carefully with various alkaloidal reagents.

Mayer's reagent - Cream precipitate

Dragendroff's reagent - Orange brown precipitate

Hager's reagent - Yellow precipitate

Wagner's reagent - Reddish brown precipitate

Test for Carbohydrates and Reducing Sugars

The minimum amount of extracts was dissolved in 5ml of distilled water & filtered. The filtrate was subjected to test for carbohydrates & glycosides.

a) Molisch's test

The filtrate 1 ml was treated with 2-3 drops of 1% alcoholic alpha naphthol& 2ml concentrated sulphuric acid was added along the sides of test tube. Violet ring was observed at the junction of 2 layers which showed the presence of carbohydrate.

b) Benedict's test

The filtrate 1 ml was treated with Benedict's reagent and heated gently. Orange red precipitate indicates the presence of reducing sugars.

c) Fehling's test

The filtrate 1 ml was treated with equal volume of Fehling's solution A and B and heated gently. Orange red precipitate indicates the presence of reducing sugars.

Test for Glycosides

The extract was hydrolyzed with dil. HCl and subjected to test for glycosides.

a) Modified Borntrager's test

To the hydrolysate extract, 1 ml of Ferric chloride solution was added and immersed in boiling water for about 5 min. The mixture was cooled and extracted with equal volume of benzene. The benzene layer was separated and treated with ammonia solution. Formation of rose pink colour in the ammoniacal layer indicates the presence of Anthranol glycosides.

b) Legal's test

The hydrolysate extract was treated with Sodium nitropruside in pyridine and sodium hydroxide. Formation of pink to blood red colour indicates the presence of Cardiac glycosides.

Test for Saponins

The extract 0.5 ml was shaken with 5 ml distilled water. The presence of saponins was indicated by formation of copious lather.

Test for Tannins

Gelatin test

To the extract, 1% gelatin solution containing sodium chloride was added. Formation of white precipitate indicates the presence of tannins.

Test for Phenolic compounds

To 0.5 ml of extract, 1 ml of alcoholic ferric chloride solution was added. Formation of bluish green or bluish black indicates the presence of Phenolic compounds.

Test for Phytosterol

Ferric chloride – acetic acid test

1 ml of extract was treated with 1 ml of chloroform and then, 2 ml of ferric chloride acetic acid reagent was added followed by 1 ml of conc. sulphuric acid. Appearance of reddish pink colour shows the presence of phytosterol.

Test for Diterpenes

Copper acetate test

1 ml of extract was dissolved in water and treated with 3-4 drops of Copper acetate solution. Formation of emerald green colour indicates the presence of diterpenes.

Test for Triterpenes

Salkowski's test

1 ml of extract was treated with 1 ml of chloroform followed by 1 ml of conc. sulphuric acid, shaken and allowed to stand. Appearance of golden yellow colour shows the presence of triterpenes.

Test for Flavonoids

a) Alkaline reagent test

To 1 ml of extract, 1 ml of 10% sodium hydroxide solution was added. Formation of dark yellow colour indicates the presence of flavonoids.

b) Lead acetate test

To 1 ml of extract, 3-4 drops of 10% lead acetate solution was added. Formation of yellow precipitate indicates the presence of flavonoids.

c) Ferric chloride test

To 1 ml of extract, 3-4 drops of ferric chloride solution was added. Formation of dark green colour indicates the presence of flavonoids.

d) Shinoda test

To 1 ml of extract, few mg of magnesium turnings was added followed by few drops of conc. hydrochloric acid and boiled for five minutes in a boiling water bath. Formation of red colour indicates the presence of flavonoids.

Test for Proteins and Free Amino Acids

a) Xanthoproteic test

To 1 ml of extract, 3-4 drops of conc. nitric acid was added. Formation of yellow precipitate indicates the presence of proteins.

b) Million's test

To 0.5 ml of extract, 2.5 ml of Million's reagent was added. Formation of white precipitate and the precipitate warmed indicates the presence of proteins.

c) Biuret test

To 0.5 ml of extract, 2.5 ml of diluted Biuret reagent was added. Appearance of purple colour or brick red precipitate showed the presence of proteins and free amino acids.

Test for Quinones

Sodium hydroxide test

To 0.5 ml of extract, 1 ml of 10% sodium hydroxide was added. Appearance of blue or green or red colour shows the presence of quinones.

Results of phytochemical analysis were noted and tabulated in Table no: 11

TLC/ HPTLC finger print studies

HPTLC finger printing was carried out as per the reference [59].

Preparation of spray reagent-vanillin-sulphuric acid reagent

Vanillin (1g) was dissolved in ice cold ethanol (95ml). Add 5ml of cooled concentrated sulphuric acid then Ice was added and stirred well. The solution was stored in refrigerator.

Chromatographic conditions

Instrument : CAMAG (Switzerland).

Sample Applicator : Camag Linomat - IV applicator with N_2 gas flow

Photo documentation System : Digi store - 2 documentation system with Win Cat &video scan software.

Scanner : Camag HPTLC scanner - 3 (030618), Win Cats - IV.

Development Chamber : Camag HPTLC 10X10, 10 X 20 twin trough linear Development chamber.

Quantity applied : 5, 10 µl for extracts and 5 µl for standards

Stationary phase : Aluminium plate pre-coated with silica gel60(E.Merck)

Plate thickness : 0.2 mm.

Mobile Phase : For Chloroform extract - Toluene: Ethyl acetate (9:1) and ethanol extract - Toluene: Ethyl acetate (1:1).

Scanning wavelength : 254 nm

Laboratory condition : 26 ± 5^{o}C and 53 % relative humidity

The plate was developed up to a height of 8 cm, air dried, spots were observed under the UV light at 254 and 366 nm. Finally the plates were derivatized using vanillin-sulphuric acid reagent heated at 105° till colour spots appeared.

HPTLC results were noted and tabulated in Table no: 12,13

4.2.4 Bio-Chemical Analysis

Preliminary Basic and Acidic radical studies

Methodology for chemical analysis

Preparation of extract

5gm of *MC* was weighed accurately and placed in a 250ml clean beaker and added with 50ml of distilled water. Then it was boiled well for about 20 minutes. Then it was cooled and filtered in a 1000ml volumetric flask and made up to 100ml distilled water.

Table No.5.Test for basic radicals

PROCEDURE	OBSERVATION	INFERENCE
Test for Potassium A pinch of sample is treated with 2ml of sodium nitrate solution and then treated with 2ml of cobalt nitrate in 30% of glacial acetic acid.	Formation of Yellow colour precipitate	Presence of Potassium
Test for Calcium Taken2 ml of extract in a clean test tube. Then acetic acid and potassium chromate solution were added.	No Yellow precipitate	Presence of Calcium
Test For Magnesium 2ml of extract was taken in a clean test tube, few drops of Magnason reagent was added in drops.	Formation of Blue colour precipitate	Presence of Magnesium
Test For Ammonium 2mlof extract was taken in a test tube and added few ml of Nessler's reagent.	Appearance of Brown colour.	Presence of Ammonium
Test For Sodium 2 pinches of *MC* was mixed with HCl and made it into paste. And introduced into the blue flame of Bunsen burner.	Appearance of intense Yellow colour	Presence of Sodium
Test for Iron (Ferrous) 2ml of extract was taken in a clean dried test tube and conc. HNO_3 and ammonium thiocyanate were added.	Appearance of Blood red colour	Presence of Ferrous iron
Test For Zinc 2 ml of the extract was taken in a test tube and Potassium ferro cyanide solution was added.	Formation of White colour precipitate	Presence of Zinc
Test For Aluminium To the 2m1of the extract was taken in a test tube sodium hydroxide drops were added to it.	White precipitate obtained	Presence of Aluminium

PROCEDURE	OBSERVATION	INFERENCE
Test For Lead: 2 ml of extract was taken in a test tube and added with 2ml of potassium iodide solution.	Formation of yellow colour precipitate	Presence of Lead
Test for Copper: To a small portion of a extract dilute hydrochloric acid was added and then hydrogen sulphide gas is passed through the solution.	Black precipitate	Presence of Copper
Test For Mercury: 2m1 of the extract was taken in a test tube and treated With 2ml of sodium hydroxide solution.	Formation of Yellow precipitate	Presence of Mercury
Test for Arsenic: 2m1 of the extract was taken in a test tube and treated with 2ml of sodium hydroxide solution.	Formation of brownish red precipitate	Presence of Arsenic

Results were noted and tabulated in Table No:14

Table No.6.Test for acidic radical

PROCEDURE	OBSERVATION	INFERENCE
Test for Sulphate: 2 ml of the extract was taken in clean, dry test tube and 5 % barium chloride solution was added to it.	Formation of white precipitate	Presence of Sulphate
Test for Chloride: The extract was taken in a test tube and then treated withSilver nitrate solution.	Formation of White precipitate	Presence of Chloride

PROCEDURE	OBSERVATION	INFERENCE
Test for Phosphate: The extract was taken in a test tube and treated with ammonium molybdate and conc. HNO_3.	Formation of Yellow precipitate	Presence of Phosphate
Test for Carbonate : The substance was taken in a clean dry test tube and then treated with Conc. HCl.	Formation of Effervescence	Presence of Carbonate
Test for Fluoride & Oxalate: 2ml of extract was taken in a test tube and added with 2ml of dil.acetic acid, 2ml calcium chloride solution and then heated.	Formation of cloudy appearance	Presence of Fluoride & Oxalate
Test For Nitrate: 1gm of the *MC* was heated with copper turnings and concentrated H2SO4 and observed the test tube vertically down.	Characteristic changes	Presence of Nitrate

Results were noted and tabulated in Table no: 15

4.2.5 Availability Of Microbial Load

Enumeration of bacteria by plate count – agar plating technique[60]

The plate count technique was one of the most routinely used procedure because of the enumeration of viable cells by this method.

Principle:

This method is based on the principle that when material containing bacteria was cultured, every viable bacterium develops into a visible colony on a nutrient agar medium. Therefore the number of colonies, are the same as the number of organisms contained in the sample.

Dilution:

A small measured volume are mixed with a large volume of sterile water or saline called the diluent or dilution blank. Dilution are usually made in multiples of ten.

A single dilution was calculated as follows:

$$\text{Dilution} = \frac{\text{Volume of the sample}}{\text{Total volume of the sample and the diluents}}$$

Requirements

- Sample or Bacterial suspension
- 9 ml dilution blanks (7)
- Sterile petri dishes (12)
- Sterile 1 ml pipettes(7)
- Nutrient agar medium (200 ml)
- Colony counter

Procedure:

- Label the dilution blanks as 10^{-1}, 10^{-2}, 10^{-3}, 10^{-4}, 10^{-5}, 10^{-6}, 10^{-7}.
- Prepare the initial dilution by adding 1 ml of the sample into a 9 ml dilution blank labelled 10^{-1} thus diluting the original sample 10 times.
- Mix the contents by rolling the tube back and forth between hands to obtain uniform distribution of organisms.
- From the first dilution transfer 1 ml of the suspension while in motion, to the dilution blank 10^{-2} with a sterile and fresh 1 ml pipette diluting the original specimen to 100 times.
- From the 10^{-2} suspension, transfer 1 ml of suspension to 10^{-3} dilution blank with a fresh sterile pipette, thus diluting the original sample to 1000 times.
- Repeat this procedure till the original sample have been diluted 10,000,000 times using every time a fresh sterile pipette.

- From the appropriate dilutions transfer 1ml of suspension while in motion, with the respective pipettes, to sterile petri dishes. Three petri dishes are to used for each dilution.
- Add approximately 15 ml of the nutrient medium, melted and cooled to 45^0c, to each petri dish containing the diluted sample. Mix the contents of each dish by rotating gently to distribute the cells throughout the medium.
- Allow the plates to solidity.
- Incubate these plates in an inverted position for 24-48 hours at 37^0c.

Observation:

Observe all the plates for the appearance of bacterial colonies. Count the number of colonies in the plates.

Calculate the number of bacteria per ml of the original suspension as follows:

$$\text{Organisms per millimeter} = \frac{\text{Number of colonies (average of 3 replates)}}{\text{Amount of plated} \times \text{dilution}}$$

4.2.6 INSTRUMENTAL ANALYSIS

Fourier Transform Infra-Red spectroscopy

Fig no:2.1 FTIR-INSTRUMENT

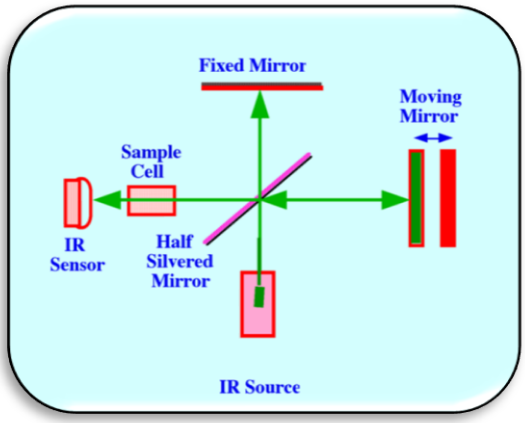


Fig no: 2.2 FTIR-MECHANISM

Model Details

Model : Spectrum one: FT-IR Spectrometer

Scan Range : MIR 450-4000 cm-1

Resolution : 1.0 cm-1

Sample required : 50 mg, solid or liquid.

It is the preferred method of infrared spectroscopy. FT-IR is an important and more advanced technique. It is used to identify the functional group, to determine the quality and consistency of the sample material and can determine the amount of compounds present in the sample. It is an excellent tool for quantitative analysis [61].In FT-IR infrared was passed from a source through a sample *(MC)*. This infrared was absorbed by the sample according to the chemical properties and some are transmitted. The spectrum that appears denotes the molecular absorption and transmission. It forms the molecular fingerprint of the sample. Like the finger print there was no two unique molecular structures producing the same infrared spectrum. It was recorded as the wavelength and the peaks seen in the spectrum indicates the amount of material present.

FT-IR is the most advanced and the major advantage is its

- Speed
- Sensitivity
- Mechanical Simplicity
- Internally Calibrated

Results were noted and tabulated in Table no: 17

XRD (X-RAY POWDER DIFFRACTION)

DEFINITION

X-ray powder diffraction is most widely used for the identification ofunknown crystalline materials (e.g. minerals, inorganic compounds). Determination of unknown solids is important to studies in geology, environmental science, material science and biology.

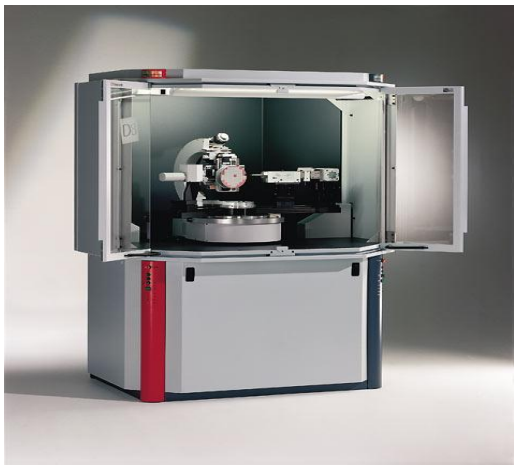


Fig no: 3 Image of XRD Analyser

Applications:

- Characterization of crystalline materials [62]
- Identification of fine-grained minerals such as clays and mixed layer clays that are difficult to determine optically
- Determination of unit cell dimensions.

With specialized techniques, XRD can be used to:

- Determine crystal structures using Rietveld refinement
- Determine of modal amounts of minerals (quantitative analysis)

Characterize thin films samples by

- determining lattice mismatch between film and substrate and toinferring stress and strain.
- determining dislocation density and quality of the film by rockingcurve measurements.

- Measuring super lattices in multilayered epitaxial structures.
- Determining the thickness, roughness and density of the film using glancing incidence X-ray reflectivity measurements.
- Make textural measurements, such as the orientation of grains, in apolycrystalline sample.

Strengths and Limitations of X-ray Powder Diffraction

Strengths

- Powerful and rapid (< 20 min) technique for identification of an unknown mineral.
- In most cases, it provides an unambiguous mineral determination
- Minimal sample preparation is required
- XRD units are widely available
- Data interpretation is relatively straight forward.

Limitations

- Homogeneous and single phase material is best for identification of unknown
- Must have access to a standard reference file of inorganic compounds
- Requires tenths of a gram of material which must be ground into a powder.For mixed materials, detection limit is ~ 2% of sample
- For unit cell determinations, indexing of patterns for non-isometric crystalsystems is complicated.

Sample Collection and Preparation

Determination of an unknown requires: the material, an instrument for grinding, and a sample holder.

- Obtain a few tenths of a gram (or more) of the material, as pure as possible
- Grind the sample to a fine powder, typically in a fluid to minimize inducing extra strain (surface energy) that can offset peak positions, and to randomize orientation.
- Powder less than ~10 μm(or 200-mesh) in size is preferred place into a sample holder or onto the sample surface

SEM (SCANNING ELECTRON MICROSCOPE)

In scanning electron microscope high-energy electron beam was focused through a probe towards the sample (*MC*) material. Variety of signals was produced on interaction with the surface of the sample. This results in the emission of electrons or photons and it was collected by a appropriate detector.

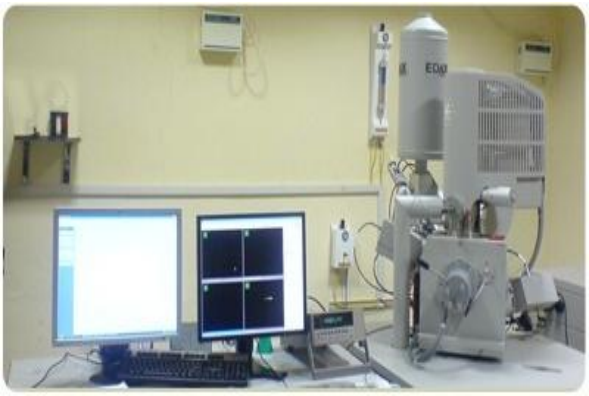


Fig no : 4.1 SEM-INSTRUMENT

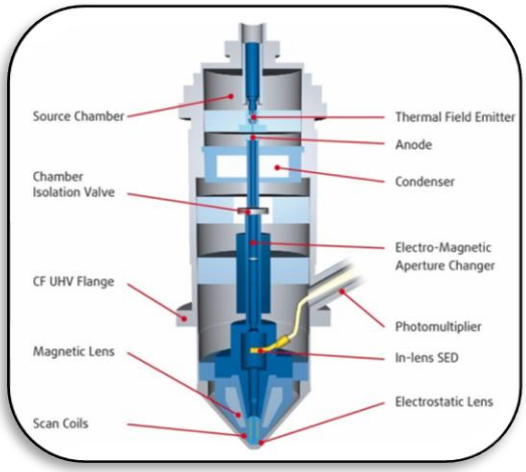


Fig no: 4.2 SEM - MECHANISM

In scanning electron microscope high-energy electron beam was focused through a probe towards the sample (*MC*) material. Variety of signals was produced on interaction with the surface of the sample. This results in the emission of electrons or photons and it was collected by a appropriate detector.

The types of signal produced by a scanning electron microscope include

- Secondary electrons
- back scattered electrons
- characteristic x-rays, light
- specimen current
- Transmitted electrons.

This gives the information about the sample and it includes external morphology, texture, its crystalline structure, chemical composition and it displays the shape of the sample [63].

ICP-OES (INDUCTIVELY COUPLED PLASMA OPTIC EMISSION SPECTROMETRY)

Fig no:5.1 ICP-OES INSTRUMENT

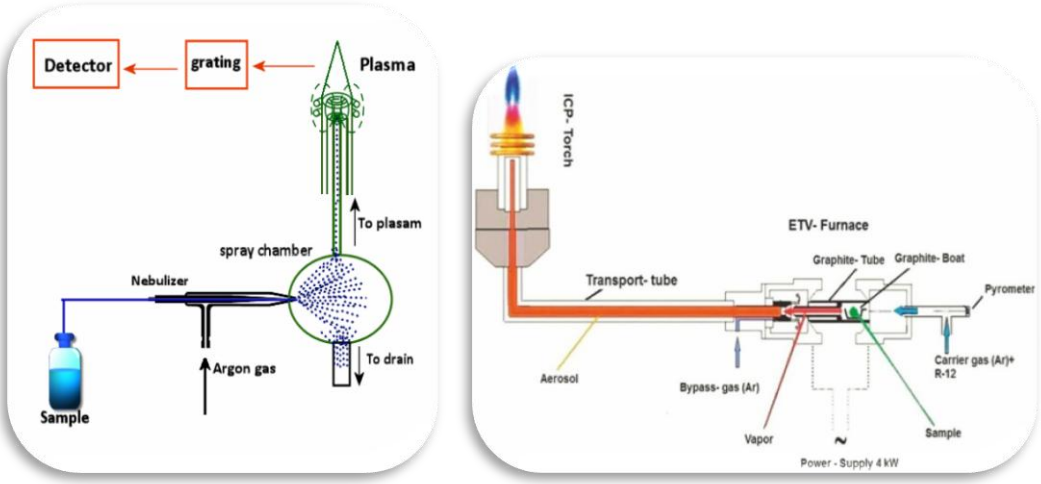


Fig no. 5.2 MECHANISM OF ICP-OES

Manufacturer : Perkin Elmer

Model : Optima 5300 DV ICP-OES Inductively Coupled Plasma Spectrometer (ICP)

Principle:

An aqueous sample *(MC)* was converted to aerosols via a nebulizer. The aerosols are transported to the inductively coupled plasma which is a high temperature zone (8,000– 10,000ºC). The analysts are heated (excited) to different (atomic and/or ionic) states and produce characteristic optical emissions (lights). These releases are separated based on their respective wavelengths and their strengths are measured (spectrometry). The intensities are proportional to the concentrations of analyses in the aqueous sample. The quantification is an external multipoint linear standardization by comparing the emission intensity of an unknown sample with that of a standard sample. Multi-element calibration standard solutions are prepared from single- and multi element primary standard solutions. With respect to other kinds of analysis where chemical speciation is relevant (such as the concentration of ferrous iron or ferric iron), only total essential concentration is analysed by ICP-OES.

Application: The analysis of major and minor elements in solution samples.

Objectives:

- Determine elemental concentrations of different metals.
- Learn principles and operation of the ICP-OES instrument
- Develop and put on a method for the ICP-OES sample analysis

- Enhance the instrumental conditions for the analysis of different elements
- Probes the outer electronic structure of atoms

Mechanism:

In plasma emission spectroscopy (OES), a sample*(MC)* solution was presented into the core of inductively coupled argon plasma (ICP), which generates temperature of approximately 8000°C. At this temperature all elements become thermally excited and emit light at their characteristic wavelengths. This light is collected by the spectrometer and passes through a diffraction grating that serves to resolve the light into a spectrum of its essential wavelengths. Within the spectrometer, this deflected light was then collected by wavelength and amplified to yield an strength of measurement that can be converted to an elemental concentration by comparison with standardizationvalues.The Inductively coupled plasma optical emission spectrometric (ICP-OES) analysis was done in SAIF, IIT MADRAS, and Chennai-36 using Perkin Elmer Optima 5300 DV [64]. Results were noted and tabulated in Table no:18

4.3 TOXICOLOGICAL STUDIES

4.3.1 ACUTE ORAL TOXICITY STUDY OF *MC*

(OECD GUIDELINE – 423)

Acute toxicity study was carried out as per OECD guideline (Organization for Economic Co - operation and Development, Guideline-423 [65].

The experimental protocol was approved by the institutional ethical committee (IAEC) under CPCSEA (IAEC no: IAEC/XLVIII/11/CLBMCP/2016).

These studies were conducted in C.L. Baid Metha College of Pharmacy, Dhuraipakkam, Chennai.

Introduction:

- The acute toxic class method is a stepwise procedure with the use of 3 animals of a single sex per step.
- Depending on the mortality and/or the moribund status of the animals, on average 2-4 steps may be necessary to allow judgement on the acute toxicity of the test substance.
- This procedure is reproducible, uses very few animals and is able to rank substances in a similar manner to the other acute toxicity testing methods.

- The acute toxic class method is based on biometric evaluations with fixed doses, adequately separated to enable a substance to be ranked for classification purposes and hazard assessment.

- In principle, the method is not intended to allow the calculation of a precise LD50, but does allow for the determination of defined exposure ranges where lethality is expected since death of a proportion of the animals is still the major endpoint of this test.

- The method allows for the determination of an LD50 value only when at least two doses result in mortality higher than 0% and lower than 100%.

- The use of a selection of pre-defined doses, regardless of test substance, with classification explicitly tied to number of animals observed in different states improves the opportunity for laboratory to laboratory reporting consistency and repeatability.

Principle of the Test:

It is the principle of the test that based on a stepwise procedure with the use of a minimum number of animals per step, sufficient information is obtained on the acute toxicity of the test substance to enable its classification. The substance is administered orally to a group of experimental animals at one of the defined doses. The substance is tested using a stepwise procedure, each step using three animals of a single sex. Absence or presence of compound-related mortality of the animals dosed at one step will determine the next step, i.e.

- no further testing is needed

- dosing of three additional animals, with the same dose

- dosing of three additional animals at the next higher or the next lower dose level. The method will enable a judgment with respect to classifying the test substance to one of a series of toxicity classes.

Methodology:

Selection of Animal Species

The preferred rodent species is the wistar albino rat, although other rodent species may be used. Healthy young adult animals are commonly used laboratory strains should be employed. Females should be nulliparous and non-pregnant. Each

animal, at the commencement of its dosing, should be between 6 to 8 weeks old and the weight (150-200gm) should fall in an interval within±20 % of the mean weight of any previously dosed animals.

Housing and Feeding Conditions

The temperature in the experimental animal room should be 22ºC + 3ºC. Although the relative humidity should be at least 30% and preferably not exceed 70% other than during room cleaning the aim should be 50-60%. Lighting should be artificial, the sequence being 12 hours light, 12 hours dark. For feeding, conventional laboratory diets may be used with an unlimited supply of drinking water. Animals may be group-caged by dose, but the number of animals per cage must not interfere with clear observations of each animal.

Preparation of animals:

The animals are randomly selected, marked to permit individual identification, and kept in their cages for at least 7 days prior to dosing to allow for acclimatization to the laboratory conditions.

Test Animals and Test Conditions: Sexually mature Female Wistar albino rats (150-200gm) were obtained from Kings institute, Guindy, Chennai. All the animals were kept under standard environmental condition (22±3°C). The animals had free access to water and standard pellet diet (Sai meera foods, Bangalore).

Preparation of animals:

The animals are randomly selected, marked to permit individual identification, and kept in their cages for at least 7 days prior to dosing to allow for acclimatization to the laboratory conditions.

Preparation for Acute Toxicity Studies

Rats were deprived of food overnight (but not water 16-18 hr) prior to administration of the, *Munthirikai Choornam*.

The principles of laboratory animal care were followed and the Institutional Animal Ethical Committee approved the use of the animals and the study design

Test Substance	**:**	***MUNTHIRIKAI CHOORNAM***
Animal Source	**:**	Kings institute, Guindy, Chennai
Animals	**:**	Wister Albino Rats (Female-3+3)
Age	**:**	6-8 weeks
Body Weight on Day 0	**:**	150-200gm.

Acclimatization : Seven days prior to dosing.

Veterinary examination : Prior and at the end of the acclimatization period.

Identification of animals : By cage number, animal number and individual marking by using Picric acid.

Number of animals : 3 Female/group,

Route of administration : Oral

Diet : Pellet feed supplied by Sai meera foods Pvt Ltd, Banglore.

Water : Aqua guard portable water in polypropylene bottles.

Housing & Environment : The animals were housed in Polypropylene cages provided with bedding of husk.

Housing temperature : between 22ºC ± 3ºC.

Relative humidity : between 30% and 70%,

Air changes : 10 to 15 per hour and

Dark and light cycle : 12:12 hours.

Duration of the study : 14 Days

Administration of Doses:

Munthirikai Choornam was suspended in water and administered to the groups of wistar albino rats in a single oral dose by gavage using a feeding needle. The control group received an equal volume of the vehicle. Animals were fasted 12 hours prior to dosing. Following the period of fasting, the animals were weighed and then the test substance was administered. Three Female animals are used for each group. The dose level of 5, 50, 300and 2000 mg/kg body weight was administered stepwise. After the substance has been administered, food was withheld for a further 3-4 hours. The principle of laboratory animal care was followed. Observations were made and recorded systematically and continuously as per the guideline after substance administration. The visual observations included skin changes, mobility, aggressively, sensitivity to sound and pain, as well as respiratory movements. Finally, the number of survivors was noted after 24 hrs and these animals were then monitored for a further 14 days and observations made daily. The toxicological effect was assessed on the basis of mortality.

Observations:

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. It should be determined by the toxic reactions, time of onset and length of recovery period, and may thus be extended when considered necessary. The times at which signs of toxicity appear and disappear are important, especially if there is a tendency for toxic signs to be delayed. All observations are systematically recorded with individual records being maintained for each animal.

Observations include changes in skin and fur, eyes and mucous membranes, and also respiratory, circulatory, autonomic and central nervous systems, and somatomotor activity and behavior pattern. Attention was directed to observations of tremors, convulsions, salivation, diarrhoea, lethargy, sleep and coma. The principles and criteria summarized in the Humane Endpoints Guidance Document taken into consideration. Animals found in a moribund condition and animals showing severe pain or enduring signs of severe distress was humanly killed. When animals are killed for human reasons or found dead, the time of death was recorded [66].

4.3.2 REPEATED DOSE 28 DAYS ORAL TOXICITY STUDY OF *Munthirikai CHOORANAM* ON RATS – (OECD-407 guidelines)[67]

Test Substance	**:**	*Munthirikai Choornam*
Animal Source	**:**	Kings institute, Guindy, Chennai
Animals	**:**	Wister Albino Rats (Male -24, and Female-24)
Age	**:**	6-8 weeks
Body Weight	**:**	150-200gm.
Acclimatization	**:**	Seven days prior to dose.
Veterinary examination	**:**	Prior and at the end of the acclimatization period.
Identification of animals	**:**	By cage number, animal number and individual marking by using Picric acid
Diet	**:**	Pellet feed supplied by Sai Meera Foods Pvt Ltd, Bangalore
Water	**:**	Aqua guard portable water in polypropylene bottles.
Housing & Environment	**:**	The animals were housed in Polypropylene cages provided with bedding of husk.
Housing temperature	**:**	between 22ºC±3ºC.
Relative humidity	**:**	between 30% and 70%,

Air changes **:** 10 to 15 per hour

Dark and light cycle **:** 12**:**12 hours.

Duration of the study **: 28 Days.**

Table 8

Groups	**No of Rats**
Group I Vehicle control (Water)	12(6male,6 female)
Group II MC- low dose X (30mg)	12 (6male,6 female)
Group III MC- Mid dose 5X (150mg)	12 (6male,6female)
Group IV MC- High dose 10X(300mg)	12(6male,6female)

MC-MUNTHIRIKAI CHOORNAM

Methodology

Randomization, Numbering and Grouping of Animals:

48 Wistar Albino Rats (24M + 24F) were selected and divided into 4 groups. Each group consist of 12 animals (Male -6, and Female-6). First group treated as a control and other three group were treated with test drug (low, mid, high) for 28 days. Animals were allowed acclimatization period of 7 days to laboratory conditions prior to the initiation of treatment. Each animal was marked with picric acid. The females were nulliparous and non-pregnant.

Justification for Dose Selection:

As per OECD guideline three dose levels were selected for the study. They are low dose (X), mid dose (5X), high dose (10X). X is calculated by multiplying the acute toxicity dose 2000mg) and the body surface area of the rat (0.018). i.e X dose is (30mg/kg), 5X dose is (150mg/kg), 10X dose is (300mg/kg).

Preparation and Administration of Dose:

Munthirikai Chooranam suspended in with water, It was administered to animals at the dose levels of X, 5X, 10X. The test substance suspensions were freshly prepared every two days once for 28 days. The control animals were administered vehicle only. The drug was administered orally by using oral gavage once daily for 28 consecutive days.

Observations:

Experimental animals were kept under observation throughout the course of study for the following:

Body Weight: Weight of each rat was recorded on day 0, at weekly intervals

throughout the course of study.

Food and water Consumption: Food and water consumed per animal was calculated for control and the treated dose groups.

Clinical signs: All animals were observed daily for clinical signs. The time of onset, intensity and duration of these symptoms, if any, were recorded.

Mortality: All animals were observed twice daily for mortality during entire course of study.

Necropsy: All the animals were sacrificed by excessive anaesthesia on day 29. Necropsy of all animals was carried out.

Laboratory Investigations:

Following laboratory investigations were carried out on day 29 in animals fasted over-night. Blood samples were collected from orbital sinus using sodium heparin (200IU/ml) for Bio chemistry and potassium EDTA (1.5 mg/ml) for Hematology as anticoagulant. Blood samples were centrifuged at 3000 r.p.m. for 10 minutes.

Haematological Investigations:

Haematological parameters were determined using Haematology analyzer.

Biochemical Investigations:

Biochemical parameters were determined using auto-analyzer.

Histopathology:

Control and highest dose group animals will be initially subjected to histopathological investigations. If any abnormality found in the highest dose group than the low, then the mid dose group will also be examined. Organs will be collected from all animals and preserved in 10% buffered neutral formalin for 24 h and washed in running water for 24 h. The organ sliced 5 or 6µm sections and were dehydrated in an auto technic on and then cleared in benzene to remove absolute alcohol. Embedding was done by passing the cleared samples through three cups containing molten paraffin at 50°C and then in a cubical block of paraffin made by the "L" moulds. It was followed by microtome and the slides were stained with Haematoxylin-eosin red.

Statistical analysis:

Findings such as body weight changes, water and food consumption, hematology and blood chemistry were subjected to One-way ANOVA followed by dunnett test using a computer software programme – Graph pad version7.

4.4 PHARMACOLOGICAL STUDIES

4.4.1 ANTI-HYPERTENSIVE ACTIVITY OF *MUNTHIRIKAI CHOORANAM* IN SPOTANEOUSLY HYPERTENSIVE RATS

Cardiovascular disease is a leading cause of death, and hypertension is a critical risk factor for cardiovascular events. The pathogenesis of hypertension is accompanied by decreased nitric oxide (NO) bioavailability in the vasculature and increased cardiovascular remodelling. Hypertensive patients frequently develop clinically evident cardiac hypertrophy 10 to 20 years after the onset of hypertension, as a result of adaptive and maladaptive responses to pressure overload. Cardiac hypertrophy has been linked to the development of a variety of cardiovascular diseases, including myocardial ischemia, arrhythmias, and sudden cardiac death. Therefore, treatment options that not only maintain stable pressure levels but also delay or even regress the structural and functional changes in resistance arteries and the heart are needed. Despite the current availability of multiple anti-hypertensive medication types, a significant number of patients do not respond to treatment and remain hypertensive. As multiple mechanisms likely contribute to the development of hypertension, including angiotensin, oxidative stress and hemodynamic changes, multi-targeted therapeutic interventions will likely be required for effective management of hypertension.

Animals:

All animal experiments were performed in accordance with the Guidelines of OECD. All experiments were performed with the approval of IAEC of C.L. BAID METHA COLLEGE OF PHARMACY. SHR (9 weeks old) and age-matched Wistar rats male, weighing 250±20 g, were purchased from King Institute of Preventive Medicine and Research, Rats were kept in a room temperature controlled room (25 °C), with 12 hours dark and 12 hours artificial illumination daily (7:00— 19:00). Food and water were available ad libitum.

GROUPING

The animals were divided into following groups:

- Group 1 control untreated group which received normal saline.
- Group 2 received Verapamil 12.5 mg/kg b.w
- Group 3 *MC*100 mg/kg b.w
- Group 4 *MC*200mg/kg b.w

The drug *MC* was administered orally and once daily for 4 weeks.

In this study, the effect of a four weeks chronic administration of daily oral doses of 100 and 200 mg/kg body weight, *MC* on blood pressure was measured.

The stock solution was prepared once every three days. Extract suspensions were stored at 4ºC and were allowed to reach room temperature before administration.

METHOD:

Systolic blood pressure (SBP) and heart rate measurement of SH rats was carried out using tail-cuff method plethysmography (LE 5001 Pressure Meter).A mean of six measurements was obtained for each animal. For blood pressure measurement, the animals were warmed up to 42°C for 5 min in a confinement cage. The animals were first submitted to a period of adaptation for 15 days before the experiments and only SHR with an SBP > 170 mmHg were selected for this study.

During the final week of the treatment, the rats were allowed to acclimatize to the experimental conditions of non invasive SBP measurements by allowing them to stand in rat restrainers for 30 min every day. SBP measurements were recorded 24 hours after the last treatment dose. At least 8-10 recordings were taken for each rat and the mean of the lowest 4 values within less than 10 mmHg difference was taken as the mean SBP [68].

4.4.2 DIURETIC ACTIVITY OF *MUNTHIRIKAI CHOORANAM*

The method of Lipchitz et al [69] was employed for the assessment of diuretic activity .

EXPERIMENTAL ANIMAL

- The animal model for diuretic was wistar albino rats of either sex.
- The weight of animals range from 150-180 gms
- The animals were housed in polypropylene cages maintained under standard conditions that was 12 hours light/dark cycle, 25±30˚c, 35-60% relative humidity.
- All the rats were fed with standard raw chow and water ad libitum.
- Initially for the assessment of diuretic activity, the urine output, sodium, potassium and chloride levels in urine of each animal were measured.

STUDY OF THE DIURETIC ACTIVITY

- The animals are segregated into four groups of six animals each.
- The animals are deprived of food and water for 15 hours prior to the experiment.
- Before the oral administration of the test drug the animals were hydrated with normal saline 20ml/kg administrated orally through a pediatric nasogastric tube [70] .

EXPERIMENTAL DESIGN

- Group I - normal water serves and as the control group.
- Group II - treated with standard diuretic drug furosemide of 20mg/kg of body weight serves as the standard group.
- Group III - treated with test drug *MC*100mg/kg body weight suspended 2ml of water serves as the test group low dose.
- Group IV - treated with test drug *MC*200mg/kg body weight suspended with2ml of water serves as the test group high dose.

Immediately after administration of the test drugs, the animal were placed in fabricated metabolic cages individually to allow separation of urine and faeces. The bottom of metabolic cages was fixed with a glass funnel and the stem of the funnel was inserted in a measuring cylinder containing mineral oil. The presence of mineral oil in the measuring cylinder prevents loss of urine through evaporation. The urine was collected for 5^{th} hour and 24^{th} hour after administration control, standard and test drug. The bladder was emptied by pull the base of tail of each rat[71][72] .

OBSERVATION

- Animals are subjected to collect urine periodically by metabolic cages.
- Diuretic assay parameters were observed for each rat.
- The total volume of urine was measured.
- Urinary pH, urinary sodium excretion, urinary potassium excretion, urinary chloride excretions are determined. The concentration of sodium, pottassium and chloride levels excreted in the urine were measured by flame photometry[73] and the chloride concentration was estimated by titration with silver nitrate solution(N/50) using 3 drops of 5% potassium chromate as indicator [74]
- The data was analysed using one way analysis of variance (ANOVA).
- The statistical significance of the difference of the means was evaluated by Dunnet's multiple comparison test

4.4.3 ANTI-OXIDANT ACTIVITY OF *MUNTHIRIKAI CHOORANAM*

DPPH ASSAY (2, 2-diphenyl -1-picrylhydrazyl) in IN-VITRO

The radical scavenging activity of different extracts was determined by using DPPH assay according to [75] Chang et al[2001].The decrease in the absorption of the DPPH solution after the addition of an antioxidant was measured at 517 nm.

Ascorbic acid (10mg/ml DMSO) was used as reference.

PRINCIPLE

1,1-diphenyl-2-picryl hydrazyl is a stable free radical with red colour which turns yellow when scavenged. The DPPH assay uses this character to show free radical scavenging activity. The scavenging reaction between (DPPH) and an antioxidant (H-A) can be written as,

$$DPPH + [H\text{-}A] \rightarrow DPPH\text{-}H + (A)$$

Antioxidants react with DPPH and reduce it to DPPH-H and as consequence the absorbance decreases. The degree of discoloration indicates the scavenging potential of the antioxidant compounds or extracts in terms of hydrogen donating ability.

REAGENT PREPARATION

0.1mm DPPH solution was prepared by dissolving 4mg of DPPH in 100ml of ethanol.

PROCEDURE

Different volumes (1.25-20µg/µl) of *MC* extracts were made upto 40µl with DMSO and 2.96ml DPPH (0.1mM) solution was added. There action mixture was incubated in dark condition at room temperature for 20min. After 20min, the absorbance of the mixture was read at 517 nm. 3ml of DPPH was taken as control. The % radical scavenging activity of the *MC* extracts was calculated using the following formula,

$$\% \text{ inhibition} = \frac{\text{Control-Test}}{\text{Control}} \times 100$$

Ingredients of *Munthirikai Chooranam*

Fig 1.1 Vitis vinifera

Fig 1.2 Nymphaea alba

Fig 1.3 Coriandrum sativum

Fig 1.4 Vetiveri zizanioides

Fig 1.5 Piper nigrum

Fig 1.6 Zingiber officinale

Fig No.1. INGREDIENTS OF *MUNTHIRIKAI CHOORANAM*

Fig 1. 7 Piper longum

Fig 1.8 Glycyrrhiza glabra

Fig ***1.9 Plectranthus veetiveroides***

Fig 1.10Mesua nagassarium

Fig 1.11Cyperus rotandus

Fig 1.12Borneo camphor

Fig 1.13 Terminalia chebula

Fig 1.14Phyllanthus emblica

Fig1.15Terminalia chebula

Fig 1.16 Aegle marmelos

Fig 1.17 Oryza sativa

Fig 1.18 Santalum album

Fig 1.19 Cinnamomum tamla

Fig 1.20 Root of Piper longum

Fig 1.21 Phoenix dactylifera

Fig 1.22 Rock candy

Fig 1.23 Maranta arundinacea

Fig 1.24 Eletaria cardamom

PREPARATION OF *MUNTHIRIKAI CHOORANAM*

A. Pounding

B.Grinding

C.Munthirikai Chooranam

Fig.No .2 A & B Shows preparation of Munthirikai Chooranam

5. RESULTS AND DISCUSSION

Many studies have been carried out to bring the efficacy and potency of the drug "***Munthirikai Chooranam".*** The study includes Literary Collections, Organoleptic Characters, Physicochemical Analysis, Phytochemical Analysis, Acid-Base radical test, Bacterial load, Instrumental Analysis, Toxicological Study and Pharmacological Study. The drug "***Munthirikai Chooranam"*** has been selected for **Anti-Hypertensive** activity in reference with the text ***"Aathma Ratchamirtha Vaithiya Saara Sangiragam". pg no: 206.***

- Literary collections about the drug from various text books were done. Siddha literatures related to the drug state the evidence and importance of its utility in treating the hypertension.
- Botanical aspect explains the identification, description, active principle and medicinal uses of the plants.
- *Gunapadam* review brings the effectiveness of the drug in treating hypertension.
- Pharmaceutical review describes about the *Chooranam* and its properties.
- The pharmacological review explains about the methodology of Anti-Hypertensive Activity and the drugs used. Modern and Siddha aspect of the disease was also reviewed.

STANDARDISATION OF THE TEST DRUG

Standardization of the drug is more essential to derive the efficacy, potency of the drug by analyzing it by various studies. Following are the results of physicochemical and phytochemical analysis. Physical characterization and estimation of basic and acidic radicals have been done and tabulated. Toxicological results of the drug and pharmacological activity of the drug were derived. Its result has been tabulated and interpretation is given below. Thus it is to give a complete justification to bring the effectiveness in treating hypertension of the trial drug **"*Munthirikai chooranam"***. Siddha parameters of testing for *Chooranam,*

- *Chooranam* tends to be amorphous.
- It should never be damp.

- ❖ The fineness of the sieve should be number 100 mesh or still finer and the *Chooranam* gave the inference of amorphous and not damp.

ORGANOLEPTIC CHARACTERS

The following characters have been noted in *Munthirikai Chooranam*.

Table No.9. Organoleptic Characters

Colour	Brown
Odour	Pleasant
Taste	Bitter
Texture	Fine powder
Particle size	Completely pass through sieve no 88

Table No.10. Physicochemical Analysis

S. No	Parameter		Result
1.	Ph		5.02
2.	Total Ash (%)		5.33
3.	Water soluble Ash (%)		3.45
4.	Acid insoluble Ash (%)		1.20
5.	Loss on drying (%)		8.00
6.	Solubility		
	i.	Distilled water	Soluble
	ii.	Benzene	Soluble
	iii.	Chloroform	Soluble
	iv.	Carbon tetra chloride	Soluble
	v.	Xylene	Soluble
	vi.	Petroleum ether	Soluble

Interpretation

The physicochemical analysis of the drug result reveals the pH, Moisture, Solubility, Water soluble ash and Acid insoluble ash.

- **pH:** It is a measure of hydrogen ion concentration; i.e., acidic or alkaline in nature. 7.0 is a neutral, above 7.0 is alkaline and below are acidic. The pH of the drug **"***Munthirikai Chooranam***"** is 5.02 which is acidic in nature. In acidic medium these acidic drugs are better absorbed from the stomach and increases the bioavailability and effectiveness [76].
- **Ash**: Ash constitutes the inorganic residues obtained after complete combustion of a drug. Thus Ash value is a valid parameter to describe and to assess the degree of purity of a given drug. Total Ash value will determine the amount of minerals and earthy material present in the drug. The total value of *MC* is 5.33 which determine the absence of inorganic content.
- **Acid insoluble ash**: The acid insoluble ash value of the drug denotes the amount of siliceous matter present in the sample. The quality of the drug is better if the acid insoluble value is low. It is 1.20 for *MC*.
- **Water soluble ash:** Water-soluble ash is the part of the total ash content, which is soluble in water. It is 3.45 for *MC.*
- **Loss on drying**: The moisture present in the drug was established in loss on drying. The moisture content of the drug reveals the stability and its shelf-life. High moisture content can adversely affect the active ingredient of the drug. Thus low moisture content could get maximum stability and better shelf life. Loss on drying of *MC* is 8.00[77].

Phytochemical Analysis

Table No. 11. Phytochemical screening test

Phytochemical Test	MC Aqueous extract
Alkaloid	Present
Glycosides	Present
Saponin	Absent
Carbohydrate	Absent
Phytosterol	Absent
Phenol	Present

Phytochemical Test	MC Aqueous extract
Triterpene	Present
Flavonoid	Present
Quinone	Present
Protein	Present

Interpretation

Phytochemicals are natural bioactive compounds, found in plants and fibers, which act as a defense system against diseases and more accurately protects the body against diseases. The phytochemical analysis reveals that the presence of Alkaloids, Glycosides, Phenol, Triterpene, Flavanoids and Quinones[78].

Alkaloids

- Alkaloids possess Vasodilator and anti-arrhythmic effects
- Alkaloids are the active principles producing many essential effects in protecting the body [79].

Glycosides

- They also protect heart from complications
- They possess Anti-oxidant activity [80].

Phenols

- They possess rich Anti-Oxidant property and protect body from oxidative stress[81].
- Phenol groups are the essential part of many anti-oxidant compounds.

Triterpenes

- The triterpenes are the best immunomodulators and also have anti-oxidant property.
- They possess vasodilator, endothelial protection effect and anti-arrhythmic effect [82].

Flavonoids

- It is the most important group of polyphenol compounds in plants.
- They improve the endothelial and capillary function.
- Reduces the risk of atherosclerosis.
- They help in strengthening and protect the inner lining of blood vessels

- ❖ Flavonoids are a group of plant metabolites which provide health benefits through cell signaling pathways and antioxidant effects.
- ❖ Flavonoids can exert their Anti-Oxidant activity by scavenging the free radicals, by chelating metal ions or by inhibiting enzymatic systems which are responsible for free radical generation[83].

Quinones

- ❖ Quinone possesses anti-oxidant activity.
- ❖ Prevent cardiovascular diseases [84].

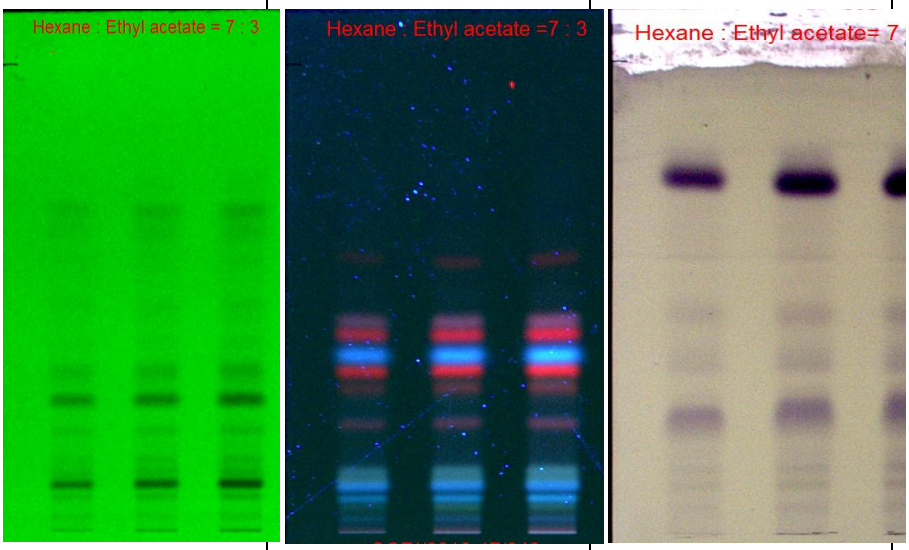
Protein

- ❖ They help in repairing cells and important for growth [85].
- ❖ A synergistic effect of all these alkaloids, glycosides, phenols, triterpenes, flavanoids, quinones increases the potency of the drug against hypertension.

TLC/HPTLC analysis of chloroform extract of *MC*

HPTLC analysis

Chloroform extract was applied in TLC aluminum sheet silica gel 60 (E. MERCK) and the plate was developed using the solvent system Toluene: Ethyl acetate (9:1).After development, the plate is allowed to dry in air and examined under UV - 254nm, 366 nm and visible light (Vanillin - Sulphuric acid)



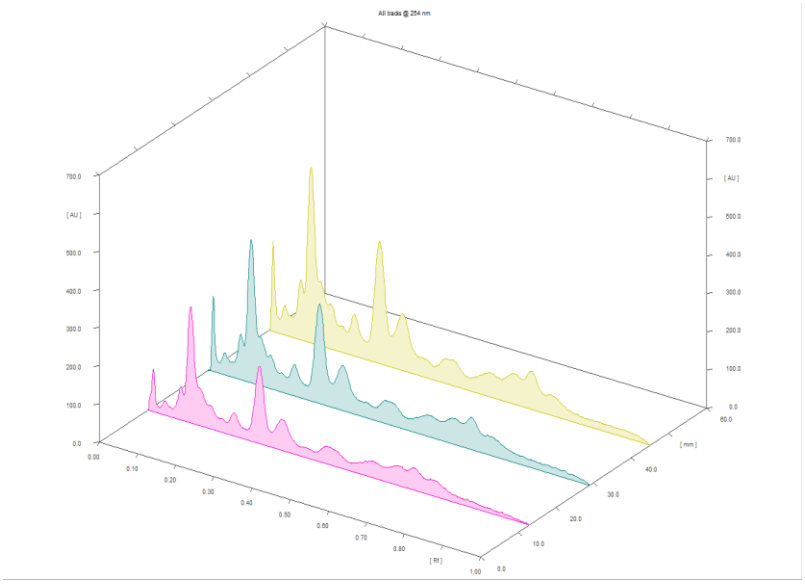
λ = 254 nm	λ = 366 nm	λ=520nm (Derivatized)

Fig.No.6.1. HPTLC plates of Chloroform Extracts

Table no :12 R_f Values for Chloroform Extract

Color	R_f value(s)	Color	R_f value(s)	Color	R_f value(s)
Green	0.04	Sky Blue	0.03	Violet	0.07
Green	0.08	Green	0.05	Green	0.12
Green	0.11	Sky Blue	0.08	Indigo	0.15
Green	0.22	Sky Blue	0.11	Violet	0.28
Green	0.29	Red	0.24	Violet	0.38
Green	0.34	Red	0.32	Violet	0.48
Green	0.50	Red	0.35	Dark	0.60
Green	0.65	Sky Blue	0.40	Violet	0.75
Green	0.69	Red	0.43		
		Red	0.58		

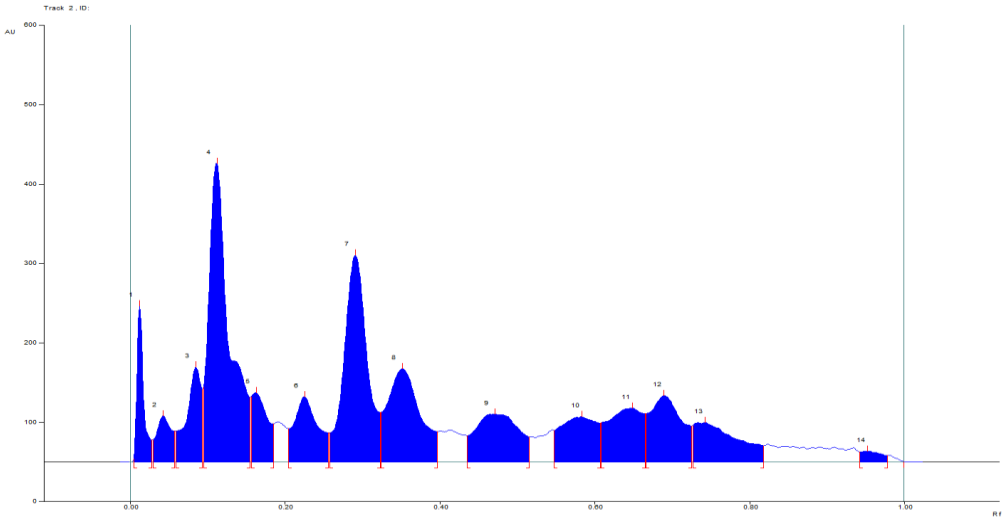
3D Chromatogram at 254 nm:



Graph.No.1. 3D Chromatogram

HPTLC finger print analysis for chloroform extract of *MC*

The finger print chromatogram was recorded at 254 nm. It showed 13 peaks of which peaks at Rf. And two were the major peaks and others were moderately smaller peaks.



Graph.No.2. HPTLC finger print for chloroform extract of *MC*

Peak Table at 254 nm

Table no.13.Chloroform extracts - Rf values in HPTLC finger print

Track 2, ID:

Peak	Start Position	Start Height	Max Position	Max Height	Max %	End Position	End Height	Area	Area %
1	0.00 Rf	3.4 AU	0.01 Rf	196.8 AU	12.06 %	0.03 Rf	27.5 AU	1545.3 AU	3.45 %
2	0.03 Rf	27.6 AU	0.04 Rf	58.1 AU	3.56 %	0.06 Rf	39.1 AU	1063.9 AU	2.37 %
3	0.06 Rf	39.1 AU	0.09 Rf	119.7 AU	7.34 %	0.09 Rf	91.2 AU	2159.8 AU	4.82 %
4	0.10 Rf	94.0 AU	0.11 Rf	376.2 AU	23.06 %	0.16 Rf	81.7 AU	9356.4 AU	20.88 %
5	0.16 Rf	82.3 AU	0.16 Rf	87.7 AU	5.38 %	0.19 Rf	48.1 AU	1674.6 AU	3.74 %
6	0.20 Rf	42.0 AU	0.23 Rf	82.5 AU	5.06 %	0.26 Rf	36.9 AU	2390.1 AU	5.33 %
7	0.26 Rf	36.9 AU	0.29 Rf	260.5 AU	15.97 %	0.32 Rf	62.3 AU	7225.2 AU	16.13 %
8	0.32 Rf	62.6 AU	0.35 Rf	117.5 AU	7.20 %	0.40 Rf	38.4 AU	4613.1 AU	10.30 %
9	0.44 Rf	33.4 AU	0.47 Rf	60.2 AU	3.69 %	0.52 Rf	31.8 AU	3221.4 AU	7.19 %
10	0.55 Rf	40.0 AU	0.58 Rf	57.2 AU	3.50 %	0.61 Rf	49.3 AU	2505.2 AU	5.59 %
11	0.61 Rf	49.5 AU	0.65 Rf	68.0 AU	4.17 %	0.67 Rf	60.9 AU	2844.7 AU	6.35 %
12	0.67 Rf	61.0 AU	0.69 Rf	83.7 AU	5.13 %	0.73 Rf	45.3 AU	3200.9 AU	7.14 %
13	0.73 Rf	45.8 AU	0.74 Rf	49.6 AU	3.04 %	0.82 Rf	20.6 AU	2649.7 AU	5.91 %
14	0.94 Rf	12.6 AU	0.95 Rf	13.9 AU	0.85 %	0.98 Rf	8.1 AU	350.2 AU	0.78 %

Interpretation:

- The quantitative estimation of compounds present in the *MC* has been performed by HPTLC. The method may be applied to identify the *MC* from other manufacturing process.
- They provide the identification of constituents, determination of impurities and quantitative determination of active substance present in the *MC* [86].
- The R_f value of the *MC* observed through these findings supports the better standardization of the drug.
- The present study revealed that *MC* showed best results in Toluene: Ethyl acetate (9:1). Solvent system. After scanning and visualizing the plates in absorbance mode at both 254 nm, 366 nm and visible light range, best results were shown at visible light range.
- TLC plate showed different colour, phytoconstituents of chloroform extract of *MC*. The bands revealed the presence of eleven greenish, four sky blue, five red, five violet, one indigo band showing the presence of alkaloids, glycosides, phenols, triterpenes, flavanoids, quinines.
- HPTLC study as recommended in this study provides a chromatographic fingerprint of phytochemicals and is suitable for confirming the identity and purity of medicinal plant raw material.
- The results from HPTLC finger print scanned for chloroform extract of *MC*. There are thirteen polyvalent phytoconstituents and corresponding ascending order of Rf values start from 0.00 to 0.94 in which highest concentrations of the phytoconstituents was found to be 23.06% and 15.97 % with its corresponding Rf value were found to be 0.10 and 0.26 respectively.

BIO CHEMICAL ANALYSIS

Table.No.14 Results of basic radicals studies of *MC*

S.No	Parameter	Observation	Result
1.	Test for Potassium	Formation of yellow colour precipitate	Positive
2.	Test for Calcium	Formation of white colour precipitate	Positive

S.No	Parameter	Observation	Result
3.	Test For Magnesium	Formation of white colour precipitate	Positive
4.	Test For Sodium	Appearance of intense yellow colour	Positive
5.	Test for Iron (Ferrous)	Appearance of blood red colour	Positive
6.	Test For Zinc	Formation of white colour precipitate	Positive

Interpretation

The results of basic radical test shows that the presence of Potassium, Magnesium, Calcium,Iron, Zinc, Sodium and absence of heavy metals such as lead, arsenic and mercury.

Potassium

- Potassium is important for muscle function especially relaxing the wall of blood vessels.
- This lowers the blood pressure and protects against muscle cramps.
- This protects against irregular heart beat.

Magnesium

- Magnesium also helps in regulation of blood pressure and relaxing the blood vessels

Calcium

- Calcium is important for healthy blood pressure because it helps in vasoconstriction and vasodilatation of blood vessels [87].

Sodium

- Sodium also important for regulation of blood pressure

Iron

- Iron helps in regulation of blood pressure
- Iron is essential for proper functioning of immune system [88].

Zinc

- Zinc have an Anti-oxidant property
- Helps to protect cells in the body from damage caused by free radicals[89]

Table no.15.Results of acid radical studies

S.NO	Parameter	Observation	Result
1.	Test for Sulphate	Formation of white precipitate	Positive
2.	Test for Chloride	Formation of white precipitate	Positive

Interpretation

The acidic radicals test shows the presence of Sulphate, Chloride, and Nitrate.

Chloride

- They helps in maintenance of proper blood volume, blood pressure, pH of blood and also helps in balance between ECF and ICF of cells [90].

Sulphate

- Nitric oxide derived from nitrate, which helps in reduction of blood pressure by the vasodilatation of blood vessels [91].

Table no.16.Availability of Microbial load in *MC*

MICROBES	DILUTION	RESULT
BACTERIA	**10^{-4}**	**7**
BACTERIA	**10^{-6}**	**5**
FUNGI	**10^{-2}**	**4**
FUNGI	**10^{-3}**	**2**

Interpretation

- The availability of bacterial load in the *MC* has been performed by Plate count-Agar plate technique.

- *MC* is a herbo-mineral drug prepared by plants and mineral. It is easy to get contamination if any contamination present in drug that decreases the potency and efficacy.

The contamination of *MC* has been examined by bacterial and fungal load.

Total bacterial load in 10^{-4} dilution is 7and 10^{-6} dilution is 5

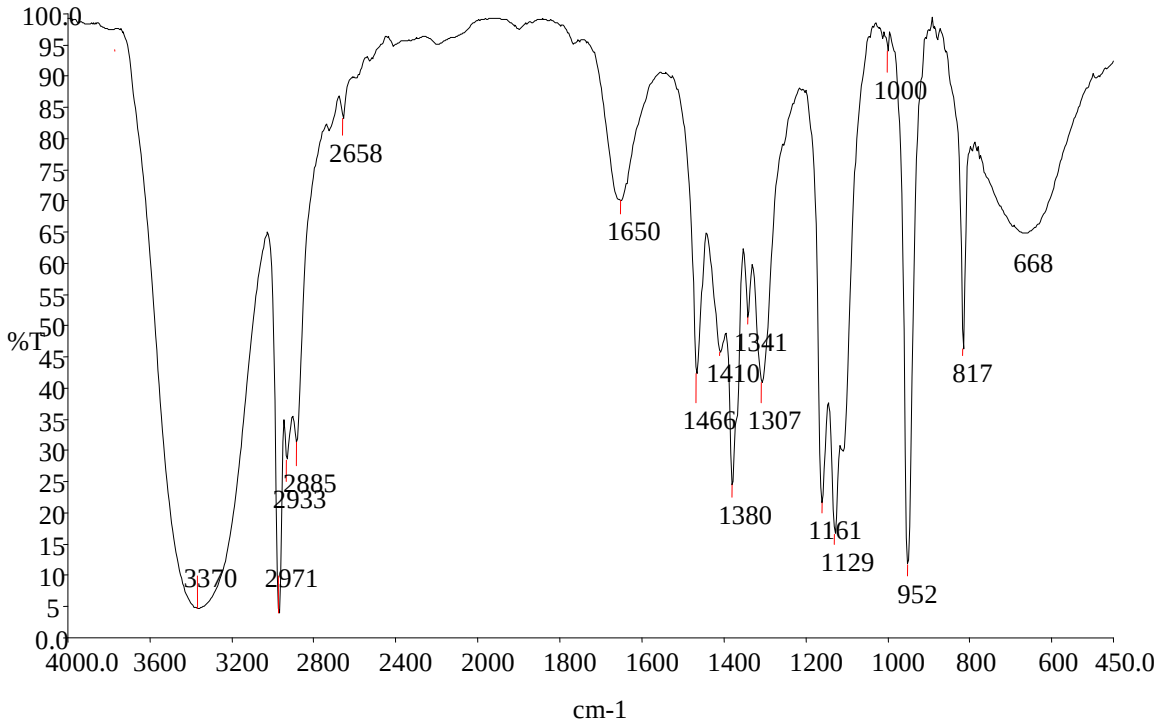
Total fungal load in 10^{-2} dilution is 4 and 10^{-3} dilution is 2

Here, the result shows presence of bacterial and fungal load in the trial drug (*MC*). They present within the normal limits.

INSTRUMENTAL ANALYSIS

FT-IR (Fourier Transform Infra Red spectroscopy)

Fourier Transform Infra-Red Spectroscopy (FTIR) analysis results in absorption spectra provide information about the functional group and molecular structure of a material. The results of Table no.17 and Graph no. 3 shows the presence of functional group and inorganic compounds of *MC*



Graph.no.3.FT-IR (Fourier Transform Infra Red)

Table no: 17 FTIR spectra of *MC*

Sl.No	Wave number (cm-1)	Vibrational modes of *MC* in IR region	Functional group
1	3370	N-H stretch	1^o,2^o amines, amides
2	2971	C-H Stretch	Alkanes
3	2933	C-H Stretch	Alkanes
4	2885	C-H Stretch	Alkanes
5	2658	H-C=O:C-H	Aldehydes
6	1650	C=O stretch	Acarbonyls
7	1466	C-H bend	Alkanes
8	1410	C-H bend	Alkanes
9	1380	C-F rock	Alkanes
10	1341	C-F rock	Alkanes
11	1307	C-O Stretch	Alcohols, carboxylicacids
12	1161	C-N Stretch	Aliphatic amines
13	1129	C-N Stretch	Aliphatic amines
14	1000	=C-H bend	Alkenes
15	952	O-H bend	Alkenes
16	817	C-Cl Stretch	Alkyl halide
17	668	C-Cl Stretch	Alkyl halide

FTIR Interpretation of *MC*

In the FT-IR Spectra analysis, this *MC* exhibits the peak value shows in at the wave number of 3370, 2971, 2933, 2885, 2658, 1650, 1466, 1410, 1380, 1341, 1307, 1161, 1129, 1000, 952, 817,668 having C=H Stretch, C=O amide, C=O Stretch, C-H bend, C-N Stretch, C-O Stretch, =C-H bending, C-Cl Stretch. This indicates the presence of some organic functional groups such as alcohol, alkane, acid, alkyl halide, amine, alkenes. The alkyl halide group is found in this sample predominantly.

SEM (SCANNING ELECTRON MICROSCOPE)

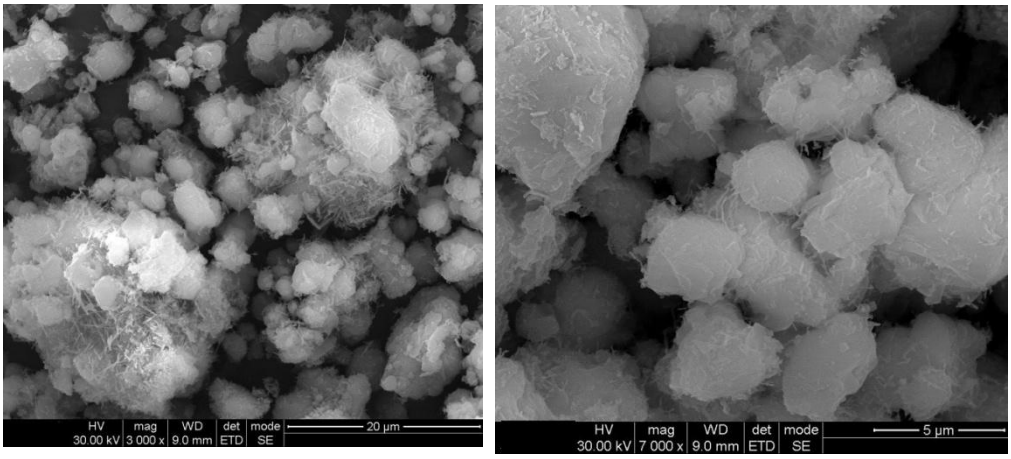
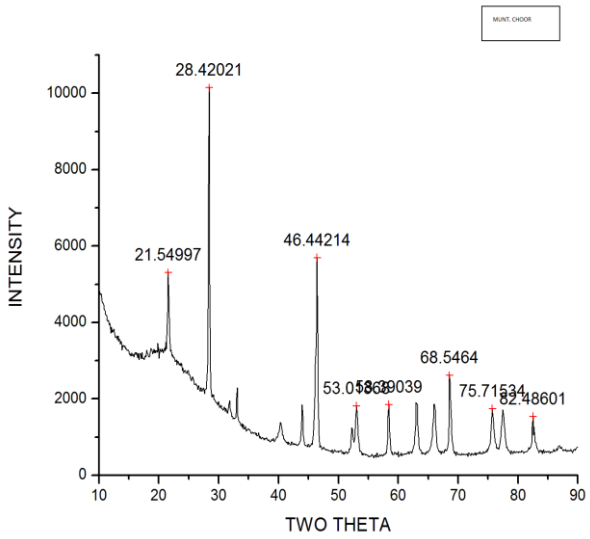


Fig No :7 SEM images of *MC*

The particle morphology can be identified through these SEM images of Siddha medicine *Munthirikai chooranam*. The particles are not spherical in shape. The size of the particles was approximately identified between 1 to 3 µm[92].

XRD:



Graph no.4 XRD image of MC

Interpretation

The structure, the size and shape of the particles are highly dependent on the route of synthesis and high lights the efficacy of the drug. The micro particles may enhance bio absorption of the drug.

The major diffraction peaks are identified after XRD analysis MC concluded that range nm is association with organic molecules probably plays an important role in making in biocompatible and nontoxic at therapeutic doses. Other elements present in MC act as additional supplement and possibly helps in increase the efficacy of the formulation [93].

ICP-OES (Inductively Coupled Plasma Optical Emission Spectroscopy):

The drug sample *MC* was analysed by the Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES) to detect the trace elements and other elements quantitatively. The result of ICP-OES is given on the

Table No.18. ICP-OES findings of MC

S. no	Elements	Detected levels
1.	Aluminium	BDL
2.	Arsenic	BDL
3.	Calcium	02.170 mg/L
4.	Cadmium	BDL
5.	Copper	BDL
6.	Iron	05.316 mg/L
7.	Mercury	BDL
8.	Potassium	53.401 mg/L
9.	Magnesium	01.384 mg/L
10.	Sodium	14.710 mg/L
11.	Nickel	BDL
12.	Lead	BDL
13.	Phosphorus	78.341 mg/L
14.	Sulfur	01.304 mg/L

BDL:Below Detectable Limit

1% = 10000ppm,

1ppm = 1/1000000 or 1ppm = 0.0001%

Table no.19 The toxic metals and the permissible limits

Heavy metals	WHO & FDA limits
Arsenic (As)	3ppm
Mercury (Hg)	1ppm
Lead (Pb)	10ppm
Cadmium (Cd)	0.30ppm

Interpretation :

The amount of presence of metals in Siddha herbo-mineral formulation *MC* was estimated through ICP-OES analysis study and their range is mentioned here. The presence of major heavy metal such as Mercury, arsenic, cadmium, Lead were identified as BDL which means their presence in the test drug is within the WHO permissible limits. So, the drug may be considered as safe for therapeutic use.

TOXICITY STUDY

Acute oral toxicity study of *MC*

Wistar albino rat was treated with the test drug *Munthirikai Chooranam* of single dose of 2000mg/kg in 2%CMC as suspention. This study was conducted as per the OECD guidelines. The result of acute toxicity of *MC* has been tabulated below.

Table 20: Dose finding experiment and its behavioral Signs of acute oral toxicity Observation done

S.No	Control Group	Observation	S.No	Test Group	Observation
1	Body weight	Normal	1	Body weight	Normally increased
2	Assessments of Posture	Normal	2	Assessments of posture	Normal
3	Signs of Convulsion Limb paralysis	Normal	3	Signs of Convulsion Limb paralysis	Absence of sign (-)
4	Body tone	Normal	4	Body tone	Normal
5	Lacrimation	Normal	5	Lacrimation	Absence

S.No	Control Group	Observation	S.No	Test Group	Observation
6	Salivation	Normal	6	Salivation	Absence
7	Change in skin Color	No significant color change	7	Change in skin color	No significant color change
8	Piloerection	Normal	8	Pilo erection	Normal
9	Defecation	Normal	9	Defecation	Normal
10	Sensitivity response	Normal	10	Sensitivity response	Normal
11	Locomotion	Normal	11	Locomotion	Normal
12	Muscle gripness	Normal	12	Muscle gripness	Normal
13	Rearing	Mild	13	Rearing	Mild
14	Urination	Normal	14	Urination	Normal

Table 21 (Observational study Results)

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.	**Control**	+	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2.	**2000mg**	+	-	-	+	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-

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.
(+ Present, - Absent)

Table 22 (Body weight Observation)

DOSE	DAYS		
	1	7	14
CONTROL	270.1±65.70	270.7± 09.71	270.6 ±2.10
HIGH DOSE	260.3± 4.44	260.4 ±7.12	260.2 ± 6.05

*N.S- Not Significant,**(p > 0.01), *(p >0.05), n = 10 values are mean ± S.D (One-way ANOVA followed by Dunnett's test)*

Table No.23. Water intake (ml/day) of wistar albino rats group exposed to *MC*

DOSE	DAYS		
	1	6	14
CONTROL	60 ± 1.62	60±1.10	60.1±1.04
HIGH DOSE	59.5±1.04	59.5±2.07	59.8±2.04

*N.S- Not Significant,**(p > 0.01), *(p >0.05), n = 10 values are mean ± S.D (One-way ANOVA followed by Dunnett's test)*

Table No.24. Food intake (gm/day) of wistar albino rats group exposed to *MC*

DOSE	DAYS		
	1	7	14
CONTROL	62.4±1.54	62.2±1.62	62.7±4.06
HIGH DOSE	64.0±2.24	64.4±2.10	64.6±2.70

*N.S- Not Significant,**(p > 0.01), *(p >0.05), n = 10 values are mean ± S.D (One-way ANOVA followed by Dunnett's test*

Interpretation

The results of acute toxicity studies shows the effect of drugs on different organ and system. The trial drug *MC* was given at the increasing dose level of 5mg, 50mg, 300mg, 2000mg in rats through oral administration.

There is no abnormal behavioural changes were observed. No mortality is seen. So can conclude there is no toxicity findings at the acute toxicity level determination. Based on OECD 423 the trail drug *MC* is considered non toxic up to the dose of 2000mg/kg.

Repeated Dose 28-Days Oral Toxicity (407) Study of *MC*

Table No.25. Body weight of Wistar albino rats group exposed to *MC*

DOSE	DAYS				
	1	7	14	21	28
CONTROL	282.2±05.64	282.2±10.04	282.4 ± 12.40	282.4±14.40	282.2 ± 12.10
LOWDOSE	280.7 ±57.75	279.4 ±4.19	281.3± 5.21	282 ±1.40	281.6± 6.16
MID DOSE	281.1± 1.22	280.2 ± 2.21	279.2± 1.42	280.2 ± 5.08	279.4 ± 13.12
HIGHDOSE	272.2± 2.41	273.4±3.17	274.8 ± 2.64	275.2 ± 4.18	276 ± 3.30

*NS- Not Significant, **(p > 0.01),*(p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)*

Table No.26. Water intake (ml/day) of Wistar albino rats group exposed to *MC*

DOSE	DAYS				
	1	6	14	21	28
CONTROL	56.4 ±2.34	56.2±1.07	56.7±1.30	56.8±1.10	56.4±1.70
LOW DOSE	63.6±1.81	63.6±2.43	63.6±1.72	63.7±2.36	63.7±1.30
MID DOSE	64.2±2.21	64.2±1.21	64.1±2.52	64.4±1.42	64.4±1.74
HIGH DOSE	58.2±3.40	58.2±1.42	58.4±1.44	58.6±1.78	58.8±2.62

*N.S- Not Significant, **(p > 0.01), *(p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)*

Table No. 27 Food intake (gm/day) of Wistar albino rats group exposed to *MC*

DOSE	DAYS				
	2	7	23	22	28
CONTROL	61±3.01	61.2±2.11	61.4±3.11	61.4.2±3.42	61±3.40
LOWDOSE	59.5±7.12	59.5±1.44	59.6±1.50	59.4±1.20	59.8±1.92
MID DOSE	60.2±6.70	60.2±2.20	60.6±2.24	60.6±1.46	60.7±1.74
HIGHDOSE	64.3±1.55	64.6±1.54	64.8±2.16	65.1±1.50	65.1±1.72

*N.S- Not Significant, **(p > 0.01), *(p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test*

Table No.28. Hematological parameters of wistar albino rats group expose to *MC*

Category	Control	Low dose	Mid dose	High dose
Haemoglobin(g/dl)	34.6±0.43	34.1±0.30	36.6±0.13	37.6±0.23
Total WBC (×10^3 l)	9.1±0.40	9.12±0.01	9.1±0.08	9.13±1.30
Neutrophils (%)	15.1±0.20	15.12±0.23	15.13±1.06	15.14±1.07
Lymphocyte (%)	80.10±1.36	80.10±1.20	80.12±1.24	81.20±1.34
Monocyte (%)	0.01±0.02	0.01±0.01	0.01±0.04	0.01±0.03
Eosinophil (%)	0.04±0.06	0.04±0.03	0.04±0.05	0.04±0.07
Platelets cells10^3/µl	1400.1±1.08	1400.3±4.84	1400.2±4.60	1400.4±6.32
Total RBC 10^6/µl	9.32±0.64	9.32±0.652	9.65±0.08	9.66±0.05
PCV%	34.60±0.8	34.63±6.23	34.6±1.31	34.8±8.22
MCHC g/dl	35.2±1.42	35.4±1.22	35.6±1.52	35.8±1.23
MCV fl(µm^3)	54.8±1.21	54.8±1.20	54.6±1.11	54.7±1.10

***(p > 0.01), *(p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)*

Table No.29. Biochemical Parameters of Wistar albino rats group exposed to *MC*

BIOCHEMICAL PARAMETERS	CONTOL	LOW DOSE	MID DOSE	HIGH DOSE
GLUCOSE (R) (mg/dl)	85.10±1.22	85.13±1.31	85.6±.04	85.7±6.20
T.Cholesterol(mg/dl)	105.10±3.10	98.15±2.20	96.10±1.17*	91.11±13**
TGC(mg/dl)	76.03±1.4	74.04±1.32	72.05±1.32**	69.06±1.04*
LDL	69.2±4.13	68.4±1.45	66.3±1.23	62.4±2.22**
VLDL	14.6±1.30	14.6±1.42	14.6±1.22	14.4±1.24

BIOCHEMICAL PARAMETERS	CONTOL	LOW DOSE	MID DOSE	HIGH DOSE
HDL	24.12±2.30	24.12±2.30	24.16±1.42	24.65±1.34
Ratio1(T.CHO/HDL)	5.1±1.10	5.1±1.20	5.1±1.30	5.1±1.60
Ratio 2(LDL/HDL)	2.85±2.13	2.85±1.20	2.85±2.20	2.85±04.02
Albumin(g/dL)	3.2±0.10	3.4±0.64	3.5±4.80	3.7±3.24

***(p > 0.01), * (p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)*

Table No.30. Renal function test of of Wistar albino rats group exposed to *MC*

PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE
UREA (mg/dl)	22.11±0.10	23.10±0.15	23.16±1.22	24.12±1.63
CREATININE(mg/dl)	0.6±0.02	0.7±0.03	0.7±0.05	0.9±0.09
BUN(mg/dl)	27.5±0.03	28.5±0.14	28.2±0.30	28.6±1.40
URIC ACID(mg/dl)	6.04±0.02	6.1±0.20	6.1±0.30	6.2±0.60

*NS- Not Significant, **(p > 0.01), * (p >0.05) , n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)*

Table No.31. Liver Function Test of of Wistar albino rats group exposed to *MC*

PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE
T.BILIRUBIN (mg/dl).	0.07±0.07	0.07±0.02	0.07±0.04	0.07±0.01
SGOT/AST(U/L)	132.1±1.33	132.2±0.32	132.4±1.33	132.6±1.43
SGPT/ALT(U/L)	99.10±1.44	99.14±1.10	99.24±1.64	99.23±0.20
ALP(U/L)	182.40±1.12	182.2±1.14	183±1.24	184.3±2.51
T.PROTEIN(g/dL)	6.5±0.13	6.5±0.21	6.7±0.32	6.7±0.34

*NS- Not Significant, ** (p > 0.01), * (p >0.05), n = 10 values are mean ± S.D (One way ANOVA followed by Dunnett's test)*

Discussion of Sub-acute toxicity study

Sub-acute oral toxicity repeated dose of *MC* on rats were conducted. All animals from the treated dose survived throughout the dosing period of 28 days. Various parameters were studied and the interpretation of the study result is discussed below.

Body weight

The result of the body weight of rats exposed to control and the trial drug of different dose groups exhibited overall mild weight gain throughout the dosing period of 28 days. The quantity of food taken by the animals from different dose groups and the control is comparably normal.

Haematological investigation interpretation

The haematological investigation results of the rats conducted on 28^{th} day after the repeated dose of the drug revealed the values of different parameters. There is a slight variation in the values of RBC count values in the dose group of 200 and 400 when compared with that of the control. The increase and decrease in the values obtained were all within the normal biological and laboratory limits.

Biochemical investigation interpretation

The biochemical investigations were conducted on 28^{th} day and the results are produced. The results revealed that there is no significant changes in the values of different parameters with that of the control. All the values were within the normal biological and laboratory limits.

Urine analysis

Urine analysis data of control group and the test groups of animals taken on 28^{th} day showed no abnormal results.

HISTOPATHOLOGY

Furthermore no dose related histo pathological changes were observed. Gross examination in necropsy and at microscopic examination revealed no changes that attribute to the administration of drug.

No abnormal changes observed in the behavior of rats.The haematological, biochemical parameters, body weight are all remains in the normal level. After the drug administrations, the histopathological findings were analyzed and those also revealed no abnormal findings.

This indicates that there is no observed level of toxicity findings at these fixed dose levels of low dose 100 mg and high dose 200 mg. Hence the study confirms that there is no observed level of toxicity in the 28 days repeated oral drug administration.

The above slides show the histopathology studies of sub-acute toxicity. There is no toxicological abnormality seen in the vital organs after administration of the test drug *MC*. Thus the safety of the drug is revealed, so that it can be administered for long time without any side effects.

Pharmacological Study

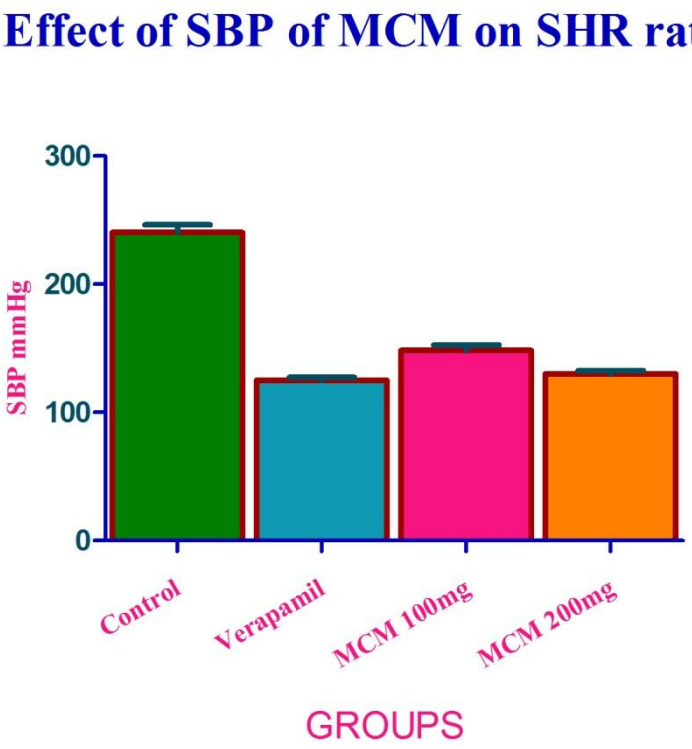
Evaluation of anti-hypertensive activity of Siddha compound *MC* in Spontaneous Hypertensive rats

Table No.32. Effect on Systolic Blood Pressure (SBP) of *MC* on various treatment groups on SHR rats

S.no	Treatment group	SBP (mm Hg)
1	Control	240.3±6.15
2	*MC* 100mg/kg b.w	148.4±4.24**
3	*MC* 200mg/kg b.w	130.2±2.42***
4	Verapamil hydrochloride12.5 mg/kg b.w	125.2±2.28***

Values represent mean ± SEM of 6 experiments.

** P< 0.05; ** P< 0.01; *** P < 0.001, treatment versus control group*



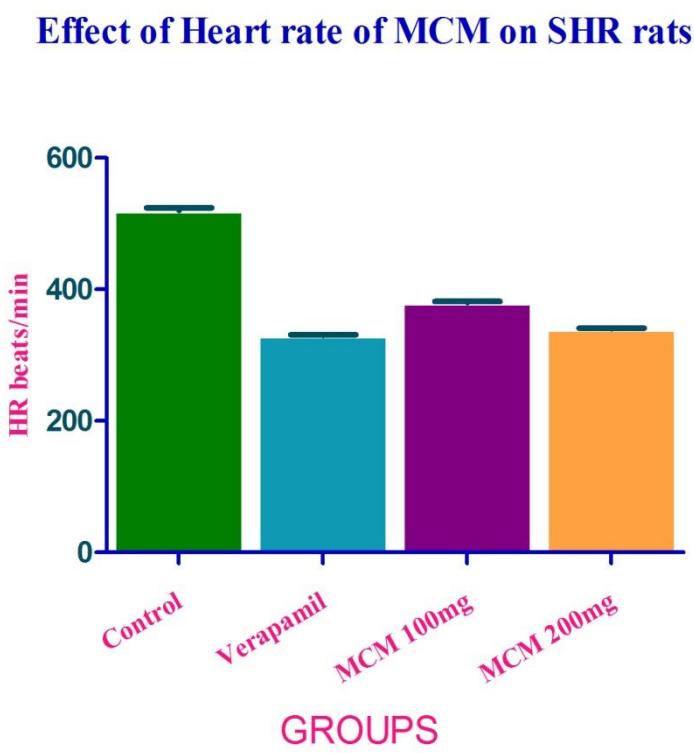
Graph No.5. **Effect of Systolic Blood Pressure (SBP) of *MC* on various treatment groups on SH-rats at 28th day**

Table No.33. Effect on Heart rate (HR) of MC on various treatment groups on SHR rats

S.no	Treatment group	Heart rate (beats/min)
1	Control	520.2±4.21
2	*MC*100mg/kg b.w	380.4±1.22**
3	*MC* 200mg/kg b.w	340.2±1.11***
4	Verapamil hydrochloride 12.5 mg/kgb.w	330.1±3.34***

Values represent mean ± SEM of 6 experiments.

** P< 0.05; ** P< 0.01; *** P < 0.001, treatment versus control group*



Graph No.6. Effect on Heart rate (HR) of *MC on* various treatment groups on SH-rats at 28th day

Interpretation:

- ❖ The systolic blood pressure and heart rate were recorded in the conscious animals by non-invasive tail cuff method.
- ❖ The results reveals that the *MC* exhibits antihypertensive effect in the form of significant lower in systolic blood pressure and heart rate after continued administration for 7 days.
- ❖ Heart rate was also decreased significantly in comparison to control
- ❖ The reduction in systolic blood pressure was measured and tabulated .The reading were compared with control group
- ❖ The systolic blood pressure on 7th day in group III treated with *MC* 200m/kg body weight showed moderate reduction in Systolic blood pressure compared with 7th day of control
- ❖ But the reduction Systolic blood pressure measured on 21st day of *MC* 200mg /kg body weight treated group showed significant reduction of Systolic blood pressure compared with 21st day of control group persistance highly significant

antihypertensive effect was noticed even after cessation of dosing 7 days earlier. This suggests absence of rebound phenomenon after withdrawal of the test drug *MC* which an advantage in the therapy of hypertension.

- The Siddha herbomineral formulation *MC*, according to their traditional uses and phytochemical constituents based on their therapeutic value leads to discovery of newer and safer alternative drug and herbal medicines having a protective role in cardiovascular diseases[94].

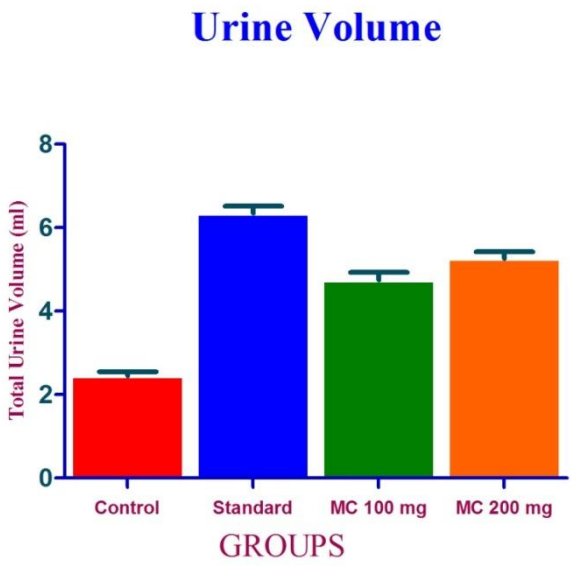
DIURETIC ACTIVITY:

Lipschitz et al was employed this method for the assessment of diuretic activity. The animals were deprived of food and water for 16tn hours prior to the experiment. Before oral administration of test drug the animals were dosed with 25ml/kg body weight of normal saline. The total volume of was measured. The urinary pH, sodium, potassium and chloride also determined. The result diuretic activity of *MC* was derived and tabulated below.

Table No.34. Effect on urine volume of *MC* on various treatment groups on SH-rats

Groups	Urine volume (ml)	Urine Ph	Diuretic Index (T/C)
Control	2.45±0.10	7.44±0.16	-
Standard	6.35±0.17***	7.50±1.28	2.59
MC 100	4.75±0.18**	7.22±0.40	1.93
MC 200	5.26±0.16***	7.42±0.52	2.14

Values represent mean ± SEM of 6 experiments. P< 0.05; ** P < 0.01; *** P < 0.001, treatment versus control group*

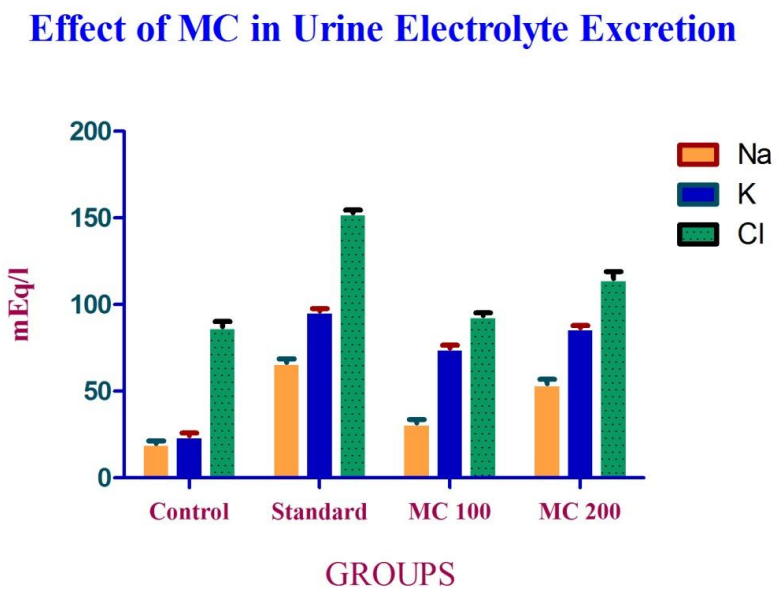


Graph No.3.Effect on urine volume of *MC* on various treatment groups on SH-rats

Table No.35. Effect on urine electrolyte excretion of *MC* on various treatment groups on SH-rats

Groups	Concentration of ions (mEq/l)			Saluretic Index			Na^+/K^+
	Na	K	Cl	Na	K	Cl	
Control	19.84±1.57	24.45±1.49	87.37 ± 2.9		-	-	
Standard	66.76±1.96**	96.18±1.65***	153.02±1.5***	3.36	3.93	1.75	0.69
MC 100	31.72±2.10*	75.12±1.42*	93.77±1.5*	1.59	3.07	1.07	0.42
MC 200	54.41±2.53**	86.73±1.12**	115.12±3.9**	2.74	3.54	1.31	0.62

Values represent mean ± SEM of 6 experiments. P< 0.05; ** P< 0.01; *** P < 0.001, treatment versus control group*

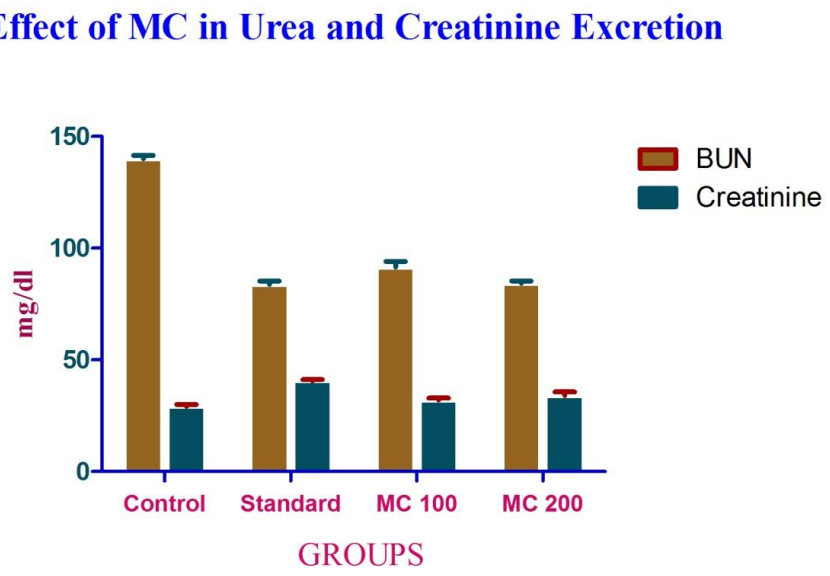


Graph No.4.Effect on urine electrolyte excretion of *MC* on various treatment groups on SH-rats

Table no.36.Effect on BUN and Creatinine excretion of *MC* on various treatment groups on SH-rats

Groups	BUN	Creatinine
Control	140.1±1.4	29.2±0.8
Standard	83.8±1.5**	40.7±0.5**
MC 100	91.6±2.5*	32.1±0.8*
MC 200	84.3±1.04*	34.05±1.6**

Values represent mean ± SEM of 6 experiments.* P< 0.05; ** P< 0.01; *** P < 0.001, treatment versus control group



Graph No.5.Effect on BUN and Creatinine excretion of *MC* on various treatment groups on SH-rats

Interpretation:

- The results of diuretic activity of *MC* showed marked increase in urine volume
- There was no evidence of dehydration of animals were found, observed normal at 5 hours and 24 hours interval.
- The standard diuretic Frusemide significantly increased in urine output when compared to normal
- The test drug *MC* at 100mg/kg b.w,200mg/kg b.w doses, showed statistically significant increase in the volume of urine with a dose dependant manner
- There is significant change in the pH level of urine
- Excretion of Na^+, Cl^- followed by similar pattern. Chloride excretion highly significant with two doses
- The diuretic activity of *MC* 5 hours after its administration was manifested in the form of an increase in urinary volume, which was highly significant with 100mg/kg b.w,200mg/kg b.w doses at 5 hours urine analysis
- Analysis of 24 hours post dosing urine sample revealed similar results with regards to urinary volume, sodium, chloride and potassium are observed in 5^{th} hour sample. That indicates a continuation of diuretic effect of *MC* upto 24 hours.

- An herbal preparation usually contains many active components (flavanoids, alkaloids, quinones etc)the phyto chemical analysis of *MC* shows significant presence of these compounds which either alone or in combination is responsible for the diuretic activity
- The diuretic study result of *MC* clearly indicates, that possesses potential diuretic activity on SH-rats and diuretics agents plays an important role in decreasing high blood pressure by decreasing plasma volume and also reducing cardiac work load and the oxygen demand[95] [96]

ANTI-OXIDANT STUDY (In-Vitro)

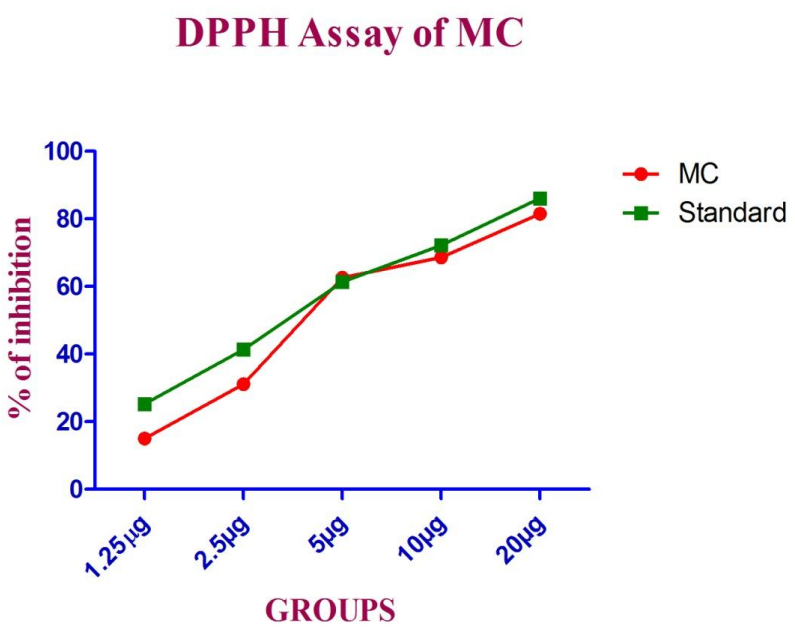
Different volumes (1.25-20µg/µl) of *MC* extracts were made up to 40µl with DMSO and 2.96ml DPPH (0.1mM) solution was added. There action mixture was incubated in dark condition at room temperature for 20min. After 20min, the absorbance of the mixture was read at 517 nm. 3ml of DPPH was taken as control. The % radical scavenging activity of the *MC* extracts was calculated using the following formula,

$$\% \text{ inhibition} = \frac{\text{Control-Test}}{\text{Control}} \times 100$$

Table No.37. DPPH Assay of *MC*

Sample concentration(µg/ml)	Absorbance		% of Inhibition	
	Drug	Standard	Drug	Standard
Control	0.5461	0.324	-	-
1.25	0.4641	0.242	15.015	25.30
2.50	0.3761	0.190	31.129	41.35
5	0.2040	0.125	62.644	61.41
10	0.1715	0.90	68.595	72.22
20	0.1009	0.45	81.523	86.11

µg/ml:microgram per millilitre. Drug : MC(1.25-20µg/µl). Standard: Ascarbic acid(10mg/ml DMSO)



Graph.No.6. DPPH Assay of *MC*

DPPH stable free radical method is an easy, rapid and sensitive way to survey the antioxidant activity of *MC* extract. The antioxidant molecules can quench DPPH free radicals by providing hydrogen atomor by electron donation and a colourless stable molecule 1, 1 diphenyl-2-picrylhydrazil is formed and as a result of which the absorbance at 517nm of the solution is decreased.

In the present study, the extract of *MC* was found to possess concentration dependent scavenging activity on DPPH radicals. The values of DPPH free radical scavenging activity of the *MC* extract was given in (Table.37). The extract of *MC* showed the highest DPPH scavenging activity (81.52%) at 20µg/m and the lowest percentage of inhibition (15.01%)at 1.25µg/ml. Ascorbic acid (Standard) showed highest percentage of inhibition (86.11%) at 20µg/ml and the lowest percentage of inhibition (25.30%)at1.25µg/ml. This indicated that % of inhibition increased within crease in concentration of both the standard and *MC* extract. The *MC* extract has more or less equal DPPH scavenging activity when compared to the standard. From the present study, it was concluded that the *MC* extract has a marked antioxidant activity at higher concentrations. Antioxidant compounds are highly present in plants and have protective effect s against diseases without reducing their therapeutic efficacy[97]. So, using of natural antioxidant as a protective strategy against cardiovascular related problems[98].

7. CONCLUSION

Herbals are always plays a significant role in the treatment of human diseases. ***Munthirikai Chooranam*** is a Siddha herbo mineral formulation indicated to treat hypertension, vertigo etc., Though herbal medicines are always considered as safe for human health, it is essential to scientifically validate the herbal medicines for global acceptance. The Siddha drug was subjected to many analytical studies to scientifically validate its nature especially its medicinal value.

The organoleptic characters of ***Munthirikai Chooranam*** has some features such as brown, aromatic, astringent, fine powder. The prepared drug statisfies the property of *Chooranam*. So the drug is easily soluble in nature. the aqueous extract of *Munthirikai Chooranam* confirms the presence of some phytochemical such as Alkaloid, Glycosides, Phenol, Triterpene, Flavonoid, Quinine, Protein in the sample. These identified phytocomponents may chiefly responsible for its therapeutic action. The HPTLC analysis of this sample shows the components in this sample free from impurities. These radicals such as Potassium, Calcium, Magnesium, Sodium, Iron, Zinc, Sulphate, Chloride are present in this *Munthirikai Chooranam.* These identified elements helps to treat diseases. In microbial load analysis the bacterial load and fungal load were found to be within the normal range.

Sophisticated analytical equipments helps to identify the molecular nature of the drug. Using FTIR analysis the functional group such as alcohol, alkane, acid, alkyl halide, aromatic, amine, alkenes were identified in this drug. The identified each and every functional group plays a significant impact in the treatment of this disease. SEM images shows the surface morphology of the drug and XRD findings reveals crystallinity of the drug. The presence of Aluminium, Arsenic, Calcium, Cadmium, Copper, Iron, Mercury, Potassium, Magnesium, Sodium, Nickel, Lead, Phosphorus, Sulphur Were Quantitatively Measured And The Presence Of Heavy Metals Such As Mercury, Arsenic, Lead, Cadmium were identified within the WHO permissible limits through ICPOES analysis. This clearly confirms that the drug can be administered in human to treat various diseases in a safe manner. These findings are creating the fingerprints for the Standardization of this Siddha drug *Munthirikai Chooranam*.

In toxicological studies, the acute and 28 days repeated oral toxicity study was carried out according to OECD guidelines to evaluate the safety of Siddha drug *Munthirikai Chooranam*. There is no mortality seen during acute toxicity study. No remarkable abnormal toxicity findings were observed during the conduction of 28 days repeated oral toxicity study in Siddha drug *Munthirikai Chooranam*. So, the toxicological study confirmed that the Siddha drug *Munthirikai Chooranam* is free from toxicity. So the drug is safe for human use.

The anti-hypertensive potential of *Munthirikai Chooranam* was confirmed by the pharmacological study conducted on SHR rats. The diuretic activity and anti oxidant property of *Munthirikai Chooranam* was proved by study conducted using Lipchitz method and DPPH assay respectively.

Hence through these research works, the safety of the drug and the anti-hypertensive, diuretic and antioxidant nature of the drug was evaluated. This Siddha herbo mineral drug *Munthirikai Chooranam* can helps to treat hypertensive patients.

SUMMARY

Munthirikai chooranam is a wonderful Siddha herbo mineral formulation which is indicated in Siddha texts as a best drug of choice to treat hypertension, vertigo etc., in order to scientifically evaluate this formulation, this drug undergoes physico chemical standardization, toxicity and pharmacological activity.

1. The organoleptic characters of the drug *Munthirikai Chooranam* was observed as brown, aromatic, astringent, fine powder, completely pass through sieve no 88 in nature.
2. The drug possess pH is 5.02, soluble in nature.
3. In phytochemical analysis the aqueous extract showed the presence of Alkaloid, Glycosides, Phenol, Triterpene, Flavonoid, Quinine, Protein in the sample *MC.*
4. The HPTLC analysis shows the fingerprints of the compounds present in the sample.
5. The presence of basic radicals such as Potassium, Calcium, Magnesium, Sodium, Iron, Zinc were identified in this *Munthirikai Chooranam.*
6. The presence of acid radicals such as Sulphate, Chloride, Nitrate were identified in this drug.
7. In microbial load analysis, the bacterial and fungal load found within the normal limits. This confirms that the drug is safe for clinical use.
8. The FTIR characterization of the Siddha medicinal compound *Munthirikai Chooranam* confirms that the presence of some functional groups such as alcohol, alkane, acid, alkyl halide, aromatic, amine, alkenes.
9. SEM analysis confirms the surface morphology of the drug.
10. The XRD analysis confirms the crystalline nature of the drug.
11. The results of ICPOES study shows the presence of Aluminium, Arsenic, Calcium, Cadmium, Copper, Iron, Mercury, Potassium, Magnesium, Sodium, Nickel, Lead, Phosphorus, Sulphur. The heavy metals such as Lead, Arsenic, Mercury, Cadimium were identified as within the WHO permissible limits. This clearly explains that the drug *Munthirikai Chooranam* is safe for therapeutic usage.

12. There is no toxicity findings at the acute toxicity level determination. Based on OECD 423 the trail drug *Munthirigai Chooranam* is considered non toxic up to the dose of 2000mg/kg.
13. In 28 days repeated dose oral toxicity study in rats to evaluate the toxicity findings of the drug, the haematological, biochemical parameters, body weight are all remains in the normal level. After the drug administration, the histopathological findings were analyzed and those also revealed no abnormal findings. This indicates that there is no observed level of toxicity findings at these fixed dose levels of low dose 100 mg and high dose 200 mg. Hence the study confirms that there is no observed level of toxicity in the 28 days repeated oral drug administration. From toxicological study results the drug is free from toxic effects for human use at therapeutic dose level.
14. In SHR rats, the drug *Munthirikai Chooranam* reduces the blood pressure and heart rate in a dose dependant manner. This clearly explains that this Siddha medicinal compound having strong anti-hypertensive potential.
15. In DPPH assay , the drug *Munthirikai Chooranam* possess potent antioxidant property comparably higher than the synthetic antioxidant BHT. This confirms the antioxidant nature of the drug.

These research works confirms that the drug is safe for clinical use. And the studies possess that the Siddha herbo mineral formulation ***Munthirikai Chooranam*** has anti hypertensive, diuretic and anti oxidant property.

FUTURE SCOPE

Munthirikai Chooranam is a Siddha medicinal compound has no toxic effects and it has anti-hypertensive, diuretic and antioxidant property. The preparation of the drug is simple and cost effective. The research findings will be helpful in getting the knowledge regarding the molecular nature of the drug. The drug has promising therapeutic potential to manage hypertension which is highly prevalence nowadays. Followed by these research findings, if clinical trial will be conducted to manage hypertension in future this drug *Munthirikai Chooranam* can contribute a lot to the society.

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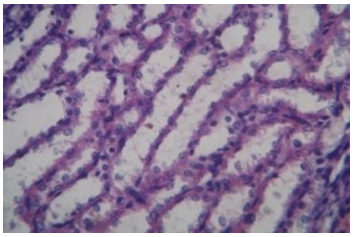
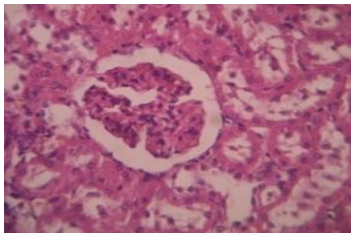
HISTOPATHOLOGY-28 DAYS REPEATED ORAL TOXICITY STUDY

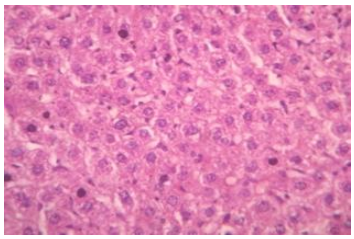
Control Group **High dose**

Control high

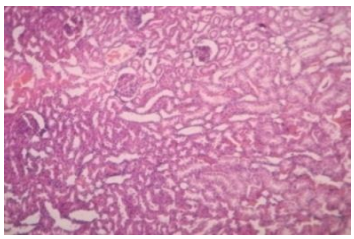


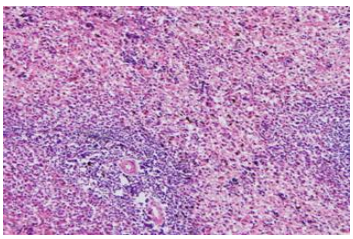
KIDNEY





LIVER





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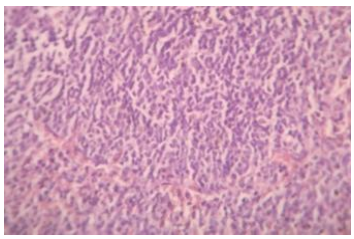

Fig.No.8 Histopathology images of *Munthirikai Chooranam*

The Tamil Nadu Dr.M.G.R.Medical University

69,Anna Salai,Guindy,Chennai - 600 032.

This Certificate is awarded to Dr/Mr/Mrs.....M. Sumithra.....

for participating as ~~Resource~~ ~~Person~~ / Delegate in the Eighteenth Workshop on

" RESEARCH METHODOLOGY & BIOSTATISTICS "

FOR AYUSH POST GRADUATES & RESEARCHERS

Organized by the Department of Siddha

The Tamil Nadu Dr. M.G.R. Medical University from 20 th to 24 th July 2015.

Dr.N.KABILAN, M.D.(Siddha)
READER,DEPT.OF SIDDHA

Prof. **Dr.P.ARUMUGAM,** M.D.,
REGISTRAR i/c

Prof. **Dr.D.SHANTHARAM,** M.D., D.Diab.,
VICE - CHANCELLOR

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SIDDHA CENTRAL RESEARCH INSTITUTE
(Central Council for Research in Siddha, Ministry of AYUSH, Govt. of India)
Anna Govt. Hospital Campus, Arumbakkam, Chennai – 600106
Phone: 044-2621 4925, Fax: 044-2621 4809

20.1.2017

CERTIFICATE

Name of the student: Dr. M. Sumithra, III year PG student, Gunapadam, Government Siddha Medical College, Arumbakkam, Chennai-600 106.

Name of the sample: Munthirikai Chooranam

Name of the Experiment	I	II	Mean
Loss on drying(at 105°C)	8.05 %	7.95 %	8.00 %
Total ash	5.35 %	5.30 %	5.33 %
Water soluble ash	3.45 %	3.45 %	3.45 %
Acid insoluble ash	1.20 %	1.20 %	1.20 %
Water soluble extractive	24.00 %	23.80 %	23.90 %
Alcohol soluble extractive	23.70 %	23.40 %	23.55 %
pH value (10%)	5.02	5.02	5.02
TLC/HPTLC	Report Enclosed		

(R. Shakila)
Research Officer (Chemistry) & Head,
Department of Chemistry

(Dr. P. Elankani) 21/01/17
Research Officer (Scientist II) (Siddha)
for Assistant Director (Siddha) I/c

C.L.BAID METHA COLLEGE OF PHARMACY

(An ISO 9001-2000 certified institute)

Jyothi Nagar, Old Mahabalipuram Road

Thoraipakkam, Chennai – 600 097

CERTIFICATE

This is to certify that the project entitled, **Toxicological and Pharmacological study on MUNTHIRIKAI CHOORANAM & ASOKA POO CHOORANAM** ***(Saraca asoca - flower)*** in rats submitted in partial fulfilment for the degree of **M.D. (siddha)** was carried out at C.L. Baid Metha college of Pharmacy, Chennai-97, in the Department of Pharmacology during the academic year of 2016-2017. It has been approved by the **IAEC**

No: IAEC/XLVIII/11/CLBMCP/2016

Dr.P.Muralidharan

IAEC Member Secretary

C.L. BAID METHA COLLEGE OF PHARMACY,
THORAIPAKKAM, CHENNAI - 600 097.

C.L. Baid Metha College of Pharmacy ★ CHENNAI-97 ★ Thoraipakkam