PRECLINICAL VALIDATION OF ANTI-ANXIETY, ANTI-DEPRESSANT AND ANTI-CONVULSANT ACTIVITY OF CLASSICAL SIDDHA DRUG "*KANDATHIRIKA CHOORANAM*" IN ANIMAL MODEL

The dissertation submitted by

Dr.C.KANIMOZHI

Reg No:321412106

Under the Guidance of

Dr. R. KAROLIN DAISY RANI, M.D(S).,

Dissertation submitted to

THE TAMILNADU DR. MGR MEDICAL UNIVERSITY

CHENNAI-600032

In partial fulfilment of the requirements

For the award of the degree of

DOCTOR OF MEDICINE (SIDDHA)

BRANCH-II-GUNAPADAM

POST GRADUATE DEPARTMENT OF GUNAPADAM

THE GOVERNMENT SIDDHA MEDICAL COLLEGE

ARUMBAKKAM, CHENNAI -106

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ACKNOWLEDGEMENT

First and foremost I would like to thank the Almighty for showering his blessings to complete this dissertation successfully.

I would like to acknowledge and extend my cordial credit to the following persons who have helped me to complete of this dissertation study fruitfully.

I express my sincere thanks to our Principal **Prof**. **Dr.K.Kanagavalli M.D(S)**, Govt. Siddha Medical College, Arumbakkam, Chennai-106 for her permission to perform this study and also for her valuable ideas and support throughout the course of the study.

I take this opportunity to express my profound gratitude and deep regards to my guide **Dr.R.Karolin Daisy Rani M.D(S)**, for her exemplary guidance, monitoring and constant encouragement throughout the course of this dissertation. The blessing, help and guidance given by her time to time shall carry me a long way in the journey of life on which I am about to embark.

I wish to express my profound gratitude to **Prof. Dr.V.Velpandian M.D(S), Ph.D.,** Head of the Department of PG Gunapadam, Govt. Siddha Medical College, Arumbakkam, Chennai-106 for his valuable guidance, encouragement and offered good advice during the course of my study.

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

I express my sincere thanks to **Dr.M.D.Saravanadevi, M.D(S)., Dr.K.Rajammal Devi Sourubarani, M.D(S)., Dr.K.Nalina Saraswathi, M.D(S)., Dr.S.Shankar, M.D(S)., Dr.C.Lakshmana Raj, M.D(S).,** Govt. Siddha Medical College, Chennai for their valuable guidance, back-up for completion of my study.

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 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.

I express my special thanks to **Mrs. R. Shakila, M.Sc.,** Research officer, Chemistry, Central Research Institution of Siddha, Chennai for his valuable precious help to conduct Physico chemical, Phytochemical and chemical analysis of the drug and help towards the successful completion of the entire study.

I extend my thanks to **Dr.R.Murugesan, Ph.D.,** IIT Madras, for giving permission to carry out instrumental analysis.

I am also thankful to **Mr.M.Selvaraj, M.Sc.,** H.O.D**,** Biochemistry dept, for helping me to prepare the test sample for instrumental analysis and biochemical analysis of the trial drug.

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 staffs** 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.A.Chandramohan, Mother Mrs.C.Gandhimathi, Husband Dr.A.Ananth B.S.M.S.,** 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.

GOVT. SIDDHA MEDICAL COLLEGE, CHENNAI-106

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **Preclinical Validation of Anti-Anxiety, Anti-Depressant and Anti-Convulsant activity of classical Siddha drug "*KANDATHIRIKA CHOORANAM*" in Animal Model** is a bonafide and genuine research work carried out by me under the guidance of **Dr.R.KAROLIN DAISY RANI M.D(S).,** Post Graduate Department of *Gunapadam*, Govt. Siddha Medical College, Arumbakkam, Chennai-600 106 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: Chennai **C.KANIMOZHI**

GOVT.SIDDHA MEDICAL COLLEGE, CHENNAI-106

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **Preclinical Validation of Anti-Anxiety, Antidepressant and Anti-Convulsant activity of classical Siddha drug "*KANDATHIRIKA CHOORANAM*" in animal model** is submitted to the TamilnaduDr.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 C.Kanimozhi 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: Chennai **Dr. R. KAROLIN DAISY RANI MD (S).,**

ENDORSEMENT BY THE HOD, PRINCIPAL OF THE INSTITUTION

This is to certify that the dissertation entitled **Preclinical Validation of Anti-Anxiety, Antidepressant and Anti-Convulsant activity of classical Siddha drug "*KANDATHIRIKA CHOORANAM*" in animal model** is a bonafide work carried out by **C. Kanimozhi** under the guidance of **Dr.R.KAROLIN DAISY RANI M.D(S),** Post Graduate Department of Gunapadam, Govt. Siddha Medical College, Chennai - 106.

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

Date : **Date :**

Place : Chennai **Place :** Chennai

ABBREVIATIONS

ADIS	**:**	**Anxiety Disorders Interview Schedule**
ANOVA	**:**	**Analysis Of Variance**
AYUSH	**:**	**Ayurveda, Yoga and Naturopathy, Unani, Siddha and Homoeopathy**
BDNF	**:**	**Brain Derived Neurotropic Factor**
BUN	**:**	**Blood Urea Nitrogen**
CNS	**:**	**Central nervous system**
CPCSEA	**:**	**Committee for the Purpose of Control Supervision and Experiments on Animals**
CSF	**:**	**Cerebro Spinal Fluid**
DPPH	**:**	**1,1-Diphenyl-2-picrylhydrazyl**
ED_{50}	:	**Effective Dose**
EPM	**:**	**Elevated Plus Maze**
FST	**:**	**Forced Swim Test**
FTIR	**:**	**Fourier Transform Infrared Spectroscopy**

HPTLC	**:**	**High Performance Thin Layer Chromatography**
IAEC	**:**	**Institutional Animal Ethical Committee**
ICPOES	**:**	**Inductively Coupled Plasma Optical Emission Spectroscopy**
IIT	**:**	**Indian Institute of Technology**
ISM	**:**	**Indian System of Medicine**
KCM	**:**	***Kandathirika Chooranam***
MAO	**:**	**Monoamine Oxidase Inhibitors**
mCPP	**:**	**1-(3-Chlorphenyl) Piperazine**
MES	**:**	**Maximal Induced Electroshock Seizure**
NEOR	**:**	**Neuroticism Extraversion and Openness Scale**
OGTT	**:**	**Oral Glucose Tolerance Test**
PTSD	**:**	**Post Traumatic Stress Disorder**
PTZ	**:**	**Pentylenetetrazole**
PCV	**:**	**Packed cell volume**
RBC	**:**	**Red blood corpuscles**
SCMC	**:**	**Sodium Carboxyl Methyl Glucose**
SEM	**:**	**Scanning Electron Microscope**

SNRIs	**:**	**Selective Serotonin Norepinephrine Reuptake Inhibitors**
SSRIs	**:**	**Selective Serotonin Reuptake Inhibitors**
TCA	**:**	**Tricyclic Antidepressants**
TLC	**:**	**Thin Layer Chromatography**
TST	**:**	**Tail Suspension Test**
UV	**:**	**Ultra violet**
WHO	**:**	**World health organization**
XRD	**:**	**X-ray Power Diffraction**
5HT	**:**	**5 Hydroxytryptymine**

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1. INTRODUCTION

Neurological disorders that can affect the brain and entire neurological pathway it results in dysfunction. Mental psychiatric illnesses are which produces primarily, thought abnormalities, emotional behaviors and functional impairment[1]. Anxiety is a frequent normal reaction to stressful conditions. It may frequently co-occurs with depression annoyance and frustration in day to day activities[2]. Depression is a sadness of mood and more pervasive experience of negative rumination that is typified by low energy levels and lack of interest in pleasurable activities[3]. Convulsion is an unexpected involuntary contraction of the muscles that may occur in an isolated muscle or throughout the whole body. It is an exaggerated activity of several brain neurons [4].

Many brain structures and chemicals are processes at works in the brain during fear or anxiety arousing conditions. These are the products of unconscious stimuli which they have appears in initial sensory perception[5]. Adrenaline, dopamine, serotonin and noradrenaline are neurotransmitters. Especially noradrenaline and serotonin are helps to control the emotional behaviors. Serotonin is also involved in the anxiety, panic and other emotional behaviors[6].

Altered thalamocortical rhythms may results in generalized seizures. Thalamic relay neurons receive ascending inputs from the neocortical pyramidal neurons and spinal cord. Activation of T-calcium channels in thalamic relay neurons are regulated by the NRT neurons[7].

According to the World Health Organization (WHO) nearly 9% of the subjects were diagnosed with anxiety neurosis. Within countries, the overall one year prevalence of mental disorders ranges from 4% to 26%[8]. The overall of prevalence in India neurosis and stress related disorders affected 3.5% of the population[9].

Epidemiological studies consisting of 33572 persons in 6550 families yielded an estimate prevalence rate of 58.2 per 1000 population. Organic psychosis 0.4, schizophrenia 2.7, mental retardation 6.9, epilepsy 4.4 and the other neurotic disorders 20.7. The findings indicated that there are 1.5 crore of people affected by severe mental disorders in India[10].

Untreated depression can be leads to emotional and health problems that affects the day to day life. Depressive condition which can leads to heart diseases, diabetes, increased intake of Alcohol, relationship difficulties, panic disorders, suicidal feelings or attempts[11]. Epilepsy leads to short term memory loss, obsessions, violent behavior, hypo-sexuality, skull or vertebral fractures suffocation, pulmonary edema and myocardial infarction [12].

Prolonged use of anti-anxiety and anti-depressant drugs causes blurred vision, difficulty in urination, hallucinations, increased ocular pressure, changes in the level of consciousness, unstable blood pressure, reduced heart rate and disturbed heart rhythm, decreased sweating, reduced sexual desire, withdrawal symptoms, coma[13] and the anticonvulsants develops endocrine disorders, visual defects, hepatotoxicity, pancreatic toxicity, erectile dysfunction, hearing loss, suicidal thoughts, neuropathic pain, behavioral problems and memory problems[14].

Ancient Tamil system of medicine is namely Siddha system. Concepts of this system on the *tridhos has* and *panchaboothas*[15].

Siddha system is more comprehensive and is classified into eight categaries; *vaadham (*chemicals), *jnanam* (scientific), *yogam* (spiritual), *maruthuvam* (medical), *anitham* (astrology), *vaidikam* (sacrifial), *mantram* (psychic) and *marmam* (martial) As it is highly integrated system, *maruthuvam* gives a detailed description of mental disorders. This system has a two-way interactive model of the mind-body relationship[16].

Physical illnesses are accompanied by psychological symptoms. The comprehensive division of psychotic disorders referred to as *Unmadam* into 18 *Kirikas*. The "*KirikaiNool*64" of *Agasthiar* is the noteworthy book of Siddha system. It describes about 18*Kirikas*.*Siddhars*believed that the diseases are occurred due to sleeplessness and breaking of varma points [17].Similar classification of mental illnesses was given by Sage *Yoogi*in *Yoogi chinthamani*-800[18].

KandhagaParpam, Abraga Parpam, PerandaParpam, Kaandha Chendhooram, Rasa Chendhooram, BrahmiNei, Vallarai Nei are used to treat the neurological disorders in the Siddha system. A valuable resource against these neurotic disorders is available in the Siddha system. From that I find a better way to treating the soul and mind without side effects from the medicines mentioned in Siddha literature for reducing neurotic conditions.

Siddhars recommended several medicines for mental illness. One of such medicine is "*Kandathirika Chooranam*" for treating mental illness in Siddha literature *Aasthiyar Vaithiya Sindhamani Venba 4000 Enum Mani 4000-part 1* it was aimed to exclusively reveals anti-anxiety, anti-depressant and anticonvulsant activities.

2. AIM AND OBJECTIVES

Aim :

The aim of this dissertation is to do a scientific review, to validate the safety and efficacy of the *Kandathirika Chooranam* for *Paithiyam* by preclinical studies.

Objectives:

Besides the scientific study, the basic concepts of Siddha science are also our aim. Hence, the following methodology was adopted to evaluate the safety and efficacy of the test drug.

- Collection of various Siddha and modern literature relevant to the study.
- Preparation of the drug according to the classical Siddha literature.
- Identification of the drugs in the ***Kandathirika Chooranam.***
- Physicochemical and phytochemical investigation of the test drug.
- Evaluate bio-chemical analysis of the test drug to derive acidic and basic radicals.
- To estimate the present of elements, functional groups and particle size through instrumental analysis of the trial drug.
- Evaluation of the Acute and 28 days repeated dose oral Toxicity of test drug according to OECD guidelines.
- Evaluation of pharmacological study of the drug through the following activities
    - Evaluation of Anti-Anxiety activity
    - Evaluation of Anti-depressant activity
    - Evaluation of Anti-Convulsant activity of ***Kandathirika Chooranam***.

3. REVEW OF LITERATURE

3.1. DRUG REVIEW

3.1.1. GUNAPADAM ASPECT

"KANDATHIRIKA CHOORANAM"

"இஞ்சிபலம் நாற்பதுசீ ரோகணந் தேசாவரங்கள்
மிஞ்சுசுக்கு சீரகமாம் விள்வகைக்கோ- ரஞ்சுபலம்
ஏலமிள கொன்றுக் கேஏந்தும் பலமுக்காலாம்
மாலவங்கத் தோலிவையா மன்.

மன்னியிடு நெல்லிமுள்ளி வந்தவகைக் கரையாம்
துன்னுபலஞ் சாதிக்காய் சொல்மதுரம் – சொன்னசிறு
நாகப்பூ நல்லவங்கம் நற்றாளி கள்வறுத்துக்
கூகைநீரோர் வகைக்காம் கூறு.

கூறுபலம் காலாம்நெய் கொள்படியும் தானரையாம்
ஊறும் சருக்கரையும் ஓர்பத்தாம் – ஏறுபலம்
முந்தவிஞ்சி தானரிந்து முசுநெய்யில் தான்வறுத்துத்
தொந்தமுடன் இடித்தே தூள்.

தூளும்பின் கற்கத்தூள் தோன்றவொன்றாய்த் தான்கலந்தா
லாளுங்கண் டாத்திரிக மாம்பெயராம் – கேளுமினி
உண்ணவன்னி மந்தம்போம் உட்டிணமாம் வாயுசயம்
நண்ணும் பைத்தியம்போம் நாடு"

-அகத்தியர் வைத்திய சிந்தாமணி வெண்பா 4000 எனும் மணி 4000-பாகம்1[19]

The following are the ingredients quoted in this song

- *Zingiber officinale – Inji*
- *Picrorhiza scrophulariflora – Kaduku rohini*
- *Piper longum – Thippili moolam*
- *Zingiber officinale – Chukku*

- *Cuminum cyminum – Chirakam*
- *Elettaria cardamomum– Elam*
- *Piper nigrum – Milagu*
- *Cinnamomum tamala – Lavanga patthiri*
- *Phyllanthus emblica – Nelli mulli*
- *Myristica fragrans– Jathi patthiri*
- *Mesua nagasarium – Sirunaga poo*
- *Abies spectabilis – Thalisa patthiri*
- *Syzygium aromaticum – Lavangam*
- *Maranta arundinaceae – Koogai neeru*
- *Nei*
- *Saccharum officinarum– Sarkarai*

Inji

Scientific name: *Zingiber officinale*

Other names : *Allam, Aarthragam, Aathiragam, Elakottai, Narumarupu mathil*

Vernacular names:

Tamil	:	Inji
English	:	Green ginger
Telugu	:	Allamu
Malayalam	:	Inji, chukka
Kannadam	:	Hashi- shunti, vona- sunthi

Parts used: Rhizome

Actions:

- Carminative
- Stomachic

- Sialogogue
- Digestive
- Rubefacient

General properties:

“ இஞ்சிக் கிழங்குக் கிருமல்ஜயம் ஓக்காளம்
வஞ்சிக்குஞ் சன்னிசுரம் வன்பேதி- விஞ்சுகின்ற
சூலையறும் வாதம்போந் தூண்டாத தீபனமாம்
வேலையுறுங் கண்ணோய்.”

-அகத்தியர் குணவாகடம்[20]

Uses:

- It cures Cough, Tuberculosis, Diarrhoea, Abdominal pain and Vomiting.

Kaduku rohini

Scientific name: *Picrorhiza scrophulariiflora*

Other names: *Kaduku rohini, Kadaga rohini*

Vernacular names:

Tamil	:	Kaduku rohini
English	:	Picrorhiza
Telugu	:	Katki
Malayalam	:	Katukurohini, Katurohini
Kannadam	:	Katukarohini

Parts used: Root

Actions:

- Antiperiodic
- Stomachic
- Cathartic
- Anthelmintic

General properties:

"மாந்தஞ் சுரமையம் வாயு கரப்பானாமஞ்
சேர்ந்தமலக்கட்டுதிரிதோடம்-போந்தபொட்டுப்
புண்வயிறுநோயிவைபோம் பொற்கொடியே பேதியுண்டாம்
திண்கடுகுரோகணிக்குத்தேர்."

-அகத்தியர் குணவாகடம்[20a]

Uses:

- It cures fever, Eczema, Abdominal pain, Amoebic dysentery and Wounds.
- Decoction of *kadugurohini* used for dropsy.

Thippili moolam

Scientific name:*Piper longum*

Other names: *Ambinadi kiranthiver, Kiranthigam, Kinthigam, Thippilikkattai, Thanman, Thanmoolam, Rathinthikam dhevasaram,Nathikaranthai, Narukkuveru, Narukku thippili,Kandanthippili, Modi ver.*

Vernacular names:

Tamil	:	Thippili moolam
Telugu	:	Pippili- mulam
Malayalam	:	Kattu- thippili
Kannadam	:	Hippifli- beru

Parts used: Root

Actions:

Stomachic

General properties:

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

-அகத்தியர் குணவாகடம்[20b]

Uses:

- It cures Cough, Syphilis, Chronic fever, Dysentery, Indigestion, Anorexia and syncope.

Chukku

Scientific name: *Zingiber officinale*

Other names: *Arukkan, Adhagam, Ularndha Inji, Sundi Sondi, Soubannam, Swarnam, Navasuru, Naagaram, Vermoodiya Amirtham,Verkombu.*

Vernacular names:

Tamil	:	Chukku
English	:	Dried Ginger
Telugu	:	Sonti
Malayalam	:	Chukku
Kannadam	:	Ona shunti or sunti

Parts used: Rhizome

Actions:

- Stimulant
- Stomachic
- Carminative

General properties:

"சூலைமந்தம் நெஞ்செரிப்பு தோடமேப் பம்மழலை
மூலம் இரைப்பிருமல் மூக்குநிர் - வலகப
தோடமதி சாரந் தொடர்வாத குன்மநிர்த்
தோடஆ மம்போக்குஞ் சுக்கு."

-அகத்தியர் குணவாகடம்[20c]

Uses:

- It cures indigestion, Asthma, Cough, Peptic ulcer, Otalgia and Anemia.
- Decoction of *Chukku* used for abdominal pain, Vomiting, Chronic fever.
- Powdered *Chukku* with sugarcane juice used for gastritis.

Chirakam

Scientific name: *Cuminum cyminum*

Other names : *Asai, Seeri, Ubakumbapesam, Narseeri, Thutthasaambalam, Prathiviga, Bosanakudori, Metthiam*

Vernacular names:

Tamil	:	Chirakam
English	:	Cumin seeds
Telugu	:	Jilakarra
Malayalam	:	Jirakam
Kannadam	:	Jirlga

Parts used: Seeds

Actions:

- Stimulant
- Stomachic
- Carminative
- Astringent

General properties:

"பித்தமெனு மந்திரியைப் பின்னப் படுத்தியவன்
சத்துருவை யுந்துறந்து சாதித்து - மத்தனெனும்
ராசனையு மிவென்று நண்பைப் பலப்படுத்தி
போசனகு பாரிசெயும் போர்".

-அகத்தியர் குணவாகடம்[20d]

Uses:

- It cures Abdominal pain, Liver diseases, Asthma, Renal calculi and Psychotic conditions.
- Powdered *chirakam* with butter used for Peptic ulcer.
- *Chiraka thylam*used for Eye diseases, Giddiness, Vomiting and Headache.

Elam

Scientific name : *Eletteria cardamomum*

Other names : *Aanji, Korangam, Thudi*

Vernacular names:

Tamil : Elam
English : Cardamom seeds
Telugu : Elakulu
Malayalam : Elattari
Kannadam : Elakki

Parts used: Seeds

Actions:

- Stimulant
- Stomachic
- Carminative

General properties:

"தொண்டை வாய்கபுள் தாலுகு தங்களில்
தோன்றும் நோயதி சாரம்பம் மேகத்தல்
உண்டை போல்எழுங் கட்டி இரிச்சரம்
உழலை வாந்தி சிலந்தி விஷச்சரம்
பண்டை வெக்கை விதாகநோய் காசமும்
பாழுஞ் சோமப் பிணீவிந்து நட்டமும்
அண்டை யீளைவன் பித்தம் இவைக்கெல்லாம்
ஆல மாங்கமழ் ஏல மருந்ததே....."

-தேரன் குணவாகடம்[20e]

Uses:

- It cures Cough, Dysuria, Dysentery and it increases the sperm count.

Milagu

Scientific name: *Piper nigrum*

Other names : *Kalinai, kari, Kaayam, Kolagam, Thirangal, Miriyal, Sarumabandham, Vallisam, Maasam, Kurumilagu, Malaiyali.*

Vernacular names:

Tamil	:	Milagu
English	:	Black pepper
Telugu	:	Miriyalu
Malayalam	:	Kurumulaku
Kannadam	:	Menasu

Parts used : Seeds and root.

Actions:

- Carminative
- Stimulant
- Stomachic
- Antiperiodic
- Rubefacient
- Antidote

General properties:

"அளவையுறாக்காராம் அடைந்திருக்கும் வாத
விளவைவையெல் லாமறுக்கும் மெய்யே - மிளகின்காய்
கண்டவர்க்கும் இன்பமாம் காரிகையே சீழ்மீலாங்
கொண்டவர்க்கும் நன்மருந்தாங் கூறு."

-அகத்தியர் குணவாகடம்[20f]

Uses:

- It cures Anaemia, Piles, Dysentery, Cough, Peptic ulcer, Indigestion, Psychotic disorder, Otalgia and Jaundice.

Lavanga pathiri

Scientific name:*Cinnamomum tamala*

Other names: *Thalisa pathiri, Thamalapathiri*

Vernacular names:

Tamil : Lavanga pathiri

English : Cassia cinnamon, Indian cassia lignea

Telugu : Adavi- lavangapatri

Malayalam : Paccila

Kannadam : Kadu lavanga patte

Parts used: Leaf

Actions:

- Carminative
- Stimulant
- Stomachic
- Diaphoretic

General properties:

"மேகசுரம் சீதசூரம் வெட்டைசுவா சங்ககம்
தாகபித்தம் வாந்திசர் வாசியநோய் - மேகத்தின்
கட்டியொடு தாதுநட்டங் கைப்பருசி போக்கிவிடும்
இட்டஇல வங்கத் திலை."

-அகத்தியர் குணவாகடம்[20g]

Uses:

- It cures Syphilis, Cough, Asthma, Abdominal pain, Vomiting and Stomatitis.

Nelli mulli

Scientific name: *Phyllanthus emblica*

Other name: *Aamalagam, Aalagam, Aambal, Aamarigam, Thaathari, Thathiri, Korangam, Miruthupala, Meethundhu.*

Vernacular names:

Tamil : Nelli

English : Indian gooseberry

Telugu : Usirika

Malayalam : Nellikay

Kannadam : Nellikai

Parts used: Leaves, flowers, bark, root, fruit, seeds.

Actions:

- Refrigerant
- Diuretic
- Laxative

General properties:

"ஆகவன லஞ்சசிஅ சிர்க்கென்யு ருக்கிகண்ணோய்
தாக முதிரவித்தந் தாது நஷ்டம் - மேகத்தின்
இல்லிமுள்ளி போலருகல் எண்கா மியவியங்கம்
நெல்லிமுள்ளி யாற்போ நினை.

நல்லநெல்லி முள்ளியது நாக்குக் குருசிதரும்
அல்லல்விரி பித்தம் அகற்றுமதை - மெல்லத்
தலை முழுகக் கண்குளிருந் தாபுபித்த வாந்தி
இலையிழிமே கங்கலும் போம் எண்."

-தேரன் குணவாகடம்[20h]

Uses:

- It cures vomiting, psychotic disorders, hypertension, menorrhagia, leucorrhoea, constipation, giddiness and tuberculosis.
- Decoction of *nelli mulli* used for giddiness and regurgitation.

Chathi pathiri

Scientific name : *Myristica fragrans*

Other name : Jathipathiri, Vasuvasi

Vernacular names:

Tamil : Chathipathiri

English : Arillus of the nut

Telugu : Japtri

Malayalam : Jatipattiri

Kannadam : Japatri

Parts used: Skin

Actions:

- Aphrodisiac
- Carminative
- Stimulant
- Hypnotic

General properties:

"சாதிதரும் பத்திரிக்குத் தாபச் சுரந்தணியும்
ஓதுகின்ற பித்தம் உயருங்காண் - தாதுவிர்த்தி
யுண்டாங் கிரகணியோ டோதக் கழிச்சலரும்
பண்டாங்க குறையே பகர்."

-அகத்தியர் குணவாகடம்[20i]

Uses:

- It cures Amoebic dysentery and fever.

Sirunaga poo

Scientific name : *Mesua nagassarium*

Other name : *Nagam, Nagaputpam, Nagesaram, Kesaram, Saambeyam*

Vernacular names:

Tamil	:	Sirunaga poo
English	:	Ceylon lorn wood
Telugu	:	Naga- kesara
Malayalam	:	Nakappuvu
Kannadam	:	Naga- kesara

Parts used: Leaves, flowers, seeds, roots and bark

Actions:

- Astringent

- Carminative
- Aromatic
- Acrid
- Purgative

General properties:

‘‘ சிறுநாகப் புவினது செய்கைதனைச் சொல்வொம்
குறியாகும் மேகத்தைக் ககொல்லும் - நெறிவிட்டுத்
தீதாய்ச் செல்வாயுவையுந் தீர்க்குமிரு மற்போக்கும்
கோதாய் இதையறிந்து கொள்.’’

-அகத்தியர் குணவாகடம்[20j]

Uses:

- It cures Cough, Leucorrhoea, Diarrhoea and Anuria.
- Paste of sirunaga poo with butter and candy used for over bleeding.
- Paste of dried sirunaga poo with ghee applied in the leg for burning sensation.
- Preparation of *manapagu* used for bacillary dysentery.

Thalisa pathiri

Scientific name : *Abies spectabilis*

Vernacular names:

Tamil : Thalisa pathiri
English : Flaurtia calaphracta
Telugu : Talispatram
Malayalam : Talisapatri
Kannadam : Talispatram

Parts used: Leaves

Actions:

- Stomachic
- Carminative
- Expectorant
- Tonic

General properties:

"நாசி களப்பிணிகள் நாட்பட்ட- காசஞ்சு
வாசம் அருசி வனமங்கால்-வீசிவரு
மேகமந்தம் அத்திசுரம் விட்டேகுந் தாளிச்சத்தால்
ஆகுஞ் சுகப்பிரச வம்."

-அகத்தியர் குணவாகடம்[20k]

Uses:

- It cures fever, chronic cough, asthma, vomiting, indigestion and diarrhoea.
- Powdered leaves of thalisa pathiri with adathoda juice and honey used for asthma and cough.
- Extract of thalisa pathiri leaves used for fever, cough and bacillary dysentery in children.

Athimathuram

Scientific name : *Glycyrrhiza glabra*

Other name : *Athingam, Atti, Madhugam, Aundri ver.*

Vernacular names:

Tamil	:	Athimathuram
English	:	Jequility, indian or Jamaica liquorice
Telugu	:	Ati- Madhuramu
Malayalam	:	Ati- Madhuram
Sans	:	Yashti- Madhukam

Parts used: Root

Actions:

- Mild expectorant
- Laxative
- Tonic
- Demulcent

General properties:

"கத்தியரி முப்பிணியால் வருபுண் தாகங்
கண்ணோய்உன் மாதம்விக்கல் வலிவெண்-குட்டம்
பித்தமெலும் புருக்கி கிரிச்சரம் ஆவர்த்த
பித்தமத மூர்ச்சை விடபாகம் வெப்பந்

தத்திவரு வாதசோ ணிதங்கா மாலை
சருவவிடங் காமியநோய் தாது நட்டங்
குத்திருமல் ஆசியங்கம் இதழ்நோய் இந்து
குயப்புணும்போம் மதுாகமெனக் கூறுங்காலே.

-தேரன் குணவாகடம்[20l]

Uses:

- It cures Eye diseases, Psychotic disorders, Hi-cough, Leucoderma, Jaundice, Burning micturition and Bone diseases.

Lavangam

Scientific name: *Syzygium aromaticum*

Other names : *Anjugam, Urkadam, Karuvaik krambu, Sosam, Thirali, Varaangam*.

Vernacular names:

Tamil : Lavangam
English : Cloves, clove tree
Telugu : Lavangalu, Lavanga-pu
Malayalam : Karampu
Kannadam : Lavanga

Parts used: Flower buds

Actions:

- Antispasmodic
- Carminative
- Stomachic

General properties:

"பித்த மயக்கம் பேதியொடு வாந்தியும்போம்
சுத்தவிரத் தக்கடுப்புந் தோன்றுமோ - மெத்த
இலவங்கங் கொண்டவருக் கேற் சுகமாகும்
மலமங்கே கட்டுமென வாழ்த்து.

சுக்கிலநட் டங்கர்ண சூர்வியங்க லாஞ்சனந்தாட்
சிக்கல்விடாச் சர்வா சியப்பிணியு - மக்கிகுட்
டங்கப் புவோடு திரிபடருந் தோன்றிலில்
வங்கப்பு வோடுரைத்து வா"

-அகத்தியர் குணவாகடம்[20m]

Uses:

- It cures Vomiting, Giddiness, Chronic diarrhoea, Ear diseases and Eye diseases.
- Paste of *Lavangam* used for Sinusitis.

Koogai neeru

Scientific name: *Maranta arundinaceae*

Other name : *Ararootkizhangu, Koovamakkizhangu, Koogai kizhangu*

Vernacular names:

Tamil : Kuvaik kizhangu
English : East Indian arrow root
Telugu : Ararut- gaddalu
Malayalam : Kuva, kuva- kizhanna
Kannadam : Koove- Gedde

Parts used: Tuberous root

Actions:

- Refrigerant
- Demulcent
- Nutrient

General properties:

"மேனியிடும் வாய்க்கு மிருதுவாம் ஆக்கியூண்ணத்
தானிருமல் வெப்பதிக தாகமிலை ஏனிருக்கும்
அம்பே றிளங்கிடிங்கி தியாவர்க்கு மாமணப்புங்
கொம்பே கூகைக்கிழங்கைக் கூறு."

-அகத்தியர் குணவாகடம்[20n]

Uses:

- It cures fever and cough.
- Preparation of *kuvaikizhangu kanji* used for bacillary dysentery.

Associated drugs:

Nei

General properties:

"நெய்யுண வுண்டவை நேர்வுறச் செய்துமேன்
மெய்யையுந் திண்ணிய மேருவெனச் செய்யும்."

- குணபாடம் தாதுசீவகுப்பு[21]

When ghee taken in required quantities along with usual diet, it helps in proper digestion and utilisation of the diet and gives strength and vigor to the body.

Cow's ghee:

It controls thirst, Vomiting, Excessive *Pitha,* Burning sensation of the stomach, *Pittha* hi-cough, Abdominal pain, Dryness, Prickly heat, Cough, Hyper motility of the gut, Weakness of bones, Piles etc.

Uses:

- When ghee is mixed in hot rice and eaten, it enhances the healing of peptic ulcer. It also stimulates bone marrow growth. Ghee should be eaten only after melting(liquid form)
- Dried ginger, Pepper, Cuminum seeds are fried, powdered and taken along with ghee for indigestion and dysentery.
- For curing stomach pain, the ghee is taken with boiled rice water and if it is taken with palm sugar candy, it cures body heat and whooping cough.
- Ghee is also used as an adjuvant for many *Parpams, Chendhooram, Leghiums, Thailams* and *Kiruthams.*

- By taking ghee bath, the burning sensation, *Pitha*, Unconsciousness, Haematemesis etc. are cured.

Sarkarai

Scientific name: *Saccharum officinarum*

Other name : *Punarpoosam, Ekku, Vei.*

Vernacular names:

Tamil	:	Karumbu
English	:	Sugarcane, Noble cane
Telugu	:	Cheruku
Malayalam	:	Karinpa
Kannadam	:	Khabbu

Parts used: Sugarcane juice, Sugar, Root

Actions:

- Demulcent
- Antiseptic
- Stimulant
- Diuretic
- Nutrient

General properties:

"சீனிச் சர்க்கரைக்குத் தீராத வன்சுரமுங்
கூனிக்கும் வாதத்தின் கூட்டுறவும் - ஏனிற்கும்
வாந்தி யொடுகிருமி மாறாத விக்கலுமே
போந்திசையை விட்டுப் புரண்டு".

-அகத்தியர் குணவாகடம்[20o]

Uses:

- It cures Fever, Vomiting and Hiccough.
- It cures *Vatha* fever, common cold & Sinusitis.
- Paste of sugar with bee wax used to treat acne.
- It cures eye diseases.

3.1.2. BOTANICAL ASPECT

Zingiber officinale

Scientific classification

Botanical name : *Zingiber officinale*

Kingdom : Plantae

Class : Liliopsida

Order : Zingeberales

Family : Zingiberaceae

Genus : *Zingiber*

Species : *Officinale*

Description: A Slinder, perennial rhizomatus herb; leaves linear, sessile, glabrous; flowers yellowish green in oblong, cylindric spikes, ensheathed in a few scarious, glabrous bracts; fruits along capsules. The rhizomes are white to yellowish brown in colour, irregularly branched, somewhat annulated and laterally flattened. The growing tips are covered over by a few scales. The surface of the rhizome is smooth and if broken a few fibrous elements of the vascular bundles project out from the cut ends.

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

Parts used : Rhizomes [22]

Chemical constituents: The characteristic fragrance and flavor of ginger result from volatile oils that compose 1-3% of the weight of fresh ginger, primarily consisting of zingerone, shogaols and gingerols with gingerol as the major pungent compound.Zingerone is produced from gingerols during drying, having lower pungency and a spicy-sweet aroma [23].

Properties: The raw ginger is Acrid, Thermogenic, Carminative, Laxative and Digestive.

Uses:

- It is useful in anorexia, vitiated conditions of *Vatha* and *Kapha*, Dyspepsia and Inflammations.[22]

Picrorhiza scorphulariiflora

Scientific classification

Botanical name	**:**	*Picrorhiza scrophulariiflora*
Kingdom	**:**	Plantae
Class	**:**	Dicotyledonae
Order	**:**	Lamiales
Family	**:**	Scrophuraiaceae
Genus	**:**	*Picrorhiza*
Species	**:**	*Scrophulariiflora*

Description: A small nearly hairy perennial herb with a woody elongate creeping root stock; leaves capsulate, serrate; flowers of white or bluish in dense terminal spicate raceme; fruits ovoid capsules.

Distribution: In the Himalayas, from Kashmir to Sikkim at an elevation of 2,700-4,500m.

Parts used: Dried rhizomes[24]

Chemical constituents: Main chemical constituents are glycosidesscroneoside B, 2-β-glucosyloxy, tetrahydroxy-9-methyl-19-norlanosta-5,23-diene-22-one, picroside I, 6-isoferuloylcatalpol, androsin, scroside A, scroside D[25]

Properties: The rhizomes are Bitter, Acrid, Cooling, Laxative, Carminative, Digestive, Stomachic, Anthelmintic, Anti-inflammatory, Expectorant, Antipyretic, and Purgative in large doses.

Uses:

- They are useful in burning sensation, Constipation, Gastropathy, Flatulence, Colic, Anorexia, Inflammations, Leucoderma, Leprosy, Skin diseases,

- It Cures Cardiac disorders, Hypotension, Cough, Asthma, Bronchitis, Hiccough, Fever, Intermittent fever, Diabetes, Jaundice, Haemorrhoids and General debility [24].

Piper longum- Root

Scientific classification

Botanical name	**:**	Piper longum
Kingdom	**:**	Plantae
Class	**:**	Magnolipsida
Order	**:**	Piperales
Family	**:**	Piperaceae
Genus	**:**	*Piper*
Species	**:**	*Longum*

Description : A slender aromatic climber, rooting at the nodes, the branches erect, subscandent, swollen at the nodes; leaves alternate, lower ones broadly ovate, cordate, upper ones oblong, oval, all entire, smooth, thin with reticulate venation, vein raised beneath; flowers in solitary spikes; fruits berries, small, red when ripe, completely sunk in solid fleshy spike.

The mature spikes collected and dried from the commercial form of pippali, roots are known as pippili moolam.

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

Parts used: Roots, dried spikes[24a]

Chemical constituents: Volatile Oil, Resin, Piperin, Piperlongumine, Piperlatin, Brachyamide A, Brachyamide B, Brachystine, Sterols, Glycosides.[26]

Properties: The roots are bitter, Tonic, Diuretic, Purgative, Expectorant, Stomachic, Digestive and Emmenagogue.

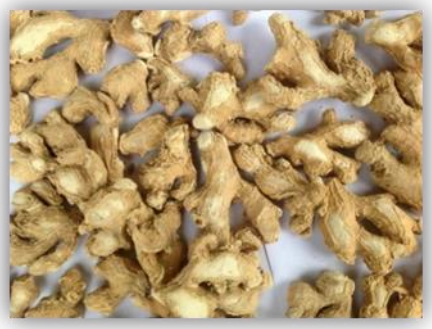
Use:

- They are useful in Gout, Dyspepsia, Stomachalgia and Spleenopathy.
- It cures Anorexia, Dyspepsia, Asthma, Bronchitis, Hiccough, Epilepsy, Fever, Gonorrhoea, Haemorrhoids and Lumbago.[24a]

Zingiber officinale

Scientific Classification

Botanical name : *Zingiber officinale*
Kingdom : Plantae
Class : Liliopsida
Order : Zingiberales
Family : Zingiberaceae
Genus : *Zingiber*
Species : *Officinale*



Description: A Slinder, perennial rhizomatous herb; leaves linear, sessile, glabrous; flowers yellowish green in oblong, cylindrical spikes, en-sheathed in a few scarious, glabrous bracts; fruits along capsules. The rhizomes are white to yellowish brown in colour, irregularly branched, somewhat annulated and laterally flattened. The growing tips are covered over by a few scales. The surface of the rhizome is smooth and if broken a few fibrous elements of the vascular bundles project out from the cut ends.

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

Parts used: Rhizome [22]

Chemical constituents: The characteristic fragrance and flavour of ginger result from volatile oils that compose 1-3% of the weight of fresh ginger, primarily consisting of zingerone, shogaols and gingerols with gingerol (1-[4'-hydroxy-3'-methoxyphenyl]-5-hydroxy-3-decanone) as the major pungent compound. Zingerone is produced from gingerols during drying, having lower pungency and a spicy-sweet aroma.[23]

Properties: The dry ginger is Acrid, Thermo-genic, Emollient, Appetiser, Laxative, Stomachic, Stimulant, Rubefacient, Aphrodisiac, Expectorant, Anthelmintic and Carminative.

Uses:

- It is useful in Dropsy, Otalgia, Cephalic, Asthma, Cough, Colic, Diarrhoea, Anorexia, Dyspepsia, Cardiopathy, Cholera, Nausea, Vomiting, Elephantiasis and Inflammations. It is also much used in several domestic preparatrions[22].

Cuminum cyminum

Scientific classification

Botanical name	**:**	*Cuminum cyminum*
Kingdom	**:**	Plantae
Class	**:**	Dictotyledonae
Order	**:**	Apiales
Family	**:**	Apiaceae
Genus	**:**	*Cuminum*
Species	**:**	*Cyminum*

Description : A Small slender glabrous annual herb about 30cm in height with much branched angular or striated stem; leaves bluish green, two or three partite, ultimate segments filiform, leafbase sheathing; flowers small, white or rose coloured in compound umbels; fruits greyish, tapering towards both ends and compressed laterally with ridges covered over by papilose hairs.

Distribution: Cultivated throughout India.

Parts used: Fruits [27]

Chemical constituents: *C. cyminum* contained cuminlaldehyde (39.48%), gamma-terpinene (15.21%), O-cymene (11.82%), beta-pinene (11.13%), 2-caren-10-al (7.93%), *trans*-carveol (4.49%) and myrtenal (3.5%) as a major components[28].

Properties: The fruits are Acrid, Sweet, Cooling, Aphrodisiac, Astringent, Digestive, Carminative, Anthelmintic, Anti- inflammatory, Anodyne, Stomachic, Stimulant, Depurative, Galactagogue, Uterine and Nervine stimulant.

Uses:

- The fruits are useful in Dyspepsia, Colic, Helminthiasis, Inflammations, Flatulence, Anorexia, Vomiting, Haemorrhoids, Renal and Vesical calculi, Leucorrhoea, Chronic diarrhoea, Skin diseases, Leprosy, Leucoderma, Fever, Cough, Asthma and Ulcers[27].

Elettaria cardamomum

Scientific Classification

Botanical name	**:**	*Elettaria cardamomum*
Kingdom	**:**	Plantae
Class	**:**	Monochlamydeae
Order	**:**	Zingiberales
Family	**:**	Zingiberaceae
Genus	**:**	*Elettaria*
Species	**:**	*Cardomum*

Description: A tall herbaceous perennial with subterranean branching root stock, 1.5- 5 m in height; leaves subsessile, elliptic or lanceolate with sheathing base; flowers in panicles which are many for a plant arising from the base of the vegetative shoots upright first and becoming prostrate, lip of the corolla white, streaked with violet; fruits trilocular, subglobose capsules, marked with many fine vertical ribs, seeds 15-20 per pod, brownish black covered by a thin mucilaginous membrane.

Distribution: Throughout India.

Parts used: Seeds, oil[27a]

Chemical constituents: The volatile oil of *E.cardamomum* Maton seeds contains trace waxes; alpha-terpinyl acetate, 42.3%; 1,8-cineole, 21.4%; linalyl acetate, 8.2%; limonene, 5.6%; and linalool, 5.4%; limonene, 36.4%; 1,8-cineole, 23.5%; terpinolene, 8.6%; and myrcene, 6.6%.[29]

Properties: The seeds are Aromatic, Acrid, Sweet, Stimulant, Carminative, Digestive, Stomachic, Diuretic, Cardio tonic, Abortifacient, Expectorant and Tonic.

Uses:

- The seeds are useful in asthma, bronchitis, haemorrhoids, cardiac disorders, anorexia, dyspepsia and burning sensation.
- Cardamom oil is used in several pharmaceutical preparations[27a].

Piper nigrum

Scientific classification

Botanical name	**:**	*Piper nigrum*
Kingdom	**:**	Plantae
Class	**:**	Dicot
Order	**:**	Microembreya
Family	**:**	Piperaceae
Genus	**:**	*Piper*
Species	**:**	*Nigrum*

Description: A climbing perennial, rooting at the nodes, leaves are cordate or round based; flowers minute in spikes usually dioeciously. Fruiting spikes very variable in length, fruits ovoid or globes one seeded berries, bright red when ripe, seeds are globose, albumin hard and test a thin greyish-black to black, perisperm hard, wrinkled and white, 0.4 to 0.5 cm in diameter; Odour aromatics, taste pungent. Flowers are flowering in the rainy season and fruits ripening in the autumn season (December to April).

Distribution: The plant cultivated in the hotter and moist parts of India, in evergreen forest up to 1500 meters.

Parts used: Dried fruits.[24b]

Chemical constituents: Black pepper has been found to contain piperine, alkamides, piptigrine, wisanine, dipiperamide D and dipiperamide E.[30]

Properties: The fruits are Acrid, Bitter, Anthelmintic, Carminative, Aphrodisiac, Antiperiodic, Diuretic, Digestive, Emmenagogue, Stimulant and Stomachic.

Uses:

- They are useful in Arthritis, Asthma, Fever, Cough, Dysentery, Dyspepsia, Hiccough, Haemorrhoids and Dermatopathy.[24b]

Cinnamomum tamala

Scientific classification

Botanical name	**:**	*Cinnamomum tamala*
Kingdom	**:**	Plantae
Class	**:**	Magnoliophyta
Order	**:**	Laurales
Family	**:**	Lauraceae
Genus	**:**	*Cinnamomum*
Species	**:**	*Tamala*

Description: A moderate sized evergreen tree 7.5m in height with dark brown or blackish rough bark and pinkish or reddish brown blaze; leaves simple, sub-opposite or alternate, ovate- lanceolate or ovate-oblong, acuminate, coriaceous,glabrous, 3 nerved from base to apex; flowers pale yellowish in axillary and terminal, lax puberulous panicles; fruits ovoid, fleshy, black drupe, supported by enlarged perianth tube.

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

Parts used: Leaves. [27b]

Chemical constituents: Monoterpenes, trans-sabinene hydrate, β-ocimene(17.9%), myrcene(4.6%), α pinene(3.1%), β- subinene, germacrene A and α-gurjunene.[31]

Properties: The leaves are Bitter, Sweet, Aromatic, Anthelmintic, Diuretic, Stimulant, Carminative and Tonic.

Uses:

- The leaves are useful in Cardiac disorders, Inflammations, Helminthiasis, Dyspepsia, Colic, Diarrhoea, Hepatopathy and Spleenopathy.[27b]

Phyllanthus emblica

Scientific classification

Botanical name	**:**	*Phyllanthus emblica*
Kingdom	**:**	Plantae
Class	**:**	Eudicots
Order	**:**	Malpighiales
Family	**:**	Euphorbiaceae
Genus	**:**	*Phyllanthus*
Species	**:**	*Emblica*

Description: A small or medium sized tree, found both in natural state in mixed deciduous forests of the country ascending to 1300 m on hills; cultivated in gardens, homeyards or grown as a road side tree.

Distribution: Throughout India, in deciduous, forests and on hill slopes upto 200m, also cultivated in plains.

Parts used: Fruit, seed, leaves, root, bark and flowers.[24c]

Chemical constituents: Fruit is a rich source of vitamin C. It also contains, Gallic acid, Ellagic acid, 1-0-galloyl-beta-D-glucose, Chebulinic acid, Quercetin, Chebulagic acid, Corilagin, 3-ethygallic acid and Isostrictiniin. [32]

Properties: The fruits are sour, astringent, bitter, acrid, sweet, ophthalmic, carminative, digestive, stomachic, laxative, alter ant, diuretic, aphrodisiac, antipyretic, tonic.

Uses:

- They are useful in Diabetes, Cough, Asthma, Bronchitis, Cephalgia, Opthalmopathy, Dyspepsia, Colic, Hyperacidity, Peptic ulcer, Skin diseases, Leprosy, Inflammations, Anaemia, Hepatopathy, Jaundice, Menorrhagia, Dysentery, Leucorrhoea, Cardiac disorders, Intermittent fevers and Greyness of hair. [24c]

Myristica fragrans

Scientific classification

Botanical name	**:**	*Myristica fragrans*
Kingdom	**:**	Plantae
Class	**:**	Magnoliposida
Order	**:**	Magnolialse
Family	**:**	Myristicaceae
Genus	**:**	*Myristica*
Species	**:**	*Fragrans*

Description: A moderate sized, usually dioecious, aromatic, evergreen tree with greyish black bark having lenticular spots on the outside and red juice on the inner side; Leaves elliptic or oblong-lanceolate, thinly coriaceous, shiny above, dull beneath; flowers creamy yellow, fragrant in umbellate cymes, stamina column of male flowers stalked, anthers 10-14, linear, ovary of female flowers sessile, ovoid-globose; fruits yellow, pericarp fleshy, splitting into two halves at maturity, seeds oblong, obtuse, testa shiny, aril yellowish red, irregularly lobed, extending to the apex of the seed.

Distribution: Cultivated in the hotter parts of India upto 750 m with a rainfall of 150-300 cm per annum.

Parts used: Seed (nutmeg), aril (mace)[24d]

Chemical constituents: Sabinene, myristicin, safrole and elemicin, α-pinene, β- pinene and sabinene.[33]

Properties: The nutmeg and mace are Bitter, Acrid, Astringent, Sweet, Thermogenic, Aromatic, Aphrodisiac, Anti-inflammatory, Anthelmintic, Deodorant, Digestive, Carminative, Stomachic, Expectorant, Diuretic, Emmenagogue, Antispasmodic, Febrifuge, Narcotic, Stimulant, Anticonvulsant, Antiseptic and Tonic.

Uses:

- They are useful in Inflammations, Dyspepsia, Colic, Cough, Asthma, Diarrhoea, Vomiting, Amenorrhoea, Dysmenorrhoea, Ulcers, Hepatopathy, Spleenopathy, Impotency, Skin diseases, Insomnia, Hyperpiesia, Cardiac disorders, Fever and General debility.[24d]

Mesua nagassarium

Scientific classification

Botanical name	**:**	Mesua nagassarium
Kingdom	**:**	Plantae
Class	**:**	Dicotyledone
Order	**:**	Malphigiales
Family	**:**	Calophyllaceae
Genus	**:**	*Mesua*
Species	**:**	*Nagassarium*

Description: A medium sized to large handsome globrous, evergreen tree, 18-30 m in height and reddish brown bark which peels off in thin flakes; leaves simple, opposite, thick, lanceolate, coriaceous, covered with waxy bloom underneath, red when young, acute or acuminate, nerves inconspicuous; flowers white, very fragrant, axillary or terminal, solitary or in pairs, 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.

Distribution: Throughout India, in evergreen forests up to 1500 m.

Parts used: Flowers, oil.[24e]

Chemical constituents: Mesuaferron, Euxanthon, Mesuaferrol, Mesuagin, Mammegin, Mesuol, Mammeuisin and bioflavin[34]

Properties: The flowers are Astringent, Bitter, Acrid, Digestive, Carminative, Constipating, Anthelmintic, Diuretic, Expectorant, Stomachic, Haemostatic, Aphrodisiac and Cardiotonic.

Uses:

- They are useful in Asthma, Cough, Hiccough, Leprosy, Scabies, Pruritus, Vomiting, Dysentery, Haemorrhoids and Ulcers, Burning sensation of the feet, Impotency, Leucorrhoea, Fever and Cardiac debility.
- Seed oil is used in vitiated conditions of *vata* and skin diseases.[24e]

Abies spectabilis

Scientific classification

Botanical name	**:**	Abies spectabilis
Kingdom	**:**	Plantae
Class	**:**	Pinopsida
Order	**:**	Pinales
Family	**:**	Pinaceae
Genus	**:**	*Abies*
Species	**:**	*Spectabilis*

Description: A very tall evergreen tree attaining a height of 60m with strong horizontally spreading branches, young shoots covered with short brown hair; leaves simple, densely covering the twinges spreading in all directions, but more or less distichous when the twinges are viewed from below, each leaf 1.5-2.3 cm long; the cones are bluish in colour, seeds winged.

Distribution: Upper Himalaya tracts

Parts used: Leaves[35]

Chemical constituents: The leaves contain bioflavonoid, abiesin, n-triacontanol, beta-sitosterol and betuloside. Essential oil from leaves contains alpha-pinene, l-limonene, deltacarene, dipentene, l-bornyl acetate and l-cardinene. [36]

Properties: The leaves are Bitter, Sweet, Acrid, Aromatic, Expectorant, Digestive, Carminative, Stomachic, Antispasmodic, Diuretic, Febrifuge and Tonic.

Uses:

- They are useful in Cough, Asthma, Bronchitis, Dyspepsia, Colic, Diarrhoea, Epilepsy, Vomiting, Urethritis, Hiccough, Fever and Emaciation. [35]

Glycyrrhiza glabra

Scientific classification

Botanical name	**:**	*Glycyrrhiza glabra*
Kingdom	**:**	Plantae
Class	**:**	Dicotyledoneae
Family	**:**	Fabaceae
Order	**:**	Fabales
Genus	**:**	*Glycyrrhiza*
Species	**:**	*Globra*

Description: A tall perennial under- shrub about 1 m high; leaves compound, leaflets 4-7 pairs; flowers violet in racemes; pods, oblong to linear, flattened, seeds reniform. The liquorice of commerce is the dried underground stems and roots.Its outer surface is pale chocolate brown in colour, flexible and fibrous and internally has a light yellow colour. It has a characteristic pleasant sweet taste.

Distribution: Cultivated in Punjab and the sub-Himalayan tracts.

Parts used : Roots[37]

Chemical constituents: Root is attributed to the flavonoid content, especially liquiritin and isoliquiritin. Plant gums, resins, and essential oils have been extracted; however, the root is cultivated for the principle active glycoside glycyrrhizin. The amount of glycyrrhizin varies from 7% to 10% or more depending on growing conditions. Glycyrrhizin, glycyrrhizic acid, and glycyrrhizinate amount to 10% to 25% of the root extract. [38]

Properties: The roots are Sweet, Refrigerant, Emetic, Tonic, Diuretic, Demulcent, Mild Laxative, Aphrodisiac, Expectorant, Emmenagogue and Intellect promoting.

Uses:

- They are useful in hyperpepsia, Cough, Bronchitis, Fever, Skin diseases.
- An extract of the root is good for treating gastric ulcers.
- A decoction of the root is good wash for falling and greying of hair.
- Externally the root is applied for cuts and wounds. [37]

Syzygium aromaticum

Scientific classification

Botanical name : *Syzygium aromaticum*
Kingdom : Plantea
Class : Dicotyledons
Order : Myrtales
Family : Myrtaceae
Genus : *Syzygium*
Species : *Aromaticum*

Description: A pyramidal or conical evergreen tree usually upto12 m in height with a single main stem bearing obliquely oriented branches; leaves simple, lanceolate, gland-doted, fragrant; flower buds greenish to pink, clustered at the ends of the branches, highly aromatic; fruits fleshy, dark pink drupes; seeds oblong, grooved on one side.

Distribution: Cultivated in south India.

Parts used: Dried flower buds (cloves, oil).[22a]

Chemical constituents: Cloves contain - among other compounds - Gallotannins, triterpenes, flavonoids, and phenolic acids. Oil derived from Cloves contains additional compounds including b-caryophyllene, eugenol, and eugenol acetate. [32]

Properties: The cloves are Acrid, Bitter, Aromatic, Refrigerant, Ophthalmic, Digestive, Stimulant, Antispasmodic, Antibacterial, Rubefacient, Aphrodisiac, Appetiser, Expectorant, Anthelmintic, Rejuvenating, Diuretic and Tonic.

Uses: They are useful in Halitosis, Opthalmopathy, Flatulence, Colic, Gastropathy, Anorexia, Cough, Asthma, Burning sensation, Skin diseases, Helmenthiasis, Fever, Neuralgia, Dental caries, Hyperacidity, Vomiting, Hepatopathy, General debility and tuberculosis.

- The oil useful in Cough, Bronchitis, Flatulence, Colic, Skin diseases, Dyspepsia, Vomiting, Dental cries and Cephalgia.
- Externally the oil is used as a Rubefacient and counterirritant.[22a]

Maranta arundinacea

Scientific classification

Botanical name	**:**	Maranta arundinacea
Kingdom	**:**	Plantae
Class	**:**	Magnoliopsida
Order	**:**	Zingiberales
Family	**:**	Marantaceae
Genus	**:**	*Maranta*
Species	**:**	*Arundinacea*

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

Distribution: Cultivated throughout India.

Parts used: Rhizome[24f]

Chemical constituents: The tuber consists of 27% starch, 63% water, 1.56% albumin, 4.10% sugar, gum, etc., 0.26% fiber and 1.23% ash. Extract of rhizomes contains

flavonoids, alkaloids, tannins, glycosides, steroids, phenols, cardiac glycosides, saponins, carbohydrates, and proteins. [40]

Properties: Starch obtained from rhizome is Astringent, Sweet, Refringent, Tonic, Aphrodisiac, Emollient, Expectorant, Febrifuge and Rubefacient.

Uses:

- It is useful in Dysentery, Diarrhoea, Dyspepsia, Bronchitis, Cough and also as a nourishing food for infants, invalids and convalescents.
- It is the main ingredient in biscuits, cakes, puddings, jellies and face powders. [24f]

Associated drugs

Ghee

English name: Ghee, clarified butter.

Nutritional profile:

- Ghee is relatively high in calories, containing 112 calories per tablespoon serving. A serving contains 12.7 grams of fat, minimal amounts of protein and no carbohydrates, dietary fiber or sugars.
- Ghee is high in saturated fat with 7.9 grams per serving.

Vitamin and mineral content:

- It contains only a minimal amount of calcium- 1 mg/ tsp
- Ghee also contains 108 micrograms of vitamin A, which is a significant amount for such a small serving size.
- 1 tsp provides 12 and 15 % of the recommended daily intakes of vitamin A for men and women, respectively.[41]

Saccharum officinarum

Scientific classification

Botanical name	**:**	*Saccharum officinarum*
Kingdom	**:**	Plantae
Class	**:**	Monocotyledons
Order	**:**	Poales
Family	**:**	Poaceae
Genus	**:**	*Saccharum*
Species	**:**	*Officinarum*

Description:

It is a topical, perennial grass that forms lateral shoots at the base to produce multiple stems, typically three or four meters high and about 5 cm diameter and once harvested the stalk will regrow allowing the plant to live for between 8 to 12 years. The stem grows into cane stalk, which when mature stalk, which when mature constituents approximately 75% of entire plant.

A mature stalk is typically composed of 11-16% fibre, 12-16% soluble sugars, 2-3% non-sugar and 63-73% water. The leaves are grow from the nodes of the stem, arranged in two rows on either side of the stem. The leaves are tubular and blades like, thicker in the centres than at the margins and encircle than the stem.

The inflorescence of sugar cane is a terminal panicle which possesses two spikelet and seeds protected by husks covered in silky hair.

Distribution: Sugar cane is indigenous to tropical south and Southeast Asia.

Parts used: Roots, stem.[22b]

Chemical constituents: Sucrose is the product of the sugar cane juice.The juice yielded flavones diosmetin-8-C-glucoside, vitrexin, schaftoside, isoschaftoside and 4',5'-dimethyl-luteolin-8-C glucoside.[42]

Properties: The roots are cooling and diuretic. The stems (sugar cane) are Sweet, Cooling, Emollient, Laxative, Cardio-tonic, Diuretic, Galactogogue, Aphrodisiac, Expectorant, Haemostatic and tonic.

Uses:

- The roots are useful in uropathy.
- They are useful in Dipsia, Fatigue, Leprosy, Gastropathy, Cardiac debility, Hematemesis, Cough, Bronchitis, Anaemia, Ulcers of the skin and mucous membrane, seminal weakness, Emaciation and general debility. [22b]

3.2. PHARMACEUTICAL REVIEW

Chooranam

Definition

Chooranam is a fine powder s 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. [43]

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 rancidity.

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 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!"

-அகஸ்தியர் வைத்திய இரத்தினச் சுருக்கம்[44]

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
தாமப்பா ரோகத்தை வெல்லா தப்பா
தளமான வியாதி யெல்லாம் பாரிக்கும் பார்
வேமப்பா சுத்தி செய்து கொண்டாயானால்
வெகுசுறுக்காய் தீருமா வியாதி கேளு".

-அகஸ்தியர் வைத்திய இரத்தினச் சுருக்கம்.

Then the *chooranam* is placed in the sunlight and powdered. Equal amount of sugar is added and taken internally. All type of diseases gets 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 & packed by electronic devices. Then *chooranam* is said to retain its potency for 3 months and then gradually deteriorate. However if properly packed & stored they keep good for a year. (Formulary of Siddha Medicines, 1993)

According to AYUSH guidelines shelf life of *chooranam* is one year.[45]

Table no: 1. ANALYTICAL SPECIFICATIONS OF CURNA/ *CHOORNAM*

Sl.No	TESTS
1.	Description
	Macroscopic, Microscopic
2.	Loss on drying at 1050 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-with marker (wherever possible)
9.	Test for heavy/Toxic metals
	Lead
	Cadmium
	Mercury
	Arsenic
10.	Microbial contamination
	Total bacterial count
	Total fungal count
	Test for specific Pathogen
	E. coli
11.	Salmonella spp.
	S.aureus
	Pseudomonas aeruginosa
	Pesticide residue
	Organochlorine pesticides
12.	Organophosphorus pesticides
	Pyrethroids
13	Test for Aflatoxins (B1,B2,G1,G2)

3.3. DISEASE REVIEW

3.3.1. SIDDHA ASPECT - *VERI NOI*

Other names:

- *Piththu noi,*
- *Paiyethiya noi,*
- *Piththa noi*
- *Unmadham*

Nature:

This disease changes the mental ability of a person and makes the person totally mad. The affected person will dance, talk, sing, beating others, abusing etc. are some of the actions which he performs without any commands from others.

Indications:

In this the affected person's mental strength is reduced. Either the person will be too fearful or too adamant, would like to have sex with any type of female, depression, totally looking like a different personality from a normal person.

Causes:

Excess eating, fasting for unnecessary reasons, consume excess amount of liquor, desirous for unwanted things beyond his capacity, frequent fear, angry, excess joy etc. are some of the causes of this disease. Sometimes this disease may be hereditary.

Types:

This disease is of four types. They are

- *Vali verinoi*
- *Azhal verinoi*
- *Iyam verinoi*
- *Mukkutram verinoi*

***Vali Verinoi (Vadha Unmadham)*:**

Before this disease affects a person, he will not have desire to food. Moreover he will be eager to eat the food which is hard, cheap quality, stale etc. Due to this fact

both the physical and mental health get spoiled. Stammering, singing, dancing, crying etc. are some of the indications.

***Azhal Verinoi* (*Pittha Unmadham*) :**

Consumption of very hot food made up of chillies, soar, food which generate lot of heat in the body etc. will lead a man to lose his physical health and mental health. In this type the affected person will always be agitated, impatient, removing clothes and run naked etc. are some of the indications.

***Iya Verinoi* (*Kabha Unmadham*):**

In work excess strain to the body beyond one's capacity, always thinking about some worried things etc. are some of the indications. The affected person will be desirous to have the company of women, frequent sleep, tastelessness, secretion of water in the mouth, paleness in the body etc. are some of the symptoms of this disease.

***Mukkutra Verinoi* (*Janni Unmadham)*:**

The indications stated in the above three types will also accompany and also create lot of complications.

Soga Veri:

Losing the wealth accumulated or the family life, sudden fear are some of the causes of this disease. The affected person will reveal his mind views without any hidden facts, involuntarily talk, sing and dance are some of the indications.

***Nacchu Veri*:**

In this type the disease is caused due to consumption of poisonous items or medicines etc. The indications of the above mentioned types will also appear. The body appearance, redness in the eyes and the actions of five organs will deteriorate.

General Indications:

In this disease the mental balance will be lost, inconsistency, losing self-control capacity, always thinking, talk in loud voice, sleeplessness etc. are some of the symptoms.

Treatment:

Though the disease can be cured with different types of medicines available in Siddha but when this disease affect a person who got the head injury and the eye balls hang, excretion of saliva in the mouth etc. cannot be cured forever.[46]

3.3.2. MODERN ASPECT - NEUROSIS

Neurosis

Neurosis is a term generally used to describe a non-psychotic mental illness which triggers feelings of distress and anxiety and impairs functioning. The word neurosis means "nerve disorders" and was first coined in the late 18thcentury by William Cullen, a Scottish physician. Cullen's concept of neurosis encompassed those nervous disorders and symptoms that do not have a clear organic cause. Sigmund Freud later used the term anxiety neurosis to describe mental illness or distress with extreme anxiety as a defining feature.

Neurosis can be defined as abnormal psychogenic (Psychologically caused) reactions. An anxiety neurosis would have predominantly anxiety symptoms; in neurotic depression there would be predominantly depressive symptoms. Neuroses typically have two components:

- A vulnerable personality
- Stress factors triggering the reaction.

They can thus be seen as exaggerated forms of normal reactions to stressful events, i.e. they are inappropriate to the situation or the stress, or the reaction occurs at a greater frequency or severity than normal. Classically, neurosis should have no demonstrable organic basis and there should be no loss of contact with external reality, such as occurs in psychosis. Neurotic symptoms are thus maladaptive reactions to stress and reflect excessive and inappropriate use of psychological defence mechanisms.

Neurotic symptoms are unpleasant and lead to the individual seeking relief. They are often accompanied by a decrease in social functioning, and individuals suffering from a neurosis have an increased mortality rate, including suicide and fatal head injuries.

Epidemiology

Neurotic symptoms are common and thus can be regarded as normal. These include:

- Inappropriate fears
- Anxiety and panic
- Brief bouts of depressive feelings
- Tension headaches
- Irritability
- Sleeplessness.

Neurotic symptoms are often seen in general practice and may be the predominant symptoms in one-sixth of individuals seen there and relevant in up to one-third. Neurotic disorders are clearly the commonest psychiatric condition, at any one time affecting up to 2% of all individuals. Neurosis is twice common in females than in males [47].

Aetiology

There is more than one reason why patients develop Anxiety disorders. Researchers and scientists are trying to find out more about the biological, psychological, and social factors which influence the development of anxiety disorders as there is still a lot more to learn about the role of these. The following are all believed to play a role in the occurrence of anxiety disorders;

Genetics and Heredity

There is clear evidence that anxiety disorders tend to run in families. If a parent or a sibling of a person suffers from an anxiety disorder, there are higher chances of that person developing this disorder. These findings suggest that a genetic factor combined with certain social factors predisposes certain people to develop anxiety disorders.

Chemical imbalances in the brain

Scientists strongly believe that brain chemistry plays a role in the onset of anxiety disorders. When there is an imbalance of chemicals (such as serotonin and dopamine) in the brain a person can feel anxious or depressed.

Personality types

People with certain types of personality are more prone to develop anxiety disorders. For e.g, people who have low self-esteem and poor coping skills may be more prone for anxiety development. The basic nature of an individual makes one vulnerable to specific types of disorders including anxiety.

Social factors

The role of social factors in the development of anxiety is being studied by researchers and a relationship has been between seen anxiety disorders and long-term exposure to abuse, violence, poverty, etc. Such life experiences affect an individual's susceptibility to these disorders.

Medical causes

Sometimes anxiety may be caused due to the presence of medical illnesses such as certain neurological disorders, endocrine disorders, cardiopulmonary disorders, etc.

Drugs and other substances

Anxiety can be caused due to the usage of certain drugs like amphetamines, certain over the counter medicines, tranquilizers, steroids, contraceptive pills, hormonal treatment, etc.[48]

Symptoms

The symptoms of anxiety neurosis could be physical or mental

The first symptom of anxiety neurosis is the irrational and unjustified fear and apprehension that something terrible will happen. This 'something' could be in the control of the patient (like fear of losing temper and getting into a fight) or beyond the control of the patient (terrorism, natural calamities).

- Some symptoms include listlessness and difficulty in concentration, irritability, short temper and difficulty in retaining information in the mind (forgetfulness) and,

Other physical manifestations include:

- Dryness of mouth and throat.
- Short, rapid intakes and outtakes of breath.

- Increased rate of heartbeat and palpitations.
- Shivering and trembling of hands and legs.
- Involuntary twitching of muscles
- Profuse sweating
- Feeling chilly even when the temperature is warm
- Dizziness and light headedness
- Nausea, hyperacidity, acid reflux reaction
- Insomnia or excessive sleeping
- Fatigue and being devoid of energy
- Excessive or reduced sexual drive[49]

Classification

Obsessive-compulsive disorders

Obsessive- compulsive disorders are characterized by the irresistible entry of unwanted ideas, thoughts or feelings into consciousness or by the need to repeatedly perform ritualistic actions that the sufferer perceives as unnecessary or unwarranted. Obsessive ideas may include recurrent violent or obscene thoughts; compulsive behavior includes rituals such as, repetitive hand washing or door locking.

Somatoform disorders

Somatic disorders which include the so-called hysterical, or conversion, neuroses, manifest themselves in physical symptoms, such as blindness, paralysis, or deafness that are not caused by organic disease. Hysteria was among the earliest syndromes to be understood and treated by psychoanalysts, who believe that such symptoms result from fixations or arrested stages in an individual's early psychosexual development.

Anxiety disorders

Anxiety is the principal feature, manifesting itself either in relatively short, acute anxiety attacks or in a chronic sense of nameless dread. Persons undergoing anxiety attacks may suffer from digestive upsets, excessive perspiration, headaches, heart palpitations, restlessness, insomnia, disturbances in appetite, and impaired concentration.

Phobia

A type of anxiety disorder is represented by inappropriate fears that are triggered by specific situations or objects. Some common objects of phobias are open or closed spaces, are, high places, dirt, and bacteria.

Depression

When neither excessively severe nor prolonged, is regarded as a neurosis. A depressed person feels sad, hopeless, and pessimistic and may be listless, easily fatigued, slow in thought and action, and have a reduced appetite and difficulty in sleeping.

Post-traumatic stress disorder

PTSD is a syndrome appearing in people who have endured some highly traumatic event, such as a natural disaster, torture, or incarceration in a concentration camp. The symptoms include nightmares, a diffuse anxiety, and guilt over having survived when others perished.

Depersonalization disorder

It consists of the experiencing of the world or oneself as strange, altered, unreal, or mechanical in quality. [50]

Diagnosis

Patients with symptoms of mental illness should undergo a thorough physical examination and detailed patient history to rule out organic causes (such as brain tumor or head injury). If neurotic disorder is suspected, a psychologist or psychiatrist will usually conduct an interview with the patient and administer clinical assessments (also called scales, inventories, or tests), to evaluate mental status. Tests which may be administered for the diagnosis and assessment of neurosis include the Neuroticism Extraversion and Openness (NEOR) scale, the Sixteen Personality Factor Questionnaire (16PF), and the Social Maladjustment Schedule. [51]

Laboratory tests for blood sugar (for diabetes) and thyroid function (for Hyperthyroid or Hypothyroid) are also commonly done. There are no laboratory tests

that can diagnose anxiety, although the doctor may order some specific tests to rule out disease conditions.

Although there is no psychiatric test that can provide definite diagnoses of anxiety disorders, there are several short answer interviews or symptom inventories that doctors can use to evaluate the intensity of a patient's anxiety and some of its associated features. These measures include the Hamilton Anxiety Scale and the Anxiety Disorders Interview Schedule (ADIS). [50]

3.4. PHARMACOLOGICAL REVIEW

REVIEW OF SIDDHA DRUG

List of siddha drugs used in neurosis:

- *Peranda parpam*
- *Eggu chendhooram*
- *Kaandha chendhooram*
- *Vallarai nei*
- *Abraga parpam* [46a]
- *Verpenthi ennai* [52]
- *Kaariya parpam*[52a]
- *Panjasootha melugu* [52b]
- *Pirandai chooranam* [52c]
- *Siddhathi ennai* [52d]
- *Sangu parpam* [52e]

REVIEW OF DRUG (Modern medicine)

Anti-anxiety, Anti-depressant and Anti-convulsive drugs:

Anxiolytics

Benzodiazepines

- Diazepam
- Chlordiazepoxide
- Lorazepam
- Alprazolam

5-HT agonist-antagonists

- Buspirone
- Gepirone
- Ipsapirone

Beta-blockers

- Propranolol

Others

- Meprobamate
- Hydroxyzine[53]

Antidepressants

Selective serotonin reuptake inhibitors (SSRIs)

- Fluoxetine
- Fluvoxamine
- Paroxetine

Tricyclic antidepressants (TCA)

- Imipramine
- Desipramine
- Clomipramine

Selective serotonin norepinephrine reuptake inhibitors (SNRIs)

- Venlafaxine
- Desvenlafaxine
- 5HT2 antagonists

Atypical antidepressants

- Mianserine
- Amineptine
- Amoxapine

Monoamine oxidase (MAO) inhibitors

- Phenelzine
- Tranylcypromine
- Clorgyline[53a]

Antiepileptics

Hydantoins

- Phenytoin
- Mephenytoin

Barbiturates

- Phenobarbitone
- Mephobarbitone

Deoxybarbiturate

- Primidone

Iminostilbene

- Carbamazepine

Succinimide

- Ethosuximide

GABA transaminase inhibitors

- Valporic acid
- Vigabatrin

Benzodiazepines

- Diazepam
- Clonazepam
- Lorazepam

Miscellanous

- Acetazolamide
- Magnesium sulphate.[53b]

Mechanism of anxiolytics:

Benzodiazepines have good anxiolytic actions and are the most commonly used drugs for anxiety.

They are CNS depressants. Alprazolam in addition has antidepressant properties.Buspirone is an azapirone with good anxiolytic properties.

It is a selective 5-HT1A agonist. 5-HT1A receptors are inhibitory autoreceptors and binding of buspirone inhibits the release of 5HT. It is useful in mild to moderate anxiety.

Anti-anxiety effect develops slowly over 2 weeks. IT is rapidly absorbed and metabolized in the liver, undergoes extensive first pass metabolism.[53]

Mechanism of Antidepressants:

SSRIs block the reuptake of serotonin from the synapse into the serotogenic nerve endings by inhibiting the serotonin transporter.

About 80% reuptake is inhibited and more serotonin is available at the synapse which in turn results in transcription of certain proteins leading to the production of related proteins like BDNF responsible for the effects of SSRIs.

They are well absorbed when given orally, most are bound to plasma proteins. [53a]

Mechanism of Anti-epileptics:

The strategies to treat epilepsy include enhancing GABA mediated inhibition, reducing excitatory transmission or modifying the ionic conductances.

- Blockade of Na+ channels and prolongation of their inactive and delaying their recovery e.g. phenytoin
- Blockade of low threshold Ca++ current in the thalamic neurons- controls absence seizures, e.g. ethosuximide.
- Enhancing GABA mediated inhibition, e.g. benzodiazipines.[53b]

PHARMACOLOGICAL STUDY IN ANIMAL MODELS

ANTI-ANXIETY ACTIVITY

Anti-anxiety test (Light-Dark Model) in mice and rats

Mice and rats tend to explore a novel environment, but they retreat from the observe sight of a brightly light opened field. Animals are placed in a two chambered system, where they can freely move between a brightly- light open field and a dark corner. After the treatment with anxiolytic they show more crossings between the two chambers and more locomotor activity. The number of crossings between the light and dark sites is recorded.

Animals required	:	Native mice or rats
Equipment's required	:	Dark and light chamber

Procedure

The apparatus consists of a dark and a light chamber which are divided by a photocell equipped zone. A polypropylene animal cage of 44×21×21 cm dimensions is darkened with black spray over one-third of its surface. A partition containing a 13 cm long × 5 cm high opening is used for separating the dark one-third from the bright two-thirds of the cage. This cage shows an activity monitor which counts total locomotor activity. Another electronic system consisting of four sets of photocells across the partition and records the time spent in the light and dark compartments.

Experiments are conducted on native mice or rats. They are treated 30 min before the experiments with test drugs or vehicle given i.p. placed in the cage and observed for 10 min. Groups of 6-8 animals should be used for each dose. Finally, the dose response curves are plotted and number of crossings through the partition between the light and the dark chamber are compared with total activity counts during the 10 min. It has been reported that anxiolytics like diazepam and meprobamate produce a dose dependent facilitatory effect whereas the non- anxiolytics are not effective in this model. The relative potency of anxiolytics in increasing the exploratory behaviour agrees well with their potency observed in lineal trails.

mCPP induced anxiety in rats

mCPP is a metabolite (1-(3-chlorphenyl) piperazine) of antidepressant drug trazodone, which has been classified as 5 HT 2c against. It has been shown to anxiogenic in man and in rats. mCCP includes induces hypophagia and hypolocomotion, inhibits social interaction in rats diminished exploratory activity of rats in the open field test and in the light-dark box test, induces hyperthermia and reduces ultrasound induced defensive behaviour in rats. Antagonism of these symptoms has been used for the screening of anxiolytic drugs.

Animals required : Male Sprague Dawley rats (200-250gm)
Chemicals required : mCCP 7 mg /kg (i.p)
Equipment's required : Locomotion activity cages

Procedure

Male Sprague Dawley rats (200-250gm) are housed in groups of six exposed to 12 hr light/dark cycle with free access to food and water.Locomotion study – Test compound or vehicle are administered orally 1 hr or i.p. 30 min before the locomotion test. mCCP is injected i.p. in a dose of 7 mg/kg 20 min before the test.Thereafter the animals are placed individually in an automated locomotors activity cages and locomotion is recorded for 10min. Hypophagia study-Rats are individually placed in cages on day 1. After getting acclimatized to their home cages, they are deprived of food on day 3 for 24 hr.They are then treated with the test drug or vehicle orally and returned with 5mg/kg mCCP or saline i.p. After a further 20 min weighed quantity of their normal food pellets are placed in their food hampers and the amount remaining after 1hr is measured. The quantity of food consumed by each animal during this period is calculated.

The effects of test compound of mCPP induced hypolocomotion is determined by one-way ANOVA and Newman-Keuls test and the effect on hypophagia is determined by one-way ANOVA and Dunnet's test. The dose producing 50% disinhibition of locomotion is also calculated for comparison with a standard drug. [54]

Behavioral tests

Elevated plus maze is an animal model of anxiety disorder following unconditioned reflex. It is a well-validated animal model to anxiogenic and anxiolytic

effects of drugs to assess which was developed and modified by Kulkarni et al [55]. The test apparatus is a plus-shaped cross of two open (16 x 5 cm) and two enclosed arms (16 x 5 x 12 cm) opposite each at an angle of 90^0 connected with a central area called neutral zone elevated with 25 cm from the floor [56].

Method

The experimental animals were divided into four groups of six animals each. The first group considered as a control group and was treated with vehicle (Normal saline) only. The second group considered as standard group which was treated with reference drug (Diazepam 2 mg/kg body weight). The third and fourth groups were considered as test groups and were treated with test drug at the dose levels of 100mg and 200mg/kg body weight respectively. Animals were fasted 18 h prior to the experiment. An adaptation period of about forty five minutes after the drug treatment, the experimental animals were placed individually in the centre of a platform facing one of the arms was closed, because animals naturally prefer the enclosed arms, as the aversion against the open arms predominates. Then the animal was observed for 5 minutes, recording the number of times that entered into the open or closed arms, and the average time spent by the animal was recorded.

ANTI-DEPRESSANT ACTIVITY

In vivo methods

Reserpine induces hypothermia

In this method depression is produced by inducing reserpine.

Animals required : Swiss albino mice (25-30 grams)

Chemicals required : Reserpine 2.5 mg/kg s.c

Equipment required : Temperature detector

Procedure

The test measures ability of compounds to inhibit Reserpine induced hypothermia in mice.Used to screen potential antidepressants mice (male albino Swiss 25-30 gm) 12 hr day-night cycle and free access to food and water. Reserpine in dose 2.5-5.0 mg/kg, s.c. induces ptosis, hyperthermia and catalepsy.

Reserpine given 2 hr before to test drug. Rectal body temperature is measured every 30 min for 3 hr after drug injection.Measure initial temperature. By measuring of temperature, according to intensity of temperature antidepressant activity of test drug is estimated.

Isolation induced hyperactivity

It is observed that rats when socially deprived for period of 15 days, exhibit depressive behaviour. There is a reduction in spontaneous locomotors activity, exploratory behaviour rearing and stereotypy.Adult Wistar rats of either sex (200-250gm) housed singly in cages (30cm×26cm×20cm) any visual or auditory their normally housed counter parts for 10-15 days.Animals are subjected to behaviour testing on an arbitrary scale for sleep, reduced response to external stimuli, ambulatory behaviour, and stereotype posture.Both classical and newer antidepressants reduce isolation induced depressive behaviour.[54a]

Forced swimming test (FST)

The forced swimming test adopted here is a modification of the method described by Porsolt et al[57]. In this model, rodents forced to swim in a position from which they cannot escape rapidly and become motionless, floating in an upright position and making only small movements to keep their heads above water.

Mice were individually forced to swim for 15 min in glass cylinders (height: 20 cm, diameter: 14 cm), containing 10 cm of water at 25 "C- which is a pre-test, and then mice were removed and dried before being returned to cages. Twenty-four hours later, mice were placed in the cylinders again for a 6-min test in the same system depicted above. The duration of immobility was recorded during the last 4 min of the 6-min testing period. The effect of pre-treatment with test drug was compared and analysed statistically with the tricyclic antidepressant imipramine (15 mg / kg) and recorded.

Tail suspension test (TST)

The tail suspension test (TST) was performed according to the method described by Steru et al with slight modifications [58]. Briefly, the mice were individually suspended by the tail from a metal rod using adhesive tape. The rod was

fixed 50cm above the surface of a table. The total duration of immobility was measured for 6 minutes.

Immobility' was defined as when they hung passively and were completely motionless. Control group of 6 mice were treated with vehicle (Distilled water 2 ml p.o.), test drug-treated and standard group imipramine (15 mg/kg, p.o.). After the administration, the mice were submitted to TST. The immobility of animals were observed and analysed with standard and control groups.

ANTICONVULSANT ACTIVITY

In vitro methods

(i)Hippocampal slices

In vitro brain slice systems are being increasingly used for study of neurophysiologic mechanism of epilepsies. In vitro Hippocampal slices have been especially useful due to involvement of hippocampus in generation of complex partial seizures.

Animals required: Any rodent (rat, mouse or pig)

Equipment's required: Micropipettes, holding chamber, Perspex chamber (1.5×4 cm)

Chemicals required: Saline

Procedure

Animals decapitated, brain removed hippocampus is dissected out. Using a vibratome, slices of about 0.5 mm thickness are made. Cutting approximately perpendicular to long axis of hippocampus preserves the three- neuron synaptic circuit and associated recurrent circuitry. After cutting the slices are incubated for two hours in holding chamber in which they are kept in 28℃ worm saline equilibrated with 95% 02 and 5% CO2. Slices can be kept healthy for more than 18 hr if handled properly. For recording, the slices are transferred to Perspex chamber and attached to its bottom. Slices are either kept in 3mm thick layer of 32°C warm saline or submerged in liquid artificial CSF. Intra cellular recording from the pyramidal neurons in the slice are done by passing micropipettes (tip diameter < 0.5mm) into the stratum pyramidal under microscopic control.

Reading is taken by adding drug to the slice medium and recording the spontaneous or shock evokes repetitive fixing of neurons.

(ii)Excitatory amino acid receptor binding assay

[^{3}H] CCP- binding assay

[^{3}H] TCP- binding assay

[^{3}H] Glycine- binding assay

In vivo methods:

(i)Electrically induced seizures

(a) Threshold models

(b) Maximal electroshock seizures

(c) Focal electrical stimulation such as kindling

(d) Other models of kindling- PTZ test

(a) Threshold models

Used to screen drugs with efficacy against the generalized tonic-clonic and focal seizures.

Procedure

Animals required : Mice(18-30 gm)

Equipment's required : Electrical stimulator

Group of 8-10 male mice (18-30 gm.) used for dosing. Corneal or ear electrodes are used to provide electrical stimulation from stimulator (at constant frequency of 50-60/sec for 0.2 sec duration).Threshold is usually determined current or voltage inducing hind limb extension in 50% of animals i.e., CC50 and CV50 or EV50 respectively. Control thresholds in mice are about 6-9 mA (CC50) or 90-140 with (CV50 or EV50) depending on stain age and method of stimulation.

Evaluation of test drug is taken as measure of its efficacy. Comparison of drug effects required calculation of that dose that elevates the threshold by 20%. Control threshold determination should be undertaken on each day parallel to threshold determinations in drug treated animals. Use of an animal more than once a day is not recommended as post octal rise in seizure threshold has been noted.

(b) Maximal induced Electroshock Seizure (MES) Test

Useful to primary and secondary generalized tonic- clonic seizures.

Procedure

Group of 8-10 animals used per dose of drug(rats or mice). Electrical stimulation applied with corneal or electrodes with stimulator constant voltage at frequency of 50-60/ sec. Electrodes are moistened with saline solution before application. Usually 2-5 times current strength. 50 mA in mice and 150 mA in rats. Potency is determined by calculation of ED50 for suppression of tonic hind limb extension.

(c) Pentylenetetrazole (PTZ) Test

PTZ is tetrazole derivative with consistent convulsive effect in mice, rats, cats, primates etc. Used for screening the drugs effective in petit mal or absence seizures. Threshold for clonic seizures after i.v.

Infusion of PTZ

8-10 mice are taken. 1% solution PTZ i.v. infusion at the rate of 0.3ml per min isgiven. Animals develop seizures as one or more isolated jerks followed by generalizedclonic seizures with loss of righting reflexes followed by maximal tonic-clonic seizures.

Dose for the production of generalized clonic seizures with loss of righting reflex ispreferably taken as an end point. Threshold is calculated as the mean dose of PTZ thatinduces seizures in the group tested and is about 50 mg/kg for clonic seizures and90mg/kg for maximal tonic-clonic seizures in mice.

(ii) Chemically induced convulsions

Numerous chemical compounds procedure seizures.

Chemoconvulsants including generalized seizures after systemic administration.

Examples: Pentylenetetrazole, Bicucullin, Picrotoxin, Isoniazid

Chemoconvulsants including focal seizures after central administration.

Examples: Pencillin, Kainic acid. [54b]

3.5. LATERAL RESEARCH

Immunomodulatory and Antitumor activity of Piper longum

Alcoholic extract of the fruits was 100% toxic at a concentration of 500 microg/ml to Dalton's lymphoma ascites (DLA) cells and 250 microg/ml to Ehrlich ascites carcinoma (EAC) cells. Piperine was found to be cytotoxic towards DLA and EAC cells at a concentration of 250 microg/ml. Alcoholic extract and piperine was also found to produce cytotoxicity towards L929 cells in culture at a concentration of 100 and 50 microg/ml, respectively. [59]

Anti-hyperglycemic activity of *Piper longum*

The aqueous and methanolic extracts of piper longum root produced significant anti-hyperglycemic activity at a dosage of 200 mg/kg b.w in diabetic treated rats [60].

Anti-microbial activity of *Cuminum cyminum*

Within the limitations of the present study it was concluded that *Cuminum cyminum* essential oil exhibited a strong antimicrobial activity against the microbial flora of the teeth with failed endodontic treatments and it was biocompatible for L929 mouse fibroblasts. [61]

Antioxidant activity of *Cuminum cyminum*

Antioxidant properties were assayed using DPPH free radical scavenging, inhibition of metal induced oxidation of proteins & lipids and protection of DNA against H 2 O 2-induced oxidative stress. IC 50 value of cumin was estimated by these mechanisms. Cumin extract had polyphenols (7.45±.10 mg GAE/g dry seeds) as major antioxidant principle. [62]

Anti-ulcerogenic activity of *Elettaria cardamomum*

The gastro protective action of petroleum ether soluble fractions and essential oils of *E.cardamomum* is due to increase in gastric motility and it has inhibitory effect in over production of some products of 5- lipoxygenasepathway[63].

Anti-inflammatory activity and Anti-Rheumatic activity of *Piper nigrum*

Piperine has anti-rheumatic effects in animal models and anti-inflammatory effects on IL1β-stimulated FLSs. Piperine also inhibited the activation of the transcription factor AP-1, but not NFκB, in our system [64].

Antibacterial activity of *Piper nigrum*

The acetone extract of black pepper displayed excellent inhibition on the growth of Gram positive bacteria. Staphylococcus was susceptible followed by Bacillus and Streptococcus. The MIC values are 125, 250 and 500 ppm, respectively. Among the Gram negative bacteria Pseudomonas was more susceptible to black pepper followed by E.coli, klebsiella and salmonella [65].

Antibacterial activity of *syzygium aromaticum*

Methanolic extract of clove showed maximum zone of inhibition 24mm against S. aureus while minimum was 19 mm against P. aeuginos. Ethanolic extract of clove showed maximum zone of inhibition 20 mm against P. aeuginosa while minimum was 18mm against E. coli [66].

Hepatoprotective activity of *Syzygium aromaticum*

50 % ethanolic extract of S. aromaticum can attenuate liver necrosis in animal model. Liver injury was induced by single intraperitoneal injection of thioacetamide (400 mg/kg b. w.). Oral administration of the extract (800 mg/kg b. w.) for three consecutive days could significantly ameliorate the changes associated with hepatic injury, particularly the levels serum biochemical markers of liver injury and oxidative stress.

The protective action may be attributed to eugenol, which has been shown to be present in the test extract[67].

Anti-diabetic activity of *Cinnamomum tamala*

Ethanolic leaf extract of *C tamala* exhibit significant anti-hyperglycemic activities in STZ-induced rats. The extract also showed improvement in lipid profile, body weight and oral glucose tolerance test (OGTT) results, hence might be valuable in diabetes[68].

Anti-bacterial activity of *Phyllanthus emblica*

The fruit extracts (Table 2) of *P. emblica* exhibited superior activity against S. aureus at 20mg/ml for example, 29 mm was recorded as diameter zone of inhibition. This was followed by 18 mm B. subtilis, 15 mm P. aeruginosa and E. coli 12 mm respectively[69].

Anti-inflammatory activity of *Phyllanthus emblica*

Hydroalcoholic extract of Emblica officinalis (HAEEO) at a dose of 700 mg/kg exhibited significant anti-inflammatory activity with 70.0% inhibition of paw edema and was comparable to the indomethacin group. In autacoid-induced models of inflammations (against serotonin, histamine, and PGE2), HAEEO produced significant inhibitory activity. The present study exhibited HAEEO's anti-inflammatory action by means of inhibiting the synthesis, release, or action of inflammatory mediators like histamine, serotonin, and prostaglandins that are involved in inflammation[70].

Antibacterial activity of *Myristica fragrans*

Both ethyl acetate and ethanol crude extracts from flesh, seed, and mace of *Myristica fragrans* exhibited good potential against oral pathogens. Ethyl acetate extract of flesh has strong antibacterial activity compared to the other extracts. While, ethanol extracts of seed and mace of *Myristica fragrans* gave higher inhibitory and bactericidal activities than their ethyl acetate extracts. The antibacterial activities of the extracts against both Gram-positive cariogenic and Gram-negative periodontopathic bacteria have confirmed its broad-spectrum antibacterial activity [71].

Antibacterial activity of *Mesua nagassarium*

The methanol extract of whole flowers of *Mesua ferrea* antibacterial activity. It could inhibit a large number of Gram-positive and Gram-negative bacteria at concentration ranges of 100 to50 µg/ml, or even lower, as against vibrios and *Escherichia coli.* The extract at 200 µg/g body weight dosages, could significantly reduce the viable count of the strain *Sulmonella typhimurium* ATCC 6539 in liver, spleen and heart blood of the extract treated challenged mice. [72]

4. MATERIALS AND METHODS

Drug selection

In this dissertation "***Kandathirika Chooranam"*** was taken as a trial drug for Anti-anxiety, Anti-depressant and Anti-convulsant activities from the Siddha literature[73].

Collection of the raw materials

All the raw materials were bought from the *Ramaswamysetti* country drug store in Parrys Corner, Chennai.

Identification and Authentication of the drug

All the raw materials were identified and authenticated by the Botanist and *Gunapadam* experts in Government Siddha Medical College, Arumbakkam, Chennai – 106.

The specimen sample of all the herbs have been preserved in PG *Gunapadam* department individually for future reference.

(Ref No: GSMCC/PGGM/0043-60/2014-17)

4.1. Preparation of the trial drug

Table no. 2 Ingredients

S.NO	TAMIL NAME	COMMON NAME	BOTANICAL NAME
1.	*Inji*	Ginger	*Zingiber officinale*
2.	*Kadukurohini*	Picrorhiza	*Picrorhizascorphulariflora*
3.	*Thippilimoolam*	Long pepper root	*Piper longum*
4.	*Chukku*	Dried ginger	*Zingiber officinale*

S.NO	TAMIL NAME	COMMON NAME	BOTANICAL NAME
5.	*Chirakam*	Cumin seeds	*Cuminum cyminum*
6.	*Elam*	Cardamom seeds	*Elettariacardamomum*
7.	*Milagu*	Black pepper	*Piper nigrum*
8.	*Lavangapathiri*	Cassia cinnamom	*Cinnamomum tamala*
9.	*Nellimulli*	Indian gooseberry	*Phyllanthus emblica*
10.	*Jathipathiri*	Nutmeg leaf	*Myristica fragrans*
11.	*Sirunaga poo*	Ceylon ironwood	*Mesua nagassarium*
12.	*Thalisapathiri*	Flaiurtiacalaphracta	*Abies spectabilis*
13.	*Athimathuram*	Indian liquorice	*Glycyrrhiza glabra*
14.	*Lavangam*	Cloves	*Syzygium aromaticum*
15.	*Koogaineeru*	East indian arrow root	*Maranta arundinaceae*
16.	*Nei*	Ghee	_
17.	*Sarkarai*	Sugar	*Saccarum officinarum*

Purification of the drugs

All the drugs mentioned here were purified as per the Siddha literature. [74]

- *Inji* : Skin of dried ginger was peeled off.
- *Kadukurohini* : Roots of Kattugurohini are immersed within the extract of Vitex leaf and then dried.
- *Thippilimoolam* : Nodes were removed and dried.
- *Chukku* : Skin of dried ginger was scruped off.

- *Chirakam* : Roasted in the pan.
- *Elam* : Roasted in the pan and outer skins are removed.
- *Milagu* : It was soaked in sour buttermilk for 3 hours and allowed to dry.
- *Lavangapathiri* : Roasted in the pan.
- *Nellimulli* : Driedfruit of Indian gooseberry was boiled with milk and the seeds were removed.
- *Jathipathiri* : Roasted in the pan.
- *Sirunaga poo* : Roasted in the pan.
- *Athimathuram* : The root of Indian liquorice was cleaned with water and cut into small pieces and then dried.
- *Thalisapathiri* : Roasted in the pan.
- *Lavangam* : Flower buds were removed.
- *Koogaineeru (Kizhangu)*: It was dried in sunlight.

Preparation of the drug

Procedure

Roasted the ginger with ghee and take all the purified ingredients were grounded separately as powderand then the powder was mixed with sugar. The powder was sieved through a white cloth and kept in an air tight container. It was labeled as "***Kandathirika Chooranam"*** *(KCM).*

Purification of the Chooranam:

***Pittaviyalmurai* (Steaming process):**

The *Kandathirika Chooranam* was purified by *Pittaviyal* method (steam cooking in milk) as per Siddha classical literature. A mud pot was taken and it was quarter filled by milk and quarter filled by pure water. The mouth of the pot was sealed by a cloth. This *Chooranam* then placed over the cloth and the pot was heated. The same drug was later dried and powdered then sieved again. It was used for the further study. [75]

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 the medicine	: *Chooranam*
Route of Administration	: Enteral
Dose	: 2 – 4gm twice a day.

4.2.STANDARDIZATION OF THE DRUG

Standardization 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.

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 noted. Results were noted and tabulated in Table No. 6

4.2.1. Physicochemical analysis

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

Solubility: **A.** A little of the *Kandathirika Chooranam* was shaken well with distilledwater. **B.** A little of the*KCM* wasshaken well with con Hcl andCon $H2SO_4$. Sparingly soluble character indicates the presence of Silicate.

pH value: Potentio-metrically 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.

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.

Determination of Ash Values

Total Ash

3g of the *KCM* 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 5mins. 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 is 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.

Loss on Drying

The powdered drug was taken and dried in the oven at 100- 105°C to constant weight. The result was noted. Results were noted and tabulated in Table No:7.

4.2.2. Phytochemical analysis

The phytochemical screening of *KCM* extract was assessed by standard method. Phytochemical screening was carried out on the *KCM* extract using aqueous extract to identify the major natural chemical groups such as tannins, saponins, flavonoids, phenols, terpenoids, alkaloids, glycosides, cardiac glycosides, coumarins and steroids. Generalreactions in these analyses revealed the presence or absence of these compounds in the ***Kandathirika Chooranam*** extracttested[76].

1. Test for Tannins

For tannin identification, 1 ml of the plant extract, one ml of ferric chloride (5% $FeCl_3$) was added. Formation of dark blue or greenish black indicates the presence of tannins.

2. Test for Saponines

For saponin identification, 2ml Plant extract, 2ml of distilled water was added and shaken in graduated cylinder for 15 min lengthwise, and formation of 1cm layer of foam indicates the presence of saponins.

3. Test for Quinones

For Quinonesidentification, 1ml Plant extract, 1ml of concentrated sulphuric acid (H_2SO_4) was added. Formation of red colour indicates the presence of Quinones.

4. Test for Flavonoids

For flavonoids identification, 2ml of plant extract, 1ml of 2N sodium hydroxide (NaOH) was added. Formation of yellow colour indicates the presence of flavonoids.

5. Test for Alkaloids

For Alkaloids identification, 2ml Plant extract, 2ml of concentrated Hydrochloric acid (Hcl) was added. Then few drops Mayer's reagent was added**.** Presence of green colour or white precipitate indicates the presence of alkaloids.

6. Test for Glycosides

For Glycosides identification, 2ml of the plant extract, 3ml of chloroform and 10% ammonium solution was added. Formation of pink colour indicates the presence of glycosides.

7. Test for Cardiac glycosides

For Cardiac glycosides identification, 0.5 ml of the plant extract, 2 ml of glacial acetic acid and few drops of 5 % ferric chloride were added. This was under layered with 1 ml of concentrated sulphuric acid. Formation of brown ring at interface indicates the presence of cardiac glycosides.

8. Test for Terpenoids

For Terpenoids identification, 0.5 ml of the plant extract, 2 ml of chloroform along with concentrated Sulphuric acid. Formation of red brown colour at the interface indicates the presence of Terpenoids.

9. Test for Phenols

For phenol identification, 1ml of the plant extract, 2ml of distilled water followed by few drops of 10 % ferric chloride was added. Formation of blue / green colour indicates the presence of phenols.

10. Test for Steroids

For steroid identification, 0.5 ml of the plant extract, 2 ml of chloroform and 1 ml of Sulphuric acid (H_2 SO_4) were added. Formation of reddish brown ring at interface indicates the presence of steroids.

11. Test for Coumarins

For coumarins identification, 1 ml of plant extract, 1 ml of 10 % NaOH was added. Formation of yellow colour indicates the presence of coumarins.

12. Test for Anthocyanin and Beta cyanin

For Anthocyanin and Beta cyanin identification, to 2ml of the plant extract, one ml of 2N sodium hydroxide (NaOH) was added and heated for 5 min at 100 °C. Formation of bluish green colour indicates the presence of anthocyanin and formation of yellow colour indicates the presence of betacyanin. Results were noted and tabulated in Table No. 8.

4.2.3. TLC/ HPTLC finger print studies

HPTLC finger printing was carried out as per the reference [77].

Preparation of spray reagent-vanillin-sulphuric acid reagent

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

Chromatographic conditions

Instrument	: CAMAG (Switzerland).
Sample Applicator	: CamagLinomat - 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 gel 60(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°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-sulphuricacid reagent heated at 105° till colour spots appeared. Results were noted and tabulated in Table No:9

4.2.4 Bio-chemical analysis

Methodology for chemical analysis

Preparation of extract

5gm of *KCM* 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.[78]

Table no:3Test 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 *KCM* 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 *KCM* extract was taken in a clean test tube, few drops of Magnason reagentwas added in drops.	Formation of Blue colour precipitate	Presence of Magnesium
Test For Ammonium: 2mlof *KCM* extract was taken in a test tube and added few ml of Nessler's reagent.	Appearance of Brown colour	Presence of Ammonium

PROCEDURE	OBSERVATION	INFERENCE
Test For Sodium: 2 pinches of *KCM* 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 *KCM* 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 *KCM* 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 2m1 *KCM* of the extract was taken in a test tube sodium hydroxide drops were added to it.	White precipitate obtained	Presence of Aluminium
Test For Lead: 2 ml of *KCM* 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 *KCM* 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*KCM* extract wastaken 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 *KCM* 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:13

Table no.4. Test for acidic radicals

PROCEDURE	OBSERVATION	INFERENCE
Test for Sulphate: 2 ml of the *KCM*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 *KCM* extract was taken in a test tube and then treated with Silver nitrate solution.	Formation of White precipitate	Presence of Chloride
Test for Phosphate: The *KCM* 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 *KCM* was heated with copper turnings andconcentrated H2SO4 and observed the test tube vertically down.	Characteristic changes	Presence of Nitrate

Results were noted and tabulated in Table No.14

4.2.5 ANTIMICROBIAL LOAD

Availability of microbial load:

Enumeration of bacteria by plate count – agar plating technique[79]

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.

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 toused 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:

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

Results were noted and tabulated in Table No.16

4.2.6 Following instrumental analysis is carried out to study quantitative analysis of *Kandathirika Chooranam*

FT-IR (Fourier Transform Infra-Red)

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.

In FT-IR infrared is passed from a source through a sample. This infrared is 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 is no two unique molecular structures producing the same infrared spectrum. It is 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 itsSpeed, Sensitivity, Mechanical Simplicity, and 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 of unknown crystalline materials (e.g. minerals, inorganic compounds). Determination of unknown solids is important to studies in geology, environmental science, material science and biology.

Applications:

- Characterization of crystalline materials [80]
- 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 to inferring stress and strain
    - determining dislocation density and quality of the film by rocking curve 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 a polycrystalline 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 crystal systems 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.Results were noted in Chart No:7

SEM (Scanning Electron Microscope)

In scanning electron microscope high-energy electron beam is focused through a probe towards the sample 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 is collected by an appropriate detector.

The types of signal produced by a scanning electron microscope include

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

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. Results were shows in Fig No:5.

Fig no.3. FTIR

Fig no.4. SEM

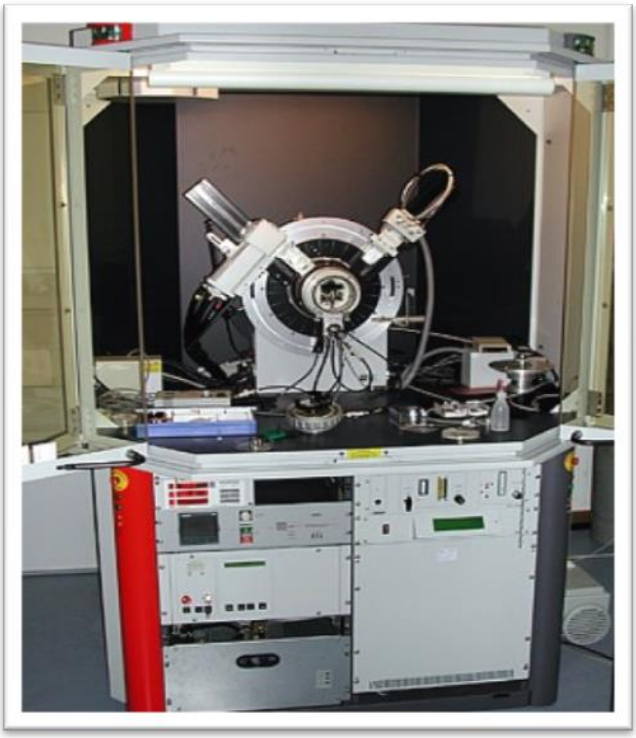


Fig no : 5 XRD

4.3 TOXICITY STUDIES

4.3.1Acute toxicity - OECD 423 Guidelines

The study was conducted as per the guidelines of Organization for Economic Cooperation and Development (OECD)-423

The experimental protocol was approved by the institutional ethical committee (IAEC) under CPCSEA **(approval No: IAEC/XLVIII/08CLBMCP/2016)**

Experiment procedure:

Acute toxicity study is used in the evaluation of the immediate effect of the trail drug after administration of a single dose. Acute toxicity studies were carried out according to the OECD (Organization of Economic Co-operation and Development) guidelines 423. Healthy female rats, weighing 100–150 g, were selected and oral administration of the single doses of *Kandathirika Chooranam* were done aseptically by suspending in 1% SCMC [81].

Experimental Animals:

The preferred rodent species is the rat, although other rodent species may be used. Normally females are used. This is because literature surveys of conventional LD50 tests show that females are generally slightly more sensitive. Females should be nulliparous and non-pregnant. Each animal, at the commencement of its dosing, should be between 8 and 12 weeks old and its weight should fall in an interval within +20 % of the mean weight of any previously dosed animals.

Administration of doses:

Kandathirika Chooranam in 1% SCMC was administered as a single oral dose by gavage using a feeding needle. Animals were fasted prior to dosing. Following the period of fasting, the animals were weighed and then the test substance was administered.

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 observed as per the guideline after substance administration. An oral (p.o) dose of 5 mg/kg, 50 mg/kg, 300 mg/kg and 2000 mg/kg was administered step by step according to the guidelines. The general behaviors of the rats were continuously monitored for 1 h after dosing, periodically during the first 24 h (with special attention given during the first 4 hours and then daily thereafter, for a total of 14 days. Changes in the normal psychomotor activity and external morphology and their body weights were monitored periodically before dosing and the time at which signs of toxicity or mortality were recorded. The visual observations included skin changes, mobility, aggressively, sensitivity to sound and pain, as well as respiratory movements. They were deprived of food, but not water 12 h prior to the administration of the test substance.

Finally, the number of survivors was noted after 24 h and these animals were then maintained for a further 14 days and observations made daily. The toxicological effect was assessed on the basis of mortality [82].

Number of animals and dose levels:

Three animals are used for each step. The dose level used as the starting dose was selected from one of four fixed levels, 5, 50, 300 and 2000 mg/kg body weight. The starting higher dose level was not likely to produce mortality in dosed animals. The available information suggests that mortality is likely at the highest dose level, so the trial or limit test was conducted. The time interval between treatment groups is determined by the onset, duration, and severity of toxic signs.

Observations:

Animals were 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 somato motor activity and behavior pattern. Attention was directed to observations of tremors, convulsions, salivation, diarrhea, 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 humanely killed. When animals are killed for humane reasons or found dead, the time of death should was recorded.

4.3.2 Repeated dose 28-day oral toxicity studies

Repeated dose 28-day oral toxicity study of *Kandathirika Chooranam* on rats (OECD – 407 guidelines)

In the assessment and evaluation of the toxic characteristics of a chemical, the determination of oral toxicity using repeated doses may be carried out after initial information on toxicity has been obtained by acute toxicity testing. This is intended to

investigate effects on a very broad variety of potential targets of toxicity. It provides information on the possible health hazards likely to arise from repeated exposure over a relatively limited period of time, including effects on the nervous, immune and endocrine systems. Regarding these particular endpoints, it should identify chemicals with neurotoxic potential, which may warrant further in depth investigation of this aspect, and chemicals that interfere with thyroid physiology. It may also provide data on chemicals that affect the male and/or female reproductive organs in young adult animals and may give an indication of immunological effects[84].

Table no.5. Repeated Dose 28-Days Oral Toxicity Studies

Test Substance	*Kandathirika Chooranam*
Animal Source	Animal house of King Institute of Preventive Medicine
Animals	Male and Female Wistar Albino Rats
Age	More than 8 weeks
Acclimatization	Seven days prior to dosing
Veterinary examination	Prior to and at the end of the acclimatization period
Identification of animals	By cage number, animal number and individual marking on fur
Diet	Pelleted feed supplied by Saimeera foods Pvt Ltd, Bangalore
Water	Aqua guard portable water in polypropylene bottles adlibitum.
Housing &Environment	The animals were housed in Polypropylene cages provided with bedding of husk
Housing temperature	Between 20 & 24°C
Relative humidity	Between 30% and 70%,
Dark and light cycle	Each of 12 hours

Justification for Dose Selection:

The results of acute toxicity studies in rats indicated that *Kandathirika Chooranam* was non- toxic and no behavioural changes were observed up to the dose level of 2000mg/kg body weight. The oral route was selected for use because oral route is considered to be a proposed therapeutic route[84].

Preparation and administration of dose:

Kandathirika Chooranam at three doses respectively was suspended in 1%SCMC. It was administered to animals at the dose levels of 100 and 200 mg/kg.The test substance suspensions were freshly prepared every day for 28 days. The control animals were administered vehicle only. Administration was by oral (gavage), once daily for 28 consecutive days.

Methodology

Randomization, Numbering and Grouping of Animals:

Ten Rats (Five Male and Five Female) in each group randomly divided into three groups for dosing up to 28 days. Animal's acclimatization period of 7 days to laboratory conditions prior to the initiation of treatment. Each animal was fur marked with picric acid. The females were nulliparous and non-pregnant.

Observations in sub-acute toxicity studies:

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 and at 5 days intervals throughout the course of study and at termination to calculate relative organ weights. From the data, group mean body weights and percent body weight gain were calculated.

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.

Terminal studies:

Laboratory Investigations:

Following laboratory investigations were carried out on day 29 in animals' fasted over-night. On 29th day, the animals were fasted for approximately 18 h, then slightly anesthetized with ether and blood samples were collected from the retro orbital plexus into two tubes:

One with EDTA for immediate analysis of haematological parameters, the other without any anticoagulant and was centrifuged at 4000 rpm at 4 °C for 10 minutes to obtain the serum. Serum was stored at 20 °C until analysed for biochemical parameters.

Haematological Investigations:

Blood samples of control and experimental rats was analysed for haemoglobin content, total red blood corpuscles (RBC), white blood corpuscles (WBC) count, MCV and PCV. From the estimated values of RBC count (millions/mm3) and PCV (volumes percent), MCV was calculated.

Biochemical Investigations:

Serum and Urine was used for the estimation of biochemical parameters. Samples of control and experimental mice were analysed for protein, bilirubin, urea, uric acid, creatinine, triglyceride, cholesterol and glucose levels was carried using standard methods. Activities of glutamate oxaloacetate transaminase/ Aspartate aminotransferase (GOT/AST), glutamate pyruvate transaminase/ Alanine amino transferase (GPT/ALT) and alkaline phosphatase were estimated as per the colorimetric procedure.

Necropsy:

All the animals were sacrificed on day 29. Necropsy of all animals was carried out and the weights of the organs including liver, kidneys, adrenals, spleen, brain, heart, uterus and testes/ovaries were recorded. The relative organ weight of each animal was then calculated as follows;

$$\text{Relative organ weight} = \frac{\text{Absolute organ weight (g)}}{\text{Body weight of rats on sacrifice day (g)}} \times 100$$

Histopathology:

Histopathological investigation of the vital organs was done. The organ pieces (3-5µm thick) of the highest dose level of 400 mg/kg were preserved and were fixed in 10% formalin for 24 h and washed in running water for 24 h. Samples were dehydrated in an auto technical 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. The organs included brain, heart, kidneys, liver and lungs of the animals were preserved they were subjected to histopathological examination.

Statistical analysis:

Findings such as clinical signs of intoxication, body weight changes, food consumption, and haematology and blood chemistry were subjected to One-way Anova. Followed by dunnet't' test using a computer software programme. (Graph Pad Prism5.0)

4.4 PHARMACOLOGICAL STUDY

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 Female

BALB/C Mice(more than 20gm) and Wister rats 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.

4.4.1 Anti-anxiety activity of *Kandathirika Chooranam*

Experimental protocols

Wister rats were randomly selected to form groups of 6 each. The animals were acclimatized one hour before for behavioral tests.

Group I: Test animals received no drugs and kept as control.

Group II: These animals received 2mg/kg of the diazepam drug as standard.

Group-III: These animals received 200mg/kg of KCM.

Group-IV: These animals received 400mg/kg of KCM.

Behavioral tests

Elevated plus maze is an animal model of anxiety disorder following unconditioned reflex. It is a well-validated animal model to anxiogenic and anxiolytic effects of drugs to assess which was developed and modified by Kulkarni et al [55]. The test apparatus is a plus-shaped cross of two open (16 x 5 cm) and two enclosed arms (16 x 5 x 12 cm) opposite each at an angle of 90^0 connected with a central area called neutral zone elevated with 25 cm from the floor [56].

Method

The experimental animals were divided into four groups of six animals each. The first group considered as a control group and was treated with vehicle (Normal saline) only. The second group considered as standard group which was treated with reference drug (Diazepam 2 mg/kg body weight). The third and fourth groups were considered as test groups and were treated with extract of *KCM* at the dose levels of 100mg and 200mg/kg body weight respectively. Animals were fasted 18 h prior to the experiment. An adaptation period of about forty five minutes after the drug treatment, the experimental animals were placed individually in the center of a platform facing one of the arms was closed, because animals naturally prefer the enclosed arms, as the aversion against the open arms predominates. Then the animal was observed for 5 minutes, recording the number of times that entered into the open or closed arms, and the average time spent by the animal was recorded.

Average time was calculated by the following formula.

Average time =total duration in the arms / number of entries.

During the experiment, all the animals were allowed to socialize to avoid unnecessary anxiety. After each animal, the test apparatus was carefully cleaned.

4.4.2 Anti- depressant activity of *Kandathirika Chooranam*

In the present study, the antidepressant-like activity was assessed in mice model of depression derived, namely, the forced swimming test (FST) and Tail suspension test (TST).

Experimental protocols

- Group 1 treated as a control group received 2 ml of distilled water.
- Group 2 considered as a test group received *Kandathirika Chooranam* (200mg/kg, p.o)
- Group 3 treated as standard group received Imipramine (15 mg/kg).

All the test drug, standard drug and vehicle were orally administered to mice 30 minutes before the experiment.

All the experiments were performed in either the morning (between 8 am and 1 pm) or in the evening (at 5 pm). The repeated treatment (10 days) with *Kandathirika Chooranam* and standard drug Imipramine were administered in the evening (at 5 pm).

Forced swimming test (FST)

The forced swimming test adopted here is a modification of the method described by Porsolt et al[57]. In this model, rodents forced to swim in a position from which they cannot escape rapidly and become motionless, floating in an upright position and making only small movements to keep their heads above water.

Mice were individually forced to swim for 15 min in glass cylinders (height: 20 cm, diameter: 14 cm), containing 10 cm of water at 25 "C- which is a pre-test, and then mice were removed and dried before being returned to cages. Twenty-four

hours later, mice were placed in the cylinders again for a 6-min test in the same system depicted above.

The duration of immobility was recorded during the last 4 min of the 6-min testing period.The effect of pretreatment with *Kandathirika Chooranam* was compared and analysed statistically with the tricyclic antidepressant imipramine (15 mg / kg) and recorded.

Tail suspension test (TST)

The tail suspension test (TST) was performed according to the method described by Steru et al[58]with slight modifications. Briefly, the mice were individually suspended by the tail from a metal rod using adhesive tape. The rod was fixed 50cm above the surface of a table. The total duration of immobility was measured for 6 minutes.

Immobility' was defined as when they hung passively and were completely motionless. Control group of 6 mice were treated with vehicle (Distilled water 2 ml p.o.), test drug-treated group (*Kandathirika Chooranam* 200mg/kg, p.o.), and standard group imipramine (15 mg/kg, p.o.). After the administration, the mice were submitted to TST. The immobility of animals were observed and analysed with standard and control groups.

4.4.3 Anti-convulsant activity of *Kandathirika Chooranam*

Experimental protocols

Albino wistar rats of either sex weighing 160 to 220 gm were divided into four groups of six animals each.

Group-I received vehicle control (1% w/v SCMC, 1ml/100 g)

Group-II received standard drug (Diazepam, 4mg/kg) intraperitoneally,

Group-III and IV, extract of *KCM* (200 and 400 mg/kg/body weight) *p.o*respectively for 20 days.

On the 20th day, Pentylenetetrazole (PTZ) (90mg/kg body weight, *s.c*) was administered to all the groups to induce clonic convulsions. Animals were observed for a period of 30mins post – PTZ administration.

Pentylenetetrazole-Induced Seizures

The method as described by Vellucci and Webster[85], and Moezi et al., [86]was used. The Chooranam extract was administered at doses of200 and 400 mg kg body weight orally. Intraperitoneal (i.p) injection of diazepam (0.1, 0.3, and 1 mg kg) was used as reference anticonvulsant drug. Animals were pretreated with the plant extract thirty minutes and diazepam fifteen minutes before administration of pentylenetetrazole (PTZ) 85 mg kg subcutaneously. Control animals were pretreated with distilled water (10 mLkg ,p.o.). The onset of, total duration as well as frequency of clonic seizures were measured within a thirty minute period.

5. RESULTS AND DISCUSSION

Many studies have been carried out to bring the efficacy and potency of the drug "***Kandathirika Chooranam".*** The study includes literary collections, organoleptic characters, physicochemical, phytochemical analysis, Acid-Base radical test, Bacterial load, instrumental analysis, toxicological study and pharmacological study. The drug "***Kandathirika Chooranam"*** has been selected for **Anti-Anxiety, Anti-depressant and Anti-convulsant**activity in reference with the text ***"Agasthiyar Vaithiya Sindhamani Venba 4000 Ennum Mani 4000 Part 1".pg no:162-163.***

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

Standardization 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 are derived. Its result has been tabulated and interpretation is made below.

Thus, it is to give a complete justification, to bring the effectiveness of the trial drug *Kandathirika Chooranam*.

Siddha parameters of testing for Chooranam

- *Chooranam* tends to be amorphous.
- It should be never damp.
- The fineness of the sieve should be100 mesh or still finer

  and the *Chooranam* gave the inference of amorphous, it doesn't damp.

ORGANOLEPTIC CHARACTERS

The following characters have been noted in *Kandathirika chooranam*.

Table no 6.Organoleptic Character

S.No	Parameter		Results
1.	Colour		Brown
2.	Odour		Aromatic
3.	Taste		Bitter
4.	Texture		Fine powder
5.	Particle size		Completely pass through sieve no 88
6.	Solubility		
	i.	Distilled water	Soluble
	ii.	Benzene	Soluble

S.No	Parameter		Results
	iii.	Chloroform	Soluble
	iv.	Carbon tetra Chloride	Soluble
	v.	Xylene	Soluble
	vi.	Petroleum ether	Soluble
	vii.	Propylene glycol	Not Soluble

Table no 7. PHYSICOCHEMICAL ANALYSIS

S.No	Parameter	Result
1.	pH	3.83
2.	Total Ash (%)	3.65
3.	Water soluble Ash(%)	2.21
4.	Acid insoluble Ash (%)	0.49
5.	Loss on drying (%)	6.33
6.	Water Soluble extractive (%)	38.75
7.	Alcohol Soluble extractive (%)	39.29

- The physicochemical analysis of the drug result reveals the pH, Moisture, Solubility, Water soluble ash, Ash and Acid insoluble ash.
- **pH:** It is a measure of hydrogen ion concentration; it is the measure of the acidic or alkaline nature. 7.0 is a neutral, above 7.0 is an alkaline and below are acidic.
- The pH of the drug *Kandathirika Chooranam* is 3.83 which is acidic in nature.

- **Ash**: Ash constitutes the inorganic residues obtained after complete combustion of a drug. Thus Ash value is a validity parameter describe and to assess the degree of purity of a given drug.

- **Acid insoluble ash**: The acid insoluble ash value of the drug denotes the amount of siliceous matter present in the plant. The quality of the drug is better if the acid insoluble value is low. It is 0.49 for KCM.
- **Water soluble ash:** Water-soluble ash is the part of the total ash content, which is soluble in water. It is 2.21 for KCM
- **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 *KCM* is 6.33[87].

PHYTOCHEMICALS ANALYSIS

Table no.8.Phytochemicals screening test

Phytochemical Test	KCM Aqueousextract
Alkaloid	Present
Glycosides	Present
Saponin	Absent
Carbohydrate	Absent
Phytosterol	Absent

Phytochemical Test	KCM Aqueousextract
Phenol	Present
Triterpene	Present
Flavonoid	Present
Tannin	Present
Protein	Present

Interpretation

Phytochemicals are natural bioactive compound, found in plants and fibers, which act as a defense system against diseases and more accurately to protect against diseases**.**The phytochemical analysis reveals the presence of Alkaloids, Glycosides, Phenol, Triterpenes, Flavonoids,Tannins and Protein[88].

- Flavonoids and glycosides which reach the brain tissues through the metabolizing process, protecting brain function from CNS disturbance and consequently, exerting an antidepressant effect[89].
- Tannins act as potential therapeutic agent, which may be beneficial in patients with neurological disease[90].

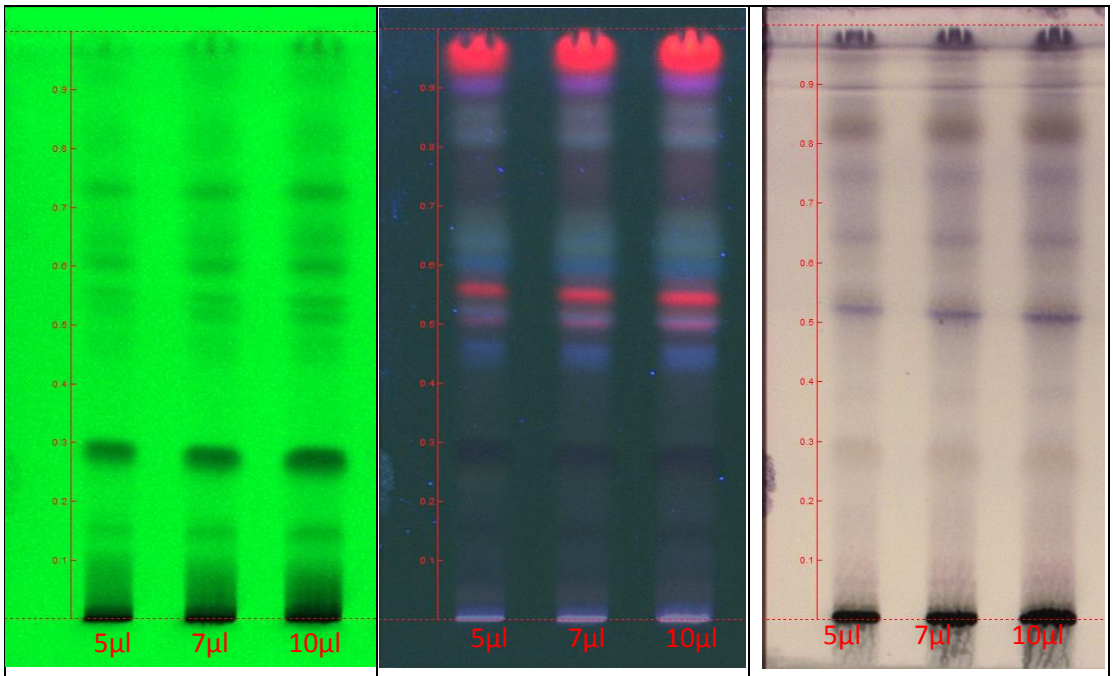
TLC/ HPTLC Analysis

TLC analysis:

Alcohol extract was applied in TLC aluminum sheet silica gel 60 F 254 (E. MERCK) and plate was developed using the solvent system Toluene: Ethyl acetate: Formic acid (1:1:0.2). After development the plate is allowed to dry in air and examined under UV (254nm), 366 nm and Visible light (Vanillin –Sulphuric acid).

Table no.9.Rf values for the Alcoholic extract

Rf	Colour	Rf	Colour	Rf	Colour
0.15	Green	0.15	Dark blue	0.28	Light brown
0.28	Green	0.27	Dark blue	0.52	Violet
0.52	Green	0.45	Blue	0.64	Grey
0.55	Green	0.52	Pink	0.75	Grey
0.61	Green	0.55	Red	0.83	Brown
0.65	Green	0.60	Blue		
0.73	Green	0.67	Light green		
0.83	Green	0.82	Light blue		



λ = 254 nm	λ = 366 nm	λ = 520nm

Chart no.1. HPTLC Alcohol extracts Photos

3D Chromatogram of 254 nm

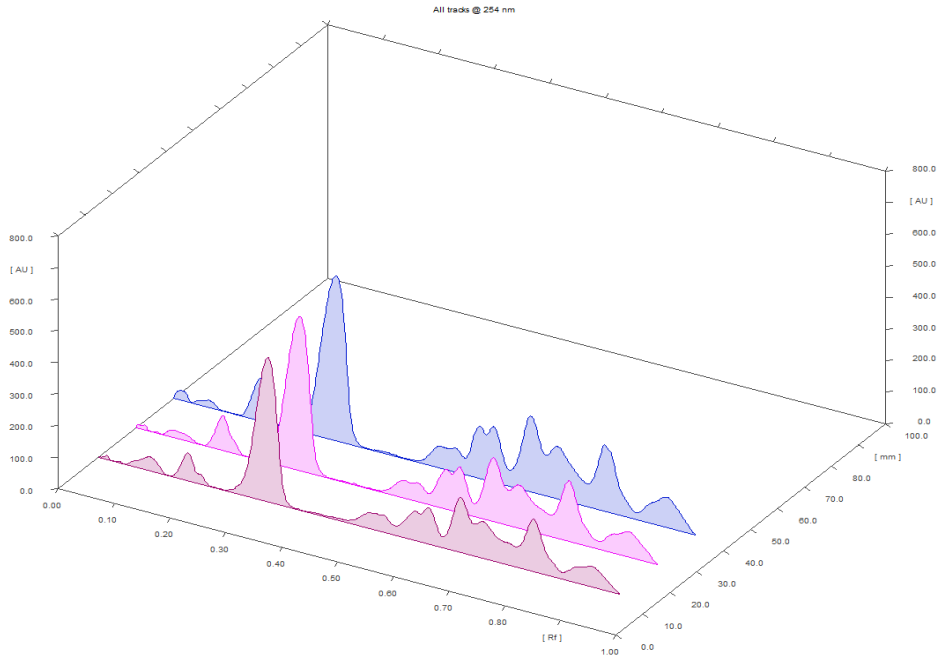


Chart no.2. 3D Chromatogram of 254 nm

HPTLC Chromatogram of SCRI/2016-2017/041 (Alcohol extract) scanning at 254 nm - 5µl

HPTLC finger print analysis for alcohol extract

The finger print chromatogram was recorded after derivatization of the plate using vanillin –sulphuric acid and scanned at 254 nm. It showed 12 peaks of which 4 peaks at Rf. 0.65, 0.69, 0.78 and 0.88 were the major peaks and others were moderately smaller peaks.

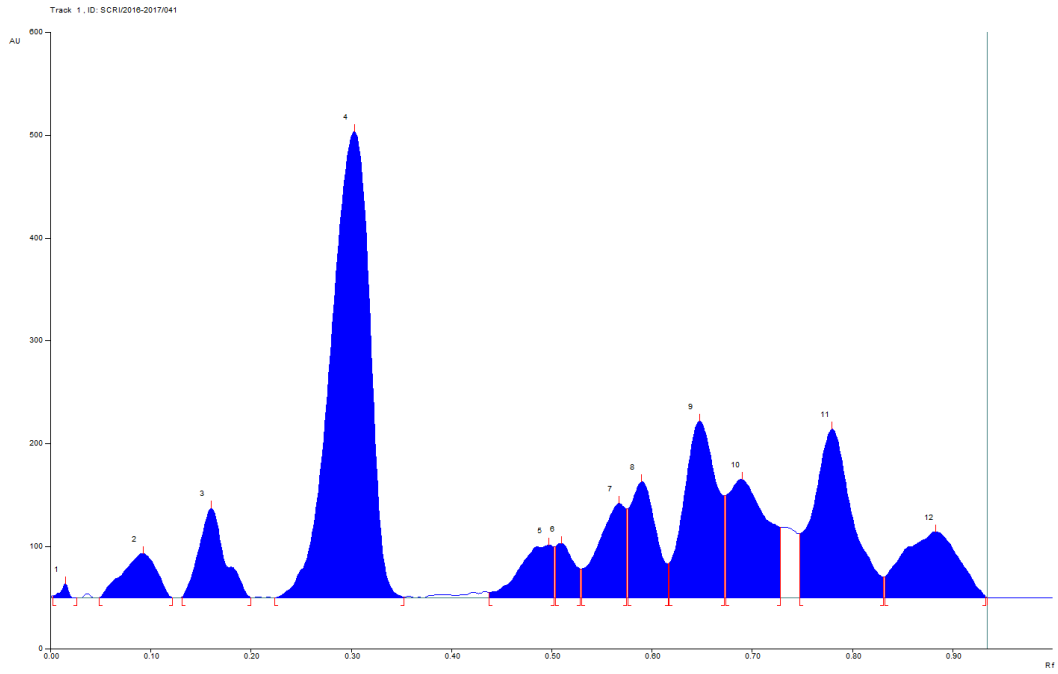


Chart no.3. HPTLC finger print for Alcohol extract of *Kandathirika Chooranam*scanning at 254 nm -5µl

Table no.10. Alcohol extracts - Rf values in HPTLC finger print scanning at 254 nm -5µl

Track 1, ID: SCRI/2016-2017/041

Peak	Start Position	Start Height	Max Position	Max Height	Max %	End Position	End Height	Area	Area %
1	0.00 Rf	1.8 AU	0.01 Rf	13.5 AU	0.95 %	0.03 Rf	0.0 AU	93.3 AU	0.20 %
2	0.05 Rf	0.0 AU	0.09 Rf	43.1 AU	3.03 %	0.12 Rf	0.1 AU	1351.9 AU	2.96 %
3	0.13 Rf	0.5 AU	0.16 Rf	87.3 AU	6.14 %	0.20 Rf	0.1 AU	2067.6 AU	4.52 %
4	0.22 Rf	0.0 AU	0.30 Rf	453.7 AU	31.89 %	0.35 Rf	0.6 AU	16179.4 AU	35.38 %
5	0.44 Rf	5.2 AU	0.50 Rf	51.6 AU	3.63 %	0.50 Rf	49.7 AU	1584.1 AU	3.46 %
6	0.50 Rf	50.0 AU	0.51 Rf	53.1 AU	3.73 %	0.53 Rf	28.1 AU	899.0 AU	1.97 %
7	0.53 Rf	28.1 AU	0.57 Rf	91.9 AU	6.46 %	0.57 Rf	86.6 AU	2325.0 AU	5.08 %
8	0.58 Rf	86.7 AU	0.59 Rf	112.9 AU	7.93 %	0.62 Rf	32.9 AU	2669.3 AU	5.84 %
9	0.62 Rf	33.8 AU	0.65 Rf	172.1 AU	12.10 %	0.67 Rf	99.5 AU	5152.4 AU	11.27 %
10	0.67 Rf	99.8 AU	0.69 Rf	115.4 AU	8.11 %	0.73 Rf	68.2 AU	4208.0 AU	9.20 %
11	0.75 Rf	62.4 AU	0.78 Rf	164.0 AU	11.53 %	0.83 Rf	20.2 AU	5901.8 AU	12.91 %
12	0.83 Rf	20.5 AU	0.88 Rf	64.1 AU	4.50 %	0.93 Rf	0.9 AU	3293.7 AU	7.20 %

HPTLC Chromatogram of SCRI/2016-2017/041 (Alcohol extract) scanning at 254 nm - 7µl

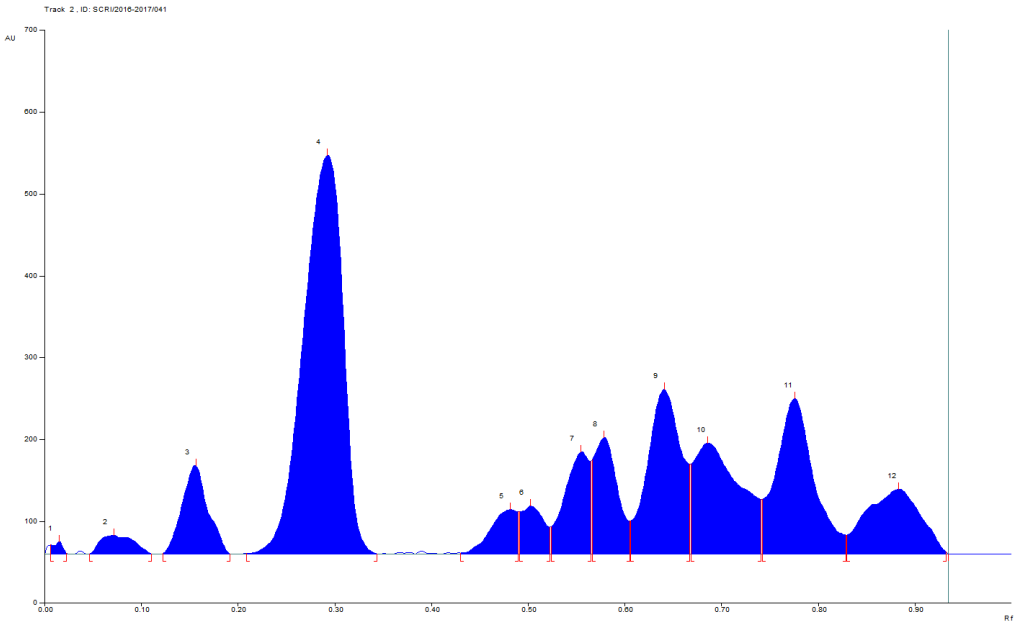


Chart no.3.1. HPTLC finger print for Alcohol extract of *Kandathirika chooranam* scanning at 254 nm -7µl

Table no.10.1. Alcohol extracts - Rf values in HPTLC finger print scanning at 254 nm -7µl

Track 2, ID: SCRI/2016-2017/041

Peak	Start Position	Start Height	Max Position	Max Height	Max %	End Position	End Height	Area	Area %
1	0.01 Rf	11.1 AU	0.01 Rf	15.1 AU	0.93 %	0.02 Rf	0.6 AU	139.4 AU	0.26 %
2	0.05 Rf	0.0 AU	0.07 Rf	22.8 AU	1.41 %	0.11 Rf	0.2 AU	738.8 AU	1.36 %
3	0.12 Rf	0.5 AU	0.16 Rf	108.3 AU	6.69 %	0.19 Rf	0.3 AU	2679.3 AU	4.93 %
4	0.21 Rf	0.5 AU	0.29 Rf	487.6 AU	30.10 %	0.34 Rf	0.2 AU	18397.0 AU	33.83 %
5	0.43 Rf	1.3 AU	0.48 Rf	54.3 AU	3.35 %	0.49 Rf	51.6 AU	1399.0 AU	2.57 %
6	0.49 Rf	51.7 AU	0.50 Rf	58.5 AU	3.61 %	0.52 Rf	33.0 AU	1284.9 AU	2.36 %
7	0.52 Rf	33.5 AU	0.56 Rf	125.0 AU	7.72 %	0.56 Rf	13.5 AU	2992.0 AU	5.50 %
8	0.57 Rf	114.8 AU	0.58 Rf	142.7 AU	8.81 %	0.61 Rf	40.1 AU	3234.9 AU	5.95 %
9	0.61 Rf	40.1 AU	0.64 Rf	201.1 AU	12.42 %	0.67 Rf	09.7 AU	6491.7 AU	11.94 %
10	0.67 Rf	110.1 AU	0.69 Rf	135.3 AU	8.35 %	0.74 Rf	66.8 AU	6043.3 AU	11.11 %
11	0.74 Rf	66.8 AU	0.78 Rf	189.8 AU	11.72 %	0.83 Rf	23.0 AU	6855.7 AU	12.61 %
12	0.83 Rf	23.1 AU	0.88 Rf	79.2 AU	4.89 %	0.93 Rf	2.7 AU	4117.5 AU	7.57 %

HPTLC Chromatogram of SCRI/2016-2017/041 (Alcohol extract) scanning at 254 nm - 10µl

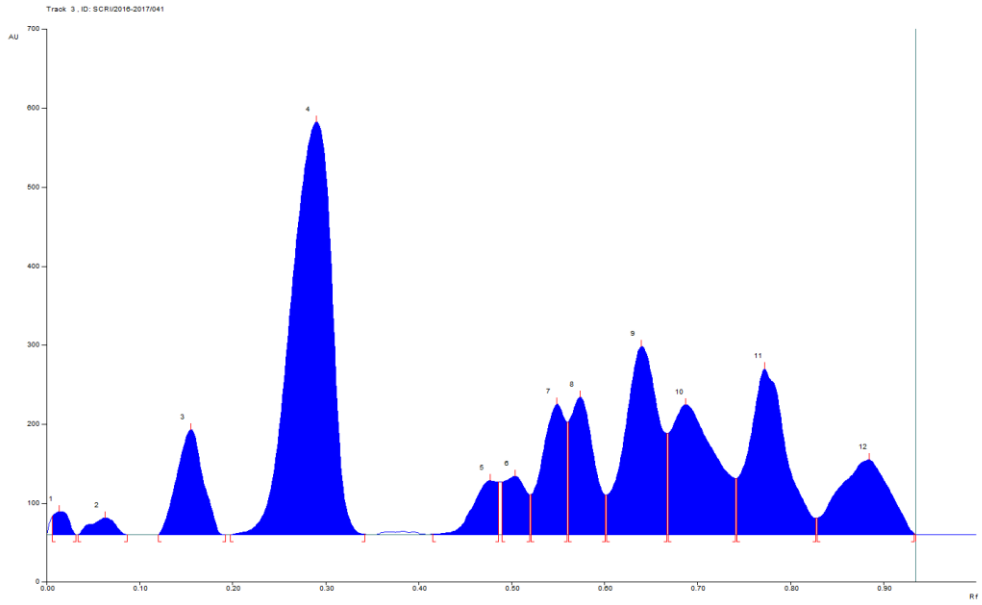


Chart no.3.2. HPTLC finger print for Alcohol extract of *Kandathirika chooranam* scanning at 254 nm -10µl

Table no.10.2. Alcohol extracts - Rf values in HPTLC finger print scanning at 254 nm -10µl

Track 3, ID: SCRI/2016-2017/041

Peak	Start Position	Start Height	Max Position	Max Height	Max %	End Position	End Height	Area	Area %
1	0.01 Rf	23.4 AU	0.01 Rf	29.4 AU	1.55 %	0.03 Rf	0.2 AU	434.5 AU	0.68 %
2	0.03 Rf	0.3 AU	0.06 Rf	21.5 AU	1.13 %	0.09 Rf	0.0 AU	508.7 AU	0.79 %
3	0.12 Rf	0.3 AU	0.16 Rf	133.1 AU	7.02 %	0.19 Rf	0.0 AU	3416.4 AU	5.32 %
4	0.20 Rf	0.0 AU	0.29 Rf	522.4 AU	27.56 %	0.34 Rf	0.5 AU	20859.6 AU	32.46 %
5	0.41 Rf	0.5 AU	0.48 Rf	68.3 AU	3.60 %	0.49 Rf	66.8 AU	1671.4 AU	2.60 %
6	0.49 Rf	66.8 AU	0.50 Rf	74.1 AU	3.91 %	0.52 Rf	50.4 AU	1652.0 AU	2.57 %
7	0.52 Rf	50.7 AU	0.55 Rf	165.2 AU	8.71 %	0.56 Rf	42.4 AU	3871.0 AU	6.02 %
8	0.56 Rf	142.8 AU	0.57 Rf	174.4 AU	9.20 %	0.60 Rf	50.5 AU	4110.8 AU	6.40 %
9	0.60 Rf	50.5 AU	0.64 Rf	238.3 AU	12.57 %	0.67 Rf	28.3 AU	8066.4 AU	12.55 %
10	0.67 Rf	128.5 AU	0.69 Rf	164.3 AU	8.67 %	0.74 Rf	71.0 AU	7235.8 AU	11.26 %
11	0.74 Rf	71.1 AU	0.77 Rf	209.8 AU	11.07 %	0.83 Rf	20.7 AU	7711.6 AU	12.00 %
12	0.83 Rf	20.9 AU	0.88 Rf	94.7 AU	5.00 %	0.93 Rf	1.7 AU	4727.8 AU	7.36 %

Discussion:

- The quantitative analysis of compounds present in the *KCM* has been performed by HPTLC. The method may be applied to identify the *KCM* from other manufacturing process.
- Theyprovide the identification of constituents,determination of impurities and quantitative determination of active substance present in the *KCM*[91].
- The Rf value of the *KCM* supports the better standardization of the drug.
- The present study revealed that *KCM* showed best results in Toluene: Ethyl acetate (9:1). Solvent system. After scanning and visualizing the plates in absorbance mode at both 254nm, 366 nm and visible light range, best results were shown at visible light range.
- TLC plate showed different colour phytoconstituents of alcohol extract of *KCM*.The bands revealed the presence of eight greenish, two dark blue, two blue, one pink, one red, one light green, one light blue, light blue, one light brown, one violet, two grey, one browns band showing the presence of alkaloids,glycosides,phenols,triterpenes,flavanoids, tannins and proteins.
- The results from HPTLC finger print scanned for chloroform extract of *KCM*. There are thirteen polyvalent phytoconstituents and corresponding ascending order of Rf values start from -0.01 to 0.98 in which highest concentrations of the phytoconstituents was found to be 34.34% and 17.88 % with its corresponding Rf value were found to be -0.01 and 0.27 respectively.

Biochemical analysis

Table no.11.Results of basic radicals studies

S.NO	Parameter	Result
1	Test for Potassium	- ve
2	Test for Calcium	+ve
3	Test For Magnesium	+ve
4	Test For Ammonium	- ve
5	Test For Sodium	- ve
6	Test for Iron (Ferrous)	-ve
7	Test For Zinc	-ve
8	Test For Aluminium	-ve
9	Test For Lead	- ve
10	Test for Copper	+ ve
11	Test For Mercury	- ve
12	Test for Arsenic	- ve

Interpretation

The basic radical test shows the presence of **Calcium, Magnesium and Copper** and absence of heavy metals such as lead, arsenic and mercury.

- Presence of Calcium in the drug improves neurotransmission and cell metabolism. [92]
- Copper plays most important roles in the human body its promoting neurological function by playing a role in antioxidant defense and neurotransmitter synthesis.[93]

Table no.12.Results of acid radical studies

S.NO	Parameter	Result
1.	Test for Sulphate	- ve
2.	Test for Chloride	+ve
3	Test for Phosphate	+ve
4	Test for Carbonate	- ve
5	Test for fluoride &oxalate	-ve
6	Test For Nitrate	- ve

Interpretation:

The acid radicals test shows the presence of **Chloride and Phosphate.**

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

The drug sample *Kandathirika Chooranam* was analysed by the Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES) to detect the trace elements and other elements quantitatively.

Table no.13.Results of ICP-OES

Elements	Wavelength(nm)	KCM
Al	396.152	BDL
As	188.979	BDL
Ca	315.807	32.140 mg/L
Cd	228.802	BDL
Cu	327.393	BDL
Fe	238.204	BDL
Hg	253.652	BDL
K	766.491	43.801 mg/L
Mg	285.213	01.104 mg/L
Na	589.592	54.220 mg/L
Ni	231.604	BDL
Pb	220.353	BDL
P	213.617	120.301 mg/L
S	180.731	01.014 mg/L

ICP-OES results of *Kandathirika Chooranam* showed the presence of calcium, Pottassium, magnesium,sodium, phosphorus and sulphur.

- Calcium is necessary for our bodies to function properly. Because calcium is needed for healthy brain function, calcium deficiency can lead to anxiety and moodiness.The electrical pulses within the nervous system depend on calcium to perform properly.[94]

- Sodium is important for the function of all of the cells in the body because it is an electrolyte. Nerve cells are particularly sensitive to the amount of sodium in the blood because they need electrolytes to function properly [95]

- Phosphorus is highly required for proper mental functions [96]

- Magnesium is the premier medicine for depression, sleep disturbances, emotionally disturbed behavior, and neurological diseases because of its strong positive effect in calming and nourishing the nervous system [97]

Table no.14. Availability Microbial load in *Kandathirika Chooranam*

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

Interpretation:

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

- *KCM* is a herbal drug prepared by plants. It is easy to get contamination,If any contamination present in drug, that decreases the potency and efficacy.The contamination of *KCM* has been examined by bacterial and fungal load.

- Total bacterial load in 10^{-4} dilution is 14 and 10^{-6} dilution is 8
- Total fungal load in 10^{-2} dilution is 8 and 10^{-3} dilution is 4

Here, the result shows presence of bacterial and fungal load in the trial drug(*KCM*).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 Chart no:6 shows the presence of functional group and inorganic compounds of *Kandathirika Chooranam.*

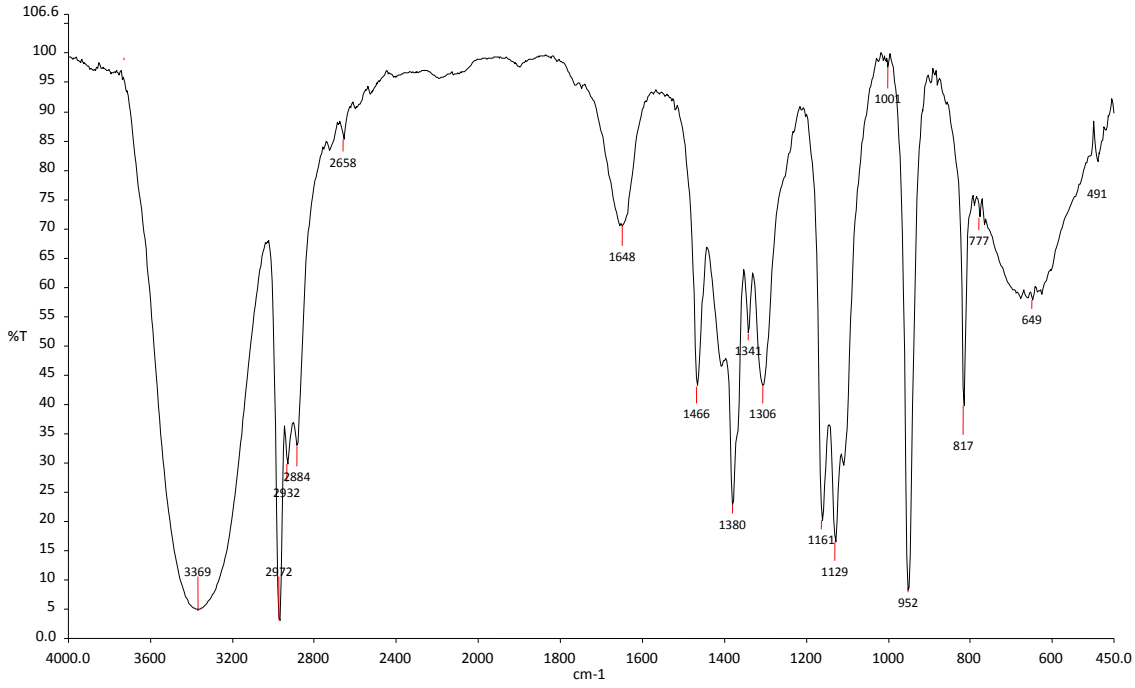


Chart no.4. FT-IR (Fourier Transform Infra Red spectroscopy)

Table.no.15.Results of FT-IR

3369	N-H stretch	1°, 2° amines, amides
2972	C-H stretch	Alkanes
2932	C-H Stretch	Alkanes
2884	C-H Stretch	Alkanes
2658	H-C=O: CH- Stretch	Aldehydes
1648	-C=C-Stretch	Alkenes
1466	C-H Bend	Alkanes
1341	N-O Symmetric stretch	Nitro compounds
1306	C-N Stretch	Aromatic amines
1161	C-H wag(-CH2X)	Alkyl halides
1129	C-N Stretch	Aliphatic amines
1001	C-O Stretch	Alcohols,carboxylic acids
952	=C-H bend	Alkenes, esters, ethers
817	N-H Wag	1°, 2° amines, amides
777	C–H “oop”	Aromatics
649	-C=C-H: C-H bend	Alkynes

Interpretation

FTIR instrumental analysis was done. The test drug was identified to have 16 peaks. They are the functional groups present in the trial drug *Kandathirika Chooranam*.

The above table shows the presence of Alkanes, amines, amides, aldehydes, nitro compounds, Aromatic amines, Alkyl halides which are represents the peak value.

- The amine neurotransmitters lies somewhere between the properties of the other small-molecule neurotransmitters and those of the neuropeptides.[98]
- Amides have played an important role in the treatment of psychopathologies such as anxiety, epilepsy and depression.[99]
- Nitro compounds have antidepressant activity.[100]

XRD (X-Ray Diffraction Analysis) results of *Kandathirika Chooranam:*

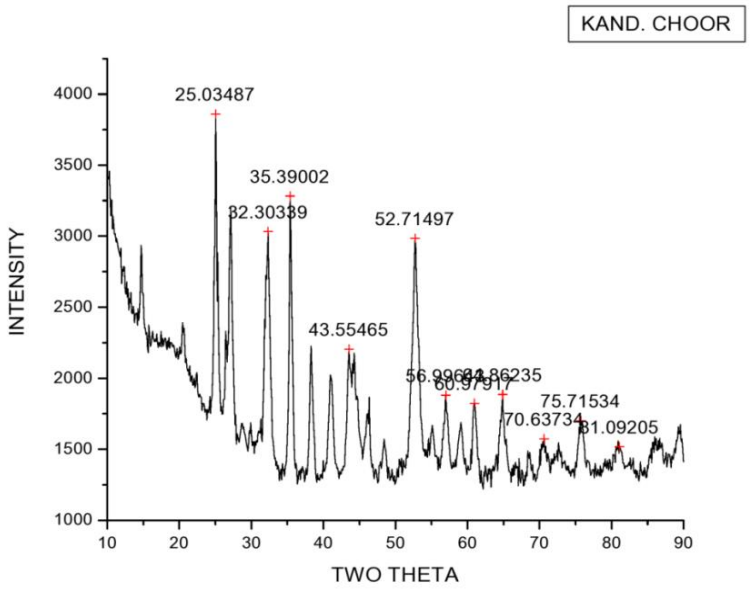


Chart no.5. XRD (X-Ray Diffraction Analysis) results of*Kandathirika Chooranam*

Interpretation:

The structure and the size 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 *KCM* concluded that range 25-55nm is associated with organic molecules probably plays an important role in making it biocompatible and nontoxic at therapeutic doses.

Other elements present in KCM act as an additional supplement and possibly helps in increase the efficacy of the formulation.

SEM: (SCANNING ELECTRON MICROSCOPE)

The particle size and the chemical elements were assessed by Scanning Electron Microscope. SEM is one of the most widely used instruments in research side. The SEM picture of *Kandathirika Chooranam* is shown below.

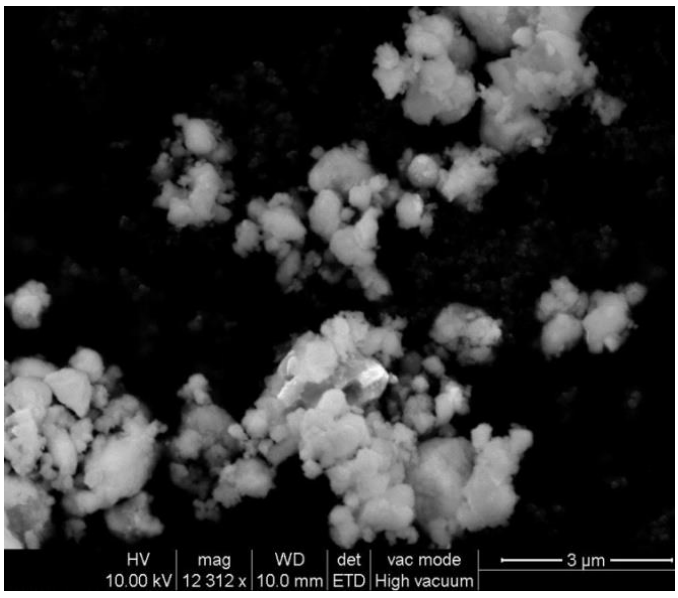


Fig no.6.SEM: (Scanning Electron Microscope)

The particle morphology can be identified through these SEM images of *Siddha* medicine *Kandathirika Chooranam* .The particles are not spherical in shape. The size

of particles was approximately identified as micro particles ranging from 100nm-1µm.

Interpretation for SEM

- Micro particles are defined as particulate dispersion or solid particles with a size in the range of 100-1000nm in diameter.
- Size and surface of micro particles can be easily manipulated to achieve both passive and active drug targeting.
- They control and sustain the release of drug during the transportation and at the site of localization, alters drug distribution in the body and subsequent clearance of the drug so as to achieve increased drug therapeutic efficacy thereby bio-availability and reduced side effects. [101]

TOXICITY STUDIES RESULTS

Acute oral toxicity study of *Kandathirika Chooranam*

Dose finding experiment and its behavioral Signs of acute oral Toxicity

Table no.16.Observation done:

SL	Group CONTROL	Observation	SL	Group 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
6	Salivation	Normal	**6**	Salivation	Absence

SL	Group CONTROL	Observation	SL	Group TEST GROUP	Observation
7	Change in skin color	No significant color change	**7**	Change in skin color	No significant color change
8	Piloerection	Normal	**8**	Piloerection	Normal
9	Defecation	Normal	**9**	Defecation	Normal
10	Sensitivity	Normal	**10**	Sensitivity	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 no.17.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.Lacrimation16.Exophthalmos 17.Diarrhea 18.Writhing 19.Respiration 20.Mortality.

(+ Present, - Absent)

Table.no.18. Body weight Observation

DOSE	DAYS		
	1	7	14
CONTROL	240.1±65.70	240.3 ± 41.11	240.6 ±02.12
HIGH DOSE	245.3± 6.64	245.7 ±7.42	245.2 ± 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)

Table.no.19. Water intake (ml/day) of Wistar albino rats group exposed to *KCM*:

DOSE	DAYS		
	1	6	14
CONTROL	53 ± 3.20	53±6.10	53 ±5.44
HIGH DOSE	54 ±1.30	54±6.70	54 ±5.64

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.20. Food intake (gm/day) of Wistar albino rats group exposed to *KCM:*

DOSE	DAYS		
	1	7	14
CONTROL	54.03±2.82	54.2±2.96	54.7±8.86
High DOSE	54.6±5.44	54.4±5.20	54.8±6.67

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 acute toxicity result shows no mortality rate up to 2000mg/kg. It showed changes in alertness, grooming, grip strength and Eye closure at touch response.The

behavioural changes are normal. Hence the test drug *KandathirikaChooranam* is a safe herbal drug and can be used for long time administration.

REPEATED DOSE 28-DAY ORAL TOXICITY (407) STUDY OF*KCM:*

Table.no.21. Body weight of wistar albino rats group exposed to *KCM*

DOSE	DAYS				
	1	7	14	21	28
CONTROL	232.4±10.40	232.2±15.04	232.4± 15.40	233.6±16.0	233.2±16.10
LOW DOSE	240.5± 55.25	241.7±16.29	241.8± 15.24	242 ±16.30	242.8±46.06
MID DOSE	246.3± 14.72	246.3±22.20	246.4 ± 17.42	246.2±35.8	247.4±34.10
HIGH DOSE	251.3± 23.51	251.7±33.07	252.4 ± 32.34	253 ± 4.08	253 ± 7.70

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.22. Water intake (ml/day) of Wistar albino rats group exposed to *KCM:*

DOSE	DAYS				
	1	6	14	21	28
CONTROL	51.3 ± 3.54	51.4±1.27	51.7±1.31	52.1±1.12	52.4±1.72
LOW DOSE	64.1±1.21	64.6±4.22	64.6±1.02	65.6±2.06	65.4±1.20
MID DOSE	62.1±1.02	62.3±1.21	62.1±2.62	63.4±4.32	63.4±1.64
HIGH DOSE	53.6±6.80	53.2±1.52	53.4±1.74	54.6±1.88	54.8±2.82

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. Food intake (gm/day) of Wistar albino rats group exposed to *KCM:*

DOSE	DAYS				
	2	7	23	22	28
CONTROL	42±5.21	42.2±4.22	42.8±3.13	43.2±6.72	44±6.80
LOW DOSE	43.6±6.22	43.8±2.42	44.4±1.50	44.5±1.30	44.8±1.12
MID DOSE	44.1±6.70	44.2±2.40	44.6±5.64	45.3±2.40	45.7±1.34
HIGH DOSE	46.4±1.45	46.6±1.34	46.8±2.36	47.2±1.70	47.6±1.62

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.24. Haematological parameters of Wistar albino rats group exposed to *KCM:*

C	Control	Low dose	Mid dose	High dose	Pvalue (p)*
Haemoglobin(g/dl)	14.5±0.43	14.60±0.32	14.8±0.23	14.84±0.33	N.S
Total WBC ($\times 10^3$ l)	12.71±0.40	12.82±0.21	12.94±0.60	13.06±1.40	N.S
Neutrophils (%)	08.12±0.40	08.22±0.32	08.31±1.50	08.04±2.20	N.S
lymphocyte (%)	90.12±1.60	90.14±1.40	90.16±1.44	91.20±1.64	N.S
Monocyte (%)	0.1±0.02	0.1±0.01	0.1±0.04	0.1±0.03	N.S
Eosinophil (%)	0.02±0.02	0.02±0.04	0.02±0.06	0.02±0.06	N.S
Platelets cells10^3/µl	700.26±2.28	702.32±2.42	702.21±2.60	702.42±3.64	N.S

C	Control	Low dose	Mid dose	High dose	Pvalue (p)*
Total RBC 10^6/µl	7.64±0.32	7.65±0.32	7.65±0.04	7.66±0.06	N.S
PCV%	40.30±0.4	40.32±5.30	40.5±2.70	41.2±1.22	N.S
MCHC g/Dl	34.7±1.61	34.8±1.32	34.8±1.35	34.13±1.36	N.S
MCV fL(µm^3)	52.7±3.04	52.7±2.40	52.9±2.20	52.9±1.20	N.S

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.25. Biochemical Parameters of Wistar albino rats group exposed to *KCM*

BIOCHEMICAL PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE
GLUCOSE (R) (mg/dl)	98.10±2.40	98.12±1.62	99.9±.08	99.9±5.25
T.CHOLESTEROL(mg/dl)	109.14±3.10	109.25±2.40	109.30±1.58	110.21±1.60
TRIGLY(mg/dl)	73.05±1.08	73.11±1.02	73.25±1.42	75.26±1.54
LDL	68.5±4.13	68.4±1.05	68.3±1.03	69.40±2.44
VLDL	15.2±1.30	15.20±1.71	15.22±1.62	15.24±1.55
HDL	25.22±2.30	25.22±2.60	25.46±1.72	26.56±1.43
Ratio1 (T.CHO/HDL)	4.36±1.10	4.37±1.20	4.64±2.32	4.74±2.63

BIOCHEMICAL PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE
Ratio 2(LDL/HDL)	2.76±2.33	2.72±1.40	2.79±2.10	2.84±04.02
Albumin (g/dL)	3.9.42±0.50	3.9.62±0.54	3.9.48±4.20	4.02±3.24

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. Renal function test of Wistar albino rats group exposed to *KCM:*

PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE	P Value (p)*
UREA (mg/dl)	24.31±0.10	24.30±0.19	24.26±1.28	25.42±1.02	N.S
CREATININE(mg/dl)	0.7±0.04	0.71±0.06	0.73±0.04	0.74±0.08	N.S
BUN(mg/dL)	15.8±0.04	15.8±0.24	15.8±0.42	15.9±1.02	NS
URIC ACID(mg/dl)	5.04±0.02	5.08±0.20	5.4±0.32	5.6±0.20	N.S

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.27. Liver Function Test of Wistar albino rats group exposed to *KCM*

PARAMETERS	CONTROL	LOW DOSE	MID DOSE	HIGH DOSE
T BILIRUBIN(mg/dl).	0.04±0.01	0.04±0.03	0.04±0.03	0.04±0.01
SGOT/AST(U/L)	51.11±1.43	51.12±0.62	52.24±1.34	53.54±1.63
SGPT/ALT(U/L)	87.11±1.43	87.24±1.14	88.44±1.36	88.33±0.21
ALP(U/L)	166.30±2.11	166.1±2.10	166±1.14	167.3±2.01
T.PROTEIN(g/dL)	6.9±0.14	6.9±0.41	7.00±0.60	7.2±0.41

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

Interpretation of 28 days repeated oral toxicity study

Sub-acute oral toxicity repeated dose of ***Kandathirika Chooranam*** 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.

General signs

No deaths or significant changes in general behaviour or other physiological activities were observed a tany point in the present study.

Body weight

No changes were observed in body weight. Treatment has not shown not show any significant differences in either the control or treated group of both sexes.

Haematological and plasma biochemical data

The haematological analysis showed no significant changes of BC, Hb, Ht, WBC, and platelets in the male and female treatment group compared to the control group. The leukocyte differential count showed no difference between groups ;some bands (upto2%) were occasionally found in some rat of the control and treatment groups. The biochemical analysis showed no significant differences in any of the parameter sex amined in either the control or treated group of the male and female rats

Tissue analysis

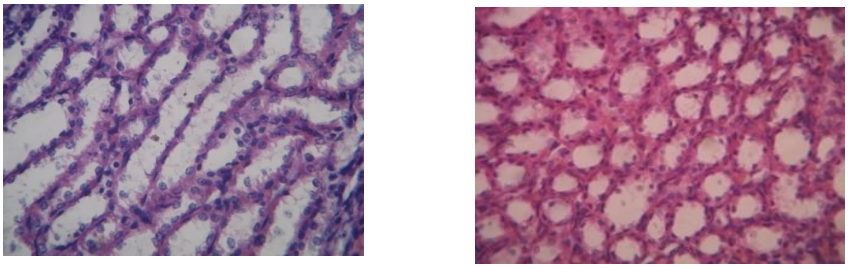
There were no significant differences between the control and treated groups in the organ weights of male and female ats .Pathological examinations of the tissues on a gross basis indicated that there were no detectable abnormalities .No alterations were seen in the microscopic examination of the internal organs; the cellular appearances were unremarkable in both group sand sexes.

REPEATED ORAL TOXICITY STUDY

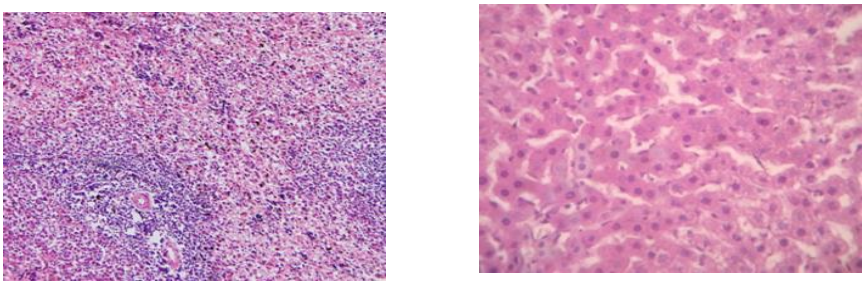
HISTO PATHOLOGY

CONTROL GROUP **TEST GROUP**

KIDNEY



LIVER



SPLEEN

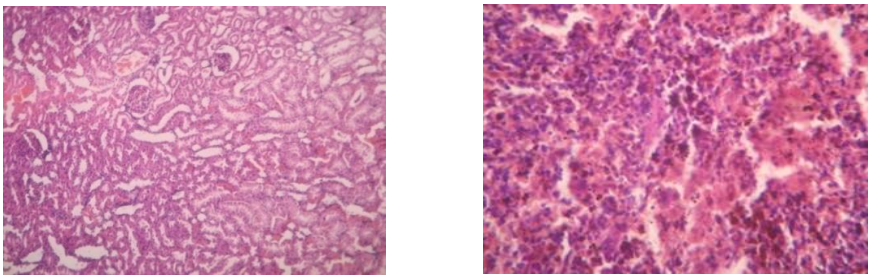


Fig no.7 Histopathology Slides of *KCM*

Interpretation

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 *Kandathirika chooranam*. Thus the safety of the drug is revealed so that it can be administered for long time without any side effects.

PHARMACOLOGICAL STUDY

ANTI-ANXIETY ACTIVITY IN ELEVATED PLUS MAZE

The elevated plus maze (EPM) is a model of anxiety that is used as a screening test for putative anxiolytic compounds and as a general research tool in neurobiological anxiety research. The test setting consists of a plus-shaped apparatus with two open 30 x 5 and two enclosed arms 30 x 5 x 25, each with an open roof, elevated 40-70cm from the floor. The model is based on rodent's aversion of open spaces. This aversion leads to the behavior termed thigmotaxis, which avoidance of open areas by confining movement to enclose.

In EPM this translates into an estimation of movement to the enclosed arms. Anxiety reduction in the plus-maze is indicated by an increase in the proportion of time spent in the open arms and an increase in the proportion of entries into the spent arms. Total number of arm entries and number of closed-arm entries are usually employed as measures of general activity.From the present study it was found that *KCM* significantly prolonged the time animals spent in the maze compared to that of the control group. Normally, when mice are placed ina maze they prefer to hide rather than explore, because they are anxious. In this test, mice generally nervous and fearful in the maze were transformed by *KCM* and mice treated with *KCM* showed a quiet curiosityin exploring their environment.

Table.no.28. Effect of *KCM* in Elevated Plus Maze

S.no	Groups	Time spent in open arm	Time spent in closed arm
1	Control	35.33±0.62	264.67±0.62

2	Standard(Diazepam)2mg/kg	131.33±0.96***	165.67±0.96**
3	*KCM* 100	92.0±0.86**	206.00±0.87*
4	*KCM* 200	117.67±0.80***	181.33±0.80**

The data is expressed as Mean ± SEM.; ANOVA followed by Dunnet's Multiple comparison test. *P<0.05vsControl.

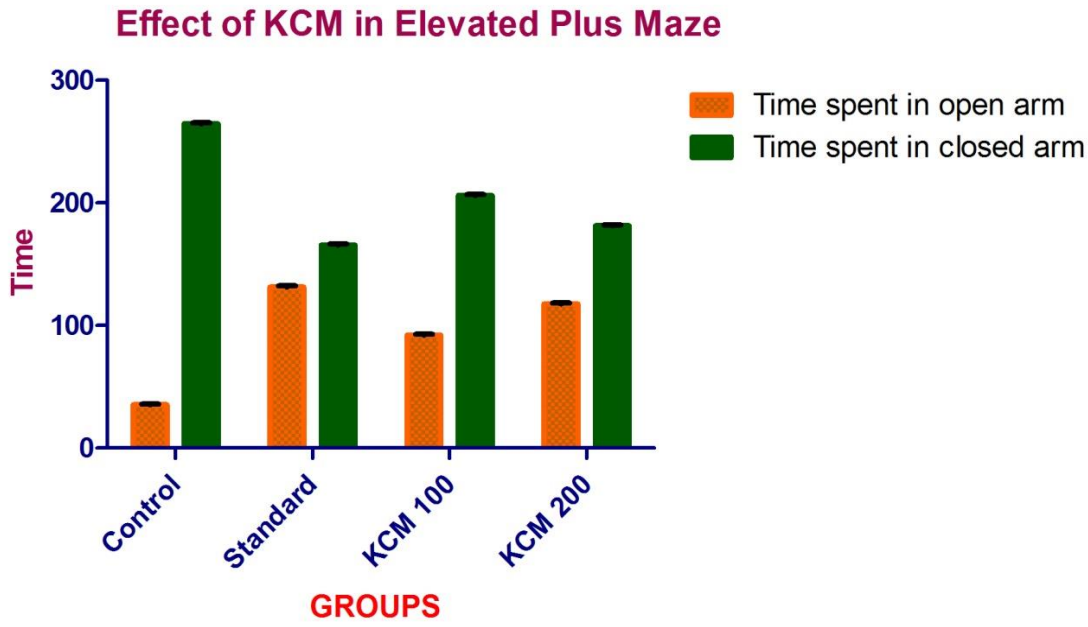


Chart no.6. Effect of *KCM* in Elevated Plus Maze

Table.no.29. Elevated plus maze number of entries & Average of time spent in open arms

Animal Groups	Total time travelled	No.of entries in open arm	Average time spent in open arms
Control	5 MINUTES	3.21±0.18	3.60±0.21

Standard(Diazepam)	5 MINUTES	7.75±0.34**	13.75±0.25*
KCM 100	5 MINUTES	5.42±0.43*	10.08±0.34*
KCM 200	5 MINUTES	6.58±0.32*	12.42±0.85*

The data is expressed as Mean ± SEM.; ANOVA followed by Dunnet's Multiple comparison test. *P<0.05vsControl.

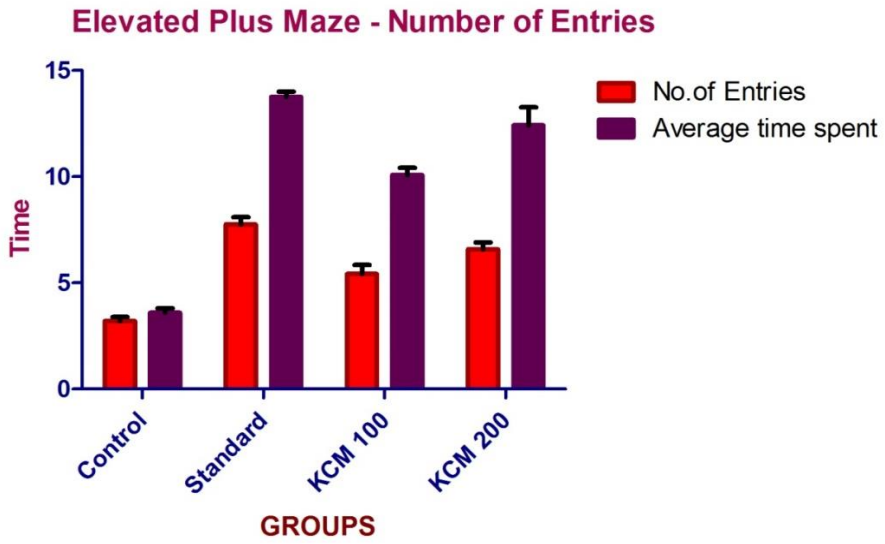


Chart no.7. Elevated Plus Maze Number of Entries

ANTI DEPRESSANT ACTIVITY OF *KANDATHIRIKA CHOORANAM*:Table.no.30. Effect of *KCM* on locomotion of mice during forced swim and tail suspension test

Treatment	Immobility period in forced swim test(sec)	Immobility period in tail suspension test(sec)
Control Distilled water	106.77± 4.08	83.73 ±2.63

Standard-Imipramine 15mg/kg,	78.75 ± 2.75*	71.29 ±1.53*
KCM 100 mg	93.20± 2.03	76.50±1.73
KCM 200 mg	82.91 ± 2.25*	73.00±1.70*

Statistical analysis of data was carried by one-way ANOVA followed by Dunnet's multiple comparisons test. *p < 0.05 vs Control.

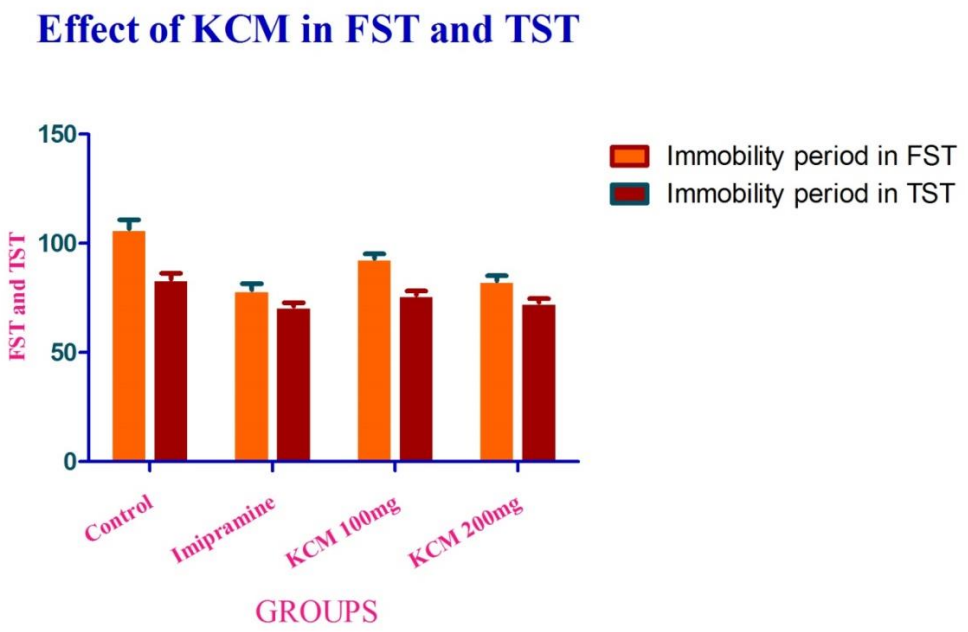


Chart no.8. Effect of *KCM* in FST and TST

Interpretation:

In this present experiment, forced swimming test and tail suspension test were used to evaluate the antidepressant effects of *Kandathirika Chooranam* in mice and are tabulated in Table No.30. Both FST and TST are widely used to screen new antidepressant drugs. These tests are quite sensitive and relatively specific to all major classes of antidepressant drugs including tricyclics, 5-HT-specific reuptake inhibitors, MAO inhibitors, and atypical antidepressant drugs.

In FST, mice are forced to swim in a restricted space from which they cannot escape, and are induced to a characteristic behavior of immobility. This behavior is reflecting a state of despair which is reduced by several agents which are therapeutically effective in human depression. The TST also induces a state of despair in animals like that in FST. This immobility referred to as behavioral despair in animals, is claimed to reproduce a condition similar to human depression.

The present study provides behavioral evidence for the antidepressant-like activities of *KCM*. From the result, it was observed that *KCM* administration showed a significant activity to reduce the immobility time at doses of 200 mg/kg in forced swimming test and tail suspension test in mice. Considering that clinical antidepressant effects often appear after chronic treatment, *KCM* was administrated orally for 10 consecutive days for the investigation of the antidepressant-like property in mice in FST and TST.

In this model, *Kandathirika Chooranam* produced a significant inhibition of the duration of immobility in FST and TST were 48.66±2.03 ($p<0.01$) and 68.16±1.94 ($p<0.01$) respectively with a profile comparable to that observed for the classical antidepressant drug imipramine 63.06±1.83 ($P<0.01$) and 79.49±4.05 ($P<0.01$) respectively.

Though the antidepressant action of *KCM* was less potent than imipramine based on the given data, the effect of *KCM* as well as other herbal medicine, is slow, mild and prolonged effect without or with mild undesirable side-effects; these are advantages over the classical antidepressants. This antidepressant effect of *KCM* may be related to a change in neither locomotor activity as demonstrated here, nor to a sedative effect.

ANTI-CONVULSANT ACTIVITY – PTZINDUCED SEIZURES

PTZ induced a sequence of events starting with myoclonic jerks which was then followed by an intense clonic convulsive phase. The KCM at doses of 200 mg/kg and 400 mg/kg significantly delayed the onset of clonic convulsions ($p<0.01$) in dose dependent manner. Whereas, the standard drug diazepam (4mg/kg, *i.p*) delayed the onset of clonic convulsions. Diazepam treated animals have shown 100% protection

against PTZ induced seizures whereas KCM 200 mg/kg and 400 mg/kg have shown 44.90% and 60.74% protection respectively.

Table.no.31. Effect of *KCM* on PTZ induced seizures in mice

Treatment	Onset of convulsion (sec)	Duration of convulsion (sec)
Control (10ml/kg)	165.07 ± 1.82	58.33 ± 1.55
Diazepam (4mg/kg)	568.66 ± 2.33**	22.63± 2.007**
KCM (200 mg/kg)	422.71 ± 2.01	28.17 ± 1.59
KCM(400 mg/kg)	529.39 ± 1.91*	27.99 ± 2.50 *

Statistical significant test for comparison was done by ANOVA, followed by Dunnet's 't' test.*$p<0.05$;** $p<0.01$; ns-non significant

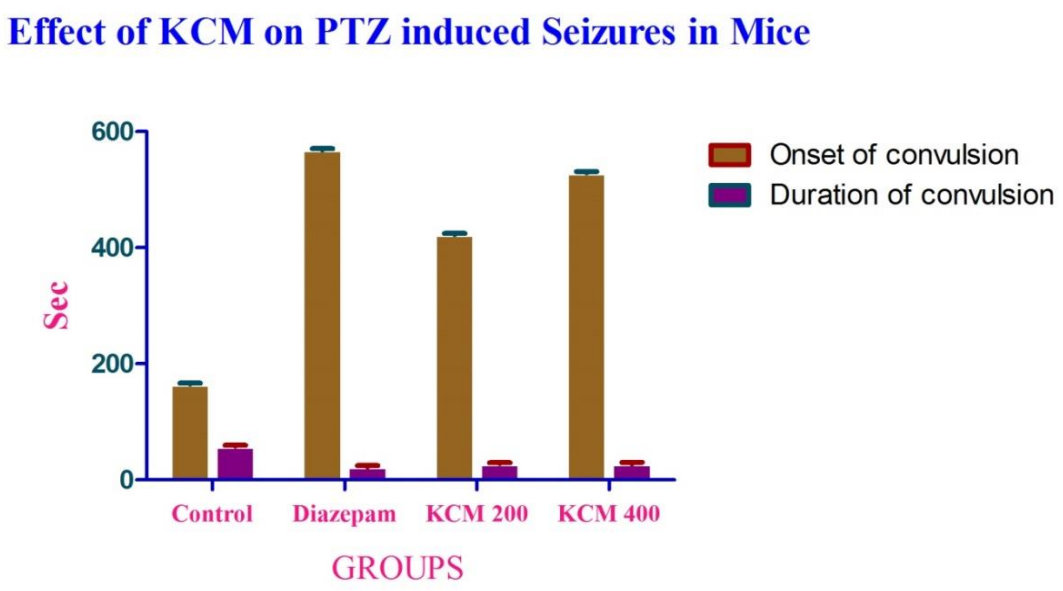


Chart no.9. Effect of *KCM* on PTZ induced Seizures in Mice

Interpretation:

PTZ test is assumed to identify anticonvulsant drugs effective against generalized to tonic-clonic partial seizures and generalized clonic seizures, respectively, the effect of KCM in these could therefore suggest anticonvulsant efficacy against the above mentioned seizures type in man.

Furthermore, PTZ might also induced convulsions by a direct excitatory effect of endogenous benzodiazepine substance.

6. CONCLUSION

- Siddha system is highly integrated system; *Maruthuvam* gives a detailed description of mental disorders. This system has a two-way interactive model of the mind-body relationship.
- Hence the author conducts the detailed scientific validation of *Kandathirika Chooranam* for Anti-anxiety activity, Anti-depressant activity and Anticonvulsant activity.
- To collect the information about the drug in various classical Siddha and modern text books, literature were referred. From them, the author came to an idea about the drug and its efficacy on neurosis.
- The Phytochemical analysis of the drug evaluates that it contains, Alkaloids, Glycosides, Phenol, Triterpenes, Flavonoids, Tannins and Protein which contributes much in relieving the symptoms of Neurosis.
- Chemical analysis of the drug contains Calcium, magnesium and copper which involves improving normal mental health in anxiety and depression.
- SEM analysis represents the drug contains Nano particles. And XRD analysis concluded that the range 25-55 nm of this drug.
- The Preclinical study showed that the drug has got safety and significant Anti-anxiety, Anti-depressant and Anticonvulsant activities.
- An incredible action of this drug value against the disease of Neurosis has been revealed from this study of *Kandathirika Chooranam.* This must be implicated in the future clinical studies and preclinical chronic toxicity studies to prove its beneficial effect in the treatment of neurosis in future.

7. SUMMARY

The trial drug ***Kandathirika Chooranam*** was selected from the Classical Siddha literature, **"*Agasthiyar Vaithiya Sinthamani Venba 4000 Enum Mani 4000"- Part I*** for the evaluation of safety and efficacy of the drug in "*Paithiyam"* (Neurosis).

The ingredients of the test drug was identified and authenticated by Siddha experts. The drug was prepared as per the procedure and subjected to various studies to reveal its potency and effectiveness against the disease.

Various analy sis such as physicochemical, phytochemical, biochemical analysis, availability of bacterial and fungal load, instrumental analysis were made. The physical character of *KCM* shows good solubility and the pH of the trial drug is 3.83 Phytochemical screening test showed the presence of Alkaloids, Glycosides, Phenol, Triterpenes, Flavonoids, Tannins and Protein. Flavonoids, Glycosides, Tannins are responsible for the anti-anxiety and antidepressant activity. The TLC/HPTLC finger prints were made and it shows 12peaks. In which the four major peaks denotes presence of phytochemicals and Rf value of the trial drug supports the better standardisation of the trial drug *(KCM).*

Biochemical analysis showed the presence of Calcium, Magnesium, Copper, Chloride and Phosphate. Calcium, Magnesium and Copper supports anti-anxiety and antidepressant activity of the trial drug *(KCM).*

The availability of bacterial load in the *KCM* has been performed and the result shows presence of bacterial and fungal load within the normal limits of trial drug. The instrumental analysis FTIR showed the peak values present which are the functional groups responsible for its activity. SEM picture described its morphology and the particle size ranging from 100nm-1µm.The result of ICPOES shows presence of Ca, K, Mg, Na, P and S has physiologically important and the heavy metals like As, Cd, Hg, Pb and Ni were below detectable level. This reveals the safety of the drug.

Toxicological study of both acute and sub-acute toxicity study were carried out in animal model Wistar albino rat according to the OECD guidelines. The test drug showed no acute toxicity as there was no mortality seen. The sub-acute toxicity after the repeated dose of 28 days was done.

The mortality, functional observations, haematological and biochemical investigations were made. There was no significant change seen in the normal values. Thus the toxicological study of the test drug greatly establishes the safety and gives the justification for long time administration.

The pharmacological study was carried out in the animal model. Three activities were seen in the drug *Kandathirika Chooranam*. The activities were

- Anti-anxiety activity in Elevated plus maze
- Anti-depressant activity in Forced swimming test and Tail suspension test
- Anticonvulsant activity –PTZ induced seizures in mice.

Anti-anxiety activity was carried out in Elevated plus maze. The trial drug *Kandathirika Chooranam*-400mg/kg b.w showed significant decrease in Anxiety condition. Thus this activity reveals the effect of the drug against Anxiety.

Antidepressant activity of *Kandathirika chooranam*-200mg/kg b.w showed significant activity to reduce depression. Thus this activity therapeutically effective in depressed condition.

Anticonvulsant activity of the test drug *Kandathirika Chooranam* was carried out in PTZ induced seizures in mice. From the present study, it was concluded that the *KCM* extract has a marked Anti-convulsant activity at higher concentrations.

Thus by scrutinizing all the above mentioned factors it is concluded that the trial drug ***Kandathirika Chooranam*** is a safe and a potent Anti-anxiety, Antidepressant and Anticonvulsant drug. Modern medicine has its own limit in treating Neurosis.

8. FUTURE SCOPE

The trial drug ***Kandathirika Chooranam*** has its own potency in treating Anxiety, Depression and Convulsion in animal model which has been established in this study. An incredible action of this drug value against the disease of Neurosis has been revealed from this study of *Kandathirika Chooranam.* This must be implicated in the future clinical studies and preclinical chronic toxicity studies. So it could be used worldwide in treatment of Neurosis.

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20.1.2017

CERTIFICATE

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

Name of the sample: Kandathirika Chooranam

Name of the Experiment	**I**	**II**	**Mean**
Loss on drying(at 105°C)	6.33 %	6.32 %	6.33 %
Total ash	3.60 %	3.70 %	3.65 %
Water soluble ash	2.09 %	2.33 %	2.21 %
Acid insoluble ash	0.49 %	0.49 %	0.49 %
Water soluble extractive	39.09 %	38.40 %	38.75 %
Alcohol soluble extractive	39.9 %	38.67 %	39.29 %
pH value (10%)	3.82	3.84	3.83
TLC/HPTLC	Report Enclosed		

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

(Dr. P. Elankani)
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 KANDATHIRIKA CHOORANAM & MANALI KEERAI *(Gisekia pharnaceoides)* KUDINEER** 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/08/CLBMCP/2016**

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

(Dr.P.Muralidharan)

IAEC Member Secretary

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

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

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

This Certificate is awarded to Dr/Mr/Mrs.....C.:...Kanimozhi.....

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

Fig 1 Zingiber officinale
இஞ்சி

Fig 1.1 Picrorhizakurroa
கடுகுரோகிணி

Fig 1.2 Piper longum
திப்பிலி மூலம்

Fig 1.3 Zingiber officinale
சுக்கு

Fig 1.4 Cuminum cyminum
சீரகம்

Fig 1.5 Elettaria cardamomum
ஏலம்

Fig 1.6 Piper nigrum
மிளகு

Fig 1.7 Phyllanthus emblica
நெல்லி

Fig 1.8 Cinnamomum tamala
இலவங்கபத்திரி

Fig 1.9 Myristica fragrans
சாதிபத்திரி

Fig 1.10 Mesua nagassarium
சிறுநாகப்பூ

Fig 1.11 Abies spectabilis
தாளிசபத்திரி

Fig 1.12 Glycyrrhiza glabra
அதிமதுரம்

Fig 1.13 Syzygium aromaticum
இலவங்கம்

Fig 1.14 Maranta arundinacea
கூகைநீறு

Fig 1.15 Saccharum officinarum
சர்க்கரை

Fig 1.16 Fried Ginger
வறுக்கப்பட்ட இஞ்சி

Fig 1.17 Preparation

2. Final product Kandathirika Chooranam