EVALUATION OF SAFETY AND EFFICACY OF A POLY HERBAL FORMULATION ADATHODAI CHOORANAM IN IYA ERAIPPU NOI (BRONCHIAL ASTHMA)

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Olympic Athletics, great leaders to common people achieve greater heights with Asthma.¹

**Siddha System**

Siddha system is one of the indigenous systems of medicine practised in India. The exponents of this system are Siddhars.² Siddhars classified the diseases on the basis of three humours Vatha, Pitha, Kaba and signs and symptoms. All the Siddha drugs are derived from herbs, metals, minerals and animals which are gifted by the Siddhars.³ The special nature of this system is its service to society for thousand years in fighting diseases and in maintaining the health.²

**Bronchial Asthma and Siddha System of medicine**

In siddha system of medicine the disease Iya Eraippu Noi is the Kaba disease which is compared with Bronchial Asthma.⁴

**Prevalence of Bronchial Asthma**

Asthma is the 14th common disorder⁵. Incidence of allergic diseases are increased due to urbanization.⁶ 300 million people globally affected from Asthma and this reaches to 400 million in year 2025.⁷ The epidemiology of Asthma has raised from 1970, and 4 to 7% of the people are affected world wide.⁸ UK has the highest prevalence of Bronchial Asthma in the world.⁹

India has an estimated 15-20 million Asthmatics.¹⁰ Past 30 years Asthma is a main problem in developing countries as they become more urbanized¹¹.ICMR found the Bronchial Asthma in Indian adults to be 2.38%.¹²
The global estimation of Asthma suggests that 334 million people are having Asthma. Female Sex, old age, urban area, low Socio economic, history of atopy and smoking were associated with higher prevalence of Asthma. GINA follows world Asthma day, each year on the 1st Tuesday of May to develop awareness.

Current therapies, their adverse effects and need of new therapy

Several drugs are available which may give a good relief in Asthma, but they are mainly asymptomatic and transient. Systemic side effects of long term treatment of inhaled corticosteroids include adrenal suppression and decreased bone mineral density. A recent case control study found that Asthmatics using inhaled corticosteroids have an increased risk of pneumonia when compared with asthmatics who did not have a prescription for an inhaled corticosteroids in the last three months. Tremor and tachycardia are reported with use of short acting inhaled B2-agonists, but tolerance to these effects develops rapidly. Heavy use of short acting inhaled B2-agonists is assessed with risk of Asthma related death. Adverse effects of theophylline include gastrointestinal symptoms, cardiac arrhythmias, seizures and even death. Hence continuous efforts are going on worldwide to find effective and safer remedies for these diseases preferably of natural origin to obtain negligible (or) no adverse effects for treating those epidemic diseases.

Herbal Medicine and Bronchial Asthma

The WHO identifies Asthma is an important health disorder. Due to minimal side effect 80 % people depend on the herbal medicine. Herbal medicine is the third choice of both adults 11% and children 6% suffering from Asthma. Medicinal herbs usage in all over the world has raised with serious concerns on the efficacy. Therefore the investigator selects the poly herbal formulation Adathodai Chooranam for pre clinical and clinical studies.
Adathodai Chooranam and Research Work

The trial drug Adathodaichooranam preparation was taken from the Siddha Sastric Book “Sigitcha Rathna Deepam Ennum Vaidhya Nool part I” which is approved by Drug and Cosmetics Act 1940. To support this trial drug, the previous research work in Justicia tranque Bariensis Juice has proven to reduce symptom scores and improves lung function significantly in Bronchial Asthma. WHO mentioned that Asthma cannot be cured, but could be controlled. The goal of Asthma Management include relief of patient’s current symptoms and prevention of disease progression. In the trial drug Adathodai Chooranam, the ingredients are having bitter and pungent taste, hot potency which neutralizes Kaba dhosha and reduces the symptom in Bronchial Asthma. Consequently, based on literature evidence, the trial drug possess curative effect in Bronchial Asthma.

In this research work standardization of Adathodai Chooranam was undertaken by evaluating its organolaptic properties, preliminary phyto chemical screening, physico chemical analysis, Thin Layer chromatography, High Performance Thin Layer Chromatography finger print, Heavy metal analysis, Microbial load and aflatoxin content were done for application in clinical trial of Bronchial Asthma. The toxicity study was undertaken as per WHO guidelines to establish the toxicity profile of Adathodai chooranam in experimental animal which will render strong evidence for its safety in clinical trial of Bronchial Asthma.

The clinical trial was conducted in 138 Bronchial Asthma patients of both sexes in the age group of 15-60 in Out patient Department and In-Patient Department of National Institute of Siddha with the trial drug Adathodai Chooranam. The standardization and the preclinical study of Adathodai Chooranam formulation proved encouraging results and the results obtained from the clinical trial also effective in Bronchial asthma.
2. AIM AND OBJECTIVES

AIM

The aim of this study is to standardize and evaluate the safety and efficacy of a new poly herbal drug Adathodai chooranam in the treatment of Bronchial Asthma for scientific validation and clinical use of the society.

OBJECTIVES

Primary Objective

To estimate the clinical efficacy of Aadhathodai Choornam in the treatment of Iya Eraippu Noi (Bronchial Asthma).

Secondary objective

- To screen the Preliminary Pytochemical Constituents (Qualitative Analysis) of the trial drug.
- To study the physico chemical analysis (Quantitative) of the trial drug.
- To identify the active compounds in the trial drug through GC-MS Analysis.
- To do the limit tests for heavy metals, microbial load and aflatoxin content etc.
- To evaluate the safety profile of the trial drug (Acute and long term toxicity studies) as per WHO guidelines.
- To study the Iya Eraippu Noi on the basis of Siddha Principles like three humours, Seven Body Constituents, Eight Diagnostic Methods, Neerkuri, Neikuri etc.
- To assess the influence of co factors such as age, sex, occupation, allergic factors, family history, socio economic status, habits etc on the Iya Eraippu Noi.

- To find out the Adverse Drug Reactions of the trial drug ‘Adhathodai Chooranam’ if any.
3. REVIEW OF LITERATURE

3.1. Review of Literature On Iya Eraippu Noi

Siddhars classified diseases into 4,448 single disease entities on the basis of vatha, Pitha and Kaba. Iya Eraippu noi is the type of Eraippu noi which is a kaba disease. The synonyms, definition, etiology, classification, signs and symptoms, pathology, diagnosis based on three humours, eight diagnostic methods, differential diagnosis, line of treatment, diet and prevention are elaborately dealt in this Siddha aspect.

Definition of Eraippu noi

A disease with symptoms such as pain and tightness of the chest, difficulty in breathing. In addition the expiration will be strenuous producing sounds mimicking those of musical instruments flute, and Veena. It is difficult to expectorate the accumulated mucus in the chest – Asthma.22

Synonyms of Eraippu noi

Eluppu Noi, Thoivu, Suvasam, Eelai, Suvasakasm, Suram. Breathlessness is the prominent symptom, so it is named as “Eluppu Noi” for the same reason it is called by Sanskrit term ‘swasam’. Since cough is an associated symptom in all cases of Eraippu Noi, it is called as Swasa Kasam.23

Etiology of Eraippu noi

According to siddha maruthuvam pothu

Highly irregular, unsuitable diet, excessive intake of kaba promoting diets, various fumes, dusts, inhaling irritable smelling substances, excessive smoking, more exposure to cold air.24
According to Siddhar kaiyezhuthupirathi

“Kaal perukkunavporul thanneermaal
Karuthirumal migalvaanthi kulirnthakattru
Maalseithu naalthorum varunthum kaichal
Manthanamuyir nilaiyil adigal thakkal
Ealaseethapethi vidapaandu pugaigal
Elagiya nellathimanich chunaiyut chellal
Maelvazhiyil silavarinum miraippam noyu
Mevumena munivargal vilambinaarae”

Intake of food which promotes vatham, drinking contaminated water, chronic cough, exposure to cold air, chronic fever and anemia, trauma in the vital organs, exposure to grains and house dusts.  

Preliminary signs and symptoms of Eraippu noi

Siddha Maruthuvam pothu

Eraippu Noi Patient will develop aura (Peculiar Sensation) and that he may undergo an attack of Eraippu Noi on that day and to some extent he can assess the Severity of the attack. The prominent features are rhinorrhoea, sneezing, discomfort in the chest, flatulence, sweating in the forehead, wheezing which may gradually develop dyspnoea on varying severity.
Theraiyar Vagadam

“Vanthidum vellokkaalam vaayathu thithhippagum
Nonthidum pidarimandai manthamum milaippinoigum
Munthavae thalaithanonthu sareeramugamung kuththum
Kantharath thondai naasikarakarantrudanae thummal”

Belching, feeling of sweet taste, loss of appetite, headache, pain in all over the body, sourness in the throat, irritation in the nose and sneezing.  

Siddhar kaiyezhuthupirathi

“Maarbil vilaavirandil mattrumiru neriyl saernthu
Valiththal thinaralaththaal moochu
Uppal vayitril uruthuvae murkuriyaga
Seyyumiraippu noikithanaisaer”

Pain in the chest and ribs, dyspnoea and abdominal distention.

Classification of Eraippu noi

Siddhar kaiyezhthupirathi classifies Eraippu noi into 5 types

“Siruperiraippu thinaral manththaaram
Varumae liraippaintththin maanbu”

1. Chittiraippu
2. Periraippu
3. Thimeral Eraippu
4. Manthara Eraippu
5. Mel Eraippu

**Siddha Marthuvam pothu classifies Eraippunoi into 5 types**

- Vali Eraippu Noi (Gastro-Oesophageal Reflux and Asthma)
- Iya Eraippu Noi (Bronchial Asthma)
- Iya Vali Eraippu Noi (Complications of Bronchial Asthma - Cardiac and renal symptoms)
- Mukkutra Eraippu Noi (Chronic Bronchial Asthma)
- Melnokku Eraippu Noi (Acute Severe Asthma)

I ) **Vali Eraippu Noi (Gastro-oesophageal Reflux and Asthma)**

Intake of indigestible foods and tubers, exposure to hot summer which promotes Vatham and causes decreased body strength leads to difficulty to breath. This type of Eraippu noi is curable.

II ) **Iya Eraippu Noi (Bronchial Asthma)**

Intake of excessive kaba promoting foods like cold food items, sweet tasted foods, exposure to rain and cold air which also promotes Iyam and causes running nose, nasal obstruction. These symptoms relived spontaneously followed by tightness of chest, wheezing with unproductive cough. In this case, when the sputum is expelled by cough, the symptoms are relived, otherwise dyspnoea will be severe. Sweating in the forehead, darkness of the face, chillness of the limbs, protrusion of eyeballs, dryness of the tongue, tremor, labored breathing, unable to lie in the bed also occurs.
III) Iya Vali Eraippu Noi (Complications of Bronchial Asthma - Cardiac & Renal symptoms)

In this type the deranged Kabam and Vatham affects the Uthaanan (Air of upward motion) and produces the following symptoms: Wheezing, constipation, oliguria, flatulence, dryness of the tongue, redness of the eyes, sweating, blabbering speech, fearfulness, restlessness and giddiness.

IV) Mukkutra Eraippu Noi (Chronic Bronchial Asthma)

In this type all the thirthodams, Uthaanan (Air of upward motion), Abaanan (Air of downward motion), viyanan (Air which spreads throughout), samanan (Air with upward and downward motion), seven body constituents are affected. Severe dyspnoea, tremor, fearfulness, high pitched wheezing, tightness of chest, giddiness, constipation, oliguria, flatulence, slurring speech, weakness of five sensory organs, body pain, excessive sweating in forehead are the clinical features.

V) Melnokku Eraippu Noi (Acute severe Asthma)

When the above types were not responded to any kind of the treatment, it may weakens the Uthaanan and leads to severe persistent dyspnoea associated with dryness of the tongue, protrusion of eyes, unable to speak and gasping. If it is treated immediately recovery can occur, otherwise death will happen.

**Signs and symptoms of Iya Eraippu noii**

**According to Siddha Maruthuvam pothu**

Intake of excessive kaba promoting food, due to exposure to rain and cold air which also promotes Iyam and causes running nose, congestion of nose which relived spontaneously
after sometime. Dyspnoea produces tightness of the chest with unproductive cough. In this case, when the sputum is expelled by cough, the symptoms are relived, otherwise dyspnoea will be severe. Sweating in the forehead, dryness of the tongue, prolonged expiration and not able to lie in the bed also occurs. It is otherwise called as Thamakka Swasam.

According to Vaidhya Chara Sangragam

Itching in the face and ear, irritation in the nose, sneezing, running nose, cough, pain in the chest and ribs, flatulence, diminished appetite are present in the mantharakasam.

According to yoogi vaidhya chinthamani

Yoogi classified the kaba diseases in three major categories

1. Kasa noi Padalam
2. Elaippu Noi Padalam
3. Iya Noi Padalam

The Symptoms of Iya Eraippu Noi are more or less similar to Manthara Kasam (Kasa Noi Padalam), Swasa Iyam (Iya noi padalam) and Swasakasam.

Manthaara Kasam

“Thanaana thooyathor naasithannil
Salanoi neerthaan vizhunthu thummalundaa
Maanaana marbu nenchadaiththu moochu
Valuvaagap paambupol seeralagum
Kanaana kandamodu mugamung kathum
Kaayamathung kasivagi viyarvaiyagum
Enaana erumalodu kozhaikattal
Eraippagu manthara kasamaamae”

- Yoogi vaidhya chinthamani
Running nose, sneezing, congestion of the nose, difficulty in breathing, wheezing, sweating, cough with or without expectoration and tightness of the chest are the symptoms of Mantharakasam.27

**Swasa Iyam**

“Thiramaiyai nenchuthanir kozhaikattunj
Sikkentru thanirumi mookkadaikkung
Kurumaiyai kurattentru suvasang kanum
Kulirodu karamundaai mayakkamaakum
Maramaiyai marbodu nenjadaikkum
Vaayvarandu mookkathanil neerae payum
Verumaiyai migaththanneer thabamundraai
Vidusuvasa silettumaththin vivaranththaanae”

- Yoogi vaidhya chinthamani

In Swasa Iyam, accumulation of phlegm in the lungs, running nose, nasal congestion, fever with chills, wheezing, tightness of the chest, dryness of the mouth and excessive thirst are present.28

**Swasakasam**

“Vanmaiyai kozhaikatti erumi veezhum
Maanaagam polavae vaangunj suvasam
Thinmaiyach cherumalunda madikkadikkuch
Seeranamilamalaie vayirumoothum
Nanmaiyai naasiyathu thanalpolagum
Nalinthudambu vattrivarung kuralung kammum
Unmaiayunnnaakkilooring kaeni
Yuzhanthumae suvasakasaththinoppae”

- Yoogi vaidhya chinthamani
Severe cough, expiration is similar to a hiss of a snake, frequent darning, feel of heat in both nostrils, emaciation, hoarseness of voice, indigestion, and flatulence.\textsuperscript{27}

\textbf{Uyir Kakkum Siddha Maruthuvam Ennum AathmaRatchamirtham Says}

Dryness of the skin, fever, cough, fatigue, headache, vomiting due to indigestion, wheezing, constipation with sweating, excessive thirst.\textsuperscript{29}

\textbf{Pathology for Eraippu noi}\textsuperscript{23}

In Siddha system, the manifestations of all diseases are the result of derangement of humours i.e., vatha, pitha, and kaba. The prime factor which involved in Eraippu Noi is Kabam, which is accompanied with vitiated vatham (or) pitham and produces the clinical symptoms of Eraippu Noi. This is clearly indicated by Theriyar as

\begin{quote}
“Kabaththinaiyantri kasa suvasam kanathu”
\end{quote}

Excess of Kabam in the respiratory organs affect the melnokkumkal (upwardair) and Uyirkal (air of life) and so, the air is not able to reach the terminal point of respiration, which produces gasping and labored breathing.

Some authors say that Eraippu Noi is caused by deranged vatham. This thought is also acceptable, because the obstruction of air in the respiratory tract is abnormally present.

Excessive intake of vatha promoting diet which induces the pitha humours. This type of pitham produces more heat and this heat goes to head resulting in running nose, heaviness of head and neck, sneezing and also induces the formation of water vapors in the lungs and causes narrowing of air passage which leads to the onset of the disease. This is indicated as \textquote{\textquote{Piththamae migunththal eelai erumalum balaththu nirgum’}}

-Gunavaagada naadi

[13]
Six seasons and Eraippu noi

1. Kaarkalam (early rainy season) – August and September
2. Koothirkalam (late rainy season) – October and November
3. Munpani Kalam (early winter season) – December and January
4. Pin pani Kalam (Late winter season) – February and March
5. Elavenil Kalam (Early Summer season) – April and May
6. Mudhuvenil Kalam (Late summer season) – June and July

“Kaarae koothir munpani pinpani Seerila venil entrangu Erumoontru thiranthathu theriperum pozhuthae”

-Siddha aruthhuvaanga churukkkam

The Kaar, koothir, Munpani, Pinpani aggravated the disease Iya Eraippu Noi especially at vaigarai (early morning).

Five lands and Eraippu noi

Hilly Tracts-Kurinchi Mountain and its surroundings

Sylvant Tracts-Mullai – Forest and its surroundings

Agricultural Tracts-Marthuam – Fields and its surroundings

Maritime Tracts-. Neithal- Sea and sea shore

Arid tracts-.Palai- Desert and its surroundings

Kurinchi

“Kurinchi varunilaththil kotramundi raththam
Urinchi varusuramumundam arignaraik
Persons who live in Hilly tracts are usually liable as developing Kaba Noi.

**Palai**

“Paalai nilam pol padarai pirappikka

Melai nilameeyathu viriththarku velai nila

Muppinikku millam muraiye yavattralam

Eppinikku millammaththen

...Siddha maruththuvaanga churukkam

People dwelling in these lands will suffer from all diseases due to vatha pitha and kapha. So Iya Eraippu Noi is found in this Land.

**Three humours and Iya Eraippu noí**

**A. vatham**

1. **Piranan: (Air of life)**

   It is responsible for respiration. It helps in spiting, coughing, sneezing, belching. In Iya Eraippu Noi difficulty in breathing is due to the affection of this air.

2. **Abanan: (Flatus air)**

   It helps to excrete the urine and motion. In Iya Eraippu Noi some patients had constipation.
3. **Viyanan** : (air spreads all over the body)

   It’s abode in the heart. It makes both the movable and immovable parts in the body of function making them to stretch and flex. It’s main function is distribution of rasam (Chyle) and senneer (blood) all over the body.

4. **Udhanan** : (Upward air)

   It is occupied in the chest, umbilicus and nose. It is the root cause for speech. In Iya Eraippu Noi sneezing and cough may present due to the derangement of this air.

5. **Samanan** (Balancing force)

   It is the main air for digestion. It controls all other vayus. In Iya Eraippu Noi dyspepsia may present due to the derangement of Samaanan.

6. **Nagan** : (Air of higher intellectual function)

   It maintains the opening and closure of eye lids.

7. **Koorman** : (Air of yawning)

   This is responsible for vision and yawning and gives strength.

8. **Kirukaran** : (Air of Salivation)

   It dwells in the tongue and gives greasiness and moisture to the tongue and nose. It stimulates hunger. It helps in remembering things. It helps in creating sneezing, coughing. In Iya Eraippu Noi this air may derranged with loss of appetite and excessive sneeze and coughs.

9. **Devathathan** : (Air of Laziness)

   It is responsible for tiredness, sleep and anger. It is affected in Iya Eraippu Noi due to nocturnal wheezing.
10. **Dhananjeyan** (Air acts on death)

It produces swelling of the body after death and escapes due to the separating of sutures of the skull after the third day.

b. **Pitham**

According to its site and function, it is divided into five kinds.

1. **Anal Pitham (The fire of digestion)**

   This is residing in the stomach, and helps in digestion. In Iya Eraippu Noi dyspepsia present. Therefore Anal pitham is affected.

2. **Ranjaga Pitham (Blood promoting fire)**

   This is residing in blood and regulates the quality of blood. Ranjaga pitham is responsible for decreased Hemoglobin.

3. **Sathaga Pitham (The fire of Energy)**

   In resides in heart and makes correct activities with the help of mind and brain. In this disease restlessness is present. So Saathaga pitham is affected.

4. **Aalosaga Pitham (The Fire of vision)**

   It resides in both eyes and gives correct vision.

5. **Pirasaga Pitham (The fire of brightness)**

   It resides in skin and gives complexion.
C. Kabam

1. **Avalambagam (Kabam of inspiration)**

   It is residing in lungs and heart and helps to other four types of kabam to function. Cough, wheezing, dyspnoea are present Iya Eraippu Noi due to the affected Avalambagam.

2. **Kilethagam (Kabam of digestion)**

   It is present in the stomach and gives moisture to the food materials and also helps in digestion. In Iya Eraippu noi affected kilethagam produces dyspepsia.

3. **Pothagam (Kabam of Taste)**

   It is present in the tongue and reveals the taste.

4. **Tharpagam (Kabam of vision)**

   It resides in the head and gives chillness to the eyes.

5. **Santhigam (Kabam of Joints)**

   It resides in joints and helps for free movements.

**Seven udal kattukal (body constituents) and Iya Eraippunoi**

“Thannamaama rasamirathamangisamu methai
Thasai matchaiyodu suklanththa thezhagi’’

Yougi vaithiya chinthamani 800

There are the seven basic principles which constitute the entire body, Saram (Chyle), Senneer (Blood), Oon (Muscle), Kozhuppu (Adspose tissue), Enbu (Bone), Moolai (Bone marrow), Sukkilam/Suronitham (Sperm/Ovum). ³³
In Iya Eraippu Noi Saaram and Senneer are affected. Saram is the end product of the digestive process. It strengthens the body and mind. This is deranged due to loss of appetite in Iya Eraippu Noi. Senneer is affected due to increased Eosinophil count, Absolute Eosinophil count and serum IgE level.

**Piniyarimuraimai (diagnosis) in Siddha**

Method of diagnosis is based upon three main principles

- Poriya arithal - Inspection
- Pulanaalarithal - Palpation
- Vinaathal - Interrogation

**Ennvagai thervugal (eight diagnostic methods)**

“Naadi parisam naa niram mozhi vizhi
Malam moothiramivai maruthuvarayutham”

-Siddha maruthuvanga churukkam

“Setma sadam viyarvai kondeyirukkum”

Thirattu naadi

“Setmaththin theganththanum sikkentru kulirnththirukkum”

-Naadi nithanam seyyul

“kodunjsethmarogi veluthiduvan thonthamellame”

Siddha maruththuvaanga churukkam
“kothutra silerpanaththarkkuk koor vizhi veluthhirukkum”

Siddha maruththuvaanga churukkam

“Mannunj seththumaththor malam veezhkuzhi

Ennal theera veezhum veruppannavae

Therayar yamagam

“Malamara chikkalaga veluthhiduma iyaththirku

pulippani

“veelume seththumaththor neerkkunam vilambak kelai

Naalume veluththurainthu nalam sera veezhung kandai

Siddha maruththuvanga churukkam

“Aravena neendidin aththe vaatham

Aazhipor paravin aththe piththam

Muththoththu nirgin mozhivathen kabame”

-Siddha maruththuvaanga churukkam

Envagai thervugal (eight fold system of clinical assessments) in Iya Eraippu

1. Naa thervu

(Examination of tongue)

(i) Niram (Colour) Pale/cyanosis in acute severe condition.

(ii) Thanmai (Character) Coated / denuded.

(iii) Pulan (Sense) Salaiva tend to taste sweet / sour.

(iv) Salivary secretion Decreased

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2. *Niram thervu*

(Examination of colour) Pale / red / pink

3. *Mozhi thervu*

(Examination of speech) Low pitched wheezing sound heard

(Snake’s snort) along with speech.

4. *Vizhi thervu*

(Examination of eye)

(i) *Niram* (Colour) Pale / black

(ii) *Thanmai* (Character) Normal.

(iii) *Pulan* (Sense) Normal.

5. *Malam thervu*

(Examination of stool)

(i) *Niram* (Colour) Pale

(ii) *Nurai* (Froth) Present

(iii) *Elagal/Erugal* (Consistancy) *Elagal* (loose stools)

6. *Moothiram thervu*

(Examination of urine)

(a) *Neerkuri:*

(i) *Niram* (Colour) Straw coloured

(ii) *Adarthi* (Density) Decreased

(iii) *Manam* (Odour) Flesh smell

(iv) *Nurai* (Froth) Increased

(v) *Enjal* (Deposits) Absent
(b) Neikkuri:  
*Iya neer*- Oil stands in the form of pearl.

In severe stage: The oil drops spreads
the shape of the sieve, betle leaf,
irregular margin and flower shapes.

7. *Parisam thervu*

(Examination by touch)  
Cold / clammy / pain in throat / tenderness.

8. *Naadi thervu*

(Examination of pulse)

(i) *Thanmai* (Character)  
Rapid and thin.

(ii) *Nadai* (Pattern)  
Iya Naadi and Vali Iya Naadi

**Naadi Nadai in Iya Eraippu noi**

**Kaba naadi**

“Uttridum iyanaadi ongiyae thudiththu nintraal
Patridum eelai pathariyae eraippundakki
Meththavae kozhai vaai miguthippadum”

-Agaththiyar gunavaagadam

“Iyamae kathiththa pothariyavae porumal kaanum
Eeelaiyu manthaarakaaam nalir kulir vikkal satthi
Seyyumaa moochchadaippaan teetharu kasarogam
Thoyyumaa milaippu kaasam thonru mentraran sonnaarae”

-Pathinen siddhar naadi
“Thaanamulla seththumanththanilagil veppu
Sayameelaiyirumal manthaarakaasam
Eenamurunjchanni vidathodam vikkal
Yiruthrogang karappaan viranathodam
Maananiyeer soolai thiral viyathi veekkam
Varunjchaththi suvasam nenchadaippu, thookkam
Eanamurung kamaalai paandu sobai
Eazhusurangal palathukkam vidamundaamae”
-Sathaganaadi

vadha kabam

“Pangaana vathaththil seththuma naadip
Parisiththaal thimir mevumulaichchalagum
Theengaana erumaludan sannithodam
Serntha vidam vedisoolai eruthrogam
Vangatha eelai manthaarakaasam
Valiyudane puraveechchuyul veechu veekkam
Onganunj suramudane suwasakasam
Undagum vegu noikkum uruthithaane”
-Sathaga naadi

Kaba pitham

“Edamaana seththumaththil pithanaadi
Ezhunthanugil vidamudane veekkamundaam
Thidamaana kulirkaichchal manjal novunth
Thegaththilulaichallilaip pirumal vaanthi
Vidamaana nenjadaippu suvasam vikkal

Vegusuramum naavaratchi paandu rogam

Adamaana kuvalai raththamathi saaranthaan

Anugi vegu pala noikkunth thadangkandaaye”

-Sathaganaadi

Iya vayu

‘Thonthiththa sethumaththil vaayukoodith thodarntha

Gunmam nenjdaippu suvasakaasam”

-Sathaganaadi

Iya ushnam

“Kathippaana sethumaththil uttinang koodil

Kalantha kulir sayamirumal suvasakaasam”

-Sathaganaadi

Iya seetham

“Adamaana seththumaththil seethalam patril

Anuginaal suvasamadaippu elaippu moorchai”

-Sathaganaadi
Differential diagnosis of Iya Eraippu noI

Mookkadaippu Erumal

“Seppave erumalodu kozhai veezhum

Seththumamaamilaippodu eraippundagum

Uppamaai vayirthuvumoothikkollum

Oonurakkamillamaluruntthegam

Kuppamaai malasalamunggaruthi veezhum

Kozhaiyidagunanththaan meen kavichchadikkunth

Thuppamaaich churundu vayiru valiyumaagum

Suvasapeenasamentre soottidaye”

-Yougi vaidhya chinthaamani

Cough with expectoration, increased kaba dhosha, dyspnoea, wheezing, abdominal distention, anorexia, insomnia, oliguria, constipation, abdominal pain and Sputum with fish like odour.  

Azhal Iyam

“Panbagak kanmayangik kirukirukkum

Paththiyanththaan asathyagum

Unbaga vasanamigaththanunjchella

Ooriyevaai neerthaan migavundagum

[25]
Fainting, giddiness, tiredness, due to severity of the abathiyam, anorexia, excessive salaivation, accumulation of phlegm in the throat, cough with severe dyspnoea, yellowish discoloration of the body.\textsuperscript{43}

\textbf{Kanda Kiragam}

\textit{“Vagaiyaana kuralathanaip pattri nonthu}
\textit{Maarbodu pidariyinil valiyundagi}
\textit{Nugaraana sarezamellam nontha zhaattri}
\textit{Nunukkamaaich suvasamathu purappadaamal}
\textit{Mugaiyaana naavaale moochchu maari}
\textit{Mugaththile viyarvaagi vilaano vundaam}
\textit{Pugaiyaana vannaththaip parugottathu}
\textit{Pariyanda kiragaththin panbuthaane”}

\textsuperscript{43}Yougi vaidhya chinthaamani

In Kandakiragam, there is difficulty in speech, chest pain and pain in occipital region, pain all over the body, breathlessness, oral breathing, sweating in face, pain in the ribs and loss of appetite.\textsuperscript{44}
Swasa Pitham

“Karuththaaga suvasamathu migavundagung
Kanamaaga vayirume oothikkaanum
Uruththaaga udalathuthaan migavalikku
Moorume kenipol vaaineerthaanum
Maruththaaga mayangiye kanmaraikkum
Maarbile valiyodu erumalundanth
Thuruththaaga vayirathanin pasiyovillai
Suvasamaam piththaththin sootchantthaane”

-Yougi vaidhya chinthamani

In Swasapitham, there is tachypnoea, flatulence, pain all over the body, excessive salivation, loss of consciousness, pain in the chest followed by cough, loss of appetite etc.⁴⁵

Silethuma Vatha Suronitham

“Panbaaga vudalkulirnthu vayiruveengip
Pathaippaana vidanththittaarpol novaanth
Thinbaana sirasu nettri nokkadundanj
Silettumamaaik kozhaiyodu suvasamaagum
Manbaaga mayakkamodu kanavumundaam
Vaaivaranda rusiyillaa varuththamaagum
Nanbaaga naadiyume padabadakkum
Nansiletma suronithamaam naadungkaale”

-Yougi vaidhya chinththaamani

[27]
In Silethuma vatha suronitham symptoms such as chillness of limbs, abdominal distension, malaise, headache, cough with mucoid sputum, dyspnoea, giddiness, dreaming, diminished salivation, loss of taste, rapid pulse etc. 46

**Principles of treatment in siddha**

Treatment in siddha system is depend on three concept.

- **Kaappu** - Prevention with protection
- **Neekkam** - Removal of diseases.
- **Niraivu** - Restoration of good health. 47

**Line of treatment in Iya eraippu noi** 48

**Purgative therapy**

To neutralize the changed three humours (Vazhi, azhal, iyam).

**Internal Medicine**

Bronchodilator with expectorant drugs to reduce the increased kabha.

**External Medicines**

**Fumigation**

This is an effective treatment for respiratory conditions such as sinusitis, bronchitis, allergies and asthma.

**Vapour bath**

Steam inhalation eases symptoms of bronchitis, allergy and asthma by relieving the inflammation and congestion of mucous membranes.
**Fomentation**

Hot fomentation can be used in a variety of acute conditions including bronchitis, asthma, chest congestion, muscle spasm and insomnia. Bran-fomentation is advised in perspiration skinned persons. It liquefies the phlegmatic congestion and also alleviates the chest tightness.

**Manipulative therapy**

It regulates nerve function, improper blood circulation, enhances immunity and removes excess tissues. It strengthens blood, flesh and skin, improves sleep, vitality and relaxes the whole body. Gentle massage may be given with medicated oil.

**Oleation**

Oil bath may be advised twice a week with medicated oil.

**YOGASANAMS FOR IYA ERAIPPU NOI**

Yogasanams strengthen the internal organs (especially heart, lungs, stomach, Lungs spleen, kidney and uterus) and stimulate and regulate their functions in Asthma.

**Machasanam**

Expands the chest and lungs within, becomes beneficial in case of diseases of the respiratory tract. It gives briskness and expels the sputum.

**Thirigonasam**

It strengthens the muscles of the rib (inter costal muscles) and rejuvenates the lungs, lower abdomen and back muscles.
Pujangasanam

It gives proper blood supply to the abdominal organs. It gives strength to the lungs and vertebral joins. It relieves constipation, indigestion and gives immune power.

Chakkarasanam

It gives strength to the muscles of neck, abdomen and vertebral column. It expands the chest.

Halasanam

It relaxes the thorax and strengthens the vertebral column.

Pranayamam (breathing exercise)\(^{49}\)

Prayanayamam’s role is prevention of Bronchial Asthma. Though to some extent the required amount of oxygen intake is brought about by normal respiration, all the alveoli in the lungs do not derive oxygen fully. Thus on reaching the lungs, the blood absorbs oxygen only from a limited number of alveoli. As a result, all the blood reaching the lungs cannot get oxygen from the alveoli. Unlike normal respiration, the practice of deep breathing in pranayamam ensures significantly higher amount of oxyen intake by blood circulating through the lungs. During breathing exercise, the lungs expand well and get proper supply of oxygen by proper expansion of chest. So pranayamam practice is one of the preventive methods for Asthma.

Diet for iya eraippu noi\(^{50}\)

Substances that cure kapha diseases

“Aaavinathupaal araththaimul langimayil
Thoovi narunjchaambal thooothulamthen maavomam
Thuyya sarukkarai thuzhaavithai vilaambazhagam
Iyyamathai yottum ari”

....Pathaarththaguna chinththaamani
Cow’s milk, Alpinia officinarum, radish, ash of peacock’s feather, Solanum trilobatum, honey, Carum copticum, sugarcane and seeds of Ocimum sanctum cure Kapha diseases.

**Curry for kapha persons:**

“Kaththiripeip pudalavarai erubaagal parungkalaa kandangkaari
Aththikkaikalum varukkai maapayattrai suraiyalpeerk karumpinchuver
Moiththasooranang kathalith thandugalap poomulangi murukkarumbum
Aththipoosinikkaayee rullivalli yungkabaththork kaaanamaame”

...Pathaarththagunachinththaamani

Foods made of brinjal, Trichosanthes cucumerina, country beans, small and big variety of bitter gourd, Carisa carandas, Solanum xanthocarpum, fig, bottle gourd, stem of plantain, fenugreek, radish, Butea frondosa, pumpkin, garlic and onion are good for Kapha (Iyam) persons.

**Greens for kapha persons:**

“Kaaraiyiru kovai munnai sembaipadol thuyili vazhukkai nerunjil
Aaraipuli yaaraimullai maruthaneithal melinalvallaarai ponnaa
Vaaraimusuk kaimurungai yirupinnaakkodu panna manali pillaik
Keeraimusuttai yungaara manimaadang kadalaipulik karikkalaave”

- Pathaarththagunachinththaamani

The suitable greens for Kapha persons are Oxalis corniculata, Margitea quadrifolia, Premna integrifolia, Randia dumetorum, Coccina India, Tribulus terrestris, Acalypha indica, Centalla asiatica, Cassia occidentalis, Moringa oleifera and Polygonum punctatum.
“Velaimanatht hakkaali menseethi chakravarththi
Peelai vasalaikkku pensunangan velaiyivai
Senththalirk kalaikkeerai seivarkaba thegarrnitham
Vanthaniyu naththaan magizhnthu”

-Pathaarththagunachinththaamani

Cleome penataphyla, Solanum nigrum, Alternenthera sessilis, Aerva lanata, Zingiber officinalis and portulaca quadrifida are also good for Kapha persons.

Sauces for kapha persons

“Kanthaoo manjseng kadugusatha kuppaitharaa
Venthiyang kothhumalli velaiikkku munthakaththi
Thoorukurinj chaapaagal thumbsiyitchchaa kangal ventha
Saarukaba thegarkkaanj sattru”

-Pathaarththagunachinththaamani

Sauces made of Mollugo spergula, Leucas aspera, Sesbania Grandiflora, Santalum album, Carum copticum, Brassica juncea, Ruta Graveolens, Pamania parviflora, Trigonella foenum, Coriandrum sativum, Zingiber officinalis and bitter gourd are good for kapha persons.

Dried food stuff for kapha persons

“Sundaimanath thakkaali thoothunam purandaiyaa
Thondaimulli peippudalai thondaisimmai kandaiyuru
Kaththarine lippinju kaanaraththam pinjivaigal
Oththa vattral inthe gark kun”

-Pathaarththagunachinththaamani
Dried dishes made of Trichosanthes cucumerina, Solanum xanthocarpum, Solanum torvum, Solanum nigrum, Solanum trilobatum, Cissus quadrangularis, Capparis zeylanica and phylanthus emblica are good for Kapha persons.

**Diet restriction**

“Kadugu nattrilath thennai koozhpaandang kadalai
Varuvathaagiya thengumaa varukkai narkaaya
Mazhavi laathavel lullikol pugaiyilai mathupen
Yidarupaagavo dagaththi nekkidalich chaapaththiyam.”

-Sigitchaarathnadeepam part-1

Mustard seeds, Bengal Gram, Mango, Garlic, Tobacco, Bitter Guard, Asafoetida, Gingely Oil, Coconut, Jack Fruit, Horse gram, Alcohol, Sesban, Other indulgence in sex.⁵¹

**Diets to be added**

1. **Green Leafy Vegetables like**
   - Spinach (Pasalai)
   - Solanum Nigrum (Manathakkali)
   - Alternanthera Sessilis (Ponnanganni)
   - Moringa Oleifera (Murungai)
   - Centella Asiatica (Vallarai)
   - Solanum Trilobatum (Thoothuvalai)
   - Cissus Quadrangularis (Pirandai)
   - Mukia Scavrilla (Mookirattai)
   - Erythrina variegate (Kalyana murungai)
2. **Sproutted Seeds and Grains**

3. **Fresh tender Vegetables like**

4. **Add sufficiently in diet**
- Fenugreek
- Coriander Seeds
- Anet Seeds (Sathakuppa)
- Asafoetida
- Cardamom seeds
- Dried ginger

5. **Fresh Fruits Like**

- apple
- Papaya
- Strawberries

6. **Non Vegetable Diet like**

- Crab
- Turkey
- Rabbit
- White rat
- Loach (Ayirai meen)
- Capra hircus (velladu)

**Diets to be avoided**

**Fried Foods**

- Difficult to digest Foods
- Refrigerated Foods, all refined & processed Foods
- Food Preservatives & Food Coloring
- Allergic foods.
➢ Food Additives (sulfites)
➢ Curd Preparations
➢ Cool Drinks, Ice Creams
➢ Plenty of tea & Coffee
➢ Alcoholic Beverages
➢ Pickles, Sauces
➢ Citrus Fruits like lemon, orange.
➢ Other fruits like pineapple, grapes, jackfruit, mango, pomegranate.

Principles and advice (or) guidelines for Asthmatics

1. In take of Hot water and hot Foods.
2. Taking Bath strictly in hot water
3. Avoidance of Chill weather
4. Avoidance of polluted area and dust.
5. Avoidance of Allergic Factors
6. Avoidance of smoking and snuff
7. Avoidance of stress and emotion
8. Evening meal should preferably be finished before sundown (or) atleast 3 hours before bed time.
9. Avoid cycling, mountain biking, Long distance, Running, Weight lifting.
10. Advice to practice Pranayamam and Yogasanam like buyangasanam, sarvangasanam, patchimothasanam, halasanam, badhmasanam.

11. Remove Carpets from bedrooms and vacuum regularly.

12. Keep the house clean and keep food in containers and out of bedrooms.
FIGURE 3.1 ANATOMY OF RESPIRATORY SYSTEM
FIGURE 3.2 TRIGGERS FOR BRONCHIAL ASTHMA

FIGURE 3.3 PATHOLOGICAL CHANGES OF BRONCHIAL ASTHMA

Pathological Changes of Bronchial Asthma

- Vasodilation
- Mucous plug
- Desquamation of epithelium
- Hyperplasia of mucous glands
- Smooth muscle hyperplasia
- Thickened BM
- Edematous submucosa
- Cellular infiltration
FIGURE 3.4 RADIOLOGICAL CHANGES IN BRONCHIAL ASTHMA

NORMAL CHEST X-RAY

HYPERINFLATED LUNGS
3.2. REVIEW OF LITERATURE ON BRONCHIAL ASTHMA

Definition

Bronchial Asthma is characterized by wheeze, cough, chest tightness and difficulty to expel the sputum\(^5\).

Prevalence of Bronchial asthma

Bronchial Asthma is a common respiratory disease affecting nearly 3 to 5 percent of the population. The highest prevalence is found in New Zealand (30% of the population). Each year approximately 4, 70,000 hospital admissions and 500 deaths in the United States are attributed to Asthma.\(^{5,3}\) Bronchial Asthma occurs highly in early life.\(^5\)

Table1.1: classification of asthma\(^\text{5,4}\)

<table>
<thead>
<tr>
<th>Factors</th>
<th>Allergic Asthma or Extrinsic Asthma</th>
<th>Idiosyncratic or Intrinsic Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Childhood or teenaged (early Onset)</td>
<td>Adults from 20 to 40 years (late onset)</td>
</tr>
<tr>
<td>Family history of allergic diseases</td>
<td>Usually present (Atopic)</td>
<td>Negative (Non Atopic)</td>
</tr>
<tr>
<td>Causes</td>
<td>Usually specific antigen and seasonal</td>
<td>Infection or exercise and non seasonal</td>
</tr>
<tr>
<td>Serum IgE Level</td>
<td>Increased Serum levels of IgE</td>
<td>Normal serum levels of IgE</td>
</tr>
<tr>
<td>Skin test for allergens</td>
<td>Usually positive</td>
<td>Usually negative</td>
</tr>
</tbody>
</table>
Table 1.2: Classification of Severity of Bronchial Asthma (NIH, USA)\textsuperscript{55}

<table>
<thead>
<tr>
<th>Severity</th>
<th>Symptoms</th>
<th>Night time symptoms</th>
<th>Lung Function</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 4</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Severe persistent</strong></td>
<td>• Continuous symptoms</td>
<td>• Frequent</td>
<td>• FEV or PEFR 60% or less than predicted</td>
</tr>
<tr>
<td></td>
<td>• Limited physical activity</td>
<td></td>
<td>• variability of PEFR &gt;30%</td>
</tr>
<tr>
<td></td>
<td>• Frequent exacerbations</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Step 3</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Moderate Persistent</strong></td>
<td>• Daily symptoms</td>
<td>• &gt; 1 week</td>
<td>• FEV1 or PEFR &gt;60% &gt; or = 80% predicted</td>
</tr>
<tr>
<td></td>
<td>• Daily use of inhaled $\beta_2$- agonists</td>
<td></td>
<td>• PEF variation &gt; 30%</td>
</tr>
<tr>
<td></td>
<td>• Exacerbations affect activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Exacerbation 2 or more/week</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• May last days</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Step 2</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mild persistent</strong></td>
<td>• Symptoms 2 times or less per week</td>
<td>• &lt; 2 times a month</td>
<td>• FEV\textsubscript{1}, or PEFR 80% or more</td>
</tr>
<tr>
<td></td>
<td>• Asymptomatic and normal PEFR between exacerbations</td>
<td></td>
<td>• PEF variation 20-30%</td>
</tr>
<tr>
<td></td>
<td>• Exacerbations brief</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Step 1</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mild intermittent</strong></td>
<td>• Symptoms 2 times or less per week</td>
<td>• 2 times or less per month</td>
<td>• FEV\textsubscript{1}, or PEFR 80% or more</td>
</tr>
<tr>
<td></td>
<td>• Asymptomatic and normal PEFR between exacerbations</td>
<td></td>
<td>• PEF variation &lt; 20%</td>
</tr>
<tr>
<td></td>
<td>• Exacerbations brief</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ETIOLOGY OF ASTHMA

GENETIC SUSCEPTIBILITY

Asthma which begins in childhood generally occurs in atopic individuals who produce significant amounts of IgE on exposure to small amounts of common antigens. First-degree relatives of asthmatic patients have a higher prevalence of asthma when compared to relatives of non-asthmatic patients.

ENVIRONMENT AND AIR POLLUTION

Indoor

House dusts, Pet-derived allergens, fungal spores and cockroach antigens are indoor factors. Nitrogen dioxide from gas cookers, sulphur dioxide from open fire, Passive exposure to cigarette smoke increases the risk of developing asthma.

Outdoor

Nitrogen dioxide, ozone, sulphur dioxide and air borne particulates exacerbate asthma symptoms. Sulphur dioxide is created by the burning of fossil fuels and emissions from diesel-powered vehicles. Leaves of grass and flower pollens, allergens from rapeseed, soya bean and other crops, atmospheric pollutants, aero-allergens and climate will have important effects on asthma.

DRUGS

Salicylates e.g. - Aspirin. Nonsteroidal anti inflammatory drugs eg - indomethacin, ibuprofen, fenoprofen, naproxen, mefenamic acid, phenyl butazone, zompirac sodium. Beta₂-adrenoreceptor antagonists (β Blockers) the local use of beta blockers in the eye for treatment of glaucoma is associated with worsening asthma.
Colouring agents such as tartrazine induce asthma.

Sulfiting agents who are presented in salads, fresh fruits, potatoes, shellfish and wine produce Asthma symptoms.

INFECTIONS

Rhinovirus and Influenza viruses are predominate pathogens.

EXERCISE:

Exercise provokes bronchospasm to some extent in every asthmatic patient.

COCKROACH ALLERGEN\textsuperscript{56}

The Cockroach Asthma is having perennial symptoms with high levels of Ig E.

PSYCHOLOGICAL FACTORS

Severe Anxiety, emotional stress, emotional expressions like anger, laugh, frustration, crying, fear induce the Asthma.
Table 1.3: SELECTIVE AGENTS KNOWN TO CAUSE OCCUPATIONAL ASTHMA

<table>
<thead>
<tr>
<th>Agents</th>
<th>Occupation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. Natural Organic environmental agents.</strong></td>
<td></td>
</tr>
<tr>
<td>Animal Proteins (urine, danders)</td>
<td>Laboratory workers/Veterinarians</td>
</tr>
<tr>
<td>Shellfish, egg proteins, pancreatic enzymes, papain, amylase</td>
<td>Food Processing</td>
</tr>
<tr>
<td>B. Subtilis enzymes</td>
<td>Detergent Factory</td>
</tr>
<tr>
<td>Poultry mites, droppings, feathers</td>
<td>Poultry Farmers</td>
</tr>
<tr>
<td>Flour grain</td>
<td>Bakers</td>
</tr>
<tr>
<td>Storage mites, soyabean, wheat</td>
<td>Farmers</td>
</tr>
<tr>
<td>Midges</td>
<td>Fish Food manufacturing</td>
</tr>
<tr>
<td>Silk worm moths and larvae</td>
<td>Silk workers</td>
</tr>
<tr>
<td>Castor beans, Coffee seeds bean</td>
<td>Farmers</td>
</tr>
<tr>
<td>Colophony</td>
<td>Electric soldering</td>
</tr>
<tr>
<td>Wood dusts (red cedar, oak, mahogany, etc)</td>
<td>Carpenters and Saw mill workers</td>
</tr>
<tr>
<td>Grain dust (moulds, insects, grain)</td>
<td>Shipping workers</td>
</tr>
<tr>
<td>Cotton dust</td>
<td>Cotton mill workers</td>
</tr>
<tr>
<td>Storage mites, fungi, ragweed, pollen</td>
<td>Granary Workers</td>
</tr>
<tr>
<td><strong>2. Organic chemicals</strong></td>
<td></td>
</tr>
<tr>
<td>Isocyanates (TDI, MDI, HDI)</td>
<td>Plastic and foam</td>
</tr>
<tr>
<td>Antibiotics, piperazine, methyl dopa, cimetidine</td>
<td>Manufacturing</td>
</tr>
<tr>
<td>Disinfectants</td>
<td>Hospital workers</td>
</tr>
<tr>
<td>Paraphenylene diamine</td>
<td>Fur dyeing</td>
</tr>
<tr>
<td>Formaldehyde, ethylene diamine</td>
<td>Rubber processing</td>
</tr>
<tr>
<td>Furfuryl alcohol resin</td>
<td>Foundary workers</td>
</tr>
<tr>
<td>Dimethyl ethanolamine toluene di-isocyanate</td>
<td>Automobile painting</td>
</tr>
<tr>
<td><strong>3. Inorganic chemicals</strong></td>
<td></td>
</tr>
<tr>
<td>Platinum Salts</td>
<td>Refining</td>
</tr>
<tr>
<td>Nickel Salts</td>
<td>Plating</td>
</tr>
<tr>
<td>Cobalt salts</td>
<td>Diamond polishing</td>
</tr>
<tr>
<td>Chromium salts</td>
<td>Stainless steel welding</td>
</tr>
<tr>
<td>Aluminium fluoride</td>
<td>Manufacturing</td>
</tr>
<tr>
<td>Persulphate</td>
<td>Beauty Shop</td>
</tr>
<tr>
<td>Vanadium</td>
<td>Refinery workers</td>
</tr>
<tr>
<td>Stainless fumes</td>
<td>Welding</td>
</tr>
</tbody>
</table>
CARDINAL PATHOPHYSIOLOGICAL FEATURES OF ASTHMA

Air flow limitation

Usually reverses spontaneously or with treatment.

Increased- Airway responsiveness

Bronchoconstriction to exercise, cold air, cold drink.

Airway inflammation

Eosinophils, lymphocytes, mast cells, neutrophils; associated oedema.

<table>
<thead>
<tr>
<th>Pathological changes</th>
<th>Mediator implicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchospasm</td>
<td>Histamine (H1 response), LTC4, LTD4, LTE4, Prostaglandins and TXA2, Bradykinin, Platelet activating factor, Acetylcholin</td>
</tr>
<tr>
<td>Mucosal oedema</td>
<td>Histamine (H1 response), LTC4, LTD4, LTE4, Prostaglandin E, Bradykinin, Platelet activating factor</td>
</tr>
<tr>
<td>Cellular Infiltration</td>
<td>Eosinophil chemotactic</td>
</tr>
</tbody>
</table>
(Airway Hyperreactivity) | factor  
| Neutrophil chemotactic factor  
| HETE₅  
| LTB₄  

Muscus secretion | Histamine (H₁ response)  
| LTC₄, LTD₄, LTE₄  
| Prlostaglandins generating  
| Factor of anaphylaxis  
| Prostaglandins  
| HETEs  
| Acetylcholin  
| Macrophage mucus secretagauge  
| O₂⁻  H₂  O₂  OH⁻  
| Proteolytic enzymes  

Basement Membrane thickening | O₂⁻ proteolytic enzymes  

**CLINICAL SYMPTOMS OF ASTHMA**

**EPISODIC ASTHMA**[^54]

Episodic asthma occurs during viral respiratory tract infections or after exposure to allergens. This is seen in children or young adults who are atopic.

**PERSISTENT ASTHMA**

Chronic wheeze is the cardinal sign of this type of asthma.

**NOCTURNAL ASTHMA**

Symptoms such as cough and wheeze often disturb sleep and the term ‘nocturnal asthma’ emphasizes their lowest level of serum adrenaline and cortisol and highest levels of histamine during night hours could be responsible for nocturnal episodes. Gastro oesophageal reflux leading to increased vagal tone, lowering of temperature, increased accumulation of secretions in the respiratory tract during sleep may be additional factors.

[^54]: [47]
COUGH VARIANT ASTHMA

Cough may be the dominant symptom and the lack of wheeze or breathlessness may lead to a delay in making the diagnosis of so called cough variant asthma.

EXERCISE INDUCED ASTHMA

Symptoms may be specifically provoked by exercise that is called exercise induced asthma.

PREGNANCY INDUCED ASTHMA

Physiological changes on pregnancy which improve Asthma.

GASTRO ESOPHAGEAL REFLUX WITH ASTHMA

The occurrence of GER after bedtime is strongly associated with Asthma, respiratory symptoms and obstructive sleep apnoea syndrome.

Diagnosis of Bronchial Asthma

Complete and differential blood count

An elevated peripheral blood eosinophil count

Serum IgE Level

An increased serum level of total or allergen - specific IgE (Radio Allergen sorbent test) may also be helpful in diagnostic of bronchial Asthma.

Chest X Ray:

Routine chest radiograph in patients with Asthma usually show only hyperinflation.

Sputum examination

Sputum eosinophilia ia a useful indication of an asthmatic type of airways reaction.
Skin Hypersensitivity test

To identify one particular allergen as the cause of Asthma in an individual patient and their chief value is to distinguish atopic from non atopic subjects.

Pulse oximetry

Measurement of oxygen saturation (SpO₂) is performed by pulse oxy meter for adequacy of oxygen therapy.

Peak Expiratory flow rate

While complete Spirometry can be done in a laboratory only, the patient can measure the peak expilatory flow rate himself. Patients measure their PFFR on morning and in the evening, before taking Bronchodilator.

Green Zone

It indicates all clear. Asthma is under control with no symptoms or interruption of activities or sleep PEFR are usually 80% - 100% of personal best. The variability is less than 20%

Yellow Zone

This signals caution. Some mild Asthma symptoms are present. PEFR readings are 60%-80% of personal best. There is 20%-30% variability.

Red Zone:

This indicates medical alert Asthma symptoms are present even when the patient is at rest or interfere with activity. PFFR readings are below 60% of the personal best.
Spirometry\textsuperscript{61}

All patients suspected to have bronchial Asthma should have spirometry done at least for initial assessment. In bronchial Asthma, typically one gets an obstructive pattern. Airflow obstruction is indicated by a reduced FEV1 / FVC ratio (<75%)

**COMPLICATIONS OF ACUTE BRONCHIAL ASTHMA\textsuperscript{55}**

- Pneumothorax
- Cystic Fibrosis
- Subcutaneous Emphysema
- Chronic Cor-Pulmonale
- Pneumoperi Cardium
- Allergic Bronchopulmonary Mycosis
- Myocardial infarction
- Mucus plugging
- Atelectasis
- Drug toxicity (theophylline)
- Dehydration
- Myopathy
- Lactic acidosis
- Rib fracture due to distressing cough
- Hypoxic brain injury
- Retaradation of Growth in children (Cortico steroids)

**BRONCHIAL ASThma IS DIFFERENTIATED FROM THE FOLLOWING DISEASES\textsuperscript{54}**

Glottic dysfunction, Endo bronchial disease such as foreign body aspiration, a neoplasm, bronchial stenosis. Acute left ventricular failure, Carcinoid tumour, Recurrent pulmonary emboli, Chronic bronchitis, Eosinophilic pneumonia, Systemic vasculities, COPD,
THE GOAL OF TREATMENT OF BRONCHIAL ASTHMA

1. To recognize Asthma
2. To maintain a normal activity level including exercise
3. To maintain a normal or near normal (best) pulmonary function rates
4. To prevent coughing or breathlessness in the night, early in the morning or after exertion.
5. To prevent recurrent exacerbations
6. To minimize absence from work or school
7. To enable normal growth to occur in children
8. To use least minimum drugs to avoid adverse reaction from medications used for asthma
FIGURE 3.5 THE INGREDIENTS OF ADATHODAI CHOORANAM

ADATHODAI POOKATHIR

THOOPTHUVALAI

ADATHODAI VERPATTAI

SAMBITRANI
3.3. REVIEW OF LITERATURE ON ADHATHODAI CHOORANAM

Siddha, an ancient system of Indian Medicine has recommended a number of drugs for indigenous plant sources for the treatment of Bronchial Asthma and allergic disorder. In siddha sastric text, Adhathodai chooranam a poly herbal formulation is specially indicated for Bronchial Asthma which comprises 17 ingredients. (Annexure)

Table 2.1: THE INGREDIENTS OF ADHATHODAI CHOORANAM

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Botanical Name &amp; Family</th>
<th>Tamil Name &amp; Quantity</th>
<th>part Used</th>
<th>Taste</th>
<th>Quality</th>
<th>Division</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Alpinia Galanga Wild (Zingiberaceae)</td>
<td>Perarathai 35 grams</td>
<td>Rhizome</td>
<td>Pungent</td>
<td>Hot</td>
<td>Pungent</td>
<td>Expectorant Febrifuge Stomachic Anti Allergic Anti Oxidant Immuno stimulating Anti inflammatory Anti microbial Anti Spasmodic</td>
</tr>
<tr>
<td>2.</td>
<td>Alpinia Officinarum Hance (Zingiberaceae)</td>
<td>Chittarathai 35 grams</td>
<td>Rhizome</td>
<td>Pungent</td>
<td>Cool</td>
<td>Pungent</td>
<td>Antimicrobial Antioxidant Anti inflammatory Anti Spasmodic Sialogogue Stomachic</td>
</tr>
<tr>
<td>3.</td>
<td>Justicia adhatoda Linn (Acanthaceae)</td>
<td>Adhathodai Flower 140gms Root bark35gms</td>
<td>Flowers Root Bark</td>
<td>Bitter</td>
<td>Hot</td>
<td>Pungent</td>
<td>Diuretic Expectorant Mucolytic Germicide Anti spasmodic Anti tussive Anti Histaminic Bronchodilatory Anti</td>
</tr>
<tr>
<td>No.</td>
<td>Plant Name</td>
<td>Part Used</td>
<td>Taste</td>
<td>Temperature</td>
<td>Effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Tragia involucrata Linn (Euphorbiaceae)</td>
<td>Root</td>
<td>Bitter</td>
<td>Hot, Pungent</td>
<td>Diaphoretic, Anti inflammatory, Anti Oxidant, Anti Bacterial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Embelia Ribes Burm-F (Myrsinaceae)</td>
<td>Seeds</td>
<td>Bitter</td>
<td>Hot, Pungent</td>
<td>Anthelmintic, Carminative, Stomachic, Stimulant, Anti inflammatory, Anti Histaminic, Anti Bacterial, Anti Oxidant, Anti bacterial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Cherodendrum Serratum (Linn) Moon (Verbenaceae)</td>
<td>Root</td>
<td>Astringent</td>
<td>Hot, Pungent</td>
<td>Stimulant, Sedative, Anti Inflammatory, Anti Allergic, Anti Histaminic, Anti Bacterial, Anti Oxidant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Cyperus Routundus Linn (Cyperaceae)</td>
<td>Rhizome</td>
<td>Astringent</td>
<td>Hot, Pungent</td>
<td>Stimulant, Spasmoletic, Anti inflammatory, Anti Bacterial, Anti Oxidant, Vermifuge</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Ficus Tsiela Roxtb (Moraceae)</td>
<td>Stem Bark</td>
<td>Astringent</td>
<td>Cool, Sweet</td>
<td>Astringent, Anti inflammatory, Anti oxidant, Anti bacterial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Piper longum Linn (Piperaceae)</td>
<td>Fruit</td>
<td>Sweet</td>
<td>Hot, Sweet</td>
<td>Sialagogue, Stimulant, Insecticide, Carminative, Expectorant, Immuno modulatory, Hematinic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

[58]
<table>
<thead>
<tr>
<th>No.</th>
<th>Plant Name</th>
<th>Plant Part</th>
<th>Taste</th>
<th>Temperature</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Styrax Benzoin Dryand (Styraceae)</td>
<td>Sublimate of Sambirani 17.5 grams</td>
<td>Resin</td>
<td>Pungent</td>
<td>Hot</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pungent Carminative Anti allergic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Anti inflammatory</td>
</tr>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>Anti bacterial</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Anti allergic</td>
</tr>
<tr>
<td>11</td>
<td>Curcuma Longa Linn (Zingiberaceae)</td>
<td>Karimanjal 35 grams</td>
<td>Finger Rhizome</td>
<td>Pungent &amp; Bitter</td>
<td>Hot</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pungent Carminative Stimulant</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hepatic tonic</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Anti spasmodic</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>Anti asthmatic</td>
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<td></td>
<td></td>
<td></td>
<td>Anti inflammatory</td>
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<td></td>
<td>Anti spasmody</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Anti Oxidant</td>
</tr>
<tr>
<td>12</td>
<td>Piper Nigrum Linn (Piperaceae)</td>
<td>Milagu 35 grams</td>
<td>Fruit</td>
<td>Bitter &amp; Pungent</td>
<td>Hot</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pungent Carminative Stimulant</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Antidote Resolvent</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Anti inflammatory</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Anti Oxidant</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Anti Microbial</td>
</tr>
<tr>
<td>13</td>
<td>Costus Speciosus (Koer) (Costaceae)</td>
<td>Kostum 17.5 grams</td>
<td>Root</td>
<td>Bitter</td>
<td>Hot</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pungent Stomachic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Expectorant</td>
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<td></td>
<td></td>
<td>Diaphoretic</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Anti inflammatory</td>
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<td></td>
<td></td>
<td>Anti spasmody</td>
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<td></td>
<td></td>
<td></td>
<td>Anti Oxidant</td>
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<td></td>
<td></td>
<td></td>
<td>Anti Bacterial</td>
</tr>
<tr>
<td></td>
<td>Plant Name</td>
<td>Common Name</td>
<td>Part Used</td>
<td>Tonicity</td>
<td>Temperature</td>
</tr>
<tr>
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<td>-----------------------------</td>
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<td>-------------</td>
</tr>
<tr>
<td>14</td>
<td>Woodfordia fruitcosa Kurz</td>
<td>Kattathipoo</td>
<td>Flowers</td>
<td>astringent</td>
<td>cool</td>
</tr>
<tr>
<td></td>
<td>(Lythraceae)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Solanum trilabatum Linn</td>
<td>Thoothuvalai</td>
<td>Leaf</td>
<td>Bitter &amp; Pungent</td>
<td>Hot</td>
</tr>
<tr>
<td></td>
<td>(Solanaceae)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Solanum Surattense Burm. F</td>
<td>Kandangathari</td>
<td>Whole Plant</td>
<td>Pungent</td>
<td>Hot</td>
</tr>
<tr>
<td></td>
<td>(Solanaceae)</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
4. PLAN OF WORK

4.1. PLAN OF WORK FOR PRECLINICAL STUDIES

- Identification of Ingredients Authentication
- Purification, Preparation of Formulation
- Preliminary Phytochemical Analysis, Physicochemical Evaluation, TLC, HPTLC Fingerprint
- GC-MS Analysis
- Heavy Metal Analysis, Microbial Load, AFLATOxin Content
- IAEC Clearance at NIS
- Acute Toxicity Study, Long Term Toxicity Study
- Histopathological Evaluation
- Data Analysis
4.2. PLAN OF WORK FOR CLINICAL STUDY

PATIENTS SCREENING

INCLUSION CRITERIA
- INFORM ABOUT STUDY AND TRIAL DRUG
- INFORMED CONSENT FORM
- STUDY NUMBER
- HISTORY TAKING
- LAB INVESTIGATION
- TRIAL DRUG
- CLINICAL ASSESSMENT
- OUTCOME

EXCLUSION CRITERIA
- EXCLUDED FROM TRIAL
- GENERAL TREATMENT, OPD

IF ANY ADVERSE EVENT
- PHARMACOVIGILANCE, NIS
- TREATED IN OPD
FIGURE 5.1 SAMBIRANI PATHANGAM
FIGURE 5.2 ADATHODAI CHOORANAM
5. MATERIALS AND METHODS

5.1. METHOD OF PREPARATION OF TRIAL DRUG ADATHODAI CHOORANAM

The trial drug Adhathodai chooranam is a poly herbal formulation specially indicated for Bronchial Asthma in Siddha sastric text which comprises 17 ingredients.

**Standard operating procedure for adathodai chooranam:**

**Procurement of raw drugs**

All the raw drugs were purchased from IMPCOPS, Chennai. The Adhathoda inflorescense, root bark and Solanum trilobatum leaf were collected in Herbal Garden, National Institute of Siddha, Chennai.

**Authentication of herbs**

All the ingredients were authenticated by Assistant Professor of Botany, National Institute of Siddha, Chennai (Voucher No. NIS/NB/69/2012) and were deposited in the Medicinal Botany Laboratory, NIS, Chennai.

**Method of purification:**

The raw drugs are purified and the Medicine is prepared in Gunapadam Lab of National Institute of Siddha.

1. **Perarathai Rhizome 35 grams (Alpinia galanga Wild):** Remove the outer layer and cut into small pieces and dried in sunlight.

2. **Chitiarathai Rhizome 35 grams (Alpinia officinarum Hance):** Remove the outer layer and cut into small pieces and dried in sunlight.
3. **Adathodai Flowers 140 grams** *(Justicia adhatoda Linn)*: Remove the pedicle, Stamens and Calyx then take the Corolla.

4. **Adathodai Root barks 35 grams** *(Justicia adhatoda Linn)*: It cleaned with pure white cloth and the outer layer of the root bark is removed.

5. **Poonaianchori Root 70 grams** *(Tragia involucrata Linn)*: It cleaned with pure white cloth and the outer layer of the root bark is removed.

6. **Arisi Thippili Fruit 70 grams** *(Piper longum Linn)*: Soaked in the Leaf Juice of Plumbago Zeylanica for 1 Naazhigai (24 minutes) and dry it sunlight.

7. **Karimanjal Finger rhizome 35 grams** *(Curcuma longa Linn)*: Remove the outer layer and cut into small pieces and dried it in sunlight.

8. **Kostum Root 17.5 grams** *(Costus speciosus (Koen.)*: Dry it under sunlight.

9. **Vaivilangam Seeds 35 grams** *(Embelia ribes Burm.f)*: Dry it under sunlight

10. **Siruthekku Root 35 grams** *(Clerodendrum serratum (Linn.)Moon)*: Remove the outer layer and cut into small pieces and dried it in sunlight.

11. **Koraikizhangu Rhizome 35 grams** *(Costus speciosus (Koen)) Dry it under heavy sunlight

12. **Ingipattai Stem bark 35 grams** *(Ficus tsiela Roxb)*: Double the proportion of Calcium Carbonate (Lime Stone) Solution with dry ginger is boiles for three hours, then, it is washed well with water and allowed to dry. The outer skin of dry ginger is peeled off.

13. **Kattathipoo Flowers 17.5 grams** *(Woodfordia fruticosa): Dry it under sunlight
14. **Thoothuvalai Leaf 70 grams** (Solanum trilobatum Linn): It is cleaned with pure white cloth and removes the decayed and ripens leaves.

15. **Kandangkathiri Whole plant 35 grams** (Solanum surattence Burm.f): It is cleaned with pure white cloth and remove the decayed and ripen leaves.

16. **Milagu Fruit 35 grams** (Piper nigrum Linn): Dry it under sunlight

**Preparation of Sambirani Pathangam:**

On the mouth of broad and deep earthenware vessel was tied up a silk cloth covering the vessel mouth and Pieces of frankincense were placed over the cloth and surmounted an earthenware vessel. The mouths of the vessels were sealed and descended into a pit up to the level of upper vessel mouth and stuffed up the pit with sand. Dung cakes were arranged around the upper lid and calcinated it.

**Preparation of Trial Drug:**

Barring the sublimate of frankincense (sambirani Pathangam), all the other ingredients were dried under the sunlight and powdered and filtered in sieve no: 100. Then all the ingredients were added proportionately including the Sambirani Pathangam.

**Drug Storage:**

The trial Drug Adathodai Chooranam was stored in clean and dry glass bottles.

**Dispensing:** The Adathodai Chooranam was given 1.5g in zip lock Packets.

Dose : 1.5 gram, 2 times daily

Vehicle : Milk

Course : 30 days

[67]
Indications : Cold with Broncial Asthma

Pathiyam : Itchopathiyam i.e.

Prickly Bitter gourd, mango, Bringal, Cluster Beans, Ash Pumpkin, Resbania, Grandi Flora, Undigestable Substances and Mustard Seeds and sexual activity are to be avoided during Medication.

Reference : SigitchaRathnaDeepam EnumVaidhyaNool Page No.319
5.2. METHODOLOGY FOR ANALYTICAL STUDIES

Acid insoluble ash, PH value, water soluble extractive, alcohol soluble extractive, TLC and HPTLC were carried out as per Indian Pharmacopeia in CSMDRI, Arumbakkam, Chennai. Tests for presence of certain heavy metals (mercury, arsenic, lead, cadmium), microbial contamination and Aflatoxin content were carried out at the Sargam Laboratory Pvt.Ltd, Guindy, Chennai (an approved laboratory by AYUSH) by using ICP MS and HPLC FLD as per the procedure WHO Q AS/05-131 and AOAC 990.33. Phyto chemical analysis was carried out in Bio chemistry Lab, National Institute of Siddha and Chemistry Lab, Siddha Central Research Institute, Arumbakkam, Chennai.

BIO -CHEMICAL ANALYSIS OF ADHATHODAI CHOORANAM

Preparation of Extract: 5gm of Adathodai chooranam weighed accurately and placed in a 250ml clean beaker and added with 50 ml of distilled water. Then it is boiled well for about 10 minutes. Then it is cooled and filtered and made up to 100ml with distilled water.

TABLE 3.1: BIO -CHEMICAL ANALYSIS OF ADHATHODAI CHOORANAM

<table>
<thead>
<tr>
<th>S.No</th>
<th>EXPERIMENT</th>
<th>OBSERVATION</th>
<th>INFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>I. Test of Acid Radicals</td>
<td>Cloudy appearance not found</td>
<td>Sulphate was not present.</td>
</tr>
<tr>
<td></td>
<td>Test of Sulphate: Two ml of the extract was taken in a test tube which was added with two ml of 4% diluted ammonium oxalate solution</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Test of Chloride: Two ml of extract was mixed with two ml of diluted hydrochloric acid upto the froth ceases off.</td>
<td>Cloudy appearance developed.</td>
<td>Chloride was present.</td>
</tr>
<tr>
<td></td>
<td><strong>Test of Phosphate:</strong> test extract was mixed with 2ml of diluted ammonium molybdate solution and two ml of concentrated HNo3.</td>
<td>Cloudy Yellow appearance not occurred.</td>
<td>Phosphate was present</td>
</tr>
<tr>
<td>---</td>
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<td>---</td>
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</tr>
<tr>
<td>4.</td>
<td><strong>Test of Carbonate:</strong> Two ml of the test extract was added with two ml diluted magnesium sulphate solution.</td>
<td>No Cloudy appearance</td>
<td>Absence of carbonate</td>
</tr>
<tr>
<td>5.</td>
<td><strong>Test For Nitrate:</strong> one gram of the substance was heated with the copper turning and concentrated H2So4 and viewed the test tube vertically down.</td>
<td>Brown gas was not evolved</td>
<td>Nitrate was not present</td>
</tr>
<tr>
<td>6.</td>
<td><strong>Test For Sulphide:</strong> 1gm of the substance is treated with 2ml of con. HCL</td>
<td>No Rotten Egg Smelling gas evolved</td>
<td>Absence of Sulphide</td>
</tr>
<tr>
<td>7.</td>
<td><strong>Test of Fluoride &amp; Oxalate:</strong> Two ml of extract was mixed with two ml of diluted Acetic acid and two ml diluted calcium chloride solution and heated.</td>
<td>No cloudy appearance</td>
<td>Absence of fluoride and oxalate</td>
</tr>
<tr>
<td>8.</td>
<td><strong>Test For Nitrite:</strong> Few drops of the sample was kept on a filter paper. Then few drops of diluted acetic acid and few drops of diluted Benzidine solution was placed.</td>
<td>Characteristic changes were not found.</td>
<td>Nitrite was not present</td>
</tr>
<tr>
<td>9.</td>
<td><strong>Test For Borate:</strong> 2 Pinches (50mg) of the substance is made into paste by using dil.sulphuric acid and alcohol (95%) and introduced into the blue flame.</td>
<td>Bluish green colour flame not appeared</td>
<td>Absence of borate</td>
</tr>
</tbody>
</table>

**II. Test For Basic Radicals**

<table>
<thead>
<tr>
<th></th>
<th><strong>Test For Lead:</strong> Two ml of the extract was mixed with two ml of diluted potassium iodine solution.</th>
<th>No Yellow Precipitate formed.</th>
<th>Lead was not occuredt.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.</td>
<td><strong>Test For Copper:</strong> 50mg of substance was made into paste with concentrated HCl in a watch glass and inserted over the non-luminuous of the flame.</td>
<td>No Blue colour flame and precipitate formed.</td>
<td>copper was not present.</td>
</tr>
</tbody>
</table>
3. **Test For Aluminium:** To the 2ml of extract dil.sodium hydroxide is added in 5 drops to excess. | No Yellow colour appeared | Aluminium was not present.
---|---|---
4. **Test of Iron:** Two ml thiocyanate solution and two ml of concentrated HNO3 was mixed with two ml of extract. | Blood red colour was not appeared | **Iron was present.**
---|---|---
5. **Test For Zinc:** To 2ml of extract dil.NaoH solution is added in 5 drops to excess and NH4cl2 is added. | White precipitate not formed | Absence of Zinc
---|---|---
6. **Test For Calcium:** 2ml of the extract is added with 2ml of 4% dil.ammonium oxalate solution | No Cloudy appearance and white precipitate is obtained | Absence of calcium
---|---|---
7. **Test For Magnesium:** with the two ml of extract diluted NAOH solution was added. | White precipitate was not formed | Magnesium was not present.
---|---|---
8. **Test For Ammonium:** with the test extract 1 ml of Nessler's reagent and diluted NAOH solution were added. | Brown colour developed | **Ammonium was present**
---|---|---
10. **Test For Sodium:** 50mg of the substance was made into paste by using HCl and inserted into the blue flame of Bunsen burner. | yellow colour flame not appeared | Absence of sodium
---|---|---
11. **Test For Mercury:** 2ml of dil NAOH solution was mixed wih the test extract | yellow precipitate was not obtained | mercury was not present
---|---|---
12. **Test For Arsenic:** 2ml of the extract is treated with 2ml of dil.sodium hydroxide solution. | No brownish red precipitate is obtained | Absence of arsenic
<table>
<thead>
<tr>
<th>S.No</th>
<th>EXPERIMENT</th>
<th>OBSERVATION</th>
<th>INFERENCES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Appearance of sample</td>
<td>Light Brown in colour</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td><strong>Solubility:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>a. A little (500mg) of the sample is shaken well with distilled water.</td>
<td>Sparingly soluble</td>
<td>Presence of Silicate</td>
</tr>
<tr>
<td></td>
<td>b. A little (500mg) of the sample is shaken well with con. HCl/Con. H₂SO₄</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### III. Miscellaneous

<p>| 1.   | <strong>Test For Starch:</strong>              | blue colour was not developed | starch was not present    |
|      | Two ml of test extract was mixed with weak diluted iodine solution |                           |                           |
| 2.   | <strong>Test of Reducing Sugar:</strong>       | Brick red colour was not developed | reducing sugar was not occured |
|      | Five ml of Benedict's qualitative solution was taken in a test tube and boiled it two minutes then mixed with 8 to 10 drops of the test extract. and second time boiled it for 2 minutes. The colour changes were noticed. |                           |                           |
| 4.   | <strong>Test For Tannic Acid:</strong>         | Precipitate was not formed.  | Tannic acid was not present |
|      | two ml of diluted ferric chloride solution was mixed with 2ml of extract |                           |                           |
| 5.   | <strong>Test For Unsaturated Compound:</strong>| Potassium permanganate was not decolourised | unsaturated compound was not present |
|      | Two ml of diluted Potassium permanganate solution was mixed with two ml of test extract. |                           |                           |</p>
<table>
<thead>
<tr>
<th></th>
<th><strong>Action of Heat:</strong> A small amount (500mg) of the sample is taken in a dry test tube and heated gently at first and then strong.</th>
<th>No white fumes evolved</th>
<th>Absence of Carbonate</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.</td>
<td><strong>Flame Test:</strong> A small amount (500mg) of the sample is made into a paste with con. HCl in a watch glass and introduced into non-luminous part of the Bunsen flame.</td>
<td>No Bluish green flame appeared.</td>
<td>Absence of Copper</td>
</tr>
<tr>
<td>5.</td>
<td><strong>Ash Test:</strong> A filter paper is soaked into a mixture of sample and dil. cobalt nitrate solution and introduced into the Bunsen flame and ignited</td>
<td>No Yellow colour flame appeared</td>
<td>Sodium was not present</td>
</tr>
</tbody>
</table>
Table no: 3.2 Preliminary Phytochemical Test of Adathodai chooranam

<table>
<thead>
<tr>
<th>S.No</th>
<th>EXPERIMENT</th>
<th>OBSERVATION</th>
<th>INFERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Test for Alkaloids (Dragendorff's test)</td>
<td>Orange red precipitation appeared</td>
<td>Presence of Alkaloids</td>
</tr>
<tr>
<td></td>
<td>Few mg of extract in separate test tube was warmed with 2% Sulphuric acid for two minutes. And it was filtered in separate test tube and little drops of Dragendorff's reagent were added.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Test for Flavonoids (Shinoda Test)</td>
<td>Presence of magenta colour</td>
<td>presence of flavonoids</td>
</tr>
<tr>
<td></td>
<td>Substance is dissolved in alcohol. Then magnesium bits and concentrated hydrochloric acid are added then heated over a water bath.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Test for Glycosides</td>
<td>appearance of green colour</td>
<td>presence of Glycoside</td>
</tr>
<tr>
<td></td>
<td>Substance is added with anthrone and concentrated sulphuric acid then heated over a water bath.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>Test for triterpenoid (Noller’s test)</td>
<td>Appearance of purple colour</td>
<td>presence of triterpenoids</td>
</tr>
<tr>
<td></td>
<td>To few mg of extract add tin and thionyl chloride. Then heated in water bath.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>To few mg of extract distilled water is added and shaken. The foam formation indicates the presence of saponin.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Test for Aminocides (Ninhydrin test)</td>
<td>A few drop of ninhydrin reagent was added to the test extract.</td>
<td>Violet colour appeared</td>
</tr>
<tr>
<td>---</td>
<td>-------------------------------------</td>
<td>---------------------------------------------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>10</td>
<td><strong>Test of Anthraquinones</strong></td>
<td>Aqueous ammonia was mixed with one ml of test extract. Observed colour change.</td>
<td>Pink red colour appeared</td>
</tr>
<tr>
<td></td>
<td><strong>Test for Steroids (Lieberman Burchard Test)</strong></td>
<td>To few mg of the extract, 2 ml of chloroform is mixed in a dry test tube. Few drops of acetic acid is added and heated. Then acetic anhydride and concentrated sulphuric acid were added.</td>
<td>green colour appeared</td>
</tr>
</tbody>
</table>
PHYSICOCHEMICAL EVALUATION: 69-73

The physicochemical analysis of trial drug Adathodai chooranam was done as mentioned in Indian Pharmacopoeia.

Determination of moisture content (Loss on drying):

Determination of moisture content was done to rule out moisture or water content in plant materials.

Procedure:

10 g of Adathodai chooranam was weighed in a tarred evaporating dish, dried at 105°C upto five hours and weighed. The procedure was repeated at hourly intervals till considered weight is achieved.

Percentage of loss on drying at 105°C = \[
\frac{\text{Loss in weight of the sample}}{\text{Weight of the sample taken}} \times 100
\]

Determination of Ash values

Procedure:

4 gm of Adathodai chooranam weighed placed in a previously ignited and tarred silica dish. Ignited in a muffle furnace at 600°C until it turned white in color. It indicated the absence of carbon.

Percentage of total ash = \[
\frac{\text{Weight of the ash}}{\text{Weight of the sample taken}} \times 100
\]
Determination of acid insoluble ash:

Acid insoluble ash is the filtrates obtained after boiling the total ash with dilute HCL

Procedure:

Added to the ash 15 to 25 ml of the HCL and boiled for 10 minutes, covering the dish by a watch glass to prevent sputtering. Waited some minutes to cool and filtered through the ash less filter paper. The filter paper was washed in hot water up to the washings are relieve from HCL as tested by AgNO3 solution and returned it to the dish. Evaporated on the water bath and ignited in the muffle furnace at 550±250c for one hour. The dish was allowed to cool in the desiccators and weighed.

Percentage of Acid insoluble ash = \( \frac{\text{acid insoluble residue weight x 100}}{\text{Weight of the sample taken}} \)

Determination of water soluble extractive:

4g of the Adathodai chooranam was taken in a glass – stoppered flask. Added 100 ml of distilled water and shaken at 30 minute intervals for 6 hours and allowed to stand for 18 hours. Filtered rapidly taking care not to lose any solvent and pipette out 25 ml of the filtrate in a pre-weighed 100 ml beaker and evaporate to dryness on a water bath. Kept it in an air oven at 1050c for 6 hours, cooled in a desiccators and weighed. Repeat the experiment twice and take the average value.

Percentage of water soluble extractive = \( \frac{\text{Weight of the extract x 100 x 100}}{25 \times \text{Weight of the sample taken}} \)
Determination of alcohol soluble extractive:

4g of the Adathodai chooranam was taken in a glass stoppered flask. Added 100 ml of distilled alcohol (95%) and shaken at 30 minute intervals for 6 hours and allowed to stand for 18 hours. Filtered quickly and pipette out 25 ml in a 100 ml beaker and disperse to dryness on a water bath. Placed it in an oven at 105°C for six hours, cooled in a desiccators and weighed. Repeat the experiment two times and take the average value.

Percentage of alcohol soluble extractive = \( \frac{\text{Weight of the extract} \times 100}{25 \times \text{Weight of the sample taken}} \)

TLC and HPTLC Methodology:

Four grams of the sample was saturated in 40 ml of 90 percentage ethyl alcohol and reserved allnight then boiled for ten minutes and filtered which was stronged to ten ml and made up to the mark in a ten ml standard flask. 15 µl and 20 µl of this solution were applied over the (Merck) Aluminium plate 60F 254 pre coated with silica gel of 0.2 millimeter. (Toluene Ethyl acetate 5:2) was included in making the plate. Then the plate was noticed under UV 254 nm and 366 nm UV. Then the plate was scanned at 254 nm and dipped in Vanillin sulphuric Acid and kept in the oven at 105°C till the colour of the spots appeared. The photos and finger print were taken.

GC-MS Analysis:

The GC-MS Analysis was done at Sophisticated Analytical Instrument Facility, Indian Institute of Technology, Chennai. Agilent 6890N gas chromatography with JEOL GC MATE-II HR Mass Spectrometer was used for the GC-MS Analysis study. The JEOL GCMATE II GC-MS and Data system is a high resolution, double focusing instrument.
Procedure:

The Agilent 6890N gas chromatograph type 1079 was joined with DB 5 MS capillary column. The temperature of injector was put at 280 °C, and the temperature of oven was put at 45 °C then programmed to 300 °C at the rate of 10 °C/min and lastly held at 200 °C for 5 min. Helium was used as a carrier gas in the flow rate of 1.0 ml/min. One µl of the sample (diluted in acetone 1:10) was injected to the split mode in the ratio of 1:100. The percentage of composition of the essential oil was estimated using the GC peak areas. GC–mass spectrometry (GC–MS) analysis of essential oil was performed by Agilent gas chromatography. The mass spectrometer was initiated in the electron impact mode in 70 eV. Ion source and transfer line temperature was placed at 250 °C. The mass spectra were obtained through centroid scan of the mass ranges 40 to 1000 amu. The compounds were identified based on the comparison of their RI, RT.⁷⁴
5.3. TOXICITY STUDIES

Animal Care and husbandry:

The acute and long term toxicity study protocol was approved by IAEC, NIS the Certificate Number NIS/IAEC/04/2011/11 dated on June 14, 2011. Healthy Swiss Albino Mice of either Sex with an average body weight of 20-30 g and wistar albino rats of either sex with an average body weight of 130-180 gram were obtained from the animal house of King Institute, Guindy, Chennai for acute and long term toxicity studies respectively and were housed in the Animal house of National Institute of Siddha, Chennai. Each group of animals were kept in polypropylene cages in a air cycles 15/Min : 70:30 exchange ratio, under an ambient temperature of 22 ±2°C and 40-65% relative humidity with 12 hours dark / 12 hours light photoperiod. Food were provided from Provimi Animal Nutrition India Pvt. Ltd., Bangalore) with purified water ad libitum. All the animals were kept to the laboratory conditions for 7 days prior to study.

Acute Toxicity Study:

This study was performed to evaluate the safety of herbal medicines as per WHO Guidelines (1993:94 Pages).

Dose calculation:

The recommended human dose of Adathodai chooranam is 3gram/day was converted to the dose for mice using conversion table. This dose was found to be 0.26 gram/kg for mice. This dose group was designated as therapeutic dose group. 10 times the therapeutic dose was 2.6 gram /kg.
Table no 3. 3: Groups of animals –Acute toxicity study

<table>
<thead>
<tr>
<th>S.No</th>
<th>Group</th>
<th>No of rats</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vehicle control (1ml Milk/100gbw )</td>
<td>10 (5 male, 5 female)</td>
</tr>
<tr>
<td>2</td>
<td>Toxic dose (10X therapeutic dose) (Single dose) 2.6gm/kg bw</td>
<td>10 (5 male, 5 female)</td>
</tr>
</tbody>
</table>

Overnight fasted control group received 1ml/100 gram body weight of cow’s milk. The drg treated group received one oral dose (10x Therapeutic Dose) of Aadhathodai Chooranam 2.6 gm/Kg body weight with cow’s milk.

**Study details:**

For oral administration of test drug in mice, Aadhathodai Chooranam was mixed with Cow’s milk with the help of mortar and pestle to get suspension. After the test drug administration, food was stopped for 3 hours in mice. The animals were monitored for morbidity and mortality for first 30 minutes and one hour once on the day of dosing and once a day for 14 days. Food and water intake and signs of toxicity was monitored up to 14 days. The body weight was noted recorded on 0th, 7th and 14th days. All animals were weighed and sacrificed on the 15th day and the vital organs were grossly examined.

**Long Term Toxicity Study:**

The 28 days long term toxicity study was performed according to the WHO Guideline (1993; 94 pages).

**Dose calculation:**

To evaluate the toxicity profile in rats, three doses of Aadhathodai Chooranam were selected for this animal toxicity study from clinically used human dose (3g/day in human) by
using body surface area dosing table. They were; Therapeutic dose (270 mg/kg body weight), 5x therapeutic dose (1, 350mg/ Kg body weight) and 10X therapeutic dose (2,700 mg/kg body weight).

Table no 3.4: Groups of animals-long term toxicity study

<table>
<thead>
<tr>
<th>S.No</th>
<th>Group</th>
<th>No of Rats</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Vehicle control (2ml Milk/kgbw )</td>
<td>10  (5 male, 5 female)</td>
</tr>
<tr>
<td>2.</td>
<td>1XTherapeutic dose (270mg or 0.270 g/kg bw)</td>
<td>10  (5 male, 5 female)</td>
</tr>
<tr>
<td>3.</td>
<td>5XTherapeutic dose (1350mg or 1.35 g/kgbw)</td>
<td>10  (5 male, 5 female)</td>
</tr>
<tr>
<td>4.</td>
<td>10XTherapeuticdose(2700mg or 2.7g/kgbw)</td>
<td>10  (5 male, 5 female)</td>
</tr>
</tbody>
</table>

The second to fourth group were administered test drug Aadhathodai Chooranam at the dose of (270 mg/kg bw, 1,350 mg/Kg bw, 2,700 mg/Kg body weight) respectively. Cow’s milk (2 ml/kg body weight) was given to the control group. The test drug administered orally by respective treatment daily for 28 days in the 2nd, 3rd, 4th groups.

Observation:

Body weight, food intake and water intake were recorded at weekly intervals for toxic manifestation or behavioral alterations and mortality.
Blood analysis:

After the drug administration period the overnight fasted animals were sacrificed and blood samples were collected from retro orbital puncture into tubes with and without EDTA for haematological and biochemical analysis correspondingly. Mindraj, BC-2800 Vet auto hematology analyzer was used for Hematological analysis. The biochemical analysis was done by Bayer, RA-50 analyser and electrolytes were investigated by Easilyte plus Na/K/Cl analyser. The blood was allowed to clot before centrifugation (1610g at 4°C for 10 min) to get serum to investigate Bio chemical parameters. Blood samples collected in heparinised tubes were used for Hematological investigations.

Histopathology:

After collecting the blood, the rats were dissected and organs like Heart, Lungs, Liver, Stomach, Kidney, Sex organs and Brain were removed and kept in normal Saline (0.09%) carefully and then weighed on a monoplane balance. All organs were examined and then fixed in 10% buffered formaldehyde solution for histopathological observations.

Statistical Analysis: The body weight, food and water intake, organ weight, biochemical and haematologiced parameters were statistically analyzed and significant differences were calculated by the paired t test to compare mean differences of control and test drug treated groups. p≤ 0.05 was considered statistically significant
5.4. CLINICAL STUDY

Study Type: Phase - III, An open Clinical Trial

Study Place: Ayothidass Pandithar Hospital, National Institute of Siddha
Tambaran Sanatorium, Chennai - 600 047.

Study Period: 4 years

Sample Size:

With type 1 Error - $\alpha$ = 0.05 (or) 5%

Precision = 10%

Adathodai Chooranam Success rate = 80%

The required Sample Size is = 100

Considering the drop out of = 20%

The required sample size for the Treatment = 125

Selection and withdrawal of subjects:

Inclusion criteria:

1. Patients who are having classical symptoms of Bronchial Asthma that difficulty in breathing, Tightness of Chest, Wheezing, Dry (or) Productive Cough,

2. Only new patients were included (2 years duration of illness).

3. Aged between 15 to 60 years of both sexes.

4. Willing to give blood specimen, sputum, Radiological Investigation and willing to be admitted in the hospital (or) attend the OPD once a week for 4 weeks.
Patients who are willing to estimate volume of air forcibly expired after a deep inspiration by using peak flow meter

**Exclusion criteria:**

1. Pregnancy and Lactation period.
2. Significant Systemic illness including Cardiac Diseases, Renal Diseases, Hypertension.
3. Patients with only nasal block or rhinorrhoea.
4. Other respiratory Diseases such as Tuberculosis, Pneumonia, COPD, Bronchiectasis, cystic fibrosis,
5. Endocrine Disorders like Hypo & Hyper Thyroidism, Diabetes Mellitus

**Withdrawal criteria:**

1. Adverse events which warrants withdrawal of trial drug.
2. Failure to comply with restrictions and prohibitions
3. Non Compliance with study schedule
4. Inadequate Co-operation
5. Withdrawal of consent for participation in the study

**Clinical assessment:**

Dry (or) Productive Cough, Difficulty to breath, Tightness of Chest, Wheezing.

**Siddha parameters:**

Three humours (vatham, pitham, kabam), Seven physical constituents, Eight diagnostic methods I.e. Naa, niram, mozhi, vizhi, sparisam, naadi, malam, mothiram, Neerkuri, Neikuri.
Laboratory investigations:

Routine blood test, urine test

Absolute eosinophil count, serum IgE level

Sputum examination-AFB, ECG, X-Ray chest

Pulmonary function test:

Forced expiratory volume (FEV)

Peak expiratory flow rate (PEFR).

Vital capacity (VC)

Treatment of Subjects:

<table>
<thead>
<tr>
<th>Medicine Name</th>
<th>Adathodai Chooranam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode of Administration</td>
<td>Internal Medicine</td>
</tr>
<tr>
<td>Dose</td>
<td>1.5 gm two times daily</td>
</tr>
<tr>
<td>Vehicle</td>
<td>Milk</td>
</tr>
<tr>
<td>Duration</td>
<td>30 days</td>
</tr>
<tr>
<td>Pathiyam</td>
<td>Itcha Pathiyam</td>
</tr>
<tr>
<td>Follow up period</td>
<td>3 months</td>
</tr>
</tbody>
</table>

Study Enrollment:

Patients reporting at OPD with the clinical Symptoms of Bronchial Asthma disease were referred to the investigator and 191 suspected patients were screened using screening form. As per the inclusion and exclusion criteria 138 cases were included in the clinical trial.
The study details, trial drug, possible outcomes and the objectives of the study were informed to the patients for a better understanding. After the patient’s willingness, their sign or left thumb print was obtained in consent form along with a witness.

Complete clinical history, complaints and duration, examination findings, siddha parameters, were recorded in the history proforma and clinical assessment forms respectively.

Unique registration card where in patient’s Registration Number of the study, Address, Phone number and Doctors phone number etc was given to the patients, so as to report to research scholar easily and report any complications.

**Conduct of the Study:**

For OP patients the trial drug Adathodai Chooranam was issued for 7 days and patients were asked to come for clinical assessment and treatment once in 7 days for one month. The trial drug was given as powder form in the dosage of 1.5 gram in zip lock pockets. 14 pockets were issued in each visit. At each clinical visit clinical assessment was done and prognosis was noted. Before and after treatment Asthma control questionnaire was filled to find out the clinical improvement of the patients. For IP patients the drug was provided daily and prognosis was noted. Blood and urine investigations, Sputum test, X-ray and ECG were taken before and after treatment and the results were recorded in the Laboratory investigation form. Serum IgE and spirometry were done in all cases before and after treatment in NABL certified Laboratories. All cases were educated about the procedure of PEFR measurement and requested to record their PEFR in the peak expiratory flow rate monitoring form in morning & evening using mini peak flow meter. Patients were
advised to take the trial drug and follow the appropriate dietary advice in the Diet and advice form.

**Follow up:**

Among 138 cases 13 cases were withdrawn for irregular treatment and long absence of treatment. 125 cases were treated with the trial drug Adathodai chooranam for 30 days. After treatment these 125 Patients were requested to attend the OPD at the end of first, second and third month to find the recurrence of symptoms and patient’s clinical condition were recorded in the Follow up form.

**Data management:**

After enrolling the patients in the study, a separate file for each patient was opened and all forms were filed in the file. Study No, Patient No were entered on the top of file for easy identification and arranged in a Registration Counter. During the visit of study patient, the respective patient file was taken and necessary recordings were made at the assessment form or other suitable forms. If patients do not turnup on a particular date, a post Card for reminding the patient was posted. The screening forms were filed separately. The Data recordings were monitored by Guide in presence of Investigator and statistical analysis was done by statistician. All collected datas were entered into computer using MS access software. Data Entry was 100% cross checked manually. All forms were further scrutinized in presence of Investigators by Sr. Research Officer (statistics) for logical errors and incompleteness of Data before entering onto computer to avoid any bias. No modifications in the results were permitted for unbiased report.
Statistical Analysis:

Paired t test was followed to find the significance of treatment using before and after data on haematological parameters, blood biochemistry, peak expiratory flow rate and spirometry results. The significance probability 0.05 (p<0.05) was used to observe the treatment difference. Statistical analysis was done by using independent “t” tests for pulmonary function test. ANOVA test was also used for pulmonary function parameters. P<0.05 is statistically significant.

Ethical issues:

When collecting blood sample from the patient disposable syringe, disposable gloves, with proper sterilized lab equipments were followed to avoid infection. Pulmonary function test, Serum IgE level was performed in the NABL certified labarotries and charges were borne by the investigator.

No other medicines were used on the trial period. There was no infringement on the right of patient. The data collected from the patient was kept confidentially. The patient was informed about the clinical study and treatment was given free of charge. In conditions treatment failure, patients were provided treatment at the OPD, NIS. The patients who were excluded given treatment at OPD of National Institute of Siddha.
Table 3.5: Outcome of the clinical study: Classification of Severity of Asthma.55

<table>
<thead>
<tr>
<th>Stages of Asthma</th>
<th>Symptoms</th>
<th>PEFR or FEV1 (PEFR Variability)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day</td>
<td>night</td>
</tr>
<tr>
<td>Step 1: Mild intermittent</td>
<td>≤ 2 days / week</td>
<td>≤ 2 nights / month</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 2: Mild persistent</td>
<td>&lt; 2 days / week</td>
<td>&gt; 2 nights / month</td>
</tr>
<tr>
<td></td>
<td>but &lt;1 per day</td>
<td></td>
</tr>
<tr>
<td>Step 3: Moderate persistent</td>
<td>Daily</td>
<td>&gt; 1 night / week</td>
</tr>
<tr>
<td>Step 4: Severe persistent</td>
<td>Continual</td>
<td>Frequent</td>
</tr>
</tbody>
</table>

Primary outcome: Primary outcome was measured by Curative effect of Asthma with PEF Measurement & siddha tools by using this Classification of Severity of Bronchial Asthma table.

Table 3.6: Primary outcome

<table>
<thead>
<tr>
<th>Improvement of Patient</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step4 to Step1/Step2/Normal</td>
<td>Good response</td>
</tr>
<tr>
<td>Step3 to Step1/Step2/Normal</td>
<td>Moderate response</td>
</tr>
<tr>
<td>Step4 to Step3</td>
<td>Poor response</td>
</tr>
<tr>
<td>no Significant</td>
<td></td>
</tr>
</tbody>
</table>

[90]
**Secondary Outcome:** Secondary Outcome was assessed by the changes in Eosinophils, ESR, AEC, Serum IgE level, pulmonary function tests and X-ray Chest before and after treatment.

**Data Collection:**

The clinical trial was documented in the following Case Report Forms. The detailed proforma is in an annexure.

- Informed Consent Form
- Information Form
- Form I - Screening and selection Proforma
- Form II - History Proforma
- Form III - Clinical Assessment on enrollment and on visits
- Form IV - Laboratory parameters chart
- Form V - Peak expiratory flow rate monitoring form
- Form VI - Drug Compliance Form
- Form VII - Withdrawal Form
- Form VIII - Adverse reaction Form
- Form IX - Diet & Advice Form
- Form X - Follow-up Proforma
- Asthma control questionnaire
PILOT STUDY

Pilot study was done in 5 OPD cases because of the trial drug Adathodai Chooranam is a new formulation. Patients who were having the classical symptoms of cough, tightness of chest and wheezing they were included in the pilot study. Before starting the treatment, informed consent was obtained from the participated patients and they were treated with Adathodai Chooranam 1.5g, two times a day with milk, after food for 30 days. The patients were asked to visit OPD once in 7 days for 30 days. Lab investigations were done before and after treatment.
6. RESULTS AND ANALYSIS

6.1. Results of Analytical Study:

Table 4.1 Preliminary Qualitative analysis – Interpretation of results

<table>
<thead>
<tr>
<th>S.NO</th>
<th>ANALYSIS</th>
<th>INERENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Silicate</td>
<td>Presence of silicate</td>
</tr>
<tr>
<td>2</td>
<td>Carbonate</td>
<td>Presence of carbonate</td>
</tr>
<tr>
<td>3</td>
<td>Copper</td>
<td>Absence of copper</td>
</tr>
<tr>
<td>4</td>
<td>Sodium</td>
<td>Absence of sodium</td>
</tr>
<tr>
<td>5</td>
<td>Sulphate</td>
<td>Absence of sulphate</td>
</tr>
<tr>
<td>6</td>
<td>Chloride</td>
<td>Absence of chloride</td>
</tr>
<tr>
<td>7</td>
<td>Phosphate</td>
<td>Absence of phosphate</td>
</tr>
<tr>
<td>8</td>
<td>Nitrate</td>
<td>Absence of Nitrate</td>
</tr>
<tr>
<td>9</td>
<td>Sulphide</td>
<td>Absence of sulphide</td>
</tr>
<tr>
<td>10</td>
<td>Fluoride &amp; oxalate</td>
<td>Absence of Fluoride &amp; oxalate</td>
</tr>
<tr>
<td>11</td>
<td>Nitrite</td>
<td>Absence of Nitrite</td>
</tr>
<tr>
<td>12</td>
<td>Borate</td>
<td>Absence of borate</td>
</tr>
<tr>
<td>13</td>
<td>Lead</td>
<td>Absence of lead</td>
</tr>
<tr>
<td>14</td>
<td>Aluminium</td>
<td>Absence of aluminium</td>
</tr>
<tr>
<td>15</td>
<td>Iron</td>
<td>Absence of iron</td>
</tr>
<tr>
<td>16</td>
<td>Zinc</td>
<td>Absence of zinc</td>
</tr>
<tr>
<td>17</td>
<td>Calcium</td>
<td>Absence of calcium</td>
</tr>
<tr>
<td>18</td>
<td>Magnesium</td>
<td>Absence of magnesium</td>
</tr>
<tr>
<td>19</td>
<td>Ammonium</td>
<td>Absence of ammonium</td>
</tr>
<tr>
<td>20</td>
<td>Potassium</td>
<td>Absence of potassium</td>
</tr>
<tr>
<td>21</td>
<td>Mercury</td>
<td>Absence of mercury</td>
</tr>
<tr>
<td>22</td>
<td>Arsenic</td>
<td>Absence of arsenic</td>
</tr>
<tr>
<td>23</td>
<td>Starch</td>
<td>Absence of starch</td>
</tr>
<tr>
<td>24</td>
<td>Alkaloids</td>
<td>Absence of alkaloids</td>
</tr>
<tr>
<td>25</td>
<td>Tannic acid</td>
<td>Absence of tannic acid</td>
</tr>
<tr>
<td>26</td>
<td>Unsaturated compound</td>
<td>Absence of unsaturated cpd</td>
</tr>
<tr>
<td>19</td>
<td>Amino acid</td>
<td>Presence of amino acid</td>
</tr>
</tbody>
</table>
The preliminary qualitative analysis study showed the presence of silicate, carbonate and aminoacids.

**Physicochemical Evaluation**

**Table No : 4.2 Organoleptic characters**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Characters</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Colour</td>
<td>Light brown</td>
</tr>
<tr>
<td>2.</td>
<td>Odour</td>
<td>Characteristic</td>
</tr>
<tr>
<td>3.</td>
<td>Taste</td>
<td>bitter</td>
</tr>
<tr>
<td>4.</td>
<td>Particle size</td>
<td>pass through Sieve No.100.</td>
</tr>
</tbody>
</table>

Aadathodai Choornam was light brown coloured fine powder with characteristic odour, bitter taste and completely passes through Sieve No.100

**Table No: 4.3 Physicochemical evaluation of Aadathodai Chooranam**

<table>
<thead>
<tr>
<th>Properties</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss on drying at 105° C</td>
<td>11.16%</td>
</tr>
<tr>
<td>Ash</td>
<td>7.90%</td>
</tr>
<tr>
<td>Acid insoluble ash</td>
<td>2.5%</td>
</tr>
<tr>
<td>Water soluble extractive</td>
<td>17.25%</td>
</tr>
<tr>
<td>Alcohol soluble extractive</td>
<td>12.29%</td>
</tr>
<tr>
<td>Ph</td>
<td>5.79%</td>
</tr>
</tbody>
</table>
Preliminary Phytochemical Screening

Qualitative tests were done to find the functional groups. The study showed the presence of Chloride, Phosphate, ammonium, iron, Alkaloids, flavonoids, Glycosides, terpene, saponins, Amino acids, Phenol, Tannins, Quinones, Lignans, Steroids in the Aadhathodai Chooranam.

Table 4.4: Phytochemical analysis of Aadhathodai Chooranam

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Alkaloids</td>
<td>+Ve</td>
</tr>
<tr>
<td>2.</td>
<td>Flavonoids</td>
<td>+Ve</td>
</tr>
<tr>
<td>3.</td>
<td>Glycosides</td>
<td>+Ve</td>
</tr>
<tr>
<td>4.</td>
<td>Terpenes</td>
<td>+Ve</td>
</tr>
<tr>
<td>5.</td>
<td>Saponins</td>
<td>+Ve</td>
</tr>
<tr>
<td>6.</td>
<td>Amino acids</td>
<td>+Ve</td>
</tr>
<tr>
<td>7.</td>
<td>Phenols</td>
<td>+Ve</td>
</tr>
<tr>
<td>8.</td>
<td>Tannins</td>
<td>+Ve</td>
</tr>
<tr>
<td>9.</td>
<td>Quionones</td>
<td>+Ve</td>
</tr>
<tr>
<td>10.</td>
<td>Lignans</td>
<td>+Ve</td>
</tr>
<tr>
<td>11.</td>
<td>Anthraquinones</td>
<td>-Ve</td>
</tr>
<tr>
<td>12.</td>
<td>Steroids</td>
<td>+Ve</td>
</tr>
<tr>
<td>13.</td>
<td>Organic Acids</td>
<td>-Ve</td>
</tr>
<tr>
<td>14.</td>
<td>Chloride</td>
<td>+Ve</td>
</tr>
<tr>
<td>15.</td>
<td>Phosphate</td>
<td>+Ve</td>
</tr>
<tr>
<td>16.</td>
<td>Iron</td>
<td>+Ve</td>
</tr>
<tr>
<td>17.</td>
<td>Ammonium</td>
<td>+Ve</td>
</tr>
</tbody>
</table>
Heavy Metal Analysis

Heavy metal analysis result revealed that the lead, cadmium, mercury and arsenic were within the permissible limits in the Adathodai chooranam and safe for consumption (Pb: 1.77 mg/kg, Cd: 0.25 mg/kg, As: 0.25 mg/kg, Hg: 0.25 mg/kg).75

Table 4.5 : Heavy Metal Contents of Aadathodai Chooranam

<table>
<thead>
<tr>
<th>Heavy Metal</th>
<th>Result</th>
<th>Specification as per Ayush/WHO/FDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead (Pb)</td>
<td>1.77 mg/kg</td>
<td>10.0 mg/Kg</td>
</tr>
<tr>
<td>Cadmium (Cd)</td>
<td>BLQ (LOQ : 0.25 mg/kg)</td>
<td>0.3 mg/Kg</td>
</tr>
<tr>
<td>Arsenic (As)</td>
<td>BLQ (LOQ : 0.25 mg/kg)</td>
<td>3.0 mg/kg</td>
</tr>
<tr>
<td>Mercury (Hg)</td>
<td>BLQ (LOQ : 0.25 mg/kg)</td>
<td>1.0 mg/kg</td>
</tr>
</tbody>
</table>

BLQ - Below Limit of Quantification: LOQ - Limit of Quantification

Microbial load and Aflatoxin Content of Aadathodai Chooranam

In Aadathodai Chooranam the total bacterial count was within the specified limit (79,000 CFU/g). Specifications as per AYUSH/WHO/FDA for total bacterial count is NMT 1,00,000 (CFU/g). Total fungal count was within the prescibed limit (<10 CFU/g). The permissible limit is NMT 1000 CFU/g. Enterobacteriaceae was <1 CFU/G. The specified limit is NMT 1000 CFU/g. Alfatoxin B1, B2, G1, G2 were within the permissible limits BLQ (LOQ: 0.50 µg/Kg).75
Table: 4.6 Microbial load and Aflatoxin content in Aadhathodai Chooranam

<table>
<thead>
<tr>
<th>Microbiological analysis</th>
<th>Result</th>
<th>Specification as per Ayush/WHO/FDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Bacterial Count</td>
<td>79,000 CFU/g</td>
<td>NMT 1,00,000 (CFu/g)</td>
</tr>
<tr>
<td>E. Coli</td>
<td>Absent / g</td>
<td>Absent / g</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Absent / g</td>
<td>Absent / g</td>
</tr>
<tr>
<td>Salmonella</td>
<td>Absent / g</td>
<td>Absent / g</td>
</tr>
<tr>
<td>Pseudomonas Aeruginosa</td>
<td>Absent / g</td>
<td>Absent / g</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>&lt;1CFU/g</td>
<td>NMT 1000 CFU/g</td>
</tr>
<tr>
<td>Total Fungal count</td>
<td>&lt;10CFU/g</td>
<td>NMT1000 CFU/g</td>
</tr>
<tr>
<td>Aflatoxin:B1,B2,G1,G2</td>
<td>BLQ(LOQ:0.50µg/Kg)</td>
<td>0.5PPb</td>
</tr>
</tbody>
</table>

TLC and HPTLC profile

Table 4.7 summarizes the RF values and color of sports visible in the TLC profiles of Aadhathodai Chooranam visualization was attempted by spraying vanillin sulphuric acid reagent(Figure 6.3).
HPTLC FINGER PRINT PROFILE

Table 4.8 and Figure 6.1 showed HPTLC finger print of Aadhathodai Chooranam in 254 nm UV(Figure1). The peak correspond to the Rf values 0.35 has highest peak area of 12446.9 Au in 254 nm. This 6th peak (area % is 48.98%) could serve as a Marker. Phyto components with 0.20, 0.35, 0.54, 0.63, 0.89 95th, 6th, 7th, 8th, 10th show the possibly active phyto constituents. Table 4.9 and Figure 6.2 showed HPTLC finger print of Aadhathodai Chooranam in 520nm UV (Figure2). The peak similar to the Rf value 0.35 has maximum peak area of 13576.3 AU in 520 nm. This 9th Peak (area % is 41.27%) is a Marker and Phyto components with Rf values are 0.01, 0.35, 0.76, 0.81, 0.89 (1st, 9th, 13th, 14th, 15th peaks).

Table 4.7: TLC Analysis (Rf value and colour of the Spots) of Aadhathodai Chooranam

<table>
<thead>
<tr>
<th>S. No.</th>
<th>UV 254 nm</th>
<th>Colour</th>
<th>Rf</th>
<th>UV 366 nm</th>
<th>Colour</th>
<th>Rf</th>
<th>With Vanillin Sulphuric acid Spray Reagent Colour</th>
<th>Rf</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Green</td>
<td>0.01</td>
<td></td>
<td>Pink</td>
<td>0.05</td>
<td></td>
<td>Grey</td>
<td>0.42</td>
</tr>
<tr>
<td>2.</td>
<td>Green</td>
<td>0.05</td>
<td></td>
<td>Blue</td>
<td>0.20</td>
<td></td>
<td>Grey</td>
<td>0.05</td>
</tr>
<tr>
<td>3.</td>
<td>Green</td>
<td>0.08</td>
<td></td>
<td>Blue</td>
<td>0.38</td>
<td></td>
<td>Grey</td>
<td>0.18</td>
</tr>
<tr>
<td>4.</td>
<td>Green</td>
<td>0.17</td>
<td></td>
<td>Green</td>
<td>0.42</td>
<td></td>
<td>Grey</td>
<td>0.13</td>
</tr>
<tr>
<td>5.</td>
<td>Green</td>
<td>0.27</td>
<td></td>
<td>Blue</td>
<td>0.49</td>
<td></td>
<td>Grey</td>
<td>0.17</td>
</tr>
<tr>
<td>6.</td>
<td>Green</td>
<td>0.42</td>
<td></td>
<td>Pink</td>
<td>0.54</td>
<td></td>
<td>Grey</td>
<td>0.21</td>
</tr>
<tr>
<td>7.</td>
<td>Green</td>
<td>0.58</td>
<td></td>
<td>Pink</td>
<td>0.63</td>
<td></td>
<td>Grey</td>
<td>0.24</td>
</tr>
<tr>
<td>8.</td>
<td>Green</td>
<td>0.65</td>
<td></td>
<td>Pink</td>
<td>0.70</td>
<td></td>
<td>Grey</td>
<td>0.30</td>
</tr>
<tr>
<td>9.</td>
<td>Green</td>
<td>0.71</td>
<td></td>
<td>Blue</td>
<td>0.74</td>
<td></td>
<td>Brown</td>
<td>0.43</td>
</tr>
<tr>
<td>10.</td>
<td>Green</td>
<td>0.93</td>
<td></td>
<td>Pink</td>
<td>0.81</td>
<td></td>
<td>Grey</td>
<td>0.63</td>
</tr>
<tr>
<td>11.</td>
<td>Green</td>
<td>0.99</td>
<td></td>
<td>Pink</td>
<td>0.88</td>
<td></td>
<td>Grey</td>
<td>0.71</td>
</tr>
</tbody>
</table>

[98]
Table 4.8 : HPTLC finger print of Aadathodai Chooranam in 254 nm UV

<table>
<thead>
<tr>
<th>Peak</th>
<th>Start Position Rf</th>
<th>Start Height Au</th>
<th>Max Position Rf</th>
<th>Max Height AU</th>
<th>Max %</th>
<th>End Position Rf</th>
<th>End Height Au</th>
<th>Area Au</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>0.01</td>
<td>144.8</td>
<td>0.01</td>
<td>155.7</td>
<td>11.73</td>
<td>0.03</td>
<td>0.0</td>
<td>832.3</td>
<td>1.57</td>
</tr>
<tr>
<td>2.</td>
<td>0.03</td>
<td>0.0</td>
<td>0.05</td>
<td>12.1</td>
<td>0.91</td>
<td>0.06</td>
<td>0.4</td>
<td>97.9</td>
<td>0.18</td>
</tr>
<tr>
<td>3.</td>
<td>0.06</td>
<td>0.1</td>
<td>0.06</td>
<td>20.1</td>
<td>1.51</td>
<td>0.10</td>
<td>0.0</td>
<td>243.9</td>
<td>0.46</td>
</tr>
<tr>
<td>4.</td>
<td>0.12</td>
<td>0.1</td>
<td>0.17</td>
<td>24.5</td>
<td>1.85</td>
<td>0.18</td>
<td>18.6</td>
<td>630.8</td>
<td>1.19</td>
</tr>
<tr>
<td>5.</td>
<td>0.20</td>
<td>18.3</td>
<td>0.27</td>
<td>118.1</td>
<td>8.90</td>
<td>0.34</td>
<td>0.3</td>
<td>5262.4</td>
<td>9.92</td>
</tr>
<tr>
<td>6.</td>
<td>0.35</td>
<td>0.3</td>
<td>0.42</td>
<td>408.3</td>
<td>30.76</td>
<td>0.54</td>
<td>79.3</td>
<td>25991.0</td>
<td>48.98</td>
</tr>
<tr>
<td>7.</td>
<td>0.54</td>
<td>80.1</td>
<td>0.58</td>
<td>307.6</td>
<td>23.17</td>
<td>0.62</td>
<td>36.7</td>
<td>12446.9</td>
<td>23.46</td>
</tr>
<tr>
<td>8.</td>
<td>0.63</td>
<td>87.3</td>
<td>0.65</td>
<td>141.2</td>
<td>10.64</td>
<td>0.69</td>
<td>4.7</td>
<td>4215.9</td>
<td>7.95</td>
</tr>
<tr>
<td>9.</td>
<td>0.69</td>
<td>4.9</td>
<td>0.71</td>
<td>21.7</td>
<td>1.64</td>
<td>0.74</td>
<td>2.0</td>
<td>452.2</td>
<td>0.85</td>
</tr>
<tr>
<td>10.</td>
<td>0.89</td>
<td>0.2</td>
<td>0.93</td>
<td>82.2</td>
<td>6.19</td>
<td>0.97</td>
<td>0.2</td>
<td>2524.4</td>
<td>4.76</td>
</tr>
<tr>
<td>11.</td>
<td>0.97</td>
<td>0.6</td>
<td>0.99</td>
<td>35.8</td>
<td>2.70</td>
<td>0.99</td>
<td>28.2</td>
<td>363.7</td>
<td>0.69</td>
</tr>
</tbody>
</table>

Table 4.9 : HPTLC finger print of Aadathodai Chooranam in 520 nm UV

<table>
<thead>
<tr>
<th>Peak</th>
<th>Start Position Rf</th>
<th>Start Height Au</th>
<th>Max Position Rf</th>
<th>Max Height AU</th>
<th>Max %</th>
<th>End Position Rf</th>
<th>End Height Au</th>
<th>Area Au</th>
<th>Area %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>0.01</td>
<td>84.6</td>
<td>0.02</td>
<td>171.2</td>
<td>16.55</td>
<td>0.03</td>
<td>1.8</td>
<td>1947.9</td>
<td>5.92</td>
</tr>
<tr>
<td>2.</td>
<td>0.04</td>
<td>1.0</td>
<td>0.05</td>
<td>9.5</td>
<td>0.91</td>
<td>0.06</td>
<td>0.0</td>
<td>58.3</td>
<td>0.18</td>
</tr>
<tr>
<td>3.</td>
<td>0.07</td>
<td>1.8</td>
<td>0.08</td>
<td>23.5</td>
<td>2.27</td>
<td>0.10</td>
<td>6.0</td>
<td>350.0</td>
<td>1.06</td>
</tr>
<tr>
<td>4.</td>
<td>0.11</td>
<td>0.1</td>
<td>0.13</td>
<td>12.4</td>
<td>1.20</td>
<td>0.14</td>
<td>4.1</td>
<td>151.9</td>
<td>0.46</td>
</tr>
<tr>
<td>5.</td>
<td>0.17</td>
<td>3.3</td>
<td>0.17</td>
<td>13.8</td>
<td>1.33</td>
<td>0.18</td>
<td>0.8</td>
<td>82.0</td>
<td>0.25</td>
</tr>
<tr>
<td>6.</td>
<td>0.20</td>
<td>0.6</td>
<td>0.21</td>
<td>10.1</td>
<td>0.98</td>
<td>0.22</td>
<td>7.5</td>
<td>147.3</td>
<td>0.45</td>
</tr>
<tr>
<td>7.</td>
<td>0.23</td>
<td>7.4</td>
<td>0.24</td>
<td>10.4</td>
<td>1.00</td>
<td>0.26</td>
<td>0.0</td>
<td>142.0</td>
<td>0.43</td>
</tr>
<tr>
<td>8.</td>
<td>0.28</td>
<td>4.6</td>
<td>0.30</td>
<td>25.5</td>
<td>2.47</td>
<td>0.32</td>
<td>9.3</td>
<td>584.4</td>
<td>1.78</td>
</tr>
<tr>
<td>9.</td>
<td>0.35</td>
<td>5.8</td>
<td>0.43</td>
<td>291.1</td>
<td>28.13</td>
<td>0.52</td>
<td>1.5</td>
<td>13576.3</td>
<td>41.27</td>
</tr>
<tr>
<td>10.</td>
<td>0.58</td>
<td>0.2</td>
<td>0.63</td>
<td>44.8</td>
<td>4.33</td>
<td>0.67</td>
<td>16.0</td>
<td>1802.8</td>
<td>5.48</td>
</tr>
<tr>
<td>11.</td>
<td>0.67</td>
<td>16.2</td>
<td>0.71</td>
<td>31.9</td>
<td>3.08</td>
<td>0.72</td>
<td>27.5</td>
<td>1074.4</td>
<td>3.27</td>
</tr>
<tr>
<td>12.</td>
<td>0.73</td>
<td>27.8</td>
<td>0.75</td>
<td>35.1</td>
<td>3.39</td>
<td>0.76</td>
<td>25.6</td>
<td>747.0</td>
<td>2.27</td>
</tr>
<tr>
<td>13.</td>
<td>0.76</td>
<td>25.6</td>
<td>0.80</td>
<td>95.5</td>
<td>9.23</td>
<td>0.81</td>
<td>35.8</td>
<td>2281.5</td>
<td>6.94</td>
</tr>
<tr>
<td>14.</td>
<td>0.81</td>
<td>85.9</td>
<td>0.85</td>
<td>172.7</td>
<td>16.69</td>
<td>0.87</td>
<td>78.7</td>
<td>6625.9</td>
<td>20.14</td>
</tr>
<tr>
<td>15.</td>
<td>0.89</td>
<td>5.9</td>
<td>0.94</td>
<td>87.1</td>
<td>8.42</td>
<td>0.99</td>
<td>0.1</td>
<td>3321.0</td>
<td>10.10</td>
</tr>
</tbody>
</table>
Figure 6.1: HPTLC of Adhathodai Chooranam at 254 nm uv
Figure 6.2: HPTLC of Adathodai Chooranam At 520 Nm UV
RESULTS OF GC-MS

In the present study five compounds have been identified. They are 1, 2-benzenedicarboxylic acid, butyl 2-methyl propyl ester, 8-octadecenoic acid, methyl ester (E),
Heptadecanoic acid, 16-methyl, methyl ester, (E)-9-Octadecenoic acid ethyl ester and Methyl tetradecanoate.

**TABLE 4.10: Result of Gc-MS Study of Adathodai Chooranam**

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Peak Name</th>
<th>Formula</th>
<th>Molecular weight</th>
<th>Retention time</th>
<th>% Peak area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>1, 2-Benzenedicarboxylic acid, butyl 2-methyl propyl ester</td>
<td>C_{16}H_{22}O_{4}</td>
<td>278.343</td>
<td>5</td>
<td>15.89</td>
</tr>
<tr>
<td>2.</td>
<td>8-Octadecenoic acid, methyl ester, (E)</td>
<td>C_{19}H_{36}O_{2}</td>
<td>296.49</td>
<td>17.13</td>
<td>43.10</td>
</tr>
<tr>
<td>3.</td>
<td>Heptadecanoic acid, 16-methyl methyl ester</td>
<td>C_{19}H_{38}O_{2}</td>
<td>298</td>
<td>17.36</td>
<td>8.62</td>
</tr>
<tr>
<td>4.</td>
<td>(E)-9-Octadecenoic acid ethyl ester</td>
<td>C_{20}H_{38}O_{2}</td>
<td>310</td>
<td>17.75</td>
<td>17.24</td>
</tr>
<tr>
<td>5.</td>
<td>Methyl tetradecanoate</td>
<td>C_{15}H_{30}O_{2}</td>
<td>242.397</td>
<td>5</td>
<td>15.39</td>
</tr>
</tbody>
</table>

**Figure 6.4: 1,2-Benzenedicarboxylic acid, butyl 2-methylpropyl ester**
Figure 6.5: 8-Octadecenoic acid, methyl ester, (E)

Figure 6.6: Heptadecanoic acid, 16-methyl, methyl ester

[104]
Figure 6.7: (E)-9-Octadecenoic acid ethyl ester

Figure 6.8: Methyl tetradecanoate
Figure 6.9: GC-MS Study of Adathodai choorananm
6.2. ACUTE TOXICITY STUDY RESULTS

In acute toxicity study the test drug Adhathodai Chooranam upto single oral dose (10x therapeutic dose) of 2.6 gm / Kg body weight did not reveal any abnormal clinical signs in all the animals. All animals survived and no treatment related morbidity occurred during the period of 14 days. Gross necroscopy did not reveal any abnormal pathology in all animals. Weight loss was not observed in control and test group animals.

**Table 4.11: Cage side observation for the effect of Adathodai Chooranam at 2.6 mg / kg.b.wt**

<table>
<thead>
<tr>
<th>Observation</th>
<th>AC M1</th>
<th>AC M2</th>
<th>AC M3</th>
<th>AC M4</th>
<th>AC M5</th>
<th>AC F1</th>
<th>AC F2</th>
<th>AC F3</th>
<th>AC F4</th>
<th>AC F5</th>
</tr>
</thead>
<tbody>
<tr>
<td>General behaviour</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Respiration</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cardiovascular signs</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Motor activities</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Skin</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Fur</td>
<td>+</td>
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<td>+</td>
<td>+</td>
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<td>+</td>
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<tr>
<td>Mucous membrane</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Salivation</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<td>+</td>
</tr>
<tr>
<td>Lethargy</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sleep</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
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<td>Coma</td>
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<td>-</td>
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<td>-</td>
</tr>
<tr>
<td>Convulsion</td>
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<td>-</td>
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<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tremors</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td>Diarrhoea</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Morbidity</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mortality</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

+ Normal - Nil
6.3. LONG TERM TOXICITY STUDY RESULTS

In long term toxicity study all the animals were active during the trial period and survived until 28 days treatment period. No signs of clinical toxicity attributable to Adhathodai Chooranam were observed throughout the study.

Table 4.12: Effects of different dose level of Adhathodai Chooranam on food consumption in albino rats during 28 days treatment

In food intake, there was significant difference among all groups of animals and moderate significant differences between therapeutic dose and control group.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>1x Therapeutic dose</th>
<th>5x Therapeutic dose</th>
<th>10x Therapeutic dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food in Take(g)</td>
<td>61.3 ± 1.5</td>
<td>67.4 ± 1.3</td>
<td>67.8 ± 8.6</td>
<td>71.3 ± 5.8</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD from 10 animals in each group.*p<0.05;**p<0.01.

Table 4.13: Effects of different dose level of Adhathodai Chooranam on Body Weight in albino rats during 28 days treatment

No difference in body weight was observed on 7th day, 14th day, 21st day, 28th day between control and drug treated groups.

<table>
<thead>
<tr>
<th>Days</th>
<th>Control</th>
<th>1x Therapeutic dose</th>
<th>5x Therapeutic dose</th>
<th>10x Therapeutic dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Day</td>
<td>137.8 ± 21.1</td>
<td>163.6 ± 16.8</td>
<td>150.2 ± 17.9</td>
<td>146.3 ± 11.3</td>
</tr>
<tr>
<td>7th Day</td>
<td>145.7 ± 22.3</td>
<td>168.9 ± 16.7</td>
<td>152.9 ± 17.6</td>
<td>154.9 ± 14.4</td>
</tr>
<tr>
<td>14th Day</td>
<td>153.6 ± 24.9</td>
<td>175.8 ± 19.4</td>
<td>159.8 ± 21.4</td>
<td>159.4 ± 16.6</td>
</tr>
<tr>
<td>21st Day</td>
<td>160.8 ± 28.9</td>
<td>182 ± 22.2</td>
<td>165.9 ± 25.1</td>
<td>162.9 ± 18.8</td>
</tr>
<tr>
<td>28th Day</td>
<td>169.8 ± 31.8</td>
<td>190.3 ± 25.8</td>
<td>173.2 ± 30.6</td>
<td>169.6 ± 22.3</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD from 10 animals in each group.*p<0.05;**p<0.01.
Table 4.14: Effects of different dose level of Adathodai Chooranam on Hematological parameters in albino rats after 28 days treatment

There was a moderate significant difference, among all groups of animals on RBC Count. However there was no difference between therapeutic dose and control group. No difference was observed in other hematological parameters between control and drug treated groups.

<table>
<thead>
<tr>
<th>Days</th>
<th>Control</th>
<th>1x Therapeutic dose</th>
<th>5x Therapeutic dose</th>
<th>10x Therapeutic dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total WBC</td>
<td>4.07 ± 1.8</td>
<td>5.7 ± 3.3</td>
<td>4.3 ± 3.4</td>
<td>4.6 ± 4.2</td>
</tr>
<tr>
<td>10^9/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocytes (%)</td>
<td>64.6 ± 11.6</td>
<td>58.1 ± 12.1</td>
<td>65.7 ± 9.9</td>
<td>68.0 ± 12.5</td>
</tr>
<tr>
<td>Monocytes (%)</td>
<td>3.0 ± 1.1</td>
<td>6.6 ± 7.7</td>
<td>3.3 ± 0.9</td>
<td>2.7 ± 0.8</td>
</tr>
<tr>
<td>Granulocytes (%)</td>
<td>32.2 ± 10.7</td>
<td>37.9 ± 11.3</td>
<td>30.9 ± 9.0</td>
<td>29.3 ± 12.2</td>
</tr>
<tr>
<td>Total RBC</td>
<td>6.6 ± 3.3</td>
<td>3.9 ± 2.1</td>
<td>5.2 ± 1.2</td>
<td>4.3 ± 1.9</td>
</tr>
<tr>
<td>10^12/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb (gm/dl)</td>
<td>11.0 ± 5.2</td>
<td>6.7 ± 3.5</td>
<td>8.5 ± 2.2</td>
<td>7.4 ± 3.2</td>
</tr>
<tr>
<td>HCT (%)</td>
<td>32.9 ± 16.7</td>
<td>18.9 ± 11.0</td>
<td>25.7 ± 5.9</td>
<td>21.3 ± 9.7</td>
</tr>
<tr>
<td>MCV (Fl)</td>
<td>49.7 ± 1.9</td>
<td>47.4 ± 3.7</td>
<td>49.7 ± 2.0</td>
<td>49.8 ± 2.1</td>
</tr>
<tr>
<td>MCH (Pg)</td>
<td>16.8 ± 0.6</td>
<td>17.5 ± 2.9</td>
<td>16.4 ± 2.1</td>
<td>17.4 ± 0.8</td>
</tr>
<tr>
<td>MCHC (g/dl)</td>
<td>34.1 ± 1.6</td>
<td>37.5 ± 9.3</td>
<td>33.1 ± 3.9</td>
<td>35.3 ± 1.8</td>
</tr>
<tr>
<td>Platelets (10^9/L)</td>
<td>77.6 ± 37.4</td>
<td>120.5 ± 121.6</td>
<td>101 ± 81.3</td>
<td>60.6 ± 66.7</td>
</tr>
</tbody>
</table>
Table 4.15 Effects of different dose level of Adathodai Chooranam on Biochemical parameters in albino rats after 28 days treatment

There was significant difference among all group of experimental animals on Blood Sugar level, total Cholesterol and triglycerides at the end of treatment. But there was no difference between therapeutic dose and control groups. Moderate significant difference was observed in urea level between therapeutic dose and control groups, but the difference was within the normal expected range for the rat species used in this study. No difference in Creatinine level and total Protein was observed among all groups. Moderate significant difference among all group of experimental animals on Albumin level. But there is no difference between therapeutic and control groups. There was difference among all groups of experimental animals on globulin and no difference between therapeutic dose and control groups. In serum bilirubin and SGOT, there is no difference in all groups of animals. There was difference among all groups of experimental animals on SGPT. But there was no difference between control and therapeutic dose groups.

<table>
<thead>
<tr>
<th>Days</th>
<th>Control</th>
<th>1x Therapeutic dose</th>
<th>5x Therapeutic dose</th>
<th>10x Therapeutic dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugar (mg/dl)</td>
<td>69.5 ± 10.0</td>
<td>73 ± 15.0</td>
<td>93.5 ± 13.4</td>
<td>115.2 ± 16.7</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dl)</td>
<td>118.8 ± 36.1</td>
<td>132.3 ± 23.3</td>
<td>130.6 ± 13.0</td>
<td>**87.3 ± 11.8</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>145 ± 64.9</td>
<td>129.2 ± 34.8</td>
<td>160.6 ± 45.5</td>
<td>194.5 ± 64.1</td>
</tr>
<tr>
<td>Urea (mg/dl)</td>
<td>53.4 ± 9.3</td>
<td>*41.9 ± 7.1</td>
<td>**36.8 ± 2.8</td>
<td>**35.52 ± 10.04</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>0.7 ± 0.1</td>
<td>0.75 ± 0.1</td>
<td>0.84 ± 0.18</td>
<td>0.7 ± 0.0</td>
</tr>
<tr>
<td>Total Protein (g/dl)</td>
<td>7.6 ± 0.6</td>
<td>7.78 ± 0.3</td>
<td>7.9 ± 0.1</td>
<td>7.91 ± 0.1</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>4 ± 0.4</td>
<td>3.8 ± 0.2</td>
<td>3.61 ± 0.2</td>
<td>3.88 ± 0.1</td>
</tr>
<tr>
<td>Globulin (g/dl)</td>
<td>3.6 ± 0.7</td>
<td>3.8 ± 0.3</td>
<td>*4.2 ± 0.2</td>
<td>4.0 ± 0.2</td>
</tr>
<tr>
<td>Bilirubin (mg/dl)</td>
<td>0.6 ± 0.2</td>
<td>0.7 ± 0.1</td>
<td>0.6 ± 0.1</td>
<td>0.6 ± 0.0</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>126.2 ± 50.6</td>
<td>146.8 ± 34.5</td>
<td>124.8 ± 30.1</td>
<td>133.5 ± 22.9</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>56.2 ± 13.8</td>
<td>47 ± 8.7</td>
<td>65.5 ± 8.8</td>
<td>61.4 ± 9.2</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD from 10 animals in each group.*p<0.05;**p<0.01.
Table 4.16: Effects of different dose level of Adathodai Chooranam on organs weight(g) in albino rats during 28 days treatment

There was no difference in weight of Heart, Lungs, Kidney and Brain of all groups of animals. There was significant difference among different groups of experimental animals on weight of Liver, Spleen, Stomach and male sex organs. However there was no difference between therapeutic dose and control groups. There was difference found in female sex organ weight among different groups of experimental animals but no difference between therapeutic and control groups.

<table>
<thead>
<tr>
<th>Organs</th>
<th>Control</th>
<th>1x Therapeutic dose</th>
<th>5x Therapeutic dose</th>
<th>10x Therapeutic dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>0.8 ± 0.2</td>
<td>0.8 ± 0.1</td>
<td>0.8 ± 0.2</td>
<td>0.8 ± 0.1</td>
</tr>
<tr>
<td>Lungs</td>
<td>1.4 ± 0.2</td>
<td>1.2 ± 0.2</td>
<td>1.4 ± 0.2</td>
<td>1.4 ± 0.2</td>
</tr>
<tr>
<td>Liver</td>
<td>5.5 ± 1.4</td>
<td>6.6 ± 0.7</td>
<td>*7.3 ± 1.4</td>
<td>*8.1 ± 1.2</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.5 ± 0.1</td>
<td>0.5 ± 0.1</td>
<td>*0.7 ± 0.1</td>
<td>0.6 ± 0.1</td>
</tr>
<tr>
<td>Stomach</td>
<td>1.6 ± 0.3</td>
<td>2.1 ± 1.4</td>
<td>*1.0 ± 0.5</td>
<td>2.5 ± 1.3</td>
</tr>
<tr>
<td>Brain</td>
<td>1.6 ± 0.2</td>
<td>1.3 ± 0.2</td>
<td>1.6 ± 0.4</td>
<td>1.4 ± 0.2</td>
</tr>
<tr>
<td>Male Sex Organ</td>
<td>4.5 ± 1.0</td>
<td>5.0 ± 0.6</td>
<td>5.1 ± 0.3</td>
<td>*7.1 ± 1.7</td>
</tr>
<tr>
<td>Kidney</td>
<td>1.6 ± 0.3</td>
<td>1.8 ± 0.2</td>
<td>1.9 ± 0.3</td>
<td>1.9 ± 0.2</td>
</tr>
<tr>
<td>Female Sex Organ</td>
<td>1.41 ± 0.8</td>
<td>1.3 ± 0.4</td>
<td>*5.2 ± 1.1</td>
<td>2.3 ± 0.8</td>
</tr>
</tbody>
</table>

Values are expressed as mean±SD from 10 animals in each group.*p<0.05;**p<0.01.
Histopathological studies

Histopathological studies showed normal architecture in therapeutic dose and control groups. Only the Liver has shown congestion and spleen has shown slightly hyperplastic. 5x therapeutic dose female group exhibited focal hyperplasia in non glandular area of stomach and pathological changes (squamous metaplasia) in uterus.10x therapeutic dose male group exhibits mild tubular epithelial cell degeneration in kidney and mild vacuolar degeneration in liver.10x therapeutic female group exhibited hyperplasia and Squamous melaplasia in uterus. No abnormalities detected in other organs. (Figures 6.10 to 6.17)

FIGURE 6.10 HISTOPATHOLOGY OF VEHICLE CONTROL FEMALE GROUP

<table>
<thead>
<tr>
<th>Brain</th>
<th>Stomach</th>
<th>Heart</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Brain Image" /></td>
<td><img src="image2.png" alt="Stomach Image" /></td>
<td><img src="image3.png" alt="Heart Image" /></td>
</tr>
<tr>
<td>Kidney</td>
<td>Liver</td>
<td>Lung</td>
</tr>
<tr>
<td><img src="image4.png" alt="Kidney Image" /></td>
<td><img src="image5.png" alt="Liver Image" /></td>
<td><img src="image6.png" alt="Lung Image" /></td>
</tr>
</tbody>
</table>
FIGURE 6.11 HISTOPATHOLOGY OF VEHICLE CONTROL MALE GROUP

Brain                      Glandular Stomach                      Heart
Intestine                               Kidney                               Liver

Lung                                     Non glandular Stomach                Spleen

Testicle                                 Testicles

[114]
FIGURE 6.12: HISTOPATHOLOGY OF 1 X THERAPEUTIC DOSE FEMALE GROUP

<table>
<thead>
<tr>
<th></th>
<th>Brain</th>
<th>Heart</th>
<th>Kidney</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spleen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterus</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
FIGURE 6.13: HISTOPATHOLOGY OF 1 X THERAPEUTIC DOSE MALE GROUP

Brain                               Brain                        Glandular Stomach
Heart                               Kidney                                    Liver
Lung                                Spleen                      Non Glandular Stomach
Testicle                            Testicle

[116]
FIGURE 6.14: HISTOPATHOLOGY OF 5 X THERAPEUTIC DOSE MALE GROUP

Brain | Heart | Kidney

Liver | Lung | Spleen

Stomach | Testicle
FIGURE 6.15: HISTOPATHOLOGY OF 5 X THERAPEUTIC DOSE FEMALE GROUP

Brain  Heart  Kidney

Liver  Lung  Spleen

Uterus
FIGURE 6.16: HISTOPATHOLOGY OF 10 X THERAPEUTIC DOSE FEMALE GROUP

Brain                               Heart                               Kidney

Liver                               Liver                               Lung

Ovary                                Spleen                               Uterus
FIGURE 6.17: HISTOPATHOLOGY IN 10X THERAPEUTIC DOSE MALE GROUP

<table>
<thead>
<tr>
<th>Brain</th>
<th>Heart</th>
<th>Kidney</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Brain" /></td>
<td><img src="image2" alt="Heart" /></td>
<td><img src="image3" alt="Kidney" /></td>
</tr>
<tr>
<td>Kidney</td>
<td>Kidney</td>
<td>Liver</td>
</tr>
<tr>
<td><img src="image4" alt="Kidney" /></td>
<td><img src="image5" alt="Kidney" /></td>
<td><img src="image6" alt="Liver" /></td>
</tr>
<tr>
<td>Liver</td>
<td>Lung</td>
<td>Spleen</td>
</tr>
<tr>
<td><img src="image7" alt="Liver" /></td>
<td><img src="image8" alt="Lung" /></td>
<td><img src="image9" alt="Spleen" /></td>
</tr>
<tr>
<td>Stomach</td>
<td>Testicle</td>
<td></td>
</tr>
<tr>
<td><img src="image10" alt="Stomach" /></td>
<td><img src="image11" alt="Testicle" /></td>
<td></td>
</tr>
</tbody>
</table>

[120]
6.4. PILOT STUDY RESULTS

Table 4.17: Pilot study-Case history

<table>
<thead>
<tr>
<th>Sl. No</th>
<th>Op. No</th>
<th>Age/Sex</th>
<th>Occupation</th>
<th>Habits</th>
<th>Family History</th>
<th>Treatment History</th>
<th>Duration of illness</th>
<th>Triggers</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>E18 261</td>
<td>23/Male</td>
<td>Civil Engineer</td>
<td>No Smoking Alcoholism</td>
<td>Negative</td>
<td>Siddha</td>
<td>6 Months</td>
<td>House dusts, cold exposure, paints</td>
</tr>
<tr>
<td>2</td>
<td>D79 552</td>
<td>40/Male</td>
<td>Ration Store</td>
<td>No Smoking Alcoholism</td>
<td>Positive</td>
<td>Modern drug</td>
<td>1 year</td>
<td>Dust, cold air &amp; foods, Exercise, Smoke, fumes, paints</td>
</tr>
<tr>
<td>3</td>
<td>C71 279</td>
<td>16/Male</td>
<td>Student</td>
<td>No Smoking Alcoholism</td>
<td>Positive</td>
<td>Siddha</td>
<td>2 years</td>
<td>Cold air, cold foods, dust, chalk powder, smoke, perfume</td>
</tr>
<tr>
<td>4</td>
<td>E37 760</td>
<td>19/Female</td>
<td>Student</td>
<td>-</td>
<td>Positive</td>
<td>Modern drug</td>
<td>2 years</td>
<td>Cold air, cold food, dust (cotton, flour) fumes, perfumes</td>
</tr>
<tr>
<td>5</td>
<td>E56 65</td>
<td>30/Female</td>
<td>Business</td>
<td>-</td>
<td>Negative</td>
<td>Modern drug</td>
<td>1 year</td>
<td>Cold air, cold foods, dust, paints, fumes, smoke</td>
</tr>
</tbody>
</table>

PILOT STUDY RESULTS

After treatment among 5 cases, serum Ig E level was reduced in 4 cases. The morning and evening peak expiratory flow rate was increased at the end of the treatment in all 5 cases. Before treatment, the Asthma Control questionnaire score was 0-20 in all 5 cases which means the Asthma Symptoms are not controlled. After treatment the ACQ score was increased and the symptoms were under control in one case (score 25) and reasonably well
controlled in 4 cases (score 20-24). Clinically before treatment 3 cases were having Mild persistent type of Asthma (Step II), one case was having Mild intermittent type of Asthma (step I) and another one case was having severe persistent type of Asthma (step IV). After treatment No wheezing and tightness of chest in 4 cases which is good result and one case was improved from step IV to step III (Moderate persistent Asthma) which is Moderate result
6.5. CLINICAL STUDY RESULTS

GENDER DISTRIBUTION

Inference:

Out of 138 cases 74 cases (53.62%) were female and 64 cases (46.38%) cases were male. The male female ratio is 1:1.16. The results showed that the female gender had more prevalence than male.

Fig: 6.18 Gender Distributions
AGE DISTRIBUTION

Among 138 cases, 69 cases (50%) were in the age group between 15-30 years. 52 cases (37.68%) were in the age group between 31-45 years. 17 cases (12.32%) were in the age group between 46-60 years. The mean age distribution of the cases was 31.79±11.06. The highest percentage of the patients belonged to 15-30 years.

Fig: 6.19 Age distribution
 DISTRIBUTION OF CASES BY KAALAM (LIFE SPAN)

Out of 138 cases, 83 cases (60.14%) were found to be affected in their vatha kaalam (1-33 years). 55 cases (39.86%) were found to be affected in their pitha kaalam (34-66 years).

Fig: 6.20 Distribution of cases by kaalam (life span)
THEGI DISTRIBUTION (BODY CONSTITUTION)

Out of 138 cases, 92 cases (66.67%) had kaba thegam. 29 cases (21.01%) had pitha thegam. 17 cases (12.32%) had vatha thegam.

Fig: 6.21 Thegi distributions (body constitution)
**DISTRIBUTION OF CASES BY GUNAM**

Out of 138 cases, 131 cases (94.93%) had Raso gunam. 7 cases (5.07%) had Thamo gunam.

**DISTRIBUTION OF CASES BY THINAI (LAND)**

Out of 138 cases, 82 cases (59.42%) were belonged to the Marutham (plain and its surroundings). 51 cases (36.96%) were belonged to the Neithal (costal area and its surroundings). 5 cases (3.62%) were belonged to the Kuringi (Mountain and its surroundings).

**Fig: 6.22 Distribution of cases by thinai (land)**

![Distribution of cases by thinai](image)
DISTRIBUTION OF CASES BY PARUVAKALAM (SEASONS)

Among 138 cases, in 65 cases (47.10%) the incidence of the disease seems to be higher in pinpani kaalm (Feb 16- Apr 15). In 25 cases (18.11%) the incidence of the disease occurred in Munpani kaalm (Dec 16- Feb 15). In 15 cases (10.87%) the incidence of disease occurred in kaarkaalam (Aug 16- Oct 15). In another 15 cases (10.87%) the incidence of disease occurred in Ilavenil kaalm (Apr 16- Jun 15). In 12 cases (8.70%) the incidence of disease occurred in koothirkaalam (Oct 16- Dec 15). In 6 cases (4.35%) the incidence of disease occurred in Mudhuvenilkaalam (Jun16- Aug 15).

Fig: 6.23 Distribution of cases by Paruvakalam

![DISTRIBUTION OF CASES BY PARUVAKALAM]

Kaarkaalam (Early Rainy)  Koothirkaalam (Later Rainy)
Munpani Kaalam (Early Winter)  Pinpani Kaalam (Later Winter)
Ilavenil Kaalam (Early Summer)  Mudhuvenil Kaalam (Later Summer)
DISTRIBUTION OF CASES BY RELIGION

Out of 138 cases, 119 cases (86.23%) were Hindus. 15 cases (10.87%) were Christians. 4 cases (2.90%) were Muslims.

SOCIO ECONOMIC STATUS DISTRIBUTION

Among 138 cases, 71 cases (51.45%) were Lower Class people. 56 cases (40.58%) were Middle Class people. 11 cases (7.97%) were Upper Class people.

Fig: 6.24 Socio economic status distributions
DEMOGRAPHIC DISTRIBUTION

Inference:

Out of 138 cases, 90 cases (65.22%) were belonged to the Rural Areas.

48 cases (34.78%) were belonged to the urban Areas.

Fig: 6.25 Demographic distribution
EDUCATIONAL STATUS DISTRIBUTION

Out of 138 cases, 121 (87.68%) cases were Literates. Among Literates, 12 cases (8.69%) had completed their middle school education. 38 cases (27.54%) had completed their high school education. 71 cases (51.45%) had completed their higher secondary studies and higher studies. 17 (12.32%) cases were Illiterates.

Fig: 6.26 Educational status distribution
DISTRIBUTION OF CASES BY MARITAL STATUS

Out of 138 cases, 84 cases (60.87%) were Married. 54 cases (39.13%) were unmarried.

Fig: 6.27  Distribution of cases by marital status

DISTRIBUTION OF CASES BY BODY BUILT

Among 138 cases, 15 (10.88%) cases were obese, 33 cases (23.91%) were over weight, 20 cases (14.49%) were under weight, and 70 cases (50.72%) were Normal Weight.

Fig: 6.28 Distribution of cases by body built
DISTRIBUTION OF CASES BY DIET FACTOR

Inference:

Among 138 cases, 131 cases (94.93%) were Non Vegetarian. 7 cases (5.07%) were Vegetarian.

Fig: 6.29 Distribution of cases by diet factor

![Distribution of cases by diet factor](image)
DISTRIBUTION OF CASES BY HABITS

Out of 138 cases, 3 cases (2.17%) were smokers. 2 cases (1.45%) were Alcoholic. 2 cases (1.45%) were Betel nut Chewer.

Fig: 6.30 DISTRIBUTIONS OF CASES BY HABITS

DISTRIBUTION OF FEMALE CASES BY MENOPAUSAL STATUS

Out of 74 Females, 65 Females (87.84%) not yet attained menopause, 9 Females (12.16%) had attained menopause.

Fig: 6.31 Distribution of female cases by menopausal status
TABLE NO.4.18 DISTRIBUTION OF CASES BY OCCUPATION

<table>
<thead>
<tr>
<th>S. No.</th>
<th>WORKERS</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Carpenter</td>
<td>0.72%</td>
</tr>
<tr>
<td>2</td>
<td>Farmer</td>
<td>0.72%</td>
</tr>
<tr>
<td>3</td>
<td>Leather</td>
<td>0.72%</td>
</tr>
<tr>
<td>4</td>
<td>Mosquito Repellent</td>
<td>0.72%</td>
</tr>
<tr>
<td>5</td>
<td>Nickel</td>
<td>0.72%</td>
</tr>
<tr>
<td>6</td>
<td>Petrol Bunk</td>
<td>0.72%</td>
</tr>
<tr>
<td>7</td>
<td>Policemen</td>
<td>0.72%</td>
</tr>
<tr>
<td>8</td>
<td>Rice Mill</td>
<td>0.72%</td>
</tr>
<tr>
<td>9</td>
<td>Rubber</td>
<td>0.72%</td>
</tr>
<tr>
<td>10</td>
<td>Salon</td>
<td>0.72%</td>
</tr>
<tr>
<td>11</td>
<td>Tailor</td>
<td>0.72%</td>
</tr>
<tr>
<td>12</td>
<td>Plastic</td>
<td>1.45%</td>
</tr>
<tr>
<td>13</td>
<td>Car</td>
<td>2.17%</td>
</tr>
<tr>
<td>14</td>
<td>Xerox Centre</td>
<td>2.17%</td>
</tr>
<tr>
<td>15</td>
<td>Electrician</td>
<td>2.90%</td>
</tr>
<tr>
<td>16</td>
<td>Mason</td>
<td>3.62%</td>
</tr>
<tr>
<td>17</td>
<td>Metal</td>
<td>3.62%</td>
</tr>
<tr>
<td>18</td>
<td>Teacher</td>
<td>3.62%</td>
</tr>
<tr>
<td>19</td>
<td>Painter</td>
<td>4.35%</td>
</tr>
<tr>
<td>20</td>
<td>Textile</td>
<td>4.35%</td>
</tr>
<tr>
<td>21</td>
<td>Office Worker</td>
<td>5.80%</td>
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<tr>
<td>22</td>
<td>Businessmen</td>
<td>6.52%</td>
</tr>
<tr>
<td>23</td>
<td>Store</td>
<td>7.25%</td>
</tr>
<tr>
<td>24</td>
<td>Engineers</td>
<td>10.14%</td>
</tr>
<tr>
<td>25</td>
<td>Students</td>
<td>14.49%</td>
</tr>
<tr>
<td>26</td>
<td>Housewives</td>
<td>19.57%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>
DISTRIBUTION OF CASES BY FAMILY HISTORY OF ASTHMA

Among 138 cases, 88 cases (63.77%) reported negative family history of similar illness. 50 cases (36.23%) reported positive family history of similar illness.

Fig : 6.32 Distribution of cases by family history of asthma

DISTRIBUTION OF CASES BY TREATMENT HISTORY

Among 138 cases, 98 cases (71.01%) had taken Modern Medicines. 32 cases (23.19%) had taken siddha treatment. 4 cases (2.90%) had taken Ayurvedha treatment and 4 cases (2.90%) had taken Homoeopathy treatment.

Fig: 6.33 Distribution of cases by treatment history
DISTRIBUTION OF CASES BY STAGES OF ASTHMA

Inference:

Among 138 cases, 61 cases (44.20%) had mild intermittent Asthma. 33 cases (23.91%) had mild persistent Asthma. 30 cases (21.74%) had moderate persistent Asthma. 14 cases (10.15%) had severe persistent Asthma.

Fig : 6.34 Distribution of cases by stages of asthma
**DISTRIBUTION OF CASES BY PEAK EXPIRATORY FLOW RATE**

On the basis of PEFR among 138 cases, 12 cases (8.69%) were mild Asthmatic cases, 71 cases (51.45%) were moderate Asthmatic cases. 55 cases (39.86%) were severe Asthmatic cases.

**Fig: 6.35 Distribution of cases by peak expiratory flow rate**

**DISTRIBUTION OF CASES BY FEV1**

On the basis of Spirometry result, all the 138 cases are divided into 3 stages according to their FEV1. 38 cases (27.54%) had mild Asthma. 44 cases (31.88%) had moderate Asthma. 56 cases (40.58%) had severe Asthma.

**Fig: 6.36 Distribution of cases by FEV1**
FIG: 6.37 OVERALL DISTRIBUTIONS OF CASES BY STAGES OF ASTHMA, PEFR and FEVI

DISTRIBUTION OF CASES BY TRIGGERING FACTORS

Among 138 cases cold exposure was the important trigger in majority of cases (126 cases 91.30%). Dust in 103 cases (74.64%), smoke exposure in 88 cases (63.77%), paints in 76 (55.07%) cases, fumes in 54 cases (39.13%), perfumes in 54 cases (39.13%) . Psychological factors like depression and emotion in 47 cases (34.06%), environmental pollution in 40 cases (28.99%), petrol in 34 cases (24.64%), cockroach antigens in 21 cases (15.22%), chemicals in 18 cases (13.04%), cotton dusts in 15 cases (10.87%), pet animals like cat, dog’s dander in 15 cases (10.87%), flour dusts in 14 cases (10.14%), Husks, grass and pollens in 12 cases (8.70%), Exercise in 11 cases (7.97%), wood dust in 6 cases (4.35%), cement dust in 5 cases (3.62%), Chalk powder in 5 cases (3.62%) cement dust in 5 cases (3.62%) and feathers in 2 cases (1.45%).
Fig: 6.38 Distribution of cases by triggering factors

<table>
<thead>
<tr>
<th>Triggering Factors</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold foods, cool drinks &amp; Cold air</td>
<td>91.30%</td>
</tr>
<tr>
<td>Dust</td>
<td>74.64%</td>
</tr>
<tr>
<td>Smoke Exposure</td>
<td>63.77%</td>
</tr>
<tr>
<td>Paint</td>
<td>55.07%</td>
</tr>
<tr>
<td>Perfumes</td>
<td>39.13%</td>
</tr>
<tr>
<td>Fumes</td>
<td>39.13%</td>
</tr>
<tr>
<td>Psychological factor</td>
<td>34.06%</td>
</tr>
<tr>
<td>Atmospheric Pollution</td>
<td>28.99%</td>
</tr>
<tr>
<td>Petrol</td>
<td>24.64%</td>
</tr>
<tr>
<td>Cockroaches</td>
<td>15.22%</td>
</tr>
<tr>
<td>Chemicals</td>
<td>13.04%</td>
</tr>
<tr>
<td>Pet Animal dander</td>
<td>10.87%</td>
</tr>
<tr>
<td>Cotton</td>
<td>10.87%</td>
</tr>
<tr>
<td>Flour Dust</td>
<td>10.14%</td>
</tr>
<tr>
<td>Husks, Grass &amp; Pollens</td>
<td>8.70%</td>
</tr>
<tr>
<td>Exercise</td>
<td>7.97%</td>
</tr>
<tr>
<td>Wood Dust</td>
<td>4.35%</td>
</tr>
<tr>
<td>Cement</td>
<td>3.62%</td>
</tr>
<tr>
<td>Chalk Powder</td>
<td>3.62%</td>
</tr>
<tr>
<td>Feathers</td>
<td>1.45%</td>
</tr>
</tbody>
</table>
DISTRIBUTION OF CASES BY DURATION OF ILLNESS

Out of 138 cases, 75 cases (54.35%) were affected by the illness from 1 ½ year to 2 years. 33 cases (23.91%) were affected from 6 months - 1 year, 14 cases (10.15%) were affected from 3 months to 6 months, 9 cases (6.52%) were affected from 1 year - 1 ½ year and 7 cases (5.07%) were affected from 0-3 months.

Fig: 6.39 Distribution of cases by duration of illness
CLINICAL FEATURES (BEFORE TREATMENT)

Among 138 cases, all the cases had sneezing, running Nose, cough, tightness of chest and wheezing. 123 cases (89.13%) had nocturnal wheezing and insomnia. 70 cases (50.72%) had dryness of tongue, sweating and drowsiness. 44 cases (31.88%) had indigestion and poor appetite. 10 cases (7.25%) had constipation. 5 cases (3.62%) had joint pain.

**Fig: 6.40 Clinical features (before treatment)**
DISTURBANCE IN GNANENTHIRIYAM (SENSORY ORGANS)  
(BEFORE AND AFTER TREATMENT)

Inference:

Before treatment among 138 cases, mooku was affected in all cases (100%) due to sneezing and running Nose. Mei and vai was affected in 70 cases (50.72%) due to sweating, drowsiness and dryness of tongue. After treatment among 125 cases mooku was affected in 3 cases (2.4%). Mei and vai was affected in 3 cases (2.4%).

Fig: 6.41 Disturbance in Gnanenthiriyam (sensory organs)  
(Before and after treatment)
**DISTURBANCE OF KANMENDRIYAM (MOTOR ORGANS)
(BEFORE AND AFTER TREATMENT)**

**Inference:**

Before treatment among 138 cases, kai was affected in one case (0.72%). kaal was affected in 4 cases (2.90%) which resulted in pain in upper and lower limbs. Eruvai was affected in 10 cases (7.25%) which resulted in constipation. karuvai was affected in 6 cases (4.35%) which resulted in irregular menstrual cycle in females and nocturnal emission in males.

After treatment among 125 cases, pain reduced in upper and lower limbs in all 5 cases. Constipation relieved in all 10 cases. Karuvai was normal in all 6 cases.

**Fig: 6.42 Disturbance of kanmendriyam (motor organs)
(Before and after treatment)**
DISTURBANCE IN KOSAM (SHEATHS)
(BEFORE AND AFTER TREATMENT)

Before treatment, in all 138 cases (100%) Annamaya kosam, pranamaya kosam, Manomaya kosam, Vignanamaya kosam, Anandhamayakosam were affected due to the presence of sneezing, wheezing, tightness of chest, drowsiness, sweating, and dryness of tongue. After treatment among 125 cases Annamayakosam, Pranamayakosam and Anandhamayakosam were affected in 22 cases (17.6%). Wheezing and tightness of chest was reduced in 103 cases. Manomayakosam and Vignanamayakosam were affected in 3 cases (2.4%) because of sneezing; sweating, drowsiness and dryness of tongue were reduced.

Fig: 6.43 Disturbance in kosam (sheaths)
(Before and after treatment)
DISTURBANCE IN MUKKUTRAM (THREE HUMORS)- VATHA

BEFORE AND AFTER TREATMENT

Before treatment, among 138 cases, pranan was affected in all 138 cases (100%) which resulted in breathlessness, cough, wheeze. Abanan was affected in 10 cases (7.25%) which resulted in constipation and burning micturition. Samanan was affected in all 138 cases (100%) due to the derangement of other types of vatha as it controls all vatha types. Udhanan was affected in all the 138 cases (100%) which resulted in cough. Viyanan was affected in 75 cases (54.35%) which resulted in drowsiness, pain in upper and lower limbs. Kirukaran was affected in all 138 cases (100%) which resulted in excessive cough reflex, excessive sneezing reflex and Devathathan was affected in 123 cases (89.13%) which resulted in sleep disturbance. After treatment among 125 cases, pranan was affected in 22 cases (17.6%). Abanan was normal in 10 cases. Samanan was affected in 25 cases (20%). Udhanan was affected in 4 cases (3.2%). Viyanan was affected in 3 cases (2.4%). Kirugaran was affected in 4 cases (3.2%). Devathathan was affected in 4 cases (3.2%).

Fig: 6.44 DERANGEMENT IN MUKKUTRAM - VATHA
DERANGEMENT IN PITHAM - BEFORE AND AFTER TREATMENT

Inference:

Before treatment among 138 cases, Anar pitham was affected in 44 cases (31.88%) which resulted in indigestion and poor appetite. Ranjagam was affected in 6 cases (4.35%) which resulted in Pallor with decreased hemoglobin. Saathagam was affected in 75 cases (54.35%) which resulted in drowsiness.

After treatment, among 125 cases indigestion and poor appetite reduced in all cases. Saathagam was affected in 3 cases (2.4%). Hemoglobin increased in all cases.

**Fig: 6.45 Derangement in pitham - before and after treatment**
DERANGEMENT IN KABAM - BEFORE AND AFTER TREATMENT

Inference:

Among 138 cases Avalambagam was affected in all 138 cases (100%) which resulted in the presence of tightness of chest, cough, wheezing. Kilethgam was affected in 44 cases (31.88%) which resulted in indigestion, heart burn. Santhigam was affected in 5 cases (3.62%) which resulted in joint pain. Pothagam was affected in 44 cases (31.88%) which resulted in loss of appetite.

After treatment, among 125 cases Avalambagam was affected in 22 cases (17.6%). Indigestion, heart burn and loss of appetite reduced in all cases. Joint pain was reduced in all cases.

**Fig: 6.46 Derangement in kabam - before and after treatment**

### Derangement in Mukkutram in Kaba (Before and After Treatment)

<table>
<thead>
<tr>
<th>Kabam of Respiration</th>
<th>Kabam of Digestion</th>
<th>Kabam of Taste</th>
<th>Kabam of Vision</th>
<th>Kabam of Joints</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avalambagam</td>
<td>Kilethgam</td>
<td>Pothagam</td>
<td>Tharpagam</td>
<td>Santhigam</td>
</tr>
<tr>
<td>100.00%</td>
<td>31.88%</td>
<td>31.88%</td>
<td>0.00%</td>
<td>3.62%</td>
</tr>
<tr>
<td>17.60%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
<td>0.00%</td>
</tr>
</tbody>
</table>
DERANGEMENT IN EZHU UDAL KATTUGAL (SEVEN SOMATIC COMPONENTS) BEFORE AND AFTER TREATMENT

Among 138 cases, Saaram was affected in all cases (100%) which resulted in tiredness both physically and mentally. Senneer was affected in 122 cases (88.41%) which resulted in decreased hemoglobin, increased Eosinophil count, Absolute Eosinophil count, Serum IgE level. Oon, Kozhuppu, Enbu was affected in 5 cases (3.62%) which resulted in pain in upper and lower limbs. Suronitham was affected in one case (0.72%) which resulted in irregular menstrual cycle. Sukkilam was affected in 5 cases (3.62%) which resulted in Nocturnal emission. After treatment among 125 cases, saaram was affected in 3 cases (2.4%). Senneer was affected in 34 cases (27.2%). Oon, Kozhuppu, Enbu was normal in all cases. Sukkilam and Suronitham were normal in all cases.

Fig : 6.47 Derangement in ezhu udal kattugal(seven Somatic components) before and after treatment

<table>
<thead>
<tr>
<th>SEVEN SOMATIC COMPONENTS BEFORE AND AFTER TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>After Treatment</td>
</tr>
<tr>
<td>Sukkilam / Suronitham (Sperm / Ovum)</td>
</tr>
<tr>
<td>Moolai (Bone Marrow)</td>
</tr>
<tr>
<td>Enbu (Bone)</td>
</tr>
<tr>
<td>Kozhuppu (Adipose tissue)</td>
</tr>
<tr>
<td>Oone (Muscle)</td>
</tr>
<tr>
<td>Seneer (Blood)</td>
</tr>
<tr>
<td>Saaram (Chyle)</td>
</tr>
</tbody>
</table>
ENVAGAITHERVUGAL (BEFORE AND AFTER TREATMENT)

Before treatment among 138 cases Sparisam Naa, Nozhi were affected in 70 cases (50.72%) which resulted in sweating, dryness of tongue and diminished voice. Malam was affected in 10 cases (7.25%) which resulted in constipation. Moothiram was affected in 2 cases (1.45%) which resulted in burning micturition. The Nadi was Pitha Kabam in 52 cases(37.68%), Kaba Pitham in 39 cases (28.26%), Vatha Kabam in 17 cases (12.32%), Vatha Pitham in 12 cases (8.69%), Pitha Vatham in 10 cases (7.25%) and Kaba Vatham in 8 cases (5.80%).

After treatment among 125 cases Naa, Mozhi, Sparisam was affected in 3 cases (2.44%). Constipation was relieved in all 10 cases. Burning micturition was relieved in 2 cases (1.45%). The Naadi was Vatha Pitham in 26 cases (20.8%), Vatha Kabam in 8 cases (6.4%), Pitha Vatham in 21 cases (16.8%), Pitha Kabam in 39 cases (31.2%), Kaba Vatham in 4 cases (3, 2%) and Kaba Pitham 27 cases (21.6%).

Fig: 6.48 Envagaithervugal (Eight fold examinations)
TABLE NO. 4.19

DISTRIBUTION OF CASES BY NEERKURI (URINE EXAMINATIONS) BEFORE AND AFTER TREATMENT

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Neerkuri</th>
<th>No. of cases Before Treatment</th>
<th>Percentage</th>
<th>No. of Cases after treatment</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Niram (color) white</td>
<td>19</td>
<td>13.77</td>
<td>16</td>
<td>12.8</td>
</tr>
<tr>
<td>2.</td>
<td>Slight yellow (or) straw</td>
<td>105</td>
<td>76.09</td>
<td>96</td>
<td>76.8</td>
</tr>
<tr>
<td>3.</td>
<td>Yellow</td>
<td>14</td>
<td>10.14</td>
<td>13</td>
<td>10.4</td>
</tr>
<tr>
<td>3.</td>
<td>Manam (Normal odour)</td>
<td>138</td>
<td>100%</td>
<td>125</td>
<td>100%</td>
</tr>
<tr>
<td>4.</td>
<td>Nurai (Froth not present)</td>
<td>138</td>
<td>100%</td>
<td>125</td>
<td>100%</td>
</tr>
<tr>
<td>5.</td>
<td>Edai (Normal specific Gravity)</td>
<td>138</td>
<td>100%</td>
<td>125</td>
<td>100%</td>
</tr>
<tr>
<td>6.</td>
<td>Enjal (Deposits)</td>
<td>128</td>
<td>92.75</td>
<td>90</td>
<td>72</td>
</tr>
</tbody>
</table>

Among 138 cases, Nurai was not present and Manam and Edai were normal in all 138 cases (100%). In 19 cases (13.77%) the urine was white in color and transparent. In 105 cases (76.09%) the urine was straw colour. In 14 cases (10.14%) urine was yellow colour. 128 cases (92.75%) had urinary deposits.

After treatment among 125 cases, Nurai was not present and manam and Edai were normal in all cases (100%). The urine was white and transparent in 16 cases (12.8%), the urine was slight yellow or straw colour in 96 cases (76.8%), the urine was yellow colour in 13 cases (10.4%). 90 cases (72%) had urinary deposits.
DISTRIBUTION OF CASES BY NEIKURI (BEFORE AND AFTER TREATMENT)

Before treatment among 138 cases, oil spreads like a pearl shape in 105 cases (76.09%) which is Kaba Neer. In 22 cases (15.94%) oil spreads like a ring shape which is Pitha Neer. In 11 cases (7.97%) oil spreads like a serpentine which is Vaatha Neer.

After treatment among 125 cases, oil spreads like a snake shape in 17 cases (13.6%). In 39 cases (31.2%) oil spreads like a ring shape. In 69 cases (55.2%) oil spreads like a pearl shape.

**Fig: 6.49 Distribution of cases by neikuri (Before and after treatment)**
DISTRIBUTION OF CASES BY RADIOLOGICAL FINDINGS  
(BEFORE AND AFTER TREATMENT)  

Before treatment among 138 cases, 128 cases (92.75%) showed normal study in chest radiograph-PA view. Only 10 cases (7.25%) showed hyperinflated lungs in radiological findings. After treatment there was no radiological changes in the 10 cases.

CLINICAL IMPROVEMENT OF CASES BY STAGING OF ASTHMA  

Before treatment and in the first week of treatment, among 138 cases, 61 cases (44.20%) had mild intermittent Asthma. 33 cases (23.91%) had mild persistent Asthma. 30 cases (21.74%) had moderate persistent Asthma. 14 cases (10.15%) had severe persistent Asthma.

In the second week among 133 cases, 54 cases (40.60%) had mild intermittent Asthma. 24 cases (18.05%) had mild persistent Asthma. 25 cases (18.80%) had moderate persistent Asthma. 14 cases (10.52%) had severe persistent Asthma. No Wheezing in 16 cases (12.03). 5 cases (3.76%) were withdrawn from the trial.

In the third week, among 131 cases, 61 cases (46.56%) had mild intermittent Asthma. 12 cases (9.16%) had mild persistent Asthma. Another 12 cases (9.16%) had moderate persistent Asthma. 7 cases had (5.34%) severe persistent Asthma. No wheezing in 39 cases (29.78%). 2 cases (1.53) were withdrawn from the trial.

In the fourth week (at the end of treatment) 12 cases (9.6%) were in step 1 of Asthma. One case (0.8%) was in step2 of Asthma. 5 cases (4%) were in step 3 of Asthma. 4 Cases (3.2%) were in step 4 of Asthma. 6 cases (4.87%) were withdrawn from the trial. Wheezing relieved in 103 cases (82.4%)
IMPROVEMENT OF CASES IN CLINICAL FEATURES

In the first week all 138 cases (100%) had sneezing Rhinorrhoea, wheezing and tightness of chest. 123 cases (89.13%) had nocturnal episode of Asthma, 70 cases (50.72%) had sweating, dryness of tongue and drowsiness. 5 cases (3.62%) had pain in upper and lower limb. 10 cases (7.25%) had constipation. 44 cases (31.88%) had indigestion and poor appetite.

In the second week of treatment among 133 cases, 117 cases (87.97%) had sneezing, rhinorrhoea and cough with mucoid sputum. 128 cases (96.24%) had wheezing with tightness of chest. 99 cases (74.44%) had Nocturnal Asthma, 53 cases (39.85%) had sweating, dryness of tongue and drowsiness. 4 cases (3.01%) had pain in upper and lower limbs. 6 cases (4.51%) had constipation. 32 cases (24.06%) had poor appetite and indigestion.
In third week of treatment among 131 cases, 78 cases (59.54%) had sneezing, rhinorrhoea, and cough with mucoid sputum, 92 cases (70.23%) had wheezing and tightness of chest, 53 cases (40.46%) had Nocturnal wheezing, 24 cases (18.32%) had sweating, dryness of tongue and drowsiness, 3 cases (2.29%) had pain in upper and lower limbs. 2 cases (1.53%) had constipation. (8.40%) 11 cases had indigestion and poor appetite.

In fourth week out of 125 cases, 3 cases (2.4%) had sneezing and rhinorrhoea, 4 cases (3.2%) had cough with mucoid sputum, and 22 cases (17.6%) had wheezing and tightness of chest. 4 cases (3.2%) had Nocturnal wheezing, 3 cases (2.4%) had sweating, dryness of tongue and drowsiness. Pain in upper and lower limb reduced in all cases, constipation, indigestion and poor appetite reduced in all cases.
Fig: 6.51 Improvement of cases in clinical features

Improvement of Cases in Clinical Features

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>0 Day &amp; I Week</th>
<th>II Week</th>
<th>III Week</th>
<th>IV Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sneezing &amp; Rhinorrhoea</td>
<td>100.00%</td>
<td>100.00%</td>
<td>100.00%</td>
<td>100.00%</td>
</tr>
<tr>
<td>Cough with Mucoid Sputum</td>
<td>89.13%</td>
<td>50.72%</td>
<td>50.72%</td>
<td>50.72%</td>
</tr>
<tr>
<td>Wheezing Tightness of Chest</td>
<td></td>
<td>3.62%</td>
<td>7.25%</td>
<td>31.88%</td>
</tr>
<tr>
<td>Nocturnal awakening</td>
<td>87.96%</td>
<td>39.85%</td>
<td>39.85%</td>
<td>39.85%</td>
</tr>
<tr>
<td>Sweating</td>
<td>96.24%</td>
<td>74.44%</td>
<td>39.85%</td>
<td>39.85%</td>
</tr>
<tr>
<td>Dryness of Tongue</td>
<td>74.44%</td>
<td>39.85%</td>
<td>39.85%</td>
<td>39.85%</td>
</tr>
<tr>
<td>Drowsiness</td>
<td></td>
<td>3.62%</td>
<td>7.25%</td>
<td>31.88%</td>
</tr>
<tr>
<td>Eczema</td>
<td>59.54%</td>
<td>18.32%</td>
<td>18.32%</td>
<td>18.32%</td>
</tr>
<tr>
<td>Associated Symptoms (Joint Pain etc)</td>
<td>17.60%</td>
<td>3.20%</td>
<td>2.40%</td>
<td>2.40%</td>
</tr>
<tr>
<td>Constipation</td>
<td>51.82%</td>
<td>9.54%</td>
<td>9.54%</td>
<td>9.54%</td>
</tr>
<tr>
<td>Indigestion, poor appetite</td>
<td>2.40%</td>
<td>2.40%</td>
<td>2.40%</td>
<td>2.40%</td>
</tr>
</tbody>
</table>

[156]
IMPROVEMENT OF CASES IN ACQ

(BEFORE AND AFTER TREATMENT)

Inference:

Before treatment among 138 cases, in 130 cases (94.20%) wheezing not controlled and in 8 cases (5.80%) wheezing reasonably well controlled.

After treatment among 125 cases wheezing not controlled in 9 cases (7.2%), reasonably well controlled in 40 cases (32%), under control in 76 cases (60.80%).

Fig: 6.52 Improvement of cases in ACQ

(Before and after treatment)
IMPROVEMENT OF CASES IN PEAK EXPIRATORY FLOW RATE (MORNING HOURS)

Among 133 cases in the first week of treatment the PEFR was above 80% in 12 cases (9.02%), 60% - 80% in 71 cases (53.38%), below 60% in 50 cases (37.60%) in the morning hours.

Among 133 cases in the second week of treatment the PEFR was above 80% in 51 cases (38.35%), 60% - 80% in 54 cases (40.60%) was below 60% in 28 cases (21.05%).

Among 131 cases in the third week of treatment the PEFR was above 80% or normal in 77 cases (58.78%), 60% - 80% in 39 cases (29.77%) below 60% in 15 cases (11.45%).

Among 125 cases in the Fourth week of treatment the PEFR was above 80% or normal in 95 cases (76%), 60% - 80% in 20 cases (16%), below 60% in 10 cases (8%)

Fig: 6.53 Improvement of cases in peak expiratory flow rate (morning)
IMPROVEMENT OF CASES IN PEAK EXPIRATORY FLOW RATE (EVENING HOURS)

Among 133 cases in the first week of treatment the PEFR was above 80% in 40 Cases (30.08%), 60% - 80% in 58 cases (43.60%), below 60% in 35 cases (26.32%) in the evening hours.

Among 133 cases in the second week of treatment the PEFR was above 80% in 82 cases (61.65%), 60% to 80% in 38 cases (28.57%), below 60% in 13 cases (9.78%).

Among 131 cases in the third week of treatment the PEFR was above 80% in 96 cases (73.28%), 60% to 80% in 22 cases (16.80%), below 60% in 13 cases (9.92%).

Among 125 cases in the fourth week of treatment the PEFR was 80% in 106 cases (84.80%), 60% to 80% in 12 cases (9.60%) below 60% in 7 cases (5.60%).

Fig: 6.54 Improvement of cases in peak expiratory flow rate (evening)
Primary outcome is measured by clinical improvement of cases. Among 125 cases, 110 cases (88%) were improved from step 4 or step 3 to step 2 or step 1 or normal which is good response. 5 cases (4%) were improved from step 4 to step 3 which is Moderate response. 10 cases (8%) were not improved from clinical symptoms which is poor response.

**Fig: 6.55 Primary outcomes by clinical features**
PRIMARY OUTCOME BY PEAK EXPIRATORY FLOW RATE

(Morning Hours)

Inference:

Among 125 cases Morning PEFR increased from 60% to 80% and below 60% to 80% and above in 65 cases (52%) which is good response. PEFR increased from below 60% to 60-80% in 44 cases (35.2%) which is moderate response. In 16 cases (12.8%) PEFR not increased during the treatment period which is poor response.

Fig: 6.56 primary outcomes by peak expiratory flow rate

(Morning hours)
PRIMARY OUTCOME BY PEAK EXPIRATORY FLOW RATE

(Evening Hours)

Inference:

Among 125 cases, evening PEFR increased from 60% to 80% and below 60% to 80% and above in 106 cases (84.8%) which is good response. PEFR increased from below 60% to 60% - 80% in 7 cases (5.6%) which is moderate response. In 12 cases (9.6%) PEFR not increased in the evening hours during the treatment period, which is poor response.

Fig: 6.57 Primary outcomes by peak expiratory flow rate

(Evening hours)
SECONDARY OUTCOME BY LAB ASSISTANT
(BEFORE AND AFTER TREATMENT)

Inference:

Among 138 cases, before treatment ESR increased in 30 (21.74%) cases, Eosinophil increased in 29 (21.01%) cases, AEC increased in 32(23.19%) cases and serum IgE increased in 122 (88.41%) cases.

After treatment ESR raised in 8 (6.4%) cases and Eosionophil elevated in 9 (7.2%) cases and AEC raised in 5 (4%) cases and serum IgE increased in 34 (27.2%) cases.

Fig: 6.58 Secondary outcome by lab assistant
(Before and after treatment)
Fig: 6.59 Overall Efficacy of the study drug on clinical features, ACQ, PEFR (Morning) and PEFR (Evening)
TABLE NO: 4.20 RESULTS OF HEMATOLOGICAL PARAMETERS (BEFORE AND AFTER TREATMENT)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Treatment days</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>t- value</th>
<th>p- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total count cells/cu.mm</td>
<td>Day 0</td>
<td>7847.1</td>
<td>1931.99</td>
<td>0.00194</td>
<td>0.474</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>7471.62</td>
<td>1751.33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polymorphs in %</td>
<td>Day 0</td>
<td>58.8478</td>
<td>12.2539</td>
<td>0.22</td>
<td>0.4133</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>57.992</td>
<td>8.9914</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocytes in %</td>
<td>Day 0</td>
<td>33.876</td>
<td>8.99834</td>
<td>0.05527</td>
<td>0.4783</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>35.136</td>
<td>7.511</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monocytes in %</td>
<td>Day 0</td>
<td>2.08955</td>
<td>1.3346</td>
<td>0.03</td>
<td>0.4868</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>2.448</td>
<td>1.8641</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total RBC (milli/µL)</td>
<td>Day 0</td>
<td>4.9818</td>
<td>0.5266</td>
<td>0.05171</td>
<td>0.4794</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>4.9352</td>
<td>0.4711</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hb in g/dL</td>
<td>Day 0</td>
<td>13.8377</td>
<td>1.85917</td>
<td>0.474</td>
<td>0.41401</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>13.7016</td>
<td>1.65388</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCT/PCV%</td>
<td>Day 0</td>
<td>42.3565</td>
<td>4.79685</td>
<td>0.14609</td>
<td>0.442</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>41.9632</td>
<td>4.47802</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCV (ft)</td>
<td>Day 0</td>
<td>83.2268</td>
<td>8.9157</td>
<td>0.47376</td>
<td>0.318</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>83.56</td>
<td>5.1801</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>Day 0</td>
<td>27.5043</td>
<td>2.4516</td>
<td>0.48748</td>
<td>0.3133</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>27.42</td>
<td>2.3685</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCHC (g/dl)</td>
<td>Day 0</td>
<td>32.5933</td>
<td>1.90193</td>
<td>0.49211</td>
<td>0.31178</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>32.5424</td>
<td>1.9312</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelet Count(lkhs/µl)</td>
<td>Day 0</td>
<td>3.3253</td>
<td>3.53644</td>
<td>0.1444</td>
<td>0.4426</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>3.004</td>
<td>0.82005</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
A paired sample t test was conducted to compare the hematological parameters before and after treatment. There were significant difference in scores for total WBC count before and after treatment p=<0.474.

There were no significant difference in scores for polymorphs, before and after treatment p=<0.4133. There were no significant difference in scores for Lymphocytes before and after treatment p=<0.4783.

There were no significant difference in scores for Monocytes before and after treatment p=<0.4868. There were no significant difference in scores for total RBC count before and after treatment p=<0.4794.

There were no significant difference in scores for Hemoglobin before and after treatment p=<0.41401. There were no significant difference in scores for HCT/PCV before and after treatment p=<0.4442.

There were no significant difference in scores for MCV before and after treatment p=<0.318. There were no significant difference in scores for MCH before and after treatment p=<0.3133.

There were no significant difference in scores for MCHC before and after treatment p=<0.31178. There were no significant difference in scores for Platelet count before and after treatment p=<0.4426.
**TABLE NO: 4.21 RESULTS OF EOSINOPHIL, ESR, AEC AND SERUM IgE BEFORE AND AFTER TREATMENT**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Treatment days</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>t-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eosinophil in %</strong></td>
<td>Day 0</td>
<td>5.28261</td>
<td>2.502</td>
<td>0.05601</td>
<td>0.4778</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>4.808</td>
<td>2.231</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ESR in mm(30 Minutes)</strong></td>
<td>Day 0</td>
<td>5.9927</td>
<td>5.97378</td>
<td>0.371</td>
<td>0.377</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>5.8</td>
<td>4.022</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ESR in mm(60 Minutes)</strong></td>
<td>Day 0</td>
<td>13.3551</td>
<td>12.2539</td>
<td>0.411</td>
<td>0.411</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>12.68</td>
<td>8.19</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>AEC (cells/cu.mm)</strong></td>
<td>Day 0</td>
<td>371.0869</td>
<td>250.3634</td>
<td>0.000627</td>
<td>0.499</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>310.352</td>
<td>117.504</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Serum IgE Level (IU/ML)</strong></td>
<td>Day 0</td>
<td>845.4734</td>
<td>756.37</td>
<td>1.705</td>
<td>0.045</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>653.079</td>
<td>606.97</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values represent Mean ± SEM. *P < 0.05 as compared to before treatment groups.

A paired sample t test was conducted to compare the Eosinophil count, Absolute Eosinophil count, ESR and Serum IgE level before and after treatment. There were no significant difference in scores for Eosinophil count before and after treatment p=0.4778. There were no significant difference in scores for ESR for 30 minutes before and after treatment p=0.377. There were no significant difference in scores for ESR 1 hour before and after treatment p=0.411.
There were significant difference in scores for Absolute Eosinophil count before and after treatment \( p = <0.499 \). There were significant difference in scores for Serum IgE level before and after treatment \( p = <0.045 \).

**TABLE NO: 4.22 RESULTS OF BLOOD SUGAR BEFORE AND AFTER TREATMENT**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Treatment days</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>t-value</th>
<th>p-value One-tailed probability (right tail):</th>
<th>p-value One-tailed probability (left tail):</th>
<th>p-value two-tailed probability (right tail):</th>
</tr>
</thead>
<tbody>
<tr>
<td>FBS (mg/dl)</td>
<td>Day 0</td>
<td>91.8768</td>
<td>9.4902</td>
<td>0.3539</td>
<td>0.36194</td>
<td>0.6380</td>
<td>0.723</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>91.696</td>
<td>10.3380</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPBS (mg/dl)</td>
<td>Day 0</td>
<td>117.007</td>
<td>11.858</td>
<td>0.1316</td>
<td>0.448</td>
<td>0.5522</td>
<td>0.8954</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>118.192</td>
<td>10.591</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\*P < 0.05 as compared to before treatment groups

Values represent Mean ± SEM.

A paired sample t test was conducted to compare the Fasting blood sugar and Post prandial blood sugar before and after treatment. There were no difference in scores for Fasting Blood Sugar before and after treatment \( p = <0.723 \). There were no significant difference in scores for Postprandial Blood Sugar before and after treatment \( p = <0.8954 \).
TABLE NO:4.23 RESULTS OF LIPID PROFILE BEFORE AND AFTER TREATMENT

<table>
<thead>
<tr>
<th>Variables</th>
<th>Treatment day</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>t-value</th>
<th>p-value One-tailed probability (right tail):</th>
<th>p-value One-tailed probability (left tail):</th>
<th>p-value two-tailed probability (right tail):</th>
</tr>
</thead>
<tbody>
<tr>
<td>T.Cho (mg/dl)</td>
<td>Day 0</td>
<td>183.25</td>
<td>35.50</td>
<td>0.0475</td>
<td>0.1688</td>
<td>0.8311</td>
<td>0.3376</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>179.592</td>
<td>33.473</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL(mg/dl)</td>
<td>Day 0</td>
<td>38.586</td>
<td>5.172</td>
<td>0.3801</td>
<td>0.3521</td>
<td>0.647</td>
<td>0.7043</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>38.568</td>
<td>5.821</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL(mg/dl)</td>
<td>Day 0</td>
<td>98.572</td>
<td>17.41</td>
<td>0.4142</td>
<td>0.33968</td>
<td>0.6603</td>
<td>0.6793</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>98.432</td>
<td>19.588</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VLDL (mg/dl)</td>
<td>Day 0</td>
<td>22.03</td>
<td>11.38</td>
<td>0.3583</td>
<td>0.36029</td>
<td>0.6397</td>
<td>0.725</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>22.416</td>
<td>10.88</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TGL (mg/dl)</td>
<td>Day 0</td>
<td>109.391</td>
<td>56.114</td>
<td>0.0116</td>
<td>0.99</td>
<td>0.161</td>
<td>0.838</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>101.936</td>
<td>39.3429</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*P < 0.05 as compared to before treatment groups. Values represent Mean ± SEM.

A paired sample t test was conducted to compare the Lipid profile before and after treatment. There were no significant differences in scores for lipid profile before and after treatment treatment.
**TABLE NO: 4.24 RESULTS OF RENAL FUNCTION TEST BEFORE AND AFTER TREATMENT**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Treatment day</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>t-value</th>
<th>p-value One-tailed probability (right tail):</th>
<th>p-value One-tailed probability (left tail):</th>
<th>p-value two-tailed probability (right tail):</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea (mg/dl)</td>
<td>Day 0</td>
<td>18.159</td>
<td>4.0960</td>
<td>0.0842</td>
<td>0.4664</td>
<td>0.533</td>
<td>0.9329</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>18.712</td>
<td>3.930</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>Day 0</td>
<td>0.735</td>
<td>0.0926</td>
<td>0.1518</td>
<td>0.4397</td>
<td>0.56</td>
<td>0.8794</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>0.7496</td>
<td>0.1299</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uric Acid (mg/dl)</td>
<td>Day 0</td>
<td>4.5985</td>
<td>1.296</td>
<td>0.1915</td>
<td>0.4242</td>
<td>0.5757</td>
<td>0.8484</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>5.4752</td>
<td>11.578</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*P < 0.05 as compared to before treatment groups. Values represent Mean ± SEM.

A paired sample t test was conducted to compare the renal function test before and after treatment. There were no significant difference in scores for Blood urea before and after treatment p=0.9329. There were no significant difference in scores for Creatinine before and after treatment p=0.8794. There were no significant difference in scores for Uric acid before and after treatment p=0.8484.
### TABLE NO: 4.25 RESULTS OF LIVER FUNCTION TEST BEFORE AND AFTER TREATMENT

<table>
<thead>
<tr>
<th>Variables</th>
<th>Treatment day</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>t-value</th>
<th>p-value One-tailed probability (right tail):</th>
<th>p-value One-tailed probability (left tail):</th>
<th>p-value two-tailed probability (right tail):</th>
</tr>
</thead>
<tbody>
<tr>
<td>T.bili (mg/dl)</td>
<td>Day 0</td>
<td>0.7094</td>
<td>0.563</td>
<td>0.1907</td>
<td>0.4245</td>
<td>0.5754</td>
<td>0.849</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>0.6696</td>
<td>0.249</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. bili (mg/dl)</td>
<td>Day 0</td>
<td>0.247</td>
<td>0.109</td>
<td>0.2950</td>
<td>0.38422</td>
<td>0.61577</td>
<td>0.768</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>0.24</td>
<td>0.0975</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I.bili (mg/dl)</td>
<td>Day 0</td>
<td>0.411</td>
<td>0.197</td>
<td>0.1003</td>
<td>0.46008</td>
<td>0.53991</td>
<td>0.92017</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>0.4368</td>
<td>0.1784</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SGOT (IU/L)</td>
<td>Day 0</td>
<td>20.9927</td>
<td>7.455</td>
<td>0.2078</td>
<td>0.4178</td>
<td>0.5821</td>
<td>0.8356</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>20.136</td>
<td>6.4873</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SGPT (IU/L)</td>
<td>Day 0</td>
<td>20.861</td>
<td>9.110</td>
<td>0.4470</td>
<td>0.3277</td>
<td>0.6722</td>
<td>0.655</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>20.56</td>
<td>7.75262</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alk. Phos (IU/L)</td>
<td>Day 0</td>
<td>88.340</td>
<td>23.266</td>
<td>0.2542</td>
<td>0.399</td>
<td>0.6001</td>
<td>0.7996</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>87.328</td>
<td>20.2726</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>Day 0</td>
<td>10.717</td>
<td>0.7564</td>
<td>0.4708</td>
<td>0.31923</td>
<td>0.68079</td>
<td>0.6384</td>
</tr>
<tr>
<td>Ca (mg/dl)</td>
<td>Day 30</td>
<td>10.75624</td>
<td>0.74505</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phos (mg/dl)</td>
<td>Day 0</td>
<td>3.3775</td>
<td>0.4654</td>
<td>0.4408</td>
<td>0.3299</td>
<td>0.67</td>
<td>0.6599</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>3.3616</td>
<td>0.3141</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T. protein (g/dl)</td>
<td>Day 0</td>
<td>6.6789</td>
<td>0.655</td>
<td>0.4316</td>
<td>0.3339</td>
<td>0.66</td>
<td>0.6786</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>6.7096</td>
<td>0.65935</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>Day 0</td>
<td>4.1427</td>
<td>0.5179</td>
<td>0.3044</td>
<td>0.38064</td>
<td>0.6193</td>
<td>0.7612</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>4.12</td>
<td>0.42634</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Globulin (g/dl)</td>
<td>Day 0</td>
<td>2.605</td>
<td>0.5570</td>
<td>0.0423</td>
<td>0.4831</td>
<td>0.5168</td>
<td>0.966</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>2.7032</td>
<td>0.53339</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*P < 0.05 as compared to before treatment groups Values represent Mean ± SEM.
A paired sample t test was conducted to compare the Liver function test before and after treatment. There were no significant difference in scores for total bilirubin before and after treatment $p=0.849$. There were no significant difference in scores for Direct bilirubin before and after treatment $p=0.768$. There were no significant difference in scores for Indirect bilirubin before and after treatment $p=0.92017$. There were no significant difference in scores for SGOT before and after treatment $p=0.8356$. There were no significant difference in scores for SGPT before and after treatment $p=0.655$. There were no significant difference in scores for Alkaline phosphatase before and after treatment $p=0.7996$.

There were no significant difference in scores for Calcium before and after treatment $p=0.6384$. There were no significant difference in scores for Phosphorus before and after treatment $p=0.6599$. There were no significant difference in scores for total protein before and after treatment $p=0.6786$. There were no significant difference in scores for Albumin before and after treatment $p=0.7612$. There were no significant difference in scores for Globulin before and after treatment $p=0.966$. 
TABLE NO: 4.26 STATISTICAL ANALYSIS FOR PEAK EXPIRATORY FLOW RATE (Morning Hours)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Week</td>
<td>269.318182</td>
<td>77.029222</td>
</tr>
<tr>
<td>II Week</td>
<td>310.871212</td>
<td>82.2175856</td>
</tr>
<tr>
<td>III Week</td>
<td>348.923077</td>
<td>88.1418532</td>
</tr>
<tr>
<td>IV Week</td>
<td>390.12</td>
<td>99.9041153</td>
</tr>
</tbody>
</table>

A paired sample t test was conducted to compare the Peak expiratory flow rate of morning hours for starting and end of treatment. There were significant difference in scores for Peak expiratory flow rate of first week and fourth week of treatment and the P –value is <.00001, the t- value is (-9.71747.). The result is significant at p <.05 for Peak expiratory flow rate of morning hours.

TABLE NO: 4.27 STATISTICAL ANALYSIS FOR PEAK EXPIRATORY FLOW RATE (Evening Hours)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>I Week</td>
<td>300.3076903</td>
<td>80.88597067</td>
</tr>
<tr>
<td>II Week</td>
<td>343.000</td>
<td>87.99136674</td>
</tr>
<tr>
<td>III Week</td>
<td>381.434108</td>
<td>96.93585548</td>
</tr>
<tr>
<td>IV Week</td>
<td>423.28</td>
<td>108.553301</td>
</tr>
</tbody>
</table>

A paired sample t test was conducted to compare the Peak expiratory flow rate for starting and end of treatment. There were significant difference in scores for Peak expiratory flow rate of first week and fourth week of treatment and the P –value is <.00001, the t- value is (-10.49023.). The result is significant at p <.05 for Peak expiratory flow rate of evening hours.
### TABLE NO: 4.20 SPIROMETRY RESULTS BEFORE AND AFTER TREATMENT

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before</th>
<th>% pred</th>
<th>After</th>
<th>% pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>3.378 ± 0.079</td>
<td>65.35±2.12</td>
<td>3.385±0.078</td>
<td>64.11±2.03</td>
</tr>
<tr>
<td>FEV1(L)</td>
<td>2.871 ± 0.068</td>
<td>64.72±2.33</td>
<td>2.883±0.066</td>
<td>83.81*±0.93</td>
</tr>
<tr>
<td>FEV3(L)</td>
<td>2.8 ± 0.057</td>
<td>93.04±3.399</td>
<td>2.816±0.0560</td>
<td>86.52±2.16</td>
</tr>
<tr>
<td>FEF 25-75%(L/sec).</td>
<td>3.44 ± 0.05</td>
<td>63.74±2.44</td>
<td>3.4468±0.059</td>
<td>66.10±2.43</td>
</tr>
<tr>
<td>FEF0.2-1.2 (L/sec)</td>
<td>6.36±0.123</td>
<td>55.48±2.068</td>
<td>6.32±0.123</td>
<td>55.5±2.044</td>
</tr>
<tr>
<td>PEFR (L/sec).</td>
<td>7.632 ± 0.134</td>
<td>59.52±1.82</td>
<td>7.7656±0.149</td>
<td>61.70±1.95</td>
</tr>
<tr>
<td>FEF 25%..</td>
<td>7.077 ± 0.0985</td>
<td>47.89±1.80</td>
<td>7.03±0.1070</td>
<td>48.80±1.91</td>
</tr>
<tr>
<td>FEF 50%..</td>
<td>4.368 ± 0.080</td>
<td>54.68±2.08</td>
<td>4.323±0.079</td>
<td>57±2.09</td>
</tr>
<tr>
<td>FEF 75%..</td>
<td>2.08 ± 0.054</td>
<td>70.80±3.31</td>
<td>2.046±0.054</td>
<td>74.49±3.24</td>
</tr>
<tr>
<td>FEV3% L</td>
<td>2.8 ± 0.057</td>
<td>93.04±3.39</td>
<td>2.816±0.056</td>
<td>86.52*±2.16</td>
</tr>
<tr>
<td>MVV 3%(L/min).</td>
<td>122.23 ± 2.50</td>
<td>38.409±1.27</td>
<td>120.66±2.682</td>
<td>39.18±1.21</td>
</tr>
</tbody>
</table>

*P < 0.05 as compared to before treatment groups, Values represent Mean ± SEM.

After treatment the percentage predicted values of FEV1 (L) was higher than that of before treatment and it was statistically significant. Similarly the percentage predicted values of FEF25-75%(L/sec), PEFR(L/sec), FEF 25%.. FEF 50%.. FEF 75% and MVV 3%(L/min) were increased after treatment.
<table>
<thead>
<tr>
<th>Variables</th>
<th>Treatment Days</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sneezing, Running nose</td>
<td>Day 0</td>
<td>1.000</td>
<td>0.0000</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>0.024</td>
<td>0.1536</td>
</tr>
<tr>
<td>Cough with Mucoid Sputum</td>
<td>Day 0</td>
<td>1.000</td>
<td>0.0000</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>0.024</td>
<td>0.0536</td>
</tr>
<tr>
<td>Tightness of Chest, Wheezing</td>
<td>Day 0</td>
<td>1.000</td>
<td>0.0000</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>0.176</td>
<td>0.3834</td>
</tr>
<tr>
<td>Nocturnal Wheezing with insomnia</td>
<td>Day 0</td>
<td>0.890</td>
<td>0.3124</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>0.032</td>
<td>0.1767</td>
</tr>
<tr>
<td>Dryness of Tongue, Sweating, Drowsiness</td>
<td>Day 0</td>
<td>0.510</td>
<td>0.5017</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>0.024</td>
<td>0.1537</td>
</tr>
<tr>
<td>Associated Symptoms (Joint Pain)</td>
<td>Day 0</td>
<td>0.036</td>
<td>0.1875</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>0.000</td>
<td>0.0000</td>
</tr>
<tr>
<td>Constipation</td>
<td>Day 0</td>
<td>0.072</td>
<td>0.2602</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>0.000</td>
<td>0.0000</td>
</tr>
<tr>
<td>Indigestion, Loss of Apetite</td>
<td>Day 0</td>
<td>0.320</td>
<td>0.4677</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>0.000</td>
<td>0.0000</td>
</tr>
</tbody>
</table>
While developing a new herbal drug formulation it is must to have the related information of that particular drug including its organoleptic characters to phytochemical constituents to pharmacological action to its standardization in respect to various parameters via various methods. Standardization is essential for Global acceptance, documentation, industrial scale production, prevent contamination, assess the quality of raw drug and finished product, estimate the amount of active component, achieve batch to batch constancy of finished product.

**Organoleptic characters**

Aadathodai Choornam was light brown coloured very fine powder and characteristic odour, bitter taste and completely pass in Sieve No.100.

**Physicochemical Evaluation**

**Loss on drying**

Loss on drying showed the total volatile content and moisture content of sample. High moisture contents may affect the feature of the drug. Low moisture content could get stability and better shelf life. In the trial drug the loss on drying at 105°C is 11.16% which is within the limits. It may be due to the presence of volatile component (resin of *Styrax benzoin dryand*) in the Aadathodai chooranam. The sublimate of *Styrax benzoin dryand* in the Adhathodai Chooranam has antiseptic action, so it may not affect the drug.
Ash Values

Ash value depends upon the inorganic matters present in the particular drug. Ash value is a effective parameter to assess the degree of purity of a drug. A high ash value denotes contamination, substitution and adulteration of the crude drugs. The ash value of Aadhathodai chooranam is 7.90% which is within the limits and it correlates with the inorganic substances Ammonium, Chloride, Iron and Phosphate of test drug through the phyto chemical analysis. The acid insoluble ash value of the drug denotes the amount of siliceous matter in the plant. The quality of the drug is good if the acid insoluble value is low. It is 2.5% for Aadhathodai chooranam. The value was below the specified limit, indicates that plant material had a minimal sand and silica contamination which are safe to use as internal medicine.

Extractive values

They are the approximate amount of the chemicals present in the raw drug. The percentage of soluble matters in the drug is estimated by the water extractive and ethanol extractive values. Based on the extractive value proper solvent can be selected. It gives the percentage of drug which will correlate to the metabolism reactions. Water soluble extractive value plays a important role in evaluation of crude drugs. The alcohol soluble extractive value was the same use like the water soluble extractive value.

Preliminary Phytochemical Screening

Qualitative tests were done to find the functional groups. The study revealed the presence of Chloride, Phosphate, ammonium, iron, Alkaloids, flavonoids, Glycosides, terpene, saponins, Amino acids, Phenol, Tannins, Quinones, Lignans, Steroids in the Adathodai Chooranam. As per Literature review these phytochemicals are presented in the ingredients of
Adhathoodai Choornam. The phytochemical analysis results give additional support to its use in clinical trial with potent antioxidant, anti inflammatory, anti histaminic, anti spasmodic, immunomodulator and bronchodilator action.\textsuperscript{79}

**Heavy Metal Analysis**

Heavy Metals may be present in crude drugs by atmospheric pollution and soil. Moreover minerals and metals are used in preparing indigenous formulations. However, heavy metals have been related with adverse reactions, heavy metals need to be detected in formulations.\textsuperscript{75} The result showed that the Aadhathodai Chooranam was below the WHO/FDA permissible limits of Heavy metals and safe for consumption (Pb:1.77 mg/kg,Cd:0.25 mg/kg,As:0.25 mg/kg,Hg:0.25 mg/kg).

**Microbial load and Aflatoxin Content of Aadathodai Chooranam**

Plant matters carry bacteria and moulds often originating in soil or after final drug preparation.\textsuperscript{80} In Aadhathodai Chooranam the total bacterial count was within the prescribed limit(79,000 CFU/g). Total fungal count was also within the permissible limit(<10CFU/g). AlfatoxinB1, B2, G1, G2 were within the specified limits BLQ (LOQ:0.50µg/Kg).\textsuperscript{75} This indicates that the proper hygiene followed during the preparation of drug and packing which are need to establish the quality at finished product level.

**HPTLC FINGER PRINT PROFILE**

Chromatographic study (HPTLC) was carried out in 254 nm and 520 nm UV to establish the fingerprinting profile and to show the possibly active phytochemical constituents. In 254 nm UV the peak corresponds to the Rf values 0.35 has maximum peak area of 12446.9 Au. This 6\textsuperscript{th}
peak (area % is 48.98%) is a Marker. Phyto components with 0.20, 0.35, 0.54, 0.63, 0.89 95th, 6th, 7th, 8th, 10th show the possibly active phyto constituents. In 520 nm UV the peak similar to the Rf value 0.35 has highest peak area of 13576.3 AU. This 9th Peak (area % is 41.27%) could serve as a Marker. Phyto components with Rf values 0.01, 0.35, 0.76, 0.81, 0.89 (1st, 9th, 13th, 14th, 15th peaks) in Aadhathodai Chooranam are responsible for expression of its pharmacological and therapeutic actions.

1,2-Benzenedicarboxylic acid, butyl 2- methyl propyl ester indicates α Glucosidase inhibition and the invivohypoglycemic effect and antimicrobial activity. 81 8-octadecenoic acid, methyl ester, (E) indicates Antioxidant and Anti microbial Activity 82 Heptadecanoic acid, 16 methyl; methyl ester are having the property of antioxidant and anti microbial. 83 Heptadecanoic acid have the hypocholerolemic lubricant, anti androgenic, hemolytic 5 - Alpha reductase inhibitor effect. 84 E)-9-Octadecanoic acid ethyl ester revealed that anti inflammatory, Cancer preventive, dermatigenic, hypocholesterolemic, 5-Alpha reductase inhibitor and anti androgenic effect. 84 Methyl tetradecanoate revealed that Antioxidant, Cancer preventive, hypocholesterolenic, lubricant, Nematinocide activity. 85

**DISCUSSION FOR TOXICITY STUDIES:**

The preclinical toxicity studies are essential for determining safe dose for human use. To evaluate the safety profile of Adathodai Chooranam, acute and long term toxicity studies were performed. Adathodai Chooranam did not produce any toxic symptoms or mortality at the dose level of 2.6 gm/kg body weight for 14 days. In Long Term toxicity study no behavioural abnormalities or death was observed during the whole treatment period. Long term toxicity studies assess the undesirable effect of repeated exposure of plant extracts over a portion of the
average life span of laboratory animals, like rodents. Specifically they provide details on target organ toxicity and are designed to found no observable adverse effect level.\textsuperscript{86} Since the liver and Kidneys are the main organs of Metabolism and Excretion, they are affected by potentially toxic agents and their functions should be monitored in Long term studies. Food consumption was important in the safety of a product with therapeutic purpose as proper intake of nutrients essential to the physiological condition of the animals and to the accomplishment of the correct response to the drug tested instead of a false response due to improper nutritional status.\textsuperscript{87} A uniform increase in food intake was observed in all the test drug administered groups when compared to control group during the treatment period of 28 days. On the basis of literature review of trial drug, most of the ingredients are having potent stomachic, stimulant and antioxidant action.\textsuperscript{79} Therefore the observed increase in food intake may be due to the increased appetite. The body weight changes serve as a sensitive indication of the general health status of animals.\textsuperscript{88} There was no weight changes on 7\textsuperscript{th} day, 14\textsuperscript{th} day, 21\textsuperscript{st} day and 28\textsuperscript{th} day in all test drug administered groups when compared to control group.

Evaluation of hematological parameters can be used to determine the extent of the deleterious effect of Adathodai Chooranam on the experimental animal. There was a moderate significant decrease among all groups of experimental animals in RBC Count. But there was no difference between control and therapeutic dose group. No difference was observed in other hematological parameters like Total WBC Count, Differential Count, Hemoglobin and Platelets. There were no significant alterations in Heamatological Parameters which indicate that Adathodai Chooranam did not affect blood cells production.

The clinical biochemistry analysis was made to evaluate the possible alterations in hepatic and renal functions induced by the test drug. Liver and Kidney function test is important
in the toxicity study of drugs and plant extracts as they are both essential for the survival of an organism. In the present study there was significant differences observed in blood sugar, total cholesterol, triglycerides in all groups of animals. But there was no difference between control and therapeutic dose group.

Moderate significant difference was observed in urea level between therapeutic dose and control groups, but the difference was within the normal expected range for the rat species used in this study which might be due to incidental. Total protein measurements can reflect nutritional status and may be used to screen for and help diagnose kidney and liver disease and many other conditions. There were no significant changes in total protein in rats treated with Adathodai Chooranam, which suggested that there was no sign of impaired renal function. No difference in Creatinine level was observed among all groups of experimental animals. The drug had no adverse effect on the concentration of creatinine. Moderate significant difference among all groups of experimental animals on Albumin level. But there is no difference between therapeutic and control group. There was difference among all groups of experimental animals on globulin and no difference between therapeutic dose and control groups.

Transaminases (SGOT and SGPT) are good indicators of liver function and bio markers to predict the possible toxicity of drugs. There were no significant changes in the SGPT, SGOT and serum bilirubin level between the therapeutic and control group which revealed that Adathodai Chooranam did not affect Liver Function. The normal levels of serum bilirubin concentrations at all doses of the adathodai chooranam used in this study are indicative of non adverse effect of the test drug on hemoglobin metabolism pathways.
Absolute terminal organ weight and percent relative organ weight indicative of test drug caused changes in target organs, phospholipid metabolism, secretion of enzymes and hormones hypo/hyperplasia, and possible tissue necrosis.\textsuperscript{90} There was no difference in weight of Heart, Lungs, Kidney and Brain in all groups of animals. There was significant difference among different group of experimental animals on weight of Liver, Spleen, Stomach, Male Sex Organ and Female Sex organs. However there was no difference between therapeutic dose and control groups.

Histopathological studies showed normal architecture in therapeutic dose and control groups. Only the Liver has shown congestion and spleen has shown slightly hyperplastic. These mild changes are not considered as a toxic effect because the hematological, biochemical parameters and organs weight showed no significant changes between therapeutic and control group. Subsequently clinically the trial drug Adathodai chooranam did not produce any adverse drug reactions and the hematological, biochemical parameters were within the normal range after treatment in all 125 cases.

Histopathological result of stomach showed focal hyperplasia in non glandular area of stomach in 5x therapeutic dose male group. The focal hyperplasia may be related with stress induced because of repeated drug administration.\textsuperscript{91,92} 5x therapeutic female group and 10x therapeutic female group exhibited hyperplasia and Squamous metaplasia in uterus. As per the literature evidence diffuse or focal (polypoid) hyperplasia of the endometrium is a spontaneous change in laboratory animals particularly in age advances. Hyperplasia is age related decline in sex hormone levels in which there is often relative excess estrogen. Administration of exogenous estrogens and other xenobiotics with estrogenic effects produces endometrial hyperplasia in both laboratory animals and in woman.\textsuperscript{93} Histopathological result of kidney showed mild tubular
epithelial cell degeneration in 10x therapeutic dose male group and the histopathological result of liver showed mild vacuolar degeneration. In the trial drug Adathodai Chooranam, one of the herbal ingredients is the seeds of embelia ribes. As per the literature survey administration of embelin at lower dose for short duration did not induce deleterious effect but its long term administration at higher dose was toxic with the following pathological changes. The liver showed hepatic congestion characterized by enlarged hepatic veins and accumulation of blood within the hepatic sinusoids. The kidney showed degenerative changes at the highest dose with the loss of cellular boundaries and haemosiderin deposition near the glomerular tuft. However the spleen revealed only mild pathological changes after the administration of embelin. The controls didn’t show any changes.  

7.2 Discussion for clinical studies:

Sex Distribution:

The incidence of Iya Eraippu Noi was found to be higher in females (74 cases, 53.62%). Females are more sensitive to environmental factors like smoking, cooking gas, ozone and pets. Body Mass Index is related to asthma and atopy in women. Sex hormones may play a vital role in this sex difference in Asthma prevalence.  

Age Distribution:

Varying age groups were included in this study; the maximum age distribution of Iya Eraipai Noi was in 15-30 age groups 69 cases (50%). The global Asthma Report 2014 indicates that the global burden of Asthma is 8.6% of young adults (aged 18-45).
**Kaalam Distribution:**

Most of the cases (83 cases 60.14%) were found to be affected in their Vatha Kaalam (between 1 - 33 years) in this clinical trial.

**Thegi Distribution:**

138 cases were divided into Vatha, Pitha, and Kaba thegi as per the Definition of thegam mentioned in the sidha literature. 92 cases (66.67%) had Kaba Thegam Persons with Kabam physique will have cough and increase of kaba.97

**Gunam Distribution:**

Out of 138 cases, 131 cases (94.93%) had Raso Gunam. As per Siddha Literature Promptitude, wisdom, Bravery, Benevolence, Penance, liberality, education and experience are the eight virtues attributed to Raso Gunam.98 7 cases had Thamo gunam due to the bad behavior like smoking, alcoholism and betel nut chewing.

**Thinai Distribution:**

More cases (82 cases 59.42%) were belonged to the Marutham (Plain and its surroundings). This Fertile land is surrounded by grass, pollens, hay dust and fertilizers. Therefore people dwelling in these lands are affected by Iya Eraip Noi.

**Paruvakalam Distribution:**

Highest number of cases was reported in pinpani Kaalam (Later winter season) i.e. Masi to Panguni - (February 16 - April 15). Most of the hospital admission cases for asthma occurred
in winter and it is proved that respiratory tract infection are very common in winter which precipitates asthma.\(^9\)

**Religion Distribution:**

Among the 138 trial cases, 119 cases (86.23\%) were Hindus. Hindus were more likely to report Asthma than others.

**Socio-Economic status Distribution:**

Lower class people were more suffered by Asthma (71 cases 51.45\%). Lower Socio Economic status tend to have a higher prevalence of asthma.\(^10\) Socio economic condition may produce Asthma by the indoor allergens, smoking and air pollution.\(^10\)

**Demographic Distribution:**

Majority of cases (90 cases 65.22\%) were belonged to the urban areas. People living in urban areas frequently suffer higher Asthma morbidity. Environmental risk factors to which urban people were more frequently, exposed than rural people were dust mites, vehicle emission and a westernized life style.\(^10\) Insects commonly seen in rural households in India like flies, cockroaches, mosquitoes and moths also influence bronchial Asthma. Indoor air pollution due to use of biomass fuels is very high in rural India.\(^10\)

**Educational Status Distribution:**

Highest prevalence observed in literates particularly completed higher studies (121 cases 87.68\%). Sedentary life style changes may be the predisposing factor of Asthma in literates.

[185]
**Marital Status Distribution:**

The incidence of Iya Eraippu Noi was found to be higher in married people (84 cases 60.87%). Married persons were more likely to report Asthma than those who were not married. Emotional stressful condition in married life which may be responsible for Asthmatic Symptoms.

**Body Built Distribution:**

Among 138 cases, 15 cases (10.87%) were obese, 33 cases (23.91%) were overweight, and 20 cases (14.49%) were under weight. Obesity affects the respiratory system by mass loading of the thorax, resulting in a diminution of chest wall compliance and changes in airway resistance. Results regarding the asthma symptoms suggest that Asthma Control in the underweight cases was worse than in the normal weight cases although this difference was not statistically significant.

**Diet Distribution:**

Non vegetarian were more affected than vegetarian (131 cases 94.93%). Those who consumed a non vegetarian diet were more likely to report asthma than those were vegetarian. Increased intake of fruits and vegetables decreases Asthma. Less intake of milk, vegetables, vitamin E, Magnesium, Calcium, Sodium, and Potassium were related with increased Asthma.

**Distribution of Cases by habit:**

Among 138 cases, 3 cases (2.17%) were smokers, 2 cases (1.45%) were alcoholic, 2 cases (1.45%) were Betel nut chewer. Smoking may produce the disease severity and development of COPD.
**Distribution of Female cases by Menopausal Status:**

Out of 74 females, 9 females had attained menopause. 65 females (87.84%) not yet attained menopause. When Asthma starts after menopause, it is strongly associated with an absence of allergy and with asthma severity and frequent exacerbations due to the decrease in Oestrogens.

**Distribution of cases by occupation.**

House wives are highly suffered by Bronchial Asthma (19.57%). House wives are exposed to indoor allergens which include house dust mites, dusts, cockroaches, mold, chemical irritants, fumes and poor air quality inside a building might contribute a serious environmental threat.


**Distribution of cases by family history:**

Among 138 cases, 50 cases (36.23%) reported positive family history and 88 cases (63.77%) reported negative family history of Bronchial Asthma. A family history of Asthma or atopy is a risk factor for the development of Asthma, and genetic factors are important triggers in the etiology of Asthma.
Distribution of cases by treatment history:

Among 138 cases, 98 cases (71.01%) had taken modern treatment. For immediate relief, most of the cases prefer modern medicine in Bronchial Asthma.

Distribution of cases by Symptoms of Asthma:

Bronchial Asthma can be defined as Mild, Moderate and Severe on the basis of severity of the disease defined by the (NAEP) Expert Panel of 1991. The British Guidelines are parallel to the NAEP Guidelines. However, National Heart, Lung and Blood Institute and the WHO 1995 (N1H Publication No.96-3659A) classifies severity of Asthma. Among 138 cases, 94 cases had mild Asthma. Only new patients (2 year duration) were included in this clinical trial, hence most of the cases were mild Asthmatics.

Distribution of cases by peak expiratory flow rate:

According to classification of Asthma severity table patients are divided into mild, moderate and severe on the basis of PEFR Values. In mild intermittent and mild persistent Asthma, the PEFR is $\geq 80\%$. In moderate persistent Asthma the PEFR is $> 60\% - < 80\%$. In severe persistent Asthma the PEFR is $\leq 60\%$. The classification of patients by PEFR was done by expected PEFR was calculated from the formula mentioned in the textbook of human physiology. Observed Peak expiratory flow rate was estimated as percentage of predicted value. Then the cases were divided into 3 stages. Among 138 cases, 12 cases (8.70%) were mild Asthmatic cases, 71 cases (51.45%) were moderate Asthmatic cases. 55 cases (39.86%) were severe asthmatic cases. In this classification severity assessment on the basis of symptoms and severity assessment on the basis of symptoms and PEFR does not correlate.
Distribution of cases by FEVI:

On the basis of Spirometry result, all the 138 cases are divided into 3 stages according to their FEVI. 38 cases (27.54%) had mild Asthma. 44 cases (31.88%) had moderate Asthma. 56 cases (40.58%) had severe Asthma. The division of cases by FEVI does not correlate with the distribution of cases by PEF.

Distribution of cases by triggering factors:

Among 138 cases 126 cases (91.30%) were allergic to cold exposure, 103 cases were allergic to dust (74.64%), 88 cases were allergic to smoke exposure (63.77%), 76 cases were allergic to paints (55.07%). House dust mite is the important indoor allergen linked to asthma. Exposure to environmental tobacco smoke (ETS) produce serious effects on Asthma. Cold air is a main trigger factor. Most of the hospital admission cases for asthma occurred in winter season and it is proved that respiratory tract infections are common in winter season which induces asthma. Perfumes, fumes, psychological factors, atmospheric pollution, fumes of petrol, chemicals, cockroach antigen in homes, cotton dust, pet animal’s thunder like cat, dog, flour dust, husks, grass and pollens, exercise, wood dust, chalk powder, cement and feathers were the triggering factors in this trial patients. Air pollution could increase the prevalence of asthma symptoms and their severity. Vehicular pollution from combustion of diesel has been shown to increase the prevalence of wheeze. Emotional triggers (eg. stress, intense emotion) are linked with severe Asthma, occurrence of Night time Symptoms and oral corticosteroid use. Patients with higher knowledge about asthma report a number of asthma triggers.
Distribution of cases by Duration of illness:

Among 138 cases most of the cases 75 (54.35%) were affected in the duration of one and half year to 2 years. As per the Protocol only new patients (acute cases) were included to this clinical trial, most of the cases were affected since 2 years.

Distribution of cases as per clinical features

Before treatment, all the cases had sneezing, running nose, cough with Mucoid sputum, tightness of chest and wheezing, 123 cases (89.13%) had nocturnal wheezing. sleep disturbance. Dryness of tongue, sweating and drowsiness presented in severe cases.

Disturbance in Gnanenthiriyam: (Sensory Organs)

After treatment period disturbance in gnanenthriyam was reduced due to reducing sneezing, running nose, sweating, Drowsiness and dryness of tongue.

Disturbance in kanmenthiriyam (Motor Organs)

After treatment period disturbance in kanmenthiriyam was reuced due to reducing pain in upper and lower limbs, constipation, and irregular periods in females and nocturnal emission in males.
Disturbance in kosam (sheaths)

After treatment Annamaya kosam (Digestive system), pranamaya kosam (Respiratory system), Manomaya kosam (Cardio Vascular system), vignanamaya kosam (central Nervous system) and Anandhamaya kosam (Reproductive system) were normal because of wheezing, cough, sneezing, drowsiness and indigestion reduced.

Derangement in Mukkutram (Three humors)

After treatment, derangements noted in vatham were reduced because of reducing constipation, dry cough or productive cough with mucoid spu tum, drowsiness, nocturnal wheezing and loss of sleep.

After treatment, derangements noted in pitham were reduced because of reducing indigestion and poor appetite, drowsiness and able to do normal activities. Ranjagam was normal in all cases because of hemoglobin was increased in all cases.

After treatment, derangements noted in kabam were reduced because of reducing wheezing and tightness of chest, indigestion, heart burn and joint pain.

Disturbance in Ezhu Udal kattugal (seven physical Constituents)

Senneer was affected in 128 cases (92.75%) due to decreased hemoglobin, increased eosinophil count, Absolute eosinophil count and serum IgE level. After treatment Senneer was affected in 34 (27.2%) cases. After treatment saram was normal in 122 cases due to reducing tiredness and drowsiness. Oon, Kozhuppu, Enbu, Sukkkilam and Suronitham was normal in all cases.
Disturbance in Envagaithervugal (Eight Methods of diagnosis)

Among 138 cases, Naa, Mozhi, Sparisam were affected in 44 cases (31.88%) due to Sweating, Dryness of tongue and diminished voice. In most of the cases pitha kaba Naadi, Kaba pitha Naadi and Vatha kaba Naadi was present. These three Naadies are Responsible for Iya Eraippu Noi in Sathaka Naadi Nool. After treatment among 125 cases, Naa, Mozhi, Sparisam were affected in only 3 cases (2.4%) due to reducing the Symptoms like dryness of tongue, diminished voice and sweating, constipation, burning micturition. After treatment the kabha humour was reduced and the Naadi was changed.

Distribution of cases by Neikuri

In most of the cases 105 cases (76.09%), the Neikuri was pearl shape which indicates the kaba disease. After treatment among 125 cases only 24 cases (13.6%) had kaba neer which indicates the reduction of kaba humour and the patient’s improvement.

Clinical Improvement of cases by staging of Asthma:

In this clinical study, only new patients are included to Clinical Trial. Most of the cases were belonged to step 1 and step 2. (Mild intermittent and mild persistent Asthma). No improvement was observed in the first week of treatment. In the 2nd week of treatment among 133 cases, (5 cases were withdrawn) wheezing was not present in only 11 cases (8.27%). (8.27%) of Improvement was observed in the 2nd week of treatment. In the 3rd week among 131 cases (2 cases were withdrawn) wheezing reduced in 37 cases (28.24%). 28.24% of improvement was observed in the 3rd week of treatment. In the 4th week of treatment (at the end of treatment)
among 125 cases (6 cases were withdrawn) wheezing relieved in 97 cases (77.6%). 77.6% of improvement was noted in the end of treatment. It is concluded that the trial drug Adathodai Chooranam is acting very effective after 7 days of treatment to 30 days of treatment.

**Improvement of cases in clinical features**

Weekly wise improvement in clinical features was observed in all cases at each clinical visit. Clinical improvement was observed at the end of second week, third week and fourth week which indicates the effect of trial drug in acute cases.

**Improvement of cases in Asthma control Questionnaire**

Asthma control Questionnaire is developed by using Asthma control test TM score of Asthma UK. Score 25 means Asthma appears to have been under control over the last 4 weeks. Score 20 to 24 means Asthma appears to have been reasonably well controlled during past 4 weeks. Score less than 20 means Asthma may not have been controlled during the past 4 weeks. 121

Before treatment among 138 cases, in 130 cases (94.20%) wheezing not controlled and the score is less than 20. In 8 cases (5.80%) wheezing reasonably well controlled and the score is between 20-24. After treatment among 125 cases wheezing under control in 76 cases (60.8%) and the score is 25 wheezing reasonably well controlled in 40 cases (32%) wheezing not controlled in 9 cases (7.2%). The trial drug reduces wheezing in day time and night hours.
Improvement of cases in PEFR (Morning hours)

Weekly wise improvement in PEFR (Morning hours) was observed in all cases at each clinical visit. Improvement was observed at the end of second week, third week and fourth week PEFR (Morning hours) which indicates the effect of tial drug in Acute cases.

Improvement of cases in PEFR (Evening hours)

Improvement was observed at the end of second week, third week and fourth week PEFR (evening hours) which indicates the effect of tial drug Adathodai chooranam in new cases.

Primary outcome by clinical features

Primary outcome is measured by clinical improvement of cases. Primary outcome is arrived by using classification of severity of bronchial Asthma table by the Expert panel of the National Asthma Education program by the National Heart, Lung and Blood Institute USA. If the patient is improved from severe persistent Asthma (step 4) to step 1 (mild intermittent) or step 2 (mild persistent) or Normal which is good response. If the patient is improved from symptoms of moderate Persistent Asthma (step 3) to step 1 or step 2 or normal which is good response. If the patient is improved from Step IV to Step III which is moderate response. No improvement in signs and symptoms which is poor response.

Among 125 cases 110 cases (88%) were improved from step 4 (severe persistent Asthma) or step 3 (Moderate persistent Asthma) to step 2 (mild persistent Asthma) are step 1 (mild intermittent Asthma) or Normal which is good response 5 cases (4%) were improved from step 4
to step 3 which is Moderate response. 10 cases (8%) were not improved from clinical symptoms which is poor response.

**Primary Outcome by Peak Expiratory Flow rate (Morning hours)**

A diagnosis of Asthma is made on the basis of clinical history plus and morning dipping of the peak expiratory flow rate which means peak expiratory flow measurement worse in the early morning.\(^{122}\) Patients should measure their PFER twice daily, on morning and in the evening before using a bronchodilator and perhaps four times a day during exacerbations.\(^{123}\)

On each occasion, three readings should be taken and best recorded graphically for easy inspection. While complete spirometry can be done in a laboratory only but the patient can measure the PEFR himself.\(^{124}\) All cases recorded their PEFR in the peak expiratory flow rate monitoring form in morning & evening by using mini peak flow meter.

Primary outcome is measured by curative effect of Asthma with PEFR Measurement. Improvement of patient from step 4 (severe persistent Asthma, PEFR≤60%) to step 1 or step 2 or Normal (Mild intermittent or Mild persistent PEFR ≥ 80%) which is good response. Improvement of patient from step 3 (Moderate persistent Asthma, PEFR > 60% - <80%) to step 1 or 2 or Normal which is good response. Improvement of patient from step 4 (severe persistent Asthma, PEFR≤ 60%) to Step 3 (moderate persistent Asthma PEFR (60 % - < 80%) which is moderate response. If no Improvement is noted in signs and symptoms with PEFR which is poor response.

Among 125 cases, 65 cases (52%) were improved in morning PEFR Measurement from 60% -80% (moderate persistent Asthma) and below 60% (severe persistent Asthma) to 80% and above (Mild intermittent and persistent Asthma) which is Good response. 44 cases (35.2%) were
improved from below 60% to 60-80% which is Moderate response. 16 cases (12.8%) were not improved in PEFR values during the treatment period which is poor response.

**Primary outcome by PEFR (Evening hours)**

When compared to morning PEFR value there is a slight elevation in Evening PEFR values. Among 125 cases, 106 cases (84.8%) were improved in evening PEFR Measurement from 60 to 80% and below 60% to 80% and above which is good response. 7 cases (5.6%) were improved from below 60% to 60-80% which is moderate response. 12 cases (9.6%) were not improved in PEFR in Evening hours during the treatment period which is poor response.

**Secondary outcome by lab assessment**

In 138 cases, before treatment ESR increased in 30 (21.74%) cases, Eosinophil increased in 29 (21.01%) cases, AEC increased in 32 (23.19%) cases and serum IgE increased in 122 (88.41%) cases. After treatment ESR reduced in 22 (17.6%) cases and Eosinophil reduced in 20 (16%) cases and AEC reduced in 27 (21.6%) cases and serum IgE reduced in 88 (70.4%) cases. The trial drug reduces the lab parameters Eosinophil, AEC, ESR and serum IgE and reduces the symptoms of asthma.

**STATISTICAL ANALYSIS OF CLINICAL STUDY RESULTS**

During the treatment period the trial drug did not produce any adverse drug reactions in all 138 cases. There were significant difference in scores for total WBC count before and after treatment p=<0.474. But the difference is within the normal range. There were no significant
difference in scores of other hematological parameters and biochemical parameters before and after treatment which exhibits the safety of the trial drug

There were no significant differences in scores for Eosinophil count before and after treatment. \( p=0.4778 \). There were no significant difference in scores for ESR for 30 minutes before and after treatment \( p=0.377 \). There were no significant difference in scores for ESR 1 hour before and after treatment \( p=0.411 \).

There were significant reduction in scores for Absolute Eosinophil count before and after treatment \( p=0.499 \). The result is statistically significant at \( p<0.05 \) for Absolute Eosinophil count.

There were significant reduction in scores for Serum IgE level before and after treatment \( p=0.045 \). The result is statistically significant at \( p<0.05 \) for Serum IgE level.

There were significant increase in scores for Peak expiratory flow rate of first week and fourth week of treatment and the \( P \)-value is \( <0.0001 \), the \( t \)-value is \( -9.71747 \). There were significant increase in scores for Peak expiratory flow rate of first week and fourth week of treatment and the \( P \)-value is \( <0.0001 \), the \( t \)-value is \( -10.49023 \). The result is statistically significant at \( p<0.05 \) for Peak expiratory flow rate of evening and morning.

After treatment the percentage predicted values of FEV\(_1\) (L) was higher than that of before treatment and it was statistically significant. Similarly the percentage predicted values of FEF\(_{25-75}\) (L/sec), PEFR (L/sec), FEF \(_{25\%}\), FEF \(_{50\%}\), FEF \(_{75\%}\) and MVV \(_{3\%}\) (L/min) were increased.
From the statistical analysis of Lab parameters the trial drug is proved that it is very effective in reducing Eosinophil count, AEC and Serum IgE in new Asthmatic patients (2 year duration) within the treatment period of 30 days with the trial drug Adathodai chooranam.

There were significant decrease in scores for sneezing, couh, wheezing, nocturnal wheezing, dryness of tongue, sweating, drowsiness and associated symptoms joint pain, constipation, indigestion and loss of appetite before and after treatment and the P-value is <.00001. The result is significant for symptoms score between before and after treatment. Hence it is proved that clinically the trial drug Adathodai chooranam is very effective in Bronchial Asthma cases.

Out of 138 cases the recurrence of Asthma symptoms was observed only in 13 cases (10.4%) in 3 months follow up period. Therefore the drug also reduces the recurrent of episode of Asthma symptoms.

**Socio Economic impact:**

Bronchial Asthma is one of the common respiratory disease with high incidence recurrence rate. The trial drug Adathodai chooranam is completely herbal medicine treatment effective and cost effective. So this drug can be better choice to the society.
8. SUMMARY AND CONCLUSION

The aim of the study is to estimate the clinical efficacy of a poly herbal formulation Adathodai chooranam in the treatment of Iya Eraippu Noi (Bronchial Asthma). The well designed protocol and case report forms were submitted in the Institutional Ethics committee, NIS for conducting clinical studies and approval was got from the IEC. The IEC approval Number is NIS/IEC/11/02/02. The dully filled Form B (Application for permission for Animal Experiments) was submitted in the Institutional Animal Ethics Committee, NIS and approval was got from the IAEC for conducting pre clinical studies in the Animal model. The IAEC Approval number is NIS/04/2011/11.

The clinical trial was registered in the clinical trial Registry of India and the Registration Number is CTRI/2013/12/004253. The clinical trial was also registered in International Clinical Trials Registry Platform and the ID is NIS/PPHD/11/0104.

The raw drugs were purchased from the Indian Medical practitioner’s co- operative pharmacy and stores Ltd., X-185 (IMCOPS), Thiruvanmiyur, Chennai. The fresh herbs were collected from the herbal Garden, NIS, Chennai. All the herbal drugs were authenticated by Assistant professor of Botany, National Institute of siddha, Chennai (voucher No. NIS/NB 69/2012) and deposited in the Medical Botany Laboratory NIS, Chennai. The trial drug was prepared in the Gunapadam lab of National Institute of siddha as per the Method of Preparation mentioned in the siddha sastric text and standard operating procedure mentioned in the protocol. The Medicine was then subjected to pre clinical toxicity studies (Acute and sub chronic toxicity studies) as per who Guidelines 1993 in Animal Laboratory National Institute of Siddha to evaluate the safety of the trial drug.
The qualitative (preliminary phyto chemical analysis) and quantitative (physio chemical analysis), TLC and HPTLC finger print profile were done at the Biochemistry laboratory of National Institute of siddha, Siddha Central Research Institute Arumbakkam, Chennai and Captain srinivasa Murti Drug research Institute of Ayurveda and siddha Drug Development, Arumbakkam, Chennai respectively. The Gas Chromatography - Mass Spectrometry (GC-MS) analysis was done at Sophisticated Analytical Instrument facility, Indian Institute of Technology, Chennai to identity the bio active Components of trial drug. Heavy metal analysis, Microbial load and aflatoxin content of trial drug were performed for drug standardization in sargam laboratory which is an AYUSH approved lab for drug analysis.

Pilot study was done in 5 OPD cases before starting the main study. 191 cases were screened in the OPD of maruthuvam, NIS by using screening and selection proforma and 138 cases were recruited for the clinical trial as per the inclusion and exclusion criteria. Clinical diagnosis was made by siddha and Modern Methodology.

The Informed consent was obtained from all the cases before starting the treatment. Complete clinical history, complaints and duration, examination findings were recorded in the History Proforma and clinical assessment form. Blood and urine investigations, x-ray, ECG and sputum test were taken in NIS and the results were recorded in the Laboratory parameters – chart. The serum IgE level and spirometry test were taken before and after treatment in NABL certified Laboratory. The patients are advised to record their peak expiratory flow rate in morning and evening before taking the trial drug in the peak expiratory flow rate monitoring form.

Clinical assessment was done daily in IPD cases, once in 7 days for 30 days in OPD cases and symptoms were recorded in clinical assessment form. Asthma control questionnaire was
filled before and after treatment to observe the score changes. Out of 138 cases 123 cases were treated in OPD, 2 cases were in IPD. 13 cases were withdrawn during the treatment period. The trial drug Adathodai chooranam was given in the dose of 1.5 gram, twice a day for 30 days. Patients were advised to take the trial drug with cow’s milk. During the treatment period patients were advised to take the diet as per the Dietary advice form. After the treatment period all the 125 cases were followed in OPD without treatment upto 3 months to monitor the recurrence of symptoms.

Paired t test was followed to find the significance of treatment using before and after the data on haematological parameters, blood biochemistry, peak expiratory flow rate and spirometry results. The significance probability 0.05 (p<0.05) was used to find the treatment difference. Statistical analysis was done by using independent “t” tests for comparison of pulmonary function parameters.
CONCLUSION

The quality of the drug is better if the acid insoluble ash value is low which 2.5% is for Aadhathodai Chooranam. In phyto chemical analysis Alkaloids, Flavonoids, Glycosides, Terpenes, Saponins, Aminoacids, Phenols, Tannins, Quinones, Lignans, Steroids, Chloride, Phosphate, Ammonium iron were detected. The Phytochemical analysis results correlate with the literature survey of all the ingredients of Aadhathodai Chooranam which given additional supports to its usage in clinical trial of Bronchial Asthma with potent antioxidant, anti-inflammatory, antihistaminic, antispasmodic, immnuomodulator, bronchodilator action. Heavy metal analysis, Microbial load and Aflatoxin content of Aadhathodai Chooranam revealed that the Aadhathodai Chooranam was below the WHO/FDA permissible limits and safe for consumption. HPTLC finger print of Aadhothodai Chooranam could serve as a marker and which is responsible for expression of its Biological and clinical actions. The bioactive compounds identified by GC-MS in the trial drug Adathodai Chooranam possess antioxidant, anti microbial, anti inflammatory and medicinally valuable.

In acute and long term toxicity studies, mortality or signs of toxicity were not observed because of administration of Adathodai Chooranam. The single oral dose of 2.6 gm/kg body weight was considered as non toxic drug in acute toxicity study. Long term toxicity study showed that the test drug adathodai chooranam is well tolerated at therapeutic dose level (270 mg/kg body weight and it is proved that the trial drug Adathodai Chooranam is safe as per mentioned in the siddha literature (1.5 g for human adult).

During the treatment period the trial drug did not produce any adverse drug reactions in all 125 cases. Clinically among 125 cases 110 cases (88%) showed good response. 5(4%) cases showed moderate response. 10 cases (8%) showed poor response. By PEFR measurement, Among 125
cases, 106 cases (84.8%) showed good response. 7 cases (5.6%) showed moderate response. 12 cases (9.6%) showed poor response. There were significant decrease in symptoms score before and after treatment and the P-value is <.00001. The siddha parameters like eight diagnostic methods, seven physical constituents, three humors and Neikuri showed improvement to the trial drug during the treatment.

There were significant reduction in scores for Absolute Eosinophil count before and after treatment $p=<0.499$. There were significant reduction in scores for Serum IgE level before and after treatment $p=<0.045$. There were significant increase in scores for Peak expiratory flow rate (morning) of first week and fourth week of treatment and the P-value is <.00001. There were significant increase in scores for Peak expiratory flow rate (evening) of first week and fourth week of treatment and the P-value is <.00001. After treatment the percentage predicted values of FEV$_1$ (L) was increased in spirometry and it was statistically significant $p < .05$.

All the results of clinical study showed that the trial drug is very effective in lowering symptoms of Asthma, reducing Absolute eosinophil count and serum IgE level, improving lung function in new Asthmatic patients (2 year duration) within the treatment period of 30 days. The drug also reduces the recurrent of episode of Asthma symptoms. The ingredients of Adhathodai chooranam possess anti-inflammatory, antihistaminic, antiasthmatic, antispasmodic, antimicrobial, expectorant, antitussive, bronchodilator, immunomodulator and antioxidant activities. These properties play a vital role in the treatment of Bronchial Asthma. Hence, it could be concluded that the Adhathodai chooranam is one of the very effective drug for Asthmatic patients. Additionally all the ingredients of Adathodai chooranam possess hot potency and pungent taste. These properties neutralize the kaba humour and reduce the signs and symptoms of Iya EraippuNoi in Siddha system of medicine.
9. RECOMMENDATIONS

It is recommended that the trial drug Adathodai chooranam can be used for chronic Asthma cases with more than 2 years duration of illness.

It is recommended that the duration of treatment with the trial drug Adathodai chooranam can be extended from 30 days to 3 months or one year for more efficacy. Therefore the drug can be subjected to chronic toxicity study in Animal models as per WHO guidelines.

It is also recommended that In vitro and In vivo pre clinical research work can be included for scientific validation of trial drug Adathodai chooranam.

This clinical trial can be conducted as Multi centric study or Randomized controlled trial for scientific Global acceptance.
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