PRECLINICAL AND CLINICAL EVALUATION OF SILVISHA USIDHAM (INTERNAL) AND PUZHUVETTU THYLAM (EXTERNAL) FOR PUZHUVETTU (ALOPECIA AREATA) IN CHILDREN

The Dissertation Submitted by

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Under the Guidance of

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **Preclinical and clinical evaluation of Silvisha Usidham (Internal) and Puzhuvettu Thylam (External) for Puzhuvettu in children**. Guidance of **Dr.M.Meenakshi Sundaram M.D (S)**, Associate Professor, Department of Kuzhandhai Maruthuvam, National Institute of Siddha, Chennai -47 and the dissertation work has not formed the basis for the award of any Degree, Diploma, Fellowship or other similar title.

Date:

Place: Chennai-47

Signature of the candidate

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BONAFIDE CERTIFICATE

Certified that I have gone through the dissertation submitted by **Dr.R.D.INDUMATHI,** (Reg.No.321514204) a student of final M.D(S), Branch-IV, Department of **Kuzhandhai Maruthuvam**, **National Institute of Siddha**, Tambaram Sanatorium, Chennai-47, and the dissertation work has been carried out by the individual only. This dissertation does not represent or reproduce the dissertation submitted and approved earlier.

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1. INTRODUCTION

Alopecia areata is a common skin condition characterized by localized hair loss usually over the scalp region. But the condition is frequently seen in children. Both sex are equally affected although some study report a male -to-female ratio 2:1 [1.]Prevalence is approximately 0.2% of the population and lifetime risk is believed to be between 1% and 2%.There is a history of familial occurrence in 10% - 20% of the affected individuals[2] Incidence of the disease is 17.2/100,000 population affecting 1:1000 individuals at a given time [3]. Hair loss not only in scalp region but also in hair bearing areas.

A complete hair loss of the scalp is seen in alopecia totalis. Alopecia of all hair-bearing surfaces including eye lashes, eye brows, body hair seen in alopecia universalis. In ophiasis a circumferential hair loss extending around the temporal and occipital hairlines. Scarring alopecia or cicatricial alopecia represents a group of disorders characterized by permanent and pathological destruction of the hair follicles. Scalp is the commonest site but lesion may present at other sites even without involvement of the scalp.

Alopecia areata is not a contagious disease. It is not associated with any scalp finding such as scale or inflammation. Exclamation mark hair indicates active disease. Dystrophic nail changes occur in 20% case. Recurrence of alopecia are frequently occur in over 50% . Spontaneous recovery is very common in children before puberty [1]. It affects all age group and the first episode usually occur in patient less than 25 years of age [3] . Lifetime risk of alopecia areata is increased in individuals with personal or family history of autoimmune disorders such as vitiligo, thyroid disease and pernicious anemia.

Alopecia areata is an autoimmune disease of the hair follicle. Alopecia areata typically presents with sudden appearance of one or more round or oval well defined patches of hair loss. The common cause of non-scarring hair loss in children. The hair loss may occur overnight or over a period of several days. In some children, the initial patch may not be well defined and may show scattered long hairs within the bald area. Occasionally, the initial loss may be diffuse and the patches of baldness may be apparently only after 1 or 2 weeks.

Alopecia areata associated with atopy; nail changes as pits, ridges, opacification, and serration of the free nail edge, dystrophy and red lunula.

An increased incidence of alopecia areata has been reported in patients with down's syndrome (5-10%)[4]. The cause of alopecia areata is unknown. Emotion factor and stress have been suggested as triggering factor.There is no cure for Alopecia and no universally proven therapy to induce hair growth.

The basic principle of Siddha system of Medicine is Panchapootham theory. According to Panchapootham theory the universe is made up of five elements of nature.The human body is also made up of five elements. Alerations of the three vital humours Vali, Azhal and Iyyam which leads to disease manifestation.

In siddha alopecia is denoted as puzhuvettu in the text book Sirappu Maruthuvam[5]. According to Mukkuttram concept Puzhuvettu is consider as vadha disease "Vathamaladhu meni kedadhu"[6]. In Siddha system of medicine, there are 4448 group of disease are classified in humanbeing. Among 4448 group of disease kurumi noi is described in the text of Noi Nadal Thirattu[6]. Kirumi is one of the reason of Puzhuvettu.

Prevention and treatment are the basic aim of the siddha system of medicine. Siddha system is a vast and unique system which defines health as a prefect state of physical, psychological, social and spiritual well being of an individual. In siddha medicine there is not only cure of disease but also improve the quality of life by prevention and rejunuvating. In NIS OPD a considerable number of patients in pediatric population are recorded with the symptoms of puzhuvettu.

Puzhuvettu is not a contagious disease but it may have to complex comparing in the schools and their surrounding environment. Preschool age Children who have alopecia don't experience as much emotional impact from their condition. Between the age of six and twelve they are noticing differences between themselves and others. They may be mentally affected and feel shy which reflects in their academic, attitude and performance skill. Cosmetically it remains a great problem in children and causing stress in parents.

A Siddha drug Silvisha Usidham (Internal) and Puzhuvettu thylam (External) both are indicated for the treatment of Puzhuvettu in the text book of Siddha Anuboga Vaithiya Navaneedha Thirattu[7]. All the ingredients of trail drug are a composition of herbal only. Silvisha Usidham which constitutes Elleteria cardamomum, Ficus hispida, Sesame oil and Piper longum having Anti- inflammatory activity, immunomodulator, anti microbial and anti-fungal activites. Puzhuvettu thylam which constitutes Ricinus communis (castor oil), Shorea robusta and Indigofera tinctoria having hair growth promoting activity. So it is safe and have efficacy in treating puzhuvettu in children.

Since the formulation does not undergone any clinical trial so far. In order to manage the disease with a simple herbal formulation has been selected as dissertation work. The medicine is proved to have a good impact on this condition it will serve as a great benefit to the paediatric population who suffer from alopecia areata.

2. AIM AND OBJECTIVES

AIM:

To evaluate safety and efficacy of Silvisha Usidham (Internal Medicine) and Puzhuvettu Thylam (External Medicine) for Puzhuvettu (Alopecia areata) in children.

OBJECTIVES:

1. To collect and review the ideas mentioned in the ancient Siddha literature about the disease Puzhuvettu.
2. To make correlative study of the Siddha and modern aspect of this disease.
3. To study the characteristics of Puzhuvettu with that of alopecia areata in children on the basis of uyir thathukkal, udal thathukkal, envagaithervugal, Paruvakaalangal, age, sex and economic status.
4. To study the Physiocochemical properties, Biochemical analysis and Phytochemical analysis.
5. To Study the Pharmacological activity of the Silvisha Usidham.
6. To evaluate the toxicity profile of Silvisha Usidham.

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3. REVIEW OF LITERATURE

3.1. SIDDHA ASPECT

Alopecia areata

புழுவெட்டு - தலையில் திட்டுத்திட்டாக முடி உதிர்ந்து அவ்விடங்கள் வழுக்கையாகக்காணப்படும்.

வேறு பெயர்கள் :

மயிர்உதிரல், தலை மயிர்வெட்டு, புழுக்கடி

AETIOLOGY (NOI VARUM VAZHI):

ACCORDINGN TO "GURUNAADI NOOL"

நோய் காரணம் :

"கிருமியால் வந்த தோடம் பெருகவுண்டு
கேட்கவதின் பிரிவதனைக் கிரமமாக
பொருமி வரும்வாயு வெல்லாங் கிருமியாலே
புழுக்கடி போல் காணுமது கிருமியாலே
செருமி வரும் பவுத்திரங்கள் கிருமியாலே
தேகமதில் சோகைக் குட்டம் கிருமியாலே
துருமி வருஞ் சுரோணிதங் கிருமியாலே
சூட்சமுடன் கிரிசைப்பால் தொழில் செய்வீரே "

-குருநாடி நூல்

The cause of Puzhuvettu is explained in Gurunaadi Nool."Puzhukadi pol kaanumadhu kirumiyalae" Infection is one of the reason that causing puzhuvettu.

ACCORDING TO THEYRAIYAR:

"**வாதமலாது மேனி கெடாது**"

As per the Siddha literature the body get affected mainly due to vitiation of vatha humour including skin condition.

The characteristic features of puzhuvettu described in the text Siddha Maruthuvam Sirappu. They are

1. Patchy hair loss in scalp region.
2. It is one of infectious disease.
3. Initially hair loss starts with small area after that it increase in size and baldness occur.

தலையில் திட்டுத்திட்டாக முடி உதிரிந்து அவ்விடங்கள் வழுக்கையாகக் காணப்படும், ஒருவகைக் கிருமிநோயைப் புழுவெட்டு என்கிறோம், மயிர் உதிர்ந்த இடங்கள் மினுமினுப்பாய்த் தோன்றும், ஒரு சிறிய இடத்தில் ஆரம்பித்து மயிர் உதிரல், கூடிக்கொண்டேபோய் வழுக்கைத்திட்டு பெரிதாகிக்கொண்டு வரும்[5.]

Varieties of puzhuvettu :

1. Loss of hair in scalp region.
   The main symptom of hair loss in patches and scarring is described in the text "Siddhar Aruvai Maruthuvam" [8] under kabala kirumi that too purakirumi –They cannot be treated.

2. Hair loss in eyebrows and eyelashes. This type of Puzhuvettu explained in the text of "Nagamuni Nayanavithi"

புறக்கிருமி – (**மண்டைகிருமி**)

1. **“ தானே கபாலப் புறக்கிருமி தக்க குணத்தைச் சாற்றக்கேள்**
   மானே தலையி லுரோமமெலாம் வடுவா யுதிர்ந்து தழும்பாகும்
   பேனேயூரும் போலூரும் பின்னுஞ்சாம்பல் பொருக்கு விழும்
   தேனே யிந்தக் குணமறிந்தாற் செய்யு மருந்தைத் தேர்ந்தறியே “

   - அறுவை மருத்துவம்

2. **“போதவே யிமைக னத்துப் பொங்கிய தினவுண்டாகும்**
   மூதவே யெரிப்புண்டாகு முதிர்ந்திடும் மயிர்க்கா,லெல்லாங்
   காதவே தலைகால் மெய்கள் கரகர வென்று தோன்றுங்
   கோதவே யிமைகள் தானுங் கொடும்புழுவெட்ட தாமே “

   -அகத்தியர் நயனவிதி

கொடும் புழுவெட்டின் பண்பு – இமையில் ஏற்படும் மயிர்வெட்டு

The main symptoms of Puzhuvettu are explained very well in the above verse (Agasthiyar Nayanavithi). They are

1. Itching
2. Tingling sensation
3. Hair loss
4. Inflammatory changes in hair follicles

“உள்ளிமை விளம்பி லூறு முரோம்மு முதிரும் புண்ணாய்
தெள்ளழல் போலக் காந்தும் ஓடுமே யிரத்தந் தானும்
வெள்ளிடை சிவக்க வீங்கித் தடித்திடு மிக்கு ணங்கள்
அள்ளிலை நெடுவெற் கண்ணாய் புழுக்கடிக் குணமே தாமே”

- நாகமுனி நயனவிதி

மயிர்ப்புழுவெட்டு

"நீட்டிய தினவுங் கூச்சம் நீர்வரு மிமையும் வீக்கம்
கூட்டிடும் பீளை சேரும் குறுமுளைப் போலத் தோற்றம்
நாட்டியே மயிருதிர்ந்து நற்சதை ரத்தம் வீழும்
காட்டிது மயிர்ப்புழு வெட்டு கண்டவ ருரைத்த வாறே "

- அகத்தியர் நயனவிதி

DIAGNOSTIC METHODS (PINIYARI MURAIMAI):

Piniyari Muraimai is the methods of determination of a disease. It is based on the following principles.

1. Poriyalarithal
2. Pulanal arithal
3. Vinaathal

Poriyalarithal and Pulanalarithal goes hand to hand with the concept of examining the patient's Pori and Pulan with that of physician's Pori and Pulan.

Vinaathal is a method of enquring about the details of that patients problem from his own words or from his parents or neibhours who are taking care of the patients, when the patient is not able to speak or patient may be child.

ENNVAGAI THERVUGAL (EIGHT DIAGNOSTIC TOOLS):

"நாடி ஸ்பரிசம் நாநிறம் மொழி விழி
மலம் மூத்திரமிவை மருத்துவ ராயுதம்"

- தேரன் வெண்பா

"மெய்குறி நிறம் தொனி விழி நா இருமலம் கைக்குறி"

It is also given in Agasthiyar Vaithiya Chinthamani Venba -4000

Hence the diagnosis is made by the following:

1. Naadi (Pulse reading)
2. Sparisam (Tactile sensation)
3. Naa (Tongue)
4. Niram (Colour)
5. Mozhi (Speech or voice)
6. Vizhi (Eyes)
7. Malam (Stools)
8. Moothiram (Urine)

ENVAGAI THERVUGAL:

1. NAADI :

எண்வகைத் தேர்வுகளில் பிரதானமானது. பிணியினை நாடியாலறிந்து மருந்தூட்டுதலே சிறந்தது என்று சித்த மருத்துவம் கூறுகின்றது. ஆனால் குழந்தைகளில் நாடிநடை சரியாக தோன்றாது என்பதை கீழ்கண்ட பாடலால் அறியலாம்.

“கொண்டிடவே கயரோகி காசரோகி
குறிப்பாக சிற்றின்பம் செய்த பேர்கள்
அண்டிடவே தரித்திரர்கள் விருத்தர் பாலர்
கொண்டிடவே இவர்களின் உறுப்பின் தாது
கூறவே முடியாது எவர்க்குக் கிட்டும்”

-நோய்நாடல் நோய் முதல்நாடல் திரட்டு

வாதம் மிகுதியால் வரும் நோய்கள்:

“வாதமெனும் நாடியது தோன்றில்
சீதமந்தமொடு வயிறு பொருமல் திரட்சி வாய்வு
சீதமுறுங் கிராணி மகோதரம் நீராமை
திரள்வாய்வு சூலை வலிகடுப்புத் தீரை

நீதமுறுங் கிருமிகுன்மம் அண்ட வாதம்

நிலையும்நீர்க் கிரிச்சரங்கள் தந்து மேகம்

பேதகமா முதரப்பிணி மூல ரோகம்

பேசவெகு பிணிகளுமே பொருள தாமே"

- அகத்தியனார் சிகிச்சாரத்னதீபம்

இதனை வாதத்தில் வாதம்,வாத கதித்தல்,வாதம்மீறி நடத்தல் எனவும் கூறுவர்.

2. SPARISAM :

The following points are elicited by sparisam temperature of the skin on any abnormal grounds, hypersensitiveness and thickness of the skin, swelling and dryness of the skin, excessive sweating, hair loss, ulcers, oedema, obesity, liver and spleen enlargement.

In puzhuvettu patchy hair loss in scalp region.

3. NAA :

This is the method of inspection of the tongue, gums, Teeth, lips, palate etc No Abnormalities were observed in Puzhuvettu.

4. NIRAM:

Changes in the color of the skin, teeth, eyes, nail and lips due to Mukkutra derangement are to be noticed. In Scarring alopecia there is colour change in affected area.

5. MOZHI :

Examination of mozhi includes clarity of speech, crying, low & high piched voice and slurring speech. No abnormalities were observed in puzhuvettu.

6. VIZHI:

Pallor of the conjunctiva, conjunctivitis, Cataract (any redness) In Puzhuvettu hair loss in eyebrows and eye lashes.

7. **MALAM :**

Semisolid, color froth, abnormal consistency indicating indigestion, frequency, constipation, foul smell etc.

8. MOOTHIRAM :

Collection of urine for the determination of Neerkuri and Neikuri. It is an important diagnostic method.

Neerkkuri:

The previous day of urine examination the patient should have good sleep and instructed to take a balanced diet. After waking up in the morning, the first voiding of urine is collected in a clear wide mouthed glass container and is subjected to analysis of "Neerkuri" within 1 1/2hours.

Urine has the following general features:

Niram

EdaiManam

Nurai

Enjal

In addition, frequency of micturation and sediments are noted.

NEIKKURI:

The collected specimen (Urine) is kept open in a glass dish or china clay container. It is to be examined under direct sunlight without any shaking of the vessel. Then add one drop of gingelly oil without disturbing the specimen and neikkuri was noted in direct sunlight and conclude the diagnosis as follows.

CHARACTER OF VATHANEER:

In 'Vaathaneer' oil drop lengthens like a Snake

CHARACTER OF PITHANEER:

In 'Pithaneer' oil drop spreads like a ring.

CHARACTER OF KABANEER:

In 'Kabaneer' oil drop spread like a pearl.

CHARACTER OF THONTHANEER:

Snake in the ring, ring in the snake, snake in the pearl and ring in the pearl are the characters of thonthaneer.

PARUVAKALAM: (Season)

Siddhars have classified a year into 6 seasons each constituting 2 months.

They are

1. Kaarkalam – Avani & Purattasi (Aug15 to Oct15)
2. Koothirkalam – Ippaasi & karthikai (Oct15 to Dec15)
3. Munpanikalam – Margazhi & Thai (Dec15 to Feb15)
4. Pinpanikalam – Masi & Panguni (Feb15 to Apr15)
5. Elavaenirkalam – Sithirai & Vaigasi (Apr15 to Jun15)
6. Muthuvenilkalam – Aani & Aadi (Jun15 to Aug15)

Puzhuvettu does not related with any seasonal variation.

BODY IMMUNITY (UDAL VANMAI):

The vanmai is classified into 3 kinds.

They are:

1. Iyarkai vanmai
2. Kala vanmai
3. Seyarkai vanmai

1. **Iyarkai vanmai :**

   Natural immunity of the body caused by three vital humour right from birth onwards.

2. **Kala vanmai :**

   Development of immunity according to age and environment.

3. **Seyarkai vanmai :**

Improving the health by intake of nutritients, food materials, activities and medicines.

PHYSICAL CONSTITUENTS (UDAL THATHUKKAL)

UDAL THATHUKKAL	-	**GENERAL DEFINITION OF EACH TYPE**
Saram	-	Give strength to body and mind.
Seneer	-	Responsible for knowledge, strength, boldness, healthy complexion
Oon	-	Gives structure and shape to body and is responsible for movement of the body
Kozhuppu	-	Lubricates the internal organs and helps the organs to work smoothy.
Enbu	-	Protects the vital organs and act as basis for movement and maintain body structure.
Moolai	-	Present inside the bones and it gives strength and maintains the normal condition of the bone
Sukilam/Suronitham	-	Responsible for reproductive function of species.

Human body is made up of seven udal kattugal which are important for the structure and function of the body. In case of Puzhuvettu, among the seven udal kattugal (seven physical constituents) Saram and Seneer were affected.

மருத்துவம்:

1. **வேற்றுநிலை வளர்ச்சியடைந்த வாதத்தினை தன்னிலைப்படுத்த வேண்டும்** Kazhichal Marunthugal
2. **வன்மை இழந்த உடற்கட்டுகளை வன்மை அடையச்செய்யும் வகையில் மருந்தளிக்க வேண்டும்**.

Line of treatment:

Siddha treatment is not only for complete healing but also prevention and rejuvenation. Saint Thiruvalluvar says about physician's duty, study the disease, study the cause treat subsiding way and do what is proper and effect.

" **நோய் நாடி நோய் முதல் நாடி அது தணிக்கும்**

வாய்நாடி வாய்ப்பச் செயல்"

"**உற்றான ளவும் பிணியளவுங் காலமுங்**

கற்றான் கருதிச் செயல்"

- திருக்குறள்

So it is essential to know the disease, the etiology, the nature of patients, severity of the illness, the seasons and the time of occurrence.

Line of treatment is as follows:

1. Kaappu (Prevention)
2. Neekkam (Treatment)
3. Niraivu (Restoration)

1. Kaappu (Prevention) :

Prevention and cure of the disease are the basic principle of any medical system but in our Siddha system prevention is the main aim. Siddhars have described general preventive measures and special measures. Especially in Balavagadam, the preventive measures are explained in detail. Prevention of the disease starts from the conception and goes on as the conception and goes on as the child grows up in intrauterine life and after delivery. Siddhars have dealt elaborately with the diet of pregnant women, her habit, the medicine to be taken in every month, her psychological condition and surrounding etc.

Avoid bathing in lake, pond.

Maintaining hair hygiene.

2. Neekam (Treatment) :

The aim of Neekam is based on,

To bring the deranged humours to equilibrium state.

To treat the patient according to the symptoms by Internal medicine "Silvisha Usidham" and Éxternal medicine "Puzhuvettu Thylam"

Virechanam (Purgation)

Ulmarunthu (Internal medicine)

Velimarunthu (External Medicine)

Pathiyam

3. Niraivu (Rejuvenation)

Physical, Psychological, social rehabilitation and reassurance of individuals is known as Niraivu.

Rest

Positive mental attitude

Life style modification

Modification in daily activites

Virechanam :

2-3ml of Mantha ennai with luke warm water was administered at bedtime. Before starting the treatment to bring the vitiated vatham to normal.

Internal and External medicine :

Silvisha Usidham 2-4ml twice daily for 45 days.

Puzhuvettu Thylam for external application indicated for Puzhuvettu in the text Siddha Anubhoga Vaithiya Navaneedha Thirattu.

பத்தியம் :

"**பத்தியத்தினாலே பலனுண்டாகும் மருந்து**

பத்தியங் போனால் பலன் போகும் –பத்தியத்தில்

பத்தியமே வெற்றிதரும் பண்டிதர்க்கு ஆதலினால்

பத்தியமே உத்தியென்று பார்"

- தேரையர் வெண்பா

Diet for alopecia areata :

- Non animal sources of protein, like whole grains, beans, nuts and seeds
- Foods that are high in calcium, such as soy products, nuts, nut milks, soymilk and certain leafy greens
- Healthy fats like olive oil, walnuts, flax seed
- Omega-3 fatty acids, found in , tuna and salmon
- Fresh fruits and vegetables, as they are high in antioxidants
- Vitamin B rich foods, like nuts, carrots, lettuce and tomatoes

Different foods that aggravate the condition and therefore should be strictly avoided :

- Animal fat, especially meat
- Acidic food and other substances that trigger off inflammation
- Milk and dairy products
- Sweets and other sugary foods
- Refined foods, like bakery items
- Fried, oily and greasy food

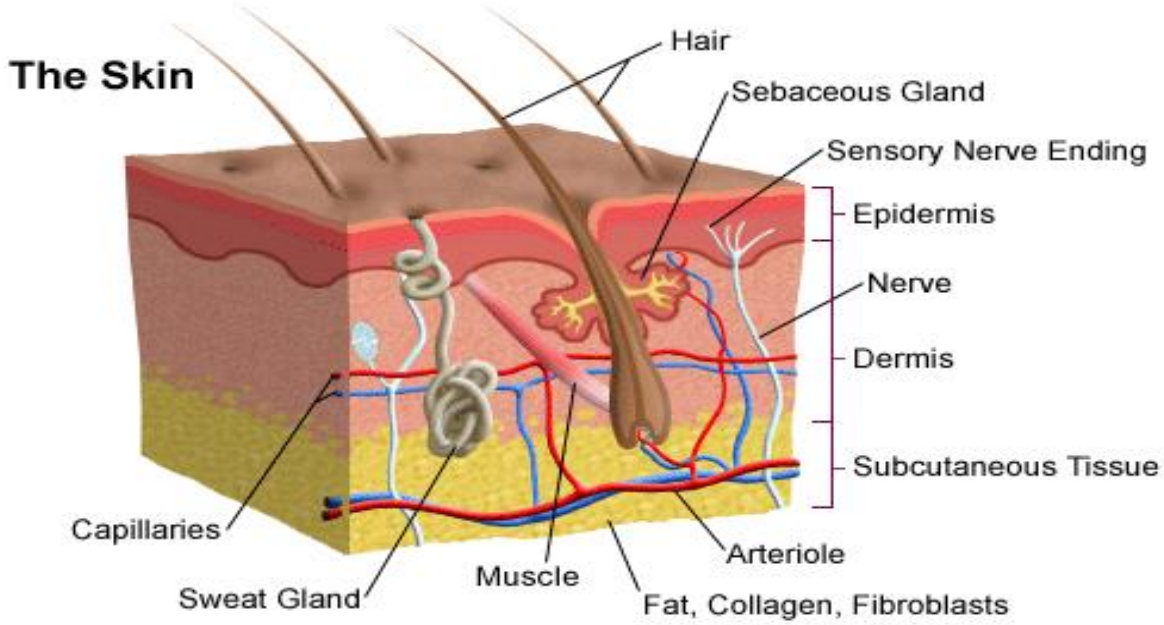
PREVENTION METHODS:

The patients were advised,

1. Good hair hygiene.
2. Good Nutrition especially adequate level of iron and vitamins.
3. Treatment of underlying medical conditions like thyroid disease, anemia and hormonal imbalance.
4. To avoid contaminated food and water
5. To take highly nutritious diet like vegetables, greens and fruit and do yoga to get their immunity developed.

3.2. MODERN ASPECT

ANATOMY OF THE SKIN- CROSS SECTION OF SKIN



The skin is a vital organ that covers the entire outside of the body, forming a protective barrier against pathogens and injuries from the environment. The skin is the Body's largest organ. The color, thickness and texture of skin vary over the body. There are two general types of skin .Thin and hairy, which is more prevalent on the body and thick and hairless, which is found on parts of the body that are used heavily and endure a large amount of friction, like the palms of the hands or the soles of the feet Basically, the skin is comprised of two layers that cover a third fatty layer. These three layers differ in function, thickness and strength. The outer layer is called the epidermis. It is a tough protective layer that contains the melanin – producing melanocytes. The second layer is called the dermis. It contains nerve endings, sweat glands, oil glands, and hair follicles. Under these two skin layers is a fatty layer of subcutaneous tissue, known as the subcutis or hypodermis.

PARTS OF THE SKIN:

- The epidermis
- Dermis
- Hypodermis /subcutaneous tissue

EPIDERMIS:

The epidermis is the most superficial layer of the skin and provides the first barrier of production from the invasion of foreign substances into the body. The principal cell of the epidermis is called a keratinocyte.

Layer of the epidermis:

Stratum corneum /corneal layer /horney layer
Stratum lucidum
Stratum granulosum/granular layer
Stratum Spinosum
Stratum basalis /basal layer

EPIDERMAL APPENDAGES:

HAIR FOLLICLE:

There are 3-5 million hair follicles, epidermal invaginations that develop during the second trimester. They occur throughout the skin, with the exception of palms, soles and parts of the genitalia (glabrous skin).

The highest density of hair follicle is on the scalp (500-1000/cm square). Newborn are covered with fine 'lanugo' hairs, which are usually non-pigmented and lack a central medulla, these are subsequently replaced by vellus hair, which is similar but more likely to be pigmented.

By contrast, scalp hair becomes terminal hair, which is thicker with a central medulla, is usually pigmented and grows longer. At puberty, vellus hair is hormonally sensitive regions, such as the axillary and genital area, become terminal.

Human hairs grow in a cycle with three phases:

1. Anagen (Active hair growth)
2. Catagen (Transitional Phase)
3. Telogen (Resting Phase)

The duration of each phase varies by site. On the scalp, Anagen lasts several years, catagen a few days and telogen around 3months.The length of hair at different sites reflects the differing lengths of anagen.

Hair Physiology :

There are three types of hair

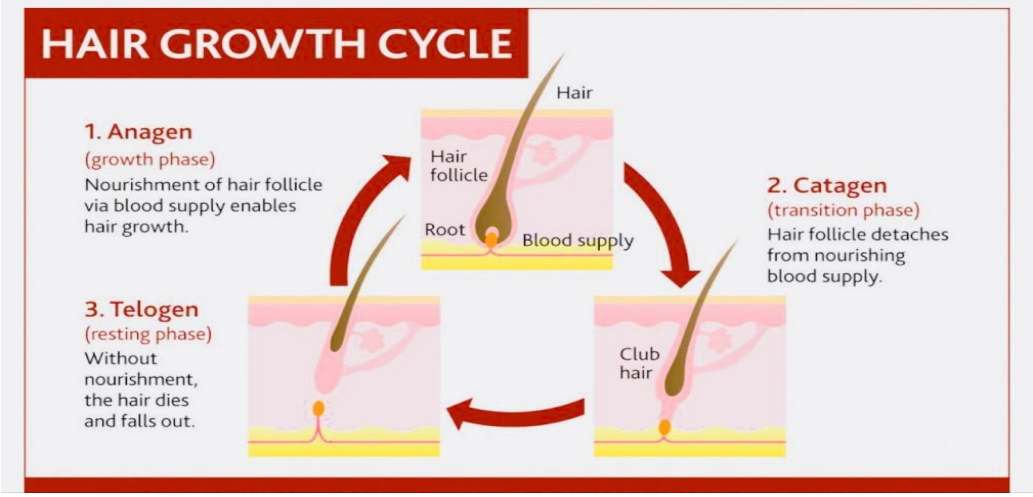
1. Lanugo Hair
2. Vellus Hair
3. Terminal Hair

Lanugo hair – Long, unmedullated hair seen in utero and are shed during the end of pregnancy and the first several months postpartum.

Vellus hair – Short, non-pigmented hair produced by follicles (Intermediate hair) that penetrate only into the papillary dermis,

Terminal hair – Terminal hair are produced by follicles that penetrate into the reticular dermis and are usually medullated and are wider than the inner root sheath of the follicle that produces them. Hair on the scalp and bread area a examples of terminal hair. In the inherited types of balding, some terminal hair are lost and vellus hair are seen instead.

CYCLES:



Anagen (Growth) Phase – About 85% to 95% of scalp hair are in this phase.

Catagen (Regressive) Phase - About 1% of scalp hair are in this phase.

Telogen (Resting) Phase – About 10% to 15% of scalp hair are in this phase.

The length of the anagen phase determines the length of the hair. The anagen for human scalp hair is usually between 2 and 6 years and the hair on the scalp grows about 1cm per month therefore, some people can never have very long hair on the scalp even if they never cut their hair.

Growth phase of hair on other body parts are much shorter than on the scalp. It is normal to lose between 50 and 100 scalp hair per day. Plucking the resting hair from follicles that have already entered anagen can advanced the onset of the hair cycle. The telogen phase is the period between the completion of follicular regression (Catagen) and the onset of the next anagen phase.

On the human scalp the telogen phase lasts about 2 to 4 months. The catagen phase on the human scalp lasts 2 to 4 weeks.

FUNCTIONS OF HAIR:

1. Cosmetic
2. Hair screens entry of irritants to nose
3. Protect Scalp from sunrays
4. Shields the eyes
5. Helps in perception of tactile stimuli

ALOPECIA AREATA

Alopecia areata is a common skin condition characterized by localized hair loss, frequently in children. Both sexes are equally affected. Alopecia areata may be associated with the atopic state and autoimmune disorders such as vitiligo, familial multiendocrine syndrome, thyroid disease (Hashimotos disease), SLE, pernicious anemia, myasthina gravis, ulcerative colitis and lichen planus.

Prevalance is estimated at approximately 0.2% of the population. Incidence of this disease is 17.2/100,000 population. There is a history of familial occurrence 10-20% of the affected individuals .It affect all age group. The first episode usually occurs in patients less than 25 years of age.

Most children develop discoid areas of alopecia in the scalp with peripheral exclamation hairs, and these areas regrow hair normally in due course.In some children,however,particularly those with an ophiasis form distribution of hair loss (invoving the temples and occipital region), the condition is progressive to become total, and regrowth is much less likely.There are also nail changes with fine pitting and horizontal depressions known as Beau's lines.Although Alopecia areata is not a life threatening condition it is obviously distressing for children for children and parents[9].

Types of alopecia areata

1. Alopecia totalis (Hair loss in whole scalp)
2. Alopecia universalis (Whole body)
3. Ophiasis (Occipito-parieto-temporal)
4. Sisaipho
5. Diffuse

- Alopecia areata (AA):

  Alopecia areata is an autoimmune condition which causes patchy hair loss.It can result in a single patch or extensive patchy hair loss

- Alopecia Totalis (AT):

  Alopecia totalis is a more advanced form of alopecia areata which results in total loss of all hair on the scalp.

- Alopecia Universalis (AU):

  Alopecia universalisis the most advanced form of alopecia areata which results in total loss of all hair on the body, including eyelashes and eyebrows.

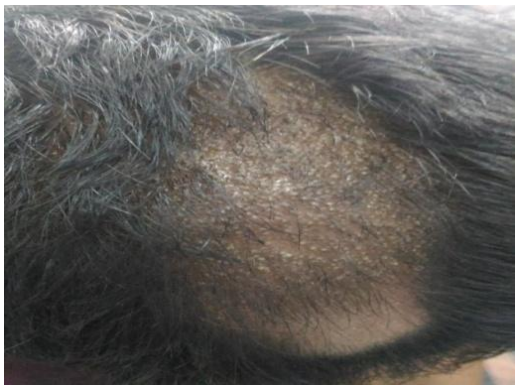
- Scarring Alopecia (Cicatricial Alopecia) :

  Scarring alopecia refers to a group of rare disorder which causes permanent hair loss. It is caused by any inflammatory processes which causes permanent damage to hair follicles.

- OPHIASIS:

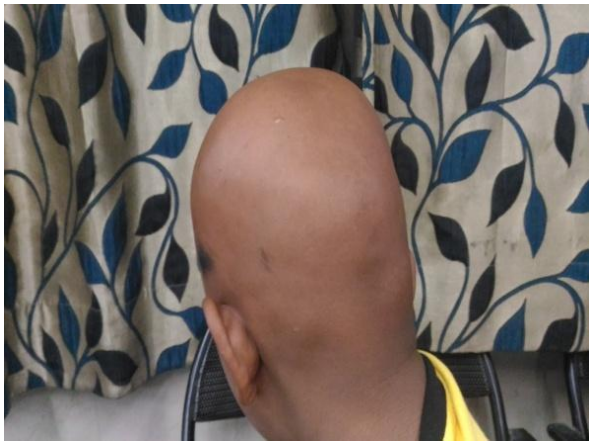
  It is a form of alopecia areata characterized by the loss of hair in the shape of a wave at the circumference of the head.'Ophis' which is a greek word snake,because of the apparent similarity to a snake –shape and the pattern of hair loss.Sisaipho is the reverse spelling of ophiasis.It is also called 'Ophiasis inversus".

DIFFUSE PATTERN ALOPECIA

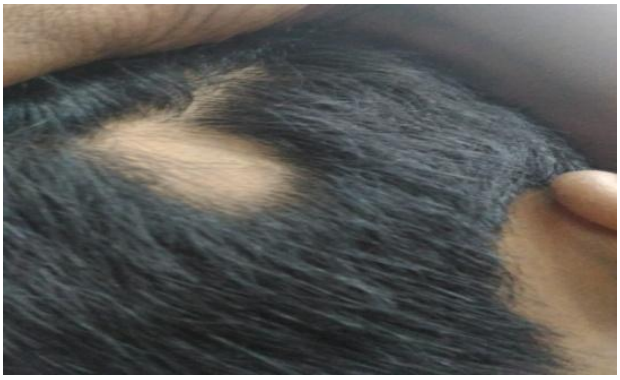


SCARRING ALOPECIA

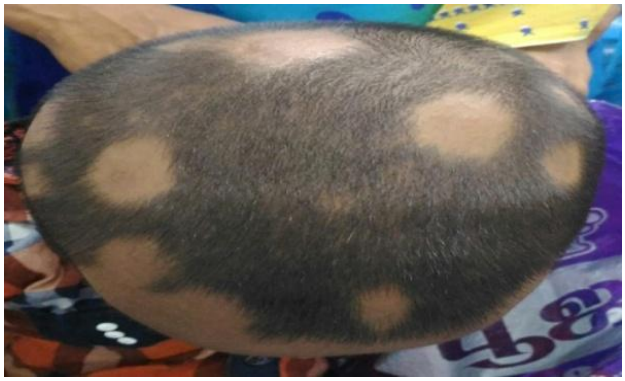
OPHIASIS PATTERN OF ALOPECIA



ALOPECIA TOTALIS



ALOPECIA AREATA (SOLITARY)



ALOPECIA AREATA(MULTIPLE)

ETIOLOGY:

1. Genetic
2. Autoimmunity
3. Infection
4. Emotional stress

CLINICAL FEATURES:

1. Sudden appearance of one or more round or oval well defined patches of hair loss.
2. The hair loss may occur overnight or over a period of several days.
3. Scattered long hairs within bald area.
4. Initial loss may be diffuse and the patches of baldness may be apparent only after 1 or 2 weeks.
5. Exclamation – mark hairs indicates progression of the patch (Active disease).
6. Dystrophic nail changes occurs (pits, longitudinal ridging and thickening).
7. Cataracts or lens opacification.
8. Associated with autoimmune diseases such as Hashimoto thyroiditis,Addison disease,Pernicious anemia,ulcerative colitis,myasthenia gravis, collagen vascular disease and vitiligo.

Indicators of poor prognosis are:

- Atopy
- Presence of other autoimmune diseases
- Family history of Alopecia areata
- Early age of onset
- Extensive hair loss
- Ophiasis
- Nail dystropy

ETIOPATHOGENISIS:

The exact etiology of alopecia areata remains unknown, but there are various postulations. It is generally believed to be an autoimmune disease.

CD4 and T lymphocytes mediate the perifollicular immune against the antigen which may be present in the follicular keratinocyte, melanocyte or dermal papilla, by triggering a cascade of events via cytokine production. Cytokines such as Interferon gamma, Interleukin – 2 and Interleukin – 1β, have been found in the affected area of the scalp.

Calcitonin gene related peptide, which has potent anti-inflammatory actions and substance P, which is capable of including hair growth, are found to be decreased in the scalp of alopecia areata patients.

HISTOPATHOLOGY:

1. Perivascular, peribulbar and outer root sheath infiltrate and follicular dystrophy (Swarm of bees appearance)
2. Lymphocytic and eosinophilic inflammatory infiltrate

DIFFERENTIAL DIAGNOSIS :

1. Tinea capitis
2. Traction alopecia
3. Trichotillomania
4. Loose anagen syndrome
5. Telogen effluvium
6. Androgenetic alopecia

TINEA CAPTIS:

- Scalling or inflammation of the scalp usually present
- Black dot hairs may be observed
- Regional lymphadenopathy may be present
- Fungal culture or potassium hydroxide preparation would be positive

TRACTION ALOPECIA:

- Symmetrical bilateral involvement typical
- Thinning or complete hair loss, especially around hairline or in areas where hair is parted Hair styling usually suggestive with tight braids and heavy hair ornaments

TRICHOTILLOMANIA

- Usually causes localized hair loss
- Irregularly shaped area of incomplete
- Hair of differing lengths in affected area

LOOSE ANAGEN SYNDROME

- Typically long history of diffusely thin and lusterless hair
- Hair grows slowly; History of no haircuts common
- Hair mount of easily extracted hairs confirms the diagnosis.

TELOGEN EFFUVUM

- Usually diffuse thinning without areas of complete hair loss
- Typically associated with preceding physical trauma/ illness believed to trigger conversion from anagen to telogen phase of hair
- Self-limited; gradual improvement within months

ANDROGENETIC ALOPECIA

- Not typically seen in younger children
- Classic distribution; symmetrical over vertex and frontal hair line
- May be associated with sign on hyper androgenic
- No associated nail changes.

INVESTIGATIONAL AGENTS

- Cytokines
- Antibodies
- Gene therapy
- Biologic therapy
- Adjunctive agents

DIAGNOSIS:

- Usually a clinical one, based on the typical finding
- In some patient, there may be associated loss of eyebrows and lashes characteristic nail changes.

- Skin biopsy rarely necessary to confirm the diagnosis, finding includes perifollicular lymphocytic infiltration.

Management for Alopecia Areata:

The treatment available for Alopecia areata at present can only control the disease, but not curative.Local treatment may help the treated areas but do not prevent further spread.The first and most important step in the management of alopecia areata is to give psychological support and counseling.A change of hair-style,caps,hats,head bands and wigs may be required for adequate camouflage.

Current Agents

- Corticosteroids
- Topical
- Intralesional
- Systemic
- PUVA(Psoralen Ultraviolet A)
- Minoxidil
- Topical sensitizers
- Anthralin
- Imiquimod

PROGNOSIS:

- Prognosis is difficult to predict and extremely variable
- Many children with isolated episodes of localized patchy hair loss will have spontaneously hair regrowth without therapy
- Children with rapid and extensive hair loss, especially when progressing to complete loss, usually respond poorly to therapy.

RESOURCES FOR FAMILIES:

- National Alopecia Areata Foundation:
- Provides information, support and resources for patients and families[10].

3.3. DRUG REVIEW

1.ஏலம்

Taxonomical classification:

Kingdom : Plantae

Phylum : Angiosperms

Order : Zingiberales

Family : Gingiberaceae

Genus : Elettaria

Species : Elettaria cardamomum

Botanical name	**:** Elettaria cardamomum
Family	: Zingiberaceae
Other name	: Aanji,Korangam,Thudi
Eng	: Cardamom
Hindi	: Chhoti elachi
Tel	: Elakulu
Mal	: Elatlari
Kan	: Elakki
Habitat	: Cultivated for its fruit in many parts of western and southern india.
Parts Used	: Dried ripe seeds ;Oil from fruits
Suvai	: Kaarppu
Thanmai	: Veppam
Pirivu	: Kaarppu

Action :

Powerful aromatic, Stimulant, Carminative, Stomachic and Diuretic [11].

These properties are due to the essential oil contained in the seeds.

தொண்டை வாய்கவுள் தாலுகு தங்களில்

தோன்றும் நோயதி சாரம்பன் மேகத்தால்

உண்டை போல்எழுங் கட்டி கிரிச்சரம்

உழலை வாந்தி சிலந்தி விஷஞ்சுரம்

பண்டை வெக்கை விதாகநோய் காசமும்

பாழுஞ் சோமப் பிணிவிந்து நட்டமும்

அண்டை யீளைவன் பித்தம் இவைக்கெல்லாம்

ஆல மாங்கமழ் ஏல மருந்ததே

-தேரையர் குணவாகடம்[11]

Chemical Constituent:

Fixed oil, Essential oil, Volatile oil of the seeds- active principle 4 to 8 p.c and 'contains considerable amount of Terpinyl acetate, cinole, free terpinol and limonene [12] α-pinenes, β-pinenes, camphene, P-Cymene, terpinene, α-terpineol and α-humulene isolated from essential oil of fruits and leaves [13] .

Therapeutic uses:

Abdominal pain, cough, Thirst, Diarrhoea, Oliguria, Sinusitis, Skin disease and Indigestion

Scientific review

1. **Immunomodulator activity :**

In vitro investigation of the potential immunomodulatory activities of cardamom. Aqueous extracts of cardamom significantly enhance spenocyte proliferation in a dose – dependent synergistic fashion. ELISA experiment reveal cardamom significantly enhance and suppress respectively, T–Helper (Th-1) cytokine release by splenocytes. Conversely, T–Helper (Th-2) cytokine release by splenocytes is significantly suppressed and enhanced by cardamom respectively. cardamom constituents can be used as potential therapeutic tools to regulate inflammatory response[14].

2. **Immunomodulator activity :**

Cardamom – essential oil is popular in skin care. Its effect on 17 protien biomarkers closely related to inflammation, immune responses and tissue remodeling using a dermal fibroblast cell culture system designed to model chronic inflammation. Its major active component is Eucalptol.CEO (Cardamom essential oil) – induced inhibition of these genes and pathway supports its anti-inflammatory and immunomodulatory properties.[15]

3. A**ntimicrobial, Antifungal Activity and Anti inflammatory activity**.

The volatile oil of the fruit of Elettaria cardamom showed significant antimicrobial activity against pathogenic bacterial and fungal strain. Cardamom essential oil had inhibitory effect against fungus growth and anti-inflammatory activity [16]

2. எள்

Taxonomical classification:

Kingdom : Plantae
Phylum : Angiosperms
Order : Lamiales
Family : Pedaliaceae
Genus : Sesamum
Species : Sesamum indicum

Botanical name : Sesamum indicum
Family : Pedaliaceae
Other name : Thilam
Eng : Gingeli oil plant, gingilly, sesame
Hindi : Thil
Tel : Nuvulu
Mal : Karuella
San : Thilam
Habitat : Annual plant

Varities : Sesamum seeds are found –Black, White and red or brown leaves, flowers.
Parts Used : Leaves, Flower, Seeds and the fixed oil expressed from the seeds

Suvai : Inippu
Thanmai : Veppam
Pirivu : Inippu

Action :

Seeds: Laxative, Emollient and demulcent, Diuretic, Nourishing, emmenagogue, lactogogue.

Oil action : Demulcent, Laxative, Nutritive, Emollient

எள்ளுமருந் தைக்கெடுக்கும் எறனலாந் திண்மைதரும்
உள்ளிலையைச் சேர்க்கும் உதிரத்தை-தள்ளுமிரு
கண்ணுக் கொளிகொடுக்குங் காசமுண்டாம் பித்தமுமாம்
பண்ணுக் கிடர்புரியும் பார்.

-அகத்தியர் குணவாகடம்

Chemical Constituent :

Diosgenin, β – sitosterol, lanosterol, solasonine, solamargine and solasodine [17]
Seed contains -protein,carbohydrate,mucilage,woody fibre,ash, fixed oil.

Oil contains - Stearin, palminitin, myristin, a crystalline substance sesamine, a phenol compound sesamol Vit –E, Phytosterol

Seeds contain fixed oil 50 to 60 p.c [18]

	Moisture	**Oil**
Black Til	2.0 to5.2 p.c	44.6 to 56.9 p.c
Red Til	-	45.7 to 55.5 p.c
White Til	2.0 to 4.4 p.c	44.9 to 58.2 p.c

Therapeutic uses:

Eye and ear releated disease, Skin disease, ulcer, Burns and cough.

Scientific review

1. **Anti Inflammatory Activity**

Anti inflammatory activity of sesame oil and sesamin – Leucocyte migration were also reduced by sesame oil and sesamin[19.]

2. **Immunomodulating activity**

The mechanism of sesame oil in ameliorating experimental autoimmune encephalomyelitis in C57BL / 6 mice . Sesame oil reducing IFN – gamma secretion.[20]

3. Piper longum - திப்பிலி

Taxonomical classification:

Kingdom : Plantae

Phylum : Angiosperms

Order : Microembryeae

Family : Piperaceae

Genus : Piper

Species : Piper longum

Botanical Name : Piper longum

Family : Piperaceae

Other name : Aargadhi, unsaram, ulavainaasi, kaaman, kudari, kolagam, koli, kozhaiyarukki, saram, saadi, thulavi, maagadhi, sondi, thandoli, kanam, kalini, baanam, pippili, vaitheyki, ambu, aadhimarundhu.

Eng : Long pepper

Tel : Pippilu

Mal : Thippilli

Kan : Hippili

Parts Used : Fruit,dried spikes and roots

Suvai : Inippu

Thanmai : Veppam

Pirivu : Inippu

Action : Stimulant, Carminative

Varieties : Arisi thippili and Yanai thippili

Habitat : Climber

இருமல் குன்மம் இரைப்பு கயப்பிணி

ஈளை பாண்டு சந்யாசம் அரோசகம்

பொருமல் ஊதை சிரப்பிணி மூர்ச்சைநோய்

பூரிக் குஞ்சல தோடம் பீலிகமும்

வரும லப்பெருக் கோடு மகோதரம்

வாதம் ஆதிமுத் தோடஞ் சுரங்குளிர்

பெருமாலைப்புரி மேகப் பிடகமும்

பேருந் திப்பிலிப் பேரங்குரைக்கவே.

-தேரையர் குணவாகடம்.

It cures cough, ulcer, bronchial asthma, kapha diseases, anaemia, headache, delirium, sinusitis and throat pain.

Chemical Constituent:

Two new piperidine alkaloids–pipernonaline and Piperundecalidine – isolated from fruits and their structures determined [21].

Volatile oil, resin, starch, gum, fatty oil, Inorganic matter and an alkaloid, Piperine, Rutin,β-caryophyllene, piperyline, piperoleines, piperamine, sabinene, chavicin, pinene, phellandrene, pentadecane, β- bisabolene, linalool and limonene.

Therapeutic uses:

Cough, ulcer, asthma, kabha disease, anemia, lethargy, flatulence, headache, delirium, sinusitis, throat disease, ear, nose, eye related disease, worm infestation.

Scientific review

1. **Anti inflammatory property:**

Piper extracts and piperine possess inhibitory activities on prostaglandin and leukotrienes COX-1 inhibitory effect and thus exhibit anti-inflammatory activity.[22]

2. **Immunomodulator Activity** :

Alcoholic extract of the fruits of the plant Piper longum and its Component Piperine was studied their immunomodulatory activity Piperinic acid moderated the pro inflammatory mediators and cytokines in the experiment, decreases of lymphocytes cytokine levels in sensitized Balb/c mice .[23]

4. பேயத்தி

Taxonomical classification:

Kingdom : Plantae

Phylum : Angiosperms

Order : Rosids

Family : Moraceae

Genus : Ficus

Species : Ficus hispida

Botanical Name : Ficus hispida

Family : Moraceae

Other name : Pe-allippayam,kattu- atthi, pe-atthi, pe- attiss, pechi, pethi

Eng : Fig tree

Hindi : Katgular

Tel : Atti - pandhlu

Parts Used : Leaves,Bark and fruit

Suvai : Thuvarppu

Thanmai : Thatppam

Pirivu : Inippu

Action : Bark-emetic, Laxative Fruit-Colling, Astringent, Sour

Habitat : Tree

Chemical Constituent:

Bergapten, Psoralen, β –Amyrin and β– sitosterol [24] Hispidine, Phenanthraindolizidines [25] n – triacontanyl, Gluanol acetates[26] ,Tannin,wax,a caoutchouc – like substance and saponin.

Therapeutic uses:

Bleeding piles, diarrhoea, leucorrhoea, menorragia, diabetic ulcer and arthritis.

Scientific review

1. **Anti – inflammatory property**

   Leaves extract of Ficus hispida leaves against cargeenan induced paw edema in rats.[27]

5.Amanakk-kenny

Taxonomical classification:

Kingdom : Plantae

Phylum : Angiosperms

Order : Euphorbiales

Family : Euphorbiaceae

Genus : Ricinus

Species : Ricinus communis

Botanical Name	:	Ricinus communis
Family	:	Euphorbiaceae
Other name	:	yerandam,Sithiram,Thalarubam
Eng	:	Castor oil
Hindi	:	Arand-kat
Tel	:	Amudam
Mal	:	Kottenna
Kan	:	Haralenne
San	:	Yeranda-tailam
Habitat	:	Two types

Small tree – 1. Chittamanakku
2. Peramanakku
3. Chevvamanakku (Ricinus tanarius)

Herb - 1. Kaatamakku
2. Yeliyamanakku

Parts Used	:	Leaves, Root and Seed.
Suvai	:	Kaippu
Thanmai	:	Veppam
Pirivu	:	Karppu
Action	:	Galactagogue, Anti-vatha, Laxative and Emollient

Chemical Constituent :

Ricin , Ricinoleic acid, Fatty acid , Linoleic acid, oleic acid, Palmitic acid, Stearic acid, linolenic acid and triacylglycerols.

	Moisture:	**Oil:**
	p.c	p.c
Castor (general)	2.97 to 6.97	38.57 to 57.40
Castor (Big variety)	2.97 to 6.25	46.63 to 55.43
Castor (Small variety)	3.17 to 6.06	43.39 to 57.40
Castor (Without awns)	4.24 to 5.20	48.28 to 51.86

பேரண்டத்துநெய் யென்பது டற்கொடு
சீரண்டத்தணி செய்திடு நிசமே.

- தேரையர்

ஆமணக்கு நெய்யால் நலமுண்டாம் யாவர்க்கும்
பூமணக்கு மேனி புரிகுழலே - வாய்மணக்கக்
கொள்ளில் வயிறுவிடுங் கோரமுள்ள வாயுவறும்
உள்ளில்வரு குன்மம்போ மோது.

அம்பொனிற மும்விந்து மாங்குடலி னெற்றமறும்
ஐம்பொறிச் சூடெரிவு மாறுங்காண் -அம்புவியிற்
பாமணக்கு மின்பமொழிப் பாவாய் ! நலஞ்செறிந்த
ஆமணக்கு நெய்யை அருந்து.

ஆமனக் கெண்ணெய் தன்னை யணிநில மறியக் கேண்மின்
பூமணச் சந்துதோறும் பொருந்திய வாதம் போக்கும்
தீமந்தந் தானும் போக்குந் திகழ்வுடன் விரைவு முண்டாம்
தீமனக் குடலில் வாதஞ் சேர்குட லேற்றம் போமே.

Therapeutic uses:

1. Castor oil is one of the cheapest, simplest and most important and useful purgatives in all delicate conditions for children and old people.
2. Chronic articular rheumatism
3. Sinusitis, Sore nipples
4. Colicky pain

6. Kungiliyam

Taxonomical classification:

Kingdom	:	Plantae
Phylum	:	Angiosperms
Order	:	Malvales
Family	:	Dipterocarpaceae
Genus	:	Shorea
Species	:	Shorea robusta
Botanical Name	:	Shorea robusta
Family	:	Dipterocarpacea
Other name	:	Kungiliyam, kungiligam, saruvrasam, gugulu, kukil
Eng	:	Sal tree, Indian Damar
Hindi	:	Dhuna, Damar
Tel	:	gugilamu
Mal	:	Kungiliyam
San	:	Guggilam
Arab	:	qaaguahar
Parts Used	:	Resin
Suvai	:	Kaippu
Thanmai	:	Veppam
Pirivu	:	Karppu
Habitat	:	Tree

Types :

1. White
2. Red

Action : Stimulant, Expectorant, Diuretic

Chemical Constituent :

Chalcone,-4-hydroxychalcone-4-O-β-`D-glucopyranoside [28]. *S. robusta* resin has been reported to contain several mono-, sesqui- and tri-terpenoids includes ursolic acid, tri and tetra hydroxy ursenoic acid, asiatic acid, α and β-amyrin, α –amyrenone, mangiferonic acid, benthamic acid and uvaol[29].

வெள்ளைக் குங்கிலியம் (சருவரசம்)

வெள்ளை யளித்த விரணநா பிக்கமலத்

தொள்ளைவிர ணம்மேகந் தோற்றுகினும் -உள்ளே

வருவரசனைமேற்புண் வரினுஞ் சுவேதச்

சருவரச மேற்பழியைச் சாற்று.

-தேரையர் குணவாகடம்.

Therapeutic uses :

- Menorrhage, Leucorrhoea, Ulcer, Abscess
- Internal hemorrhoids
- Ear, Nose, Throat Disease
- Syphilitic ulcer
- Dysentry, urticaria, Arthritis
- Disease of nail the powdered resin is mixed with sugar and given for diarrhoea in children.
- The powdered resin along with milk is taken as an alternative.
- It is used for fumigating the rooms of ill people.
- It is used as an ointment for wound as an ingredient of ointments for skin diseases and in ear troubles.
- The resin obtained from the plant is considered as an astringent and is used in dysentery and bleeding piles.
- It is also given in gonorrhea and for delayed digestion.

Scientific review

1. **Anti Inflammatory activity :**

2. Ethonolic extract of Shorea robusta resin has anti inflammatory activity-carrageen induced paw edema and sub –acute by cotton pellet- induced granuloma in male Wistar rats.[30]

7. AVURI

Taxonomical classification:

Kingdom : Plantae

Phylum : Angiosperms

Order : Fabales

Family : Fabaceae

Genus : Indigofera

Species : Indigofera tinctoria

Botanical name	:	Indigofera tinctoria
Family	:	Fabaceae
Other name	:	Neelam, nilam, Aviri, Avari
Eng	:	True indigo, Dyer's
Hindi	:	Sind
Tel	:	Aviri, Neeichettu, neli
San	:	Neela, Neelinee, Nililea
Parts Used	:	Leaf, Root, Plant and Expressed juice - Indigo
Suvai	:	Kaippu
Thanmai	:	Veppam
Pirivu	:	Kaarppu
Habitat	:	Shrub
Action	:	Stimulant, Alternative, deobstruent, Germicide, Antiperiodic and Purgative Indigo is antiseptic and astringent.

உரியலவு ரித்தழைத்தான் ஓது பதினெண்

அரியநஞ்சைத் தின்றவர்க்கும் ஆகும் -தெரிவரிய

வாதவெப்பு காமாலை மைந்தர் குறுமாந்தஞ்

சன்னி பதிமூன்றுஞ் சந்தொடித்த வாதமுதல்

உன்னு விடக்கடியும் ஓடுங்காண்-மின்னுங்

கவுரிநிறம் உண்டாகும் காசினியுள் நல்ல

அவுரியிலை தன்னால் அறி.

-அகத்தியர் குணவாகடம்.

Chemical Constituent:

Indican (Glycoside), Indigotin or Indigo-blue, Indicom, Indigotine, indirubin and Glactomannan.

Therapeutic uses :

- Amtidote, Valisuram, Mantham, Jaundice, Delirium
- Stomach Ulcer, Leucorrhoea
- Arthritis
- Skin Disease

Scientific review

1. **Immunomodulatory activity**

In vitro study of Indigofera tinctoria leaf extract - macrophage response and lymphocyte proliferation [31]

2. **Effect of UV – B radiation on biochemical and anti oxidant defence system in Indigofera tinctoria**

Indigofera tinctoria is resistant to UV -B radiation damage and the possible negative effect of additional UV-B radiation on the growth of seedling may have been effectively balanced by the UV-B radiation stress through increase in UV-B absorbing compound and antioxidant enzymes.[32]

3. **Hair Growth Promoting activity :**

Ethonol extract of Indigofera tinctoria Linn for their effect on promoting hair growth in albino wistar rats.[33]

INRGREDIENTS OF TRIAL DRUG

SILVISHA USIDHAM

Gingelly Oil

Ficus hispida

Eleteria cardamomum

Piper longum

PUZHUVETTU THYLAM

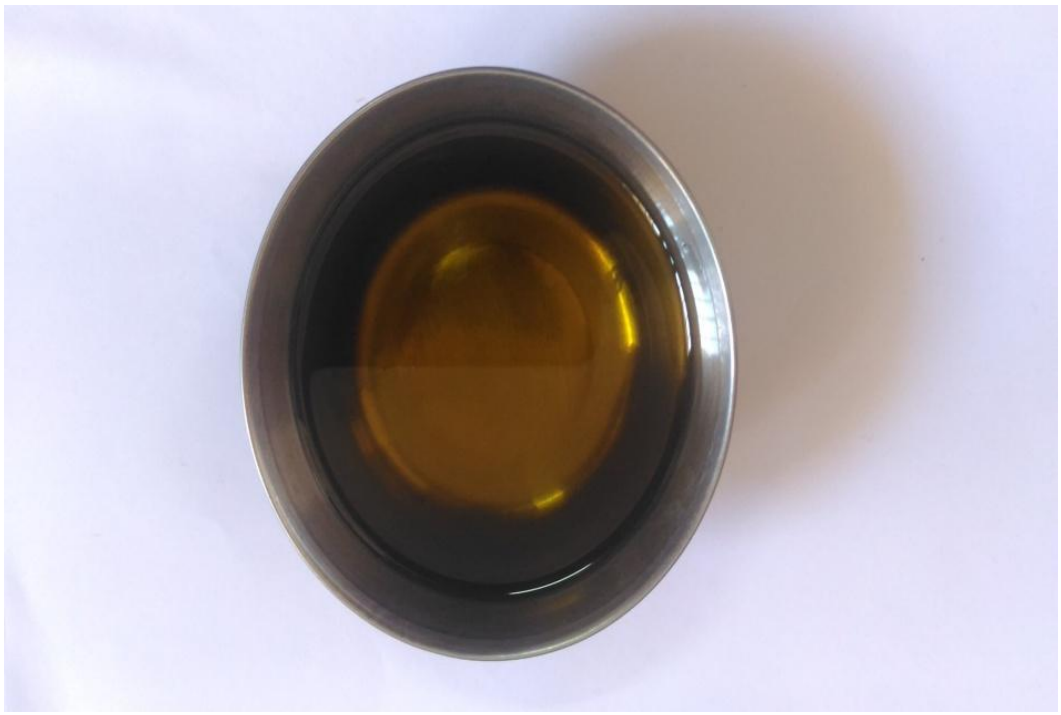
Shorea robusta

Castor oil

Indigofera tinctoria

PREPARED MEDICINE

SILVISHA USIDHAM (INTERNAL)



PUZHUVETTU THYLAM (EXTERNAL)

4. MATERIALS AND METHODS

Puzhuvettu is one of the commonest skin conditions in children. It was proposed to study about the disease. A protocol was prepared and submitted before IEC of National Institute of Siddha. After obtaining IEC approval from the committee the clinical study on Puzhuvettu (alopecia areata) in children and the drug of choice was Silvisha Usidham (Internal) and Puzhuvettu Thylam (External) was carried out as per the protocol. The IEC approval number and date is NIS/IEC/2016/11-20/14.10.2016.

The ingredients for preparation of experimental formulation Silvisha Usidham and Puzhuvettu thylam was purchased from a well reputed country shop and raw drugs were authenticated by Herbal botanist. The medicine was prepared in Gunapadam lab of national Institute of Siddha after proper purification.

4.1 PREPARATION OF MEDICINE:

Ingredients of Silvisha Usidham:

1. Gingelly oil (Sesame indicum) - 40 palam (1400gm)
2. Peyathi saru (Ficus hispida) -80 palam (2800gms)
3. Elarisithool (Elettaria cardamomum) -1 palam (35gms)
4. Arisithippili (Piper longum) -1 palam (35gms)

Method of Purification:

Peyathi : Remove petiole and vein of the leaves

Elarisithool : Fry to the extent that the contents become golden color

Arisithippili : Fruit of Piper longum was soaked in lemon juice and it was dried in sunlight until the juice gets evaporated. Then it was fried well

Method of preparation:

The above said elarisithool and arisithippili powder mixed with peyathi juice together combined with gingelly oil and heated till the waxy consistency is obtained.

Indication: Puzhuvettu [7]

Ingredients of Puzhuvettu Thylam :

1. Castor oil (Riccinus comminus) - 5 Palam (175gm)
2. Venkungiliyam (Shorea robusta) - ¼ Palam (8.75gm)
3. Avuri leaf (Indigofera tinctoria) - 5 Palam (175gm)

Method of Purification:

1. Venkungiliyam : Resin of Shorea robusta was boiled with tender coconut and then dried
2. Avuri : Whole plant wash with clean water

Method of Preparation:

Take avuri paste and venkungiliyam powder in equal quantity, then mixed with castor oil afterwards boiled it well till it reaches waxy consistency.

Indication: External application for Puzhuvettu.[7]

4.2 PRECLINICAL SAFETY STUDIES:

A. Physicochemical Analysis
B. Biochemical Analysis
C. Acute Toxicity Study
D. Phytochemical Analysis
E. Quantitative Analysis
F. Pharmacological Activity

A) PHYSICOCHEMICAL ANALYSIS OF THE SILVISHA USIDHAM

Physicochemical evaluation

Determination of specific gravity

Fill the dry sp. gravity bottle with prepared samples in such a manner to prevent entrapment of air bubbles after removing the cap of side arm. Insert the stopper, immerse in water bath at $50^{O}C$ and hold for 30 min. Carefully wipe off any substance that has come out of the capillary opening. Remove the bottle from the bath, clean and dry it thoroughly. Remove the cap of the side and quickly weigh. Calculate the weight difference between the sample and reference standard.

Determination of Iodine value

About 20 gm of test sample was transferred into Iodine flask. To which 10 ml of chloroform was added and warmed slightly and cooled for 10 minutes. Followed by this about 25 ml of Wiji's solution was added in the same flask and shaken well. The flask was allowed to stand for 30mins and refrigerated for an hour. T About10 ml of KI solution was added to this and titrated against 0.1 N Sodium thiosulphate solutions until the appearance of yellow color. 1 ml of starch indicator was added and again titrated against the sodium thiosulphate solution from the burette. Disappearance of blue colour indicates end point. Repeat the above procedure without taking sample and note the corresponding reading for blank titration.

Determination of saponification value

About 2 gm of test sample was transferred into the round bottomed flask. To this about 20 ml of 0.5 N alcoholic KOH solutions was added to the round bottomed flask. Repeat the same procedure without taking the sample for blank titration. Reflux both sample and blank round bottomed flasks for 1 hour. After reflux, allow both the round bottomed flasks to cool. Titrate the samples using 0.5 N HCl with phenolphthalein indicator. The disappearance of pink indicates the end point.

Determination of Viscosity value

Viscosity determination were been carried out using Ostwald viscometers. Measurement of viscosity involves the determination of the time required for a given volume of liquid to flow through a capillary. The liquid is added to the viscometer, pulled into the upper reservoir by suction, and then allowed to drain by gravity back into the lower reservoir. The time that it takes for the liquid to pass between two etched marks, one above and one bellow the upper reservoir, is measured.

Determination of Refractive Index

Determination of RL was carried out using Refractometer.

Determination of Weight per ml

Weight per ml was determined using the comparative weight calibration method, in which the weight of 1ml of the base of the formulation was calculated and then weight of 1 ml of finished formulation were been calculated. The difference between weight variations of the base with respect to finished formulation calculated as an index of weight per ml.

Determination of pH

Sample being liquid in nature the direct litmus evaluation method was adopted to check the pH of the sample.

Acid Value

Accurately 5 g of test sample was weighed and transferred into a 250 mL conical flask. To this, a 50 mL of neutralized alcohol solution was added. This mixture was heated for 10 min by heating mantle. Afterwards, the solution was taken out after 10 min and 1 or 2 drops of phenolphthalein indicator was added. This solution was titrated against KOH solution from the burette. The appearance of pink color indicated the end point. The volume of consumed KOH solution was determined and the titration of test sample was carried out in triplicate and the mean of the successive readings was used to calculate the acid-value of the respective sample by following expression.

Acid value = Titter Value X 0.00561X 1000 / Wt of test sample (g)

Peroxide value

5 g of the substance being examined, accurately weighed, into a 250-ml glass-stoppered conical flask, add 30 ml of a mixture of 3 volumes of glacial acetic acid and 2 volumes of chloroform, swirl until dissolved and add 0.5ml volumes of saturated potassium iodide solution. Allow to stand for exactly 1 minute, with occasional shaking, add 30 ml of water and titrate gradually, with continuous and vigorous shaking, with 0.01M sodium thiosulphate until the yellow colour almost disappears. Add 0.5 ml of starch solution and continue the titration, shaking vigorously until the blue colour just disappears (a ml). Repeat the operation omitting the substance being examined (b ml). The volume of 0.01M sodium thiosulphate in the blank determination must not exceed 0.1 ml.

$$\text{Peroxide value} = 10\ (a - b)/w$$

B. BIOCHEMICAL ANALYSIS OF SILVISHA USIDHAM:

The chemical analysis of Silvisha Usidham was carried out in Bio chemistry lab, National Institute of Siddha.

S.No	EXPERIMENT	OBSERVATION
1.	Physical Appearance of extract	Pale yellowish in colour
2.	**Test for Silicate** A 500mg of the sample was shaken well with distilled water.	Sparingly soluble
3.	**Action of Heat:** A 500mg of the sample was taken in a dry test tube and heated gently at first and then strong.	No White fumes evolved.
4.	**Flame Test:** A 500mg of the sample was made into a paste with Con. HCl in a watch glass and introduced into non-luminous part of the Bunsen flame.	No bluish green flame
5.	**Ash Test:** A filter paper was soaked into a mixture of extract and dil. cobalt nitrate solution and introduced into the Bunsen flame and ignited.	No yellow color flame

Preparation of Extract:

5gm of sample was taken in a 250ml clean beaker and added with 50ml of distilled water. Then it was boiled well for about 10 minutes. Then it was cooled and filtered in a 100ml volumetric flask and made up to 100ml with distilled water. This preparation was used for the qualitative analysis of acidic/basic radicals and biochemical constituents in it.

S.No	EXPERIMENT	OBSERVATION
	I. Test For Acid Radicals	
1.	**Test For Sulphate:** 2ml of the above prepared extract was taken in a test tube to this added 2ml of 4% dil ammonium oxalate solution	Cloudy appearance present
2.	**Test For Chloride:** 2ml of the above prepared extract was added with 2ml of dil-HCl until the effervescence ceases off.	No Cloudy appearance was formed
3.	**Test For Phosphate:** 2ml of the extract was treated with 2ml of dil.ammonium molybdate solution and 2ml of Con.HNo3	No Cloudy yellow appearance present
4.	**Test For Carbonate:** 2ml of the extract was treated with 2ml dil. magnesium sulphate solution.	Cloudy appearance present.
5.	**Test For Nitrate:** 1gm of the extract was heated with copper turning and concentrated H2So4 and viewed the test tube vertically down.	No Brown gas was evolved
6.	**Test For Sulphide:** 1gm of the extract was treated with 2ml of Con. HCL	No rotten egg smelling gas was evolved
7.	**Test For Fluoride & Oxalate:** 2ml of extract was added with 2ml of dil. Acetic acid and 2ml dil. calcium chloride solution and heated**.**	No cloudy appearance.
8.	**Test For Nitrite:** 3drops of the extract was placed on a filter paper, on that-2 drops of dil.acetic acid and 2 drops of dil.Benzidine solution were placed.	No characteristic changes were noted.

9.	**Test For Borate:** 2 Pinches (50mg) of the extract was made into paste by using dil.sulphuric acid and alcohol (95%) and introduced into the blue flame.	No Appearance of bluish green color.
II. Test For Basic Radicals		
1.	**Test For Lead:** 2ml of the extract was added with 2ml of dil.potassium iodine solution.	No Yellow precipitate was obtained
2.	**Test For Copper:** One pinch (25mg) of extract was made into paste with Con. HCl in a watch glass and introduced into the non-luminuous part of the flame.	No blue colour appeared
3.	**Test For Aluminium:** To the 2ml of extract dil.sodium hydroxide was added in 5 drops to excess.	No yellow Colour appeared
4.	**Test For Iron:** a. To the 2ml of extract, added 2ml of dil.ammonium solution b. To the 2ml of extract 2ml thiocyanate solution and 2ml of con HNO3 were added	Mild Red colour appeared
5.	**Test For Zinc:** To 2ml of the extract dil. sodium hydroxide solution was added in 5 drops to excess and dil. ammonium chloride was added.	No White precipitate was formed
6.	**Test For Calcium:** 2ml of the extract was added with 2ml of 4% dil.ammonium oxalate solution	No Cloudy appearance and white precipitate was formed
7.	**Test For Magnesium:** To 2ml of extract dil. sodium hydroxide solution was added in 5 drops to excess.	No White precipitate was obtained

8.	**Test For Ammonium:** To 2ml of extract 1 ml of Nessler's reagent and excess of dil.sodium hydroxide solution were added.	Brown colour appeared
9.	**Test For Potassium:** A pinch (25mg) of extract was treated with 2ml of dil. sodium nitrite solution and then treated with 2ml of dil. cobalt nitrate in 30% dil. glacial acetic acid.	No Yellow precipitate was obtained
10.	**Test For Sodium**: 2 pinches (50mg) of the extract was made into paste by using HCl and introduced into the blue flame of Bunsen burner.	No yellow colour flame evolved.
11.	**Test For Mercury**: 2ml of the extract was treated with 2ml of dil. sodium hydroxide solution.	No Yellow precipitate was obtained
12.	**Test For Arsenic:** 2ml of the extract was treated with 2ml of dil. sodium hydroxide solution.	No Brownish red precipitate was obtained

III. Miscellaneous		
1.	**Test For Starch:** 2ml of extract was treated with weak dil.Iodine solution	Blue colour developed
2.	**Test For Reducing Sugar:** 5ml of Benedict's qualitative solution was taken in a test tube and allowed to boil for 2 minutes and added 8 to 10 drops of the extract and again boil it for 2 minutes. The colour changes were noted.	No Brick red colour is developed

3.	**Test For The Alkaloids**: a) 2ml of the extract was treated with 2ml of dil.potassium lodide solution. b) 2ml of the extract was treated with 2ml of dil.picric acid. c) 2ml of the extract was treated with 2ml of dil.phosphotungstic acid.	Yellow colour developed
4	**Test For Tannic Acid:** 2ml of extract was treated with 2ml of dil. ferric chloride solution	No Blue-black precipitate was obtained
5	**Test For Unsaturated Compound:** To the 2ml of extract, 2ml of dil. Potassium permanganate solution was added.	Potassium permanganate was not decolourised
6	**Test For Amino Acid:** 2 drops of the extract was placed on a filter paper and dried well. 20ml of Burette reagent was added**.**	No Violet colour appeared
7	**Test For Type of Compound:** 2ml of the extract was treated with 2 ml of dil. ferric chloride solution.	No green and red colour developed No Violet colour developed No Blue colour developed.

C. ACUTE TOXICITY STUDY :

TOXICOLOGICAL EVALUATION OF SILVISHA USIDHAM (SU)

The following in vivo toxicity studies were carried out on Silvisha Usidham (SU) by World Health Organization (WHO) guideline [39]. Acute Oral Toxicity study (WHO)

The toxicity studies were carried out at National Institute of Siddha. The study was done after getting permission from the Institutional Animal Ethics Committee.
IAEC Approved No: For acute toxicity study – NIS/IAEC-IV/05/05012017

For Acute toxicity studies test animals were obtained from Tamil Nadu Veterinary and Animal Sciences University, Madhavaram. Animals were kept in animal house at National Institute of Siddha, Chennai.

DESCRIPTION OF THE METHOD

Selection of the animals:

Animals were selected as per guidelines. Healthy adult animals of Wistar albino rat, both male and female sex were used for acute oral toxicity study. The female animals used in the studies were nulliparous and non-pregnant.

Housing and feeding conditions:

The temperature in the experimental animal room: 22ºC (± 3ºC)

Humidity: 60 ± 10 %

Lighting : Artificial, the sequence being 12 hours light, 12 hours dark.

The animals were housed in polypropylene cages provided with bedding of husk. The animals had free access to RO water. For feeding, Standard pellet diet (bought from SaiMeera foods pvt. Ltd, Bangalore) was used.

Preparation of animals:

The animals were randomly selected, to permit individual identification by cage number and individual marking on the fur of each animals was made with picric acid. The animals were kept in their cages for 7 days prior to dosing to allow for acclimatization to the laboratory conditions. The principles of laboratory animal care were followed.

Test Substance:

Silvisha Usidham (SU) is pale yellowish in colour, free flowing- greasy and Slightly pungent.

Route of administration:

Oral route was selected, because it is the normal route of clinical administration.

PROCEDURE:

ACUTE ORAL TOXICITY STUDY

Experimental Animals:

Species and strain	: Wistar Albino rat
Sex	: Male and Female
Age, Weight	: 6-8 weeks, 150-175 gm
Test guideline	: WHO guideline
Groups/treatment	: Grouped by randomization
Duration of exposure to the	: Silvisha Usidham (SU) Single dose
Study duration	: 14 days
Number of animals	: 10 male, 10 female
Route of administration	: Oral

Number of animals and dose levels:

Animals are divided into two groups, each group containing 5 male and 5 female rats. One group as control and the other as test group. Control group is treated with saline and other groups were treated with test drug Silvisha Usidham (SU) ten times the therapeutic dose (5000mg per kg b.wt).

Groups	No. of Rats
Group I Vehicle control (saline)	5 male, 5 female
Group II Test drug –Silvisha Usidham (SU) (5000mg per kg b.wt)	5 male, 5 female

Administration of doses:

The test drug was administered in a single dose by using oral gavage. Animals were fasted prior to drug administration. Following the period of fasting, the animals were weighed and test drug was administered. The control groups received equal volume saline. The test drug was administered at 10 times the therapeutic dose (5000 mg per kg b.wt). The food was withheld for 3-4 hours after dosing the animal.

Observations:

Observations were made and recorded systematically and continuously observed after the substance administration as per the guidelines.

- ½ hour, 1 hour, 2 hours, 4 hours and up to 24 hours observation
- All rats were observed twice daily for 14 days
- Body weight were Calculated weekly once
- Feed & water intake were Calculated daily

Cage side observation

The animals were monitored for behavioral parameters like Alertness, Aggressiveness, piloerection, Grooming, Gripping, Touch Response, Motor Activity, Tremors, Convulsions, Muscle Spasm, Catatonia, Muscle relaxant, Hypnosis Analgesia, Lacrimation, Exophthalmos, Diarrohea, Writhing, Respiration and Mortality

Gross necropsy:

At the end of the 14th day, all the animals were sacrificed by using the injection of Pentothal sodium Gross necropsy includes examinations of the external surface of the body, all orifices, cranial, thoracic and abdominal cavities and their contents. Brain, eye, lungs, heart, spleen, liver, kidneys, adrenal and sexorgans of all animals.

D. PHYTOCHEMICAL ANALYSIS

Test for alkaloids:

Mayer's Test: To the test sample, 2ml of mayer's reagent was added, a dull white precipitate revealed the presence of alkaloids.

Test for coumarins:

To the test sample, 1 ml of 10% sodium hydroxide was added. The presence of coumarins is indicated by the formation of yellow color.

Test for saponins:

To the test sample, 5 ml of water was added and the tube was shaken vigorously. Copious lather formation indicates the presence of Saponins.

Test for tannins:

To the test sample, ferric chloride was added, formation of a dark blue or greenish black color showed the presence of tannins.

Test for glycosides- Borntrager's Test

Test drug is hydrolysed with concentrated hydrochloric acid for 2 hours on a water bath, filtered and the hydrolysate is subjected to the following tests. To 2 ml of filtered hydrolysate, 3 ml of choloroform is added and shaken, choloroform layer is separated and 10% ammomia solution is added to it. Pink colour indicates presence of glycosides.

Test for flavonoids:

To the test sample about 5 ml of dilute ammonia solution were been added followed by addition of few drops of conc. Sulfuric acid. Appearance of yellow color indicates the presence of Flavonoids.

Test for phenols:

Lead acetate test: To the test sample; 3 ml of 10% lead acetate solution was added. A bulky white precipitate indicated the presence of phenolic compounds.

Test for steroids:

To the test sample, 2ml of chloroform was added with few drops of conc. Sulphuric acid (3ml), and shaken well. The upper layer in the test tube was turns into red and sulphuric acid layer showed yellow with green fluorescence. It showed the presence of steroids.

Triterpenoids

Liebermann–Burchard test: To the chloroform solution, few drops of acetic anhydride was added then mixed well. 1 ml concentrated sulphuric acid was added from the sides of the test tube, appearance of red ring indicates the presence of triterpenoids.

Test for Cyanins

A. Aanthocyanin:

To the test sample, 1 ml of 2N sodium hydroxide was added and heated for 5 min at 100^{o}C. Formation of bluish green colour indicates the presence of anthocyanin.

Test for Carbohydrates - Benedict's test

To the test sample about 0.5 ml of Benedic's reagent is added. The mixture is heated on a boiling water bath for 2 minutes. A characteristic coloured precipitate indicates the presence of sugar.

Proteins (Biuret Test)

To extracts 1% solution of copper sulphate was added followed by 5% solution of sodium hydroxide, formation of violet purple colour indicates the presence of proteins.[34]

Fluorescence analysis in dried powder

Sample SUwas subjected to fluorescence analysis under visible light and UV – Light at 365 nm under closed circuit cabinet. Each fluorescence characteristic of the treated sample was observed under ordinary light and then under UV light of wave lengths 365 nm. The drug was treated with acids viz., Conc. HCl, Conc. H2SO4, Conc. HNO3 and glacial acetic acid. The drug was treated with alkaline solutions viz., aqueous NaOHand ferric chloride. They were subjected to fluorescence analysis in visible light and in short UV- light (254 nm) and long UV- light (365 nm).

Reference

Evans WC. In: Trease and Evans' Pharmacognosy. Harcourt Baraco and Company Asia Pvt. Ltd. Singapore; 1996: 1–437.

E. QUANTITATIVE ANALYSIS:

HEAVY METAL ANALYSIS BY AAS

Standard: Hg, As, Pb and Cd – Sigma

Methodology

Atomic Absorption Spectrometry (AAS) is a very common and reliable technique for detecting metals and metalloids in environmental samples. The total heavy metal content of the sample SU was performed by Atomic Absorption Spectrometry (AAS)

Model AA 240 Series. In order to determination the heavy metals such as mercury, arsenic, lead and cadmium concentrations in the test sample SU

Sample Digestion

Test sample SU digested with 1mol/L HCl for determination of arsenic and mercury. Similarly for the determination of lead and cadmium the sample were digested with 1mol/L of HNO3.

Standard reparation

As & Hg- 100 ppm sample in 1mol/L HCl

Cd & Pb- 100 ppm sample in 1mol/L HNO3

TLC Analysis

Test sample was subjected to thin layer chromatography (TLC) as per conventional one dimensional ascending method using silica gel 60F254, 7X6 cm (Merck) were cut with ordinary household scissors. Plate markings were made with soft pencil. Micro pipette were used to spot the sample for TLC applied sample volume 10-micro liter by using pipette at distance of 1 cm at 5 tracks. In the twin trough chamber with different solvent system Toulene: Ethyl Acetate: Acetic Acid (1.5:1:0.5) After the run plates are dried and was observed using visible light Short-wave UV light 254nm and light long-wave UV light 365 nm [35].

High Performance Thin Layer Chromatography Analysis

HPTLC method is a modern sophisticated and automated separation technique derived from TLC. Pre-coated HPTLC graded plates and auto sampler was used to achieve precision, sensitive, significant separation both qualitatively and quantitatively. High performance thin layer chromatography (HPTLC) is a valuable quality assessment tool for the evaluation of botanical materials efficiently and cost effectively. HPTLC method offers high degree of selectivity, sensitivity and rapidity combined with single-step sample preparation. In addition it is a reliable method for the quantitation of nano grams level of samples. Thus this method can be conveniently adopted for routine quality control analysis. It provides chromatographic fingerprint of phytochemicals which is suitable for confirming the identity and purity of medicinal plant raw materials.

Chromatogram Development

It was carried out in CAMAG Twin Trough chambers. Sample elution was carried out according to the adsorption capability of the component to be analysed. After elution, plates were taken out of the chamber and dried.

Scanning

Plates were scanned under UV at 366nm. The data obtained from scanning were brought into integration through CAMAG software. Chromatographic finger print was developed for the detection of phytoconstituents present in each extract and Rf values were tabulated.[36]

Test for Specific Pathogen

Methodology

About 0.5 gms of test sample was directly inoculated in to the specific pathogen medium (EMB, DCC, Mannitol, Cetrimide) by spread plate method. The plates were incubated at 37^{o}C for 24 - 72h for observation. Presence of specific pathogen identified by their characteristic color with respect to pattern of colony formation in each differential media.

Abbreviation

Organism	Abbreviation
E-coli	*EC*
Salmonella	*SA*
Staphylococcus Aureus	*ST*
Pseudomonas Aeruginosa	*PS*

Observation

No growth was observed after incubation period. Reveals the absence of specific pathogen

STERILITY TEST BY POUR PLATE METHOD

Objective

The pour plate techniques were adopted to determine the sterility of the product. Contaminated / un sterile sample (formulation) when come in contact with the nutrition rich medium it promotes the growth of the organism and after stipulated period of incubation the growth of the organism was identified by characteristic pattern of colonies. The colonies are referred to as Colony Forming Units (CFUs).

Methodology

About 1ml of the test sample was inoculated in sterile petri dish to which about 15 mL of molten agar 45^{o}C were added. Agar and sample were mixed thoroughly by tilting and swirling the dish. Agar was allowed to completely gel without disturbing it. (about 10 minutes). Plates were then inverted and incubated at 37^{o} C for 24-48 hours. Grown colonies of organism was then counted and calculated for CFU.

Observation

No growth was observed after incubation period. Reveals the absence of specific pathogen

PESTICIDE RESIDUE:

Extraction

About 10 g weight equivalent to test substance were extracted with 100 ml of acetone and followed by homogenization for brief period. Further filtration was allowed and subsequent addition of acetone to the test mixture. Heating of test sample was performed using a rotary evaporator at a temperature not exceeding 40ºC until the solvent has almost completely evaporated. To the residue add a few milliliters of toluene R and heat again until the acetone is completely removed. Resultant residue will be dissolved using toluene and filtered through membrane filter

AFALOTOXIN:

Standard

Aflatoxin B1

Aflatoxin B2

Aflatoxin G1

Aflatoxin G2

Solvent

Standard samples was dissolved in a mixture of chloroform and acetonitrile (9.8 : 0.2) to obtain a solution having concentrations of 0.5 µg per ml each of aflatoxin B1 and aflatoxin G1 and 0.1 µg per ml each of aflatoxin B2 and aflatoxin G2.

Test solution: Concentration 1 µg per ml

Procedure

Standard aflatoxin was applied on to the surface to pre coated TLC plate in the volume of 2.5 µL, 5 µL, 7.5 µL and 10 µL. Similarly the test sample was placed and Allow the spots to dry and develop the chromatogram in an saturated chamber containing a solvent system consisting of a mixture of chloroform, acetone and isopropyl alcohol (85 : 10 : 5) until the solvent front has moved not less than 15 cm from the origin. Remove the plate from the developing chamber, mark the solvent from and allow the plate to air-dry. Locate the spots on the plate by examination under UV light at 365 nm.

The Physiochemical, phytochemical analysis, heavy metal analysis, Specific pathogen test, pesticide residue, aflatoxin, TLC of the drug Silvisha Usidham was done at Noble Research Solution.

F. PHARMACOLOGICAL ACTIVITY

In-vitro Anti-Inflammatory Activity by Protein (Albumin) denaturation Assay

Albumin Denaturation Assay Procedure

In-vitro anti-inflammatory activity SUwas studied using albumin denaturation technique. The reaction mixture consisted of bovine serum albumin (5% aqueous solution) and test sample SU at varying concentration ranges from 100 to 500 µg/ml and standard Diclofenac sodium at the concentration of100 µg /ml of final volume.

pH was adjusted by using a small amount of 1N Hydrochloric acid. The samples were incubated at 37°C for 20 min and then heated at 57°C for 3 min. After cooling the sample, 2.5 ml of phosphate buffer solution was added into each test tube. Turbidity developed was measured spectrophotometrically at 660 nm, for control distilled water was used instead of test sample while product control tests lacked bovine serum albumin. The experiment was performed in triplicate. The Percentage protection from denaturation is calculated by using the formulae

$$\left[\frac{(A)_{\text{control}} - (A)_{\text{sample}}}{(A)_{\text{control}}} \right] \times 100.$$

Statistical analysis

Results are expressed as Mean ± SD. The difference between experimental groups was compared by One-Way Analysis Of Variance (ANOVA) followed by Dunnet Multiple comparison test.[37, 38].

The anti-inflammatory activity of the drug Silvisha Usidham was done at Noble Research Solution.

CLINICAL STUDIES

All the 30 cases were selected from the OPD of Kuzhandhai Maruthuvam Department, National Institute of Siddha. They were treated with the trial drug Silvisha Usidham (Internal) and Puzhuvettu Thylam (External) and observed for clinical prognosis.

STUDY DESIGN AND CONDUCT OF STUDY:

Study type : An open clinical study

Study place: OPD of Ayothidoss Pandithar Hospital
National Institute of Siddha
Tambaram sanatorium
Chennai - 47.

Study duration : 24Months

Treatment Period: 45 Days

Population and Sample:

Population consists of 30 paediatric patients attending the OPD of Ayothidoss pandithar Hospital, National Institute of Siddha, Chennai-47.

The sample consists of patients between 6-12 years of age group fulfilling all the inclusion criteria and exclusion criteria.

INCLUSION CRITERIA

- Patient who complained with symptoms of alopecia areata
- Hair loss in patches
- Non scarring
- Scattered long hairs within the bald area
- The area of hair loss may tingle or painful
- Age between 6 -12 years of both sex.
- Parents/guardian of the patient willing to sign the informed consent.

EXCLUSION CRITERIA:

- Scarring alopecia
- Alopecia Universalis
- Alopecia totalis
- Vitiligo
- Atopic dermatitis
- Thyroid disease
- Down syndrome
- Sample size: 30 patients

TREATMENT MEDICINE:

Silvisha Usidham (Internal)

Dosages:

- 6 -7years -2ml
- 8-10years -3ml
- 11-12years -4ml

Duration : 45days

Drug Storage : Prepared medicine were stored in porcelain vessel.

Dispensing : Prepared medicine were given as oil in separate tight container of individual dose.

Siddha method of assessment:

Nilam, Kalam, Uyirthathukkal, Udal thathukkal, Envagai thervugal.

OUTCOME:

SALT SCORE –Severity of Alopecia Tool Score

1. Vertex -40% (0.4) of the scalp surface area
2. Right profile of the scalp-18% (0.18)
3. Left profile of the scalp-18% (0.8)
4. Posterior aspect of scalp-24% (0.24)

SALT Score= Sum of percentage of hair loss in all above mentioned area.[40]

STUDY ENROLLMENT:

- Patient reporting at the OPD with the clinical symptoms of Hair loss in patches, Scattered long hairs within the bald area ,non scarring ,area of hair loss may tingle or painful sensation were examined clinically for enrolling in this study based on the inclusion and exclusion criteria.
- The patients who are to be enrolled will be informed about the study, trial drug, possible outcomes and the objectives of the study in the language and terms understandable to them.
- After ascertaining the patients' willingness, informed consent (Form II) were obtained in writing from their parents in the consent form.
- All these patients were given unique registration card in which patients' Registration number of the study, Address, Phone number and Doctors phone number etc. were given, so as to report easily should any complications arise.
- Complete clinical history, complaints and duration, examination findings-- all would be recorded in the prescribed Case sheet proforma and clinical assessment forms separately. Screening Form- I will be filled up. Form III, Form –IV and Form –V will be used for recording the patient's history, clinical examination of symptoms and signs and laboratory investigations respectively.

- Patient will be advised to take the trial drug and appropriate dietary advice will be given according to the patients' perfect understanding.

CONDUCT OF THE STUDY :

The trial drug Silvisha Usidham (Internal) and Puzhuvettu Thylam (External) is given for 45days.Patients should visit the hospital after 7days once. At each clinical visit clinical assessment is done and prognosis is noted. After the end of the treatment, the patient is advised to visit the OPD for another 1 month for follow-up. If any trial patient fails to collect the trial drug on the prescribed day will not be allowed to continue and will be withdrawn from the study with fresh case being inducted.

DATA MANAGEMENT :

- After enrolling the patient in the study, a separate file for each patient will be opened and all forms will be filed in the file. Study No. and Patient No. will be entered on the top of the file for easy identification. Whenever study patient visits OPD during the study period, the respective patient file will be taken and necessary recordings will be made at the assessment form or other suitable form.
- The screening forms will be filed separately.The Data recordings in all forms will be monitored and scrutinized by Professor and Head of the department of Kuzhanthai Maruthuvam .
- Data analysis were done with the help of Senior research officer (statistics) of NIS

ADVERSE EFFECT / SERIOUS EFFECT MANAGEMENT:

If the trial patient develops any adverse reaction, he/she would be immediately withdrawn from the trial and proper management will be given in OPD of National Institute of Siddha. The details of adverse reactions will be recorded in prescribed Pharmacovigilance form and the same will be reported to Regional Pharmacovigilance centre.

ETHICAL ISSUES

1. To prevent any infection, proper sterilization of lab equipments were used.
2. No other external or internal medicines were used. There will be no infringement on the rights of patient.
3. The data collected from the patient will be recorded. The patient will be informed about the diagnosis, treatment and follow-up.
4. After the consent of the patient (through consent form) they were enrolled in the study.
5. Informed consent were obtained from the patient explaining in the understandable language to the patient.
6. Treatment were provided free of cost.
7. In conditions of treatment failure, adverse reactions, patients were given alternative treatment at the National Institute of Siddha with full care throughout the end.

The following ASSESSMENT FORMS were used for data collection:

FORM I	SCREENING & SELECTION PROFORMA
FORM II	CONSENT FORM
FORM III	CASE RECORD FORM
FORM IV	CLINICAL ASSESSMENT FORM
FORM V	DRUG COMPLAINCE
FORM VI	PATIENT'S INFORMATION SHEET
FORM VII	WITHDRAWAL FORM
FORM VIII	PHARMOCOLOVIGILANCE FORM
FORM IX	DIETARY ADVICE FORM
FORM X	ASSENT FORM

5. RESULTS AND OBSERVATIONS

QUALITATIVE ANALYSIS

A.PHYSICO-CHEMICAL ANALYSIS

Sample Description

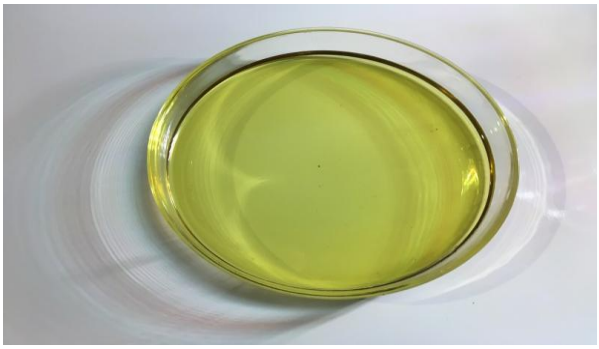


Table-1: State, appearance, Nature and odor of Silvisha Usidham

State	Liquid
Appearance	Pale Yellowish
Nature	Free flowing – Greasy
Odor	Slightly Pungent

From table 1, the Organoleptic characters shows that Silvisha Usidham is pale yellowish in colour,slightly pungent odor,liquid state and the nature is free flowing-greasy.

Table -2: Physico-chemical properties of Silvisha Usidham

Analytical Report

S.NO	Parameter	Silvisha Usidham
1	Specific Gravity	0.9760
2	Viscosity at 50^{o}C (Pa s)	6.905
3	Refractive index	1.24
5	Iodoine value (mg I2/g)	104.77

6	Saponification Value (mg of KOH to saponify 1gm of fat)	149.55
7	Ph	4
8	Weight per ml	0.029 g/ml
9	Acid Value mg KOH/g	0.766
10	Peroxidase Value mEq/kg	0.528

From table 2, The physicochemical analysis of Silvisha Usidham Explained in the parameters such as viscosity, refractive index, Iodine value, Saponification value, Peroxidase value are within limit,

B. BIOCHEMICAL ANALYSIS

Table-3: Test for Acidic radicals on Silvisha Usidham

S.NO	Parameter	Observation	Result
1	Test for Sulphate	Cloudy appearance present.	Positive
2	Test for Chloride	-	Negative
3	Test For Phosphate	-	Negative
4	Test For Carbonate	Cloudy appearance present	Positive
5	Test For Nitrate	-	Negative
6	Test for Sulphide	-	Negative
7	Test For Fluoride &oxalate	-	Negative
8	Test For Nitrite	-	Negative
9	Test For Borax	-	Negative

(+ve/-ve present or absent if component tested)

Interpretation

The acidic radicals test shows the presence of **Sulphate, Carbonate.**

Table-4: Test for Basic radicals on Silvisha Usidham

S.NO	Parameter	Observation	Result
1	Test for Lead	-	Negative
2	Test for Copper	-	Negative
3	Test For Aluminium.	-	Negative
4	Test For Iron.	Red colour appeared	Positive
5	Test For Zinc	-	Negative
6	Test for Calcium	-	Negative
7	Test For Magnesium	-	Negative
8	Test For Ammonium	Brown colour appeared	Positive
9	Test For Potassium	-	Negative
10	Test For Sodium	-	Negative
11	Test For Mercury	-	Negative
12	Test For Arsenic	-	Negative

(+ve/-ve present or absent if component tested)

Interpretation

The basic radical test shows the presence of **Iron** and **Ammonium.** Absence of heavy metals such as lead, arsenic and mercury.

Table-5 : Test for Miscellaneous on Silvisha Usidham:

S.NO	Parameter	Observation	Result
1	Test for Starch	Blue colour developed	Positive
2	Test for Reducing sugars	-	Negative
3	Test For Alkaloids.	Yellow colour developed	Positive

4	Test For Tannic acid.	-	Negative
5	Test for unsaturated compounds	-	Negative
6	Test for Amino acid	-	Negative
7	Test For Type of compounds	-	Negative

(+ve/-ve present or absent if component tested)

Interpretation:

The Miscellaneous test shows the presence of **Starch** and **Alkaloid.**

c. PHYTOCHEMICAL ANALYSIS REPORT:

Table-6 : Test fos Phytochemical Screening on Silvisha Usidham

S.NO	TEST	OBSERVATION
1.	ALKALOIDS	+
2.	FLAVANOIDS	-
3.	GLYCOSIDES	-
4.	STEROIDS	+
5.	TRITERPENOIDS	+
6.	COUMARIN	+
7.	PHENOL	-
8.	TANIN	+
9.	PROTEIN	-
10.	SAPONINS	-
11.	SUGAR	-
12.	ANTHOCYANIN	-
13.	BETACYANIN	-

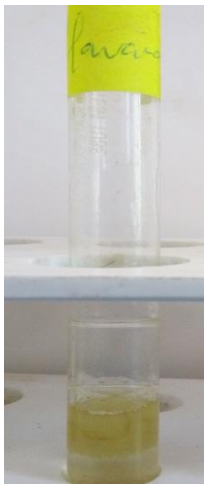
Note: +-> Indicates Presence and - -> Indicates Absence of the Phytocomponents.

Interpretation:

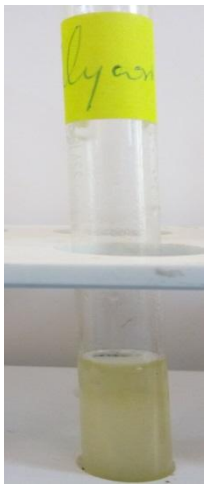
Phytochemical screening shows presence of Alkaloid, Steroid, Tritrepenoids, Coumarin and Tanin.

Test for Alkaloids

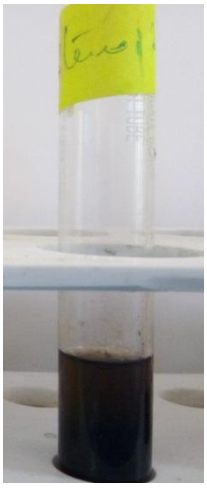
Test for Flavonoids



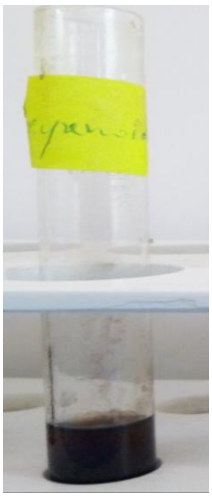
Test for Glycosides



Test for Steroids



Test for Triterpenoids



Test for Coumarins

Test for Phenols

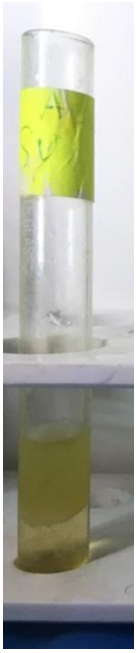
Test for Tanins

Test for Proteins

Test for Saponins

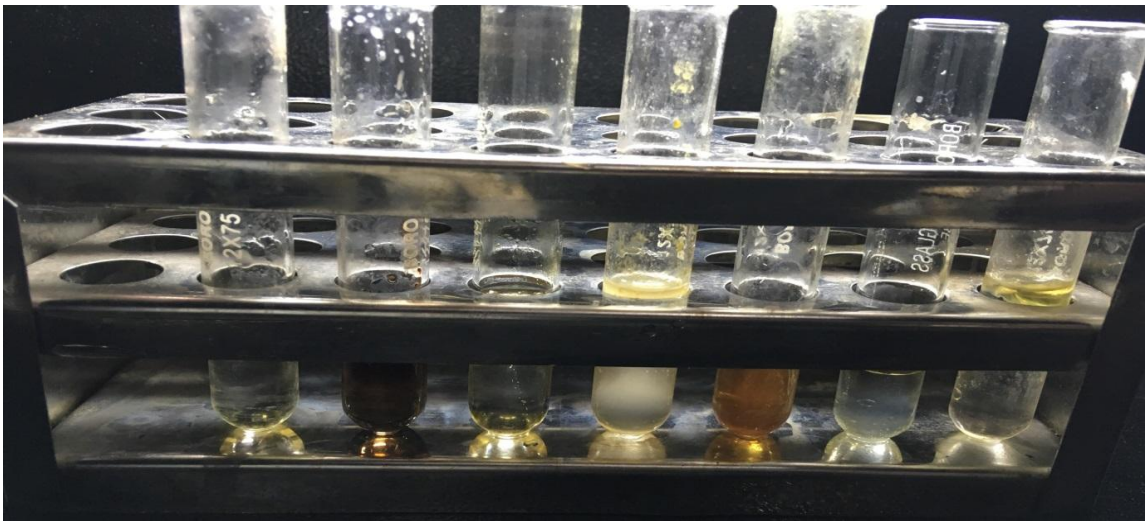
Test for Carbohydrates

Test for Anto/ Beta cyanins

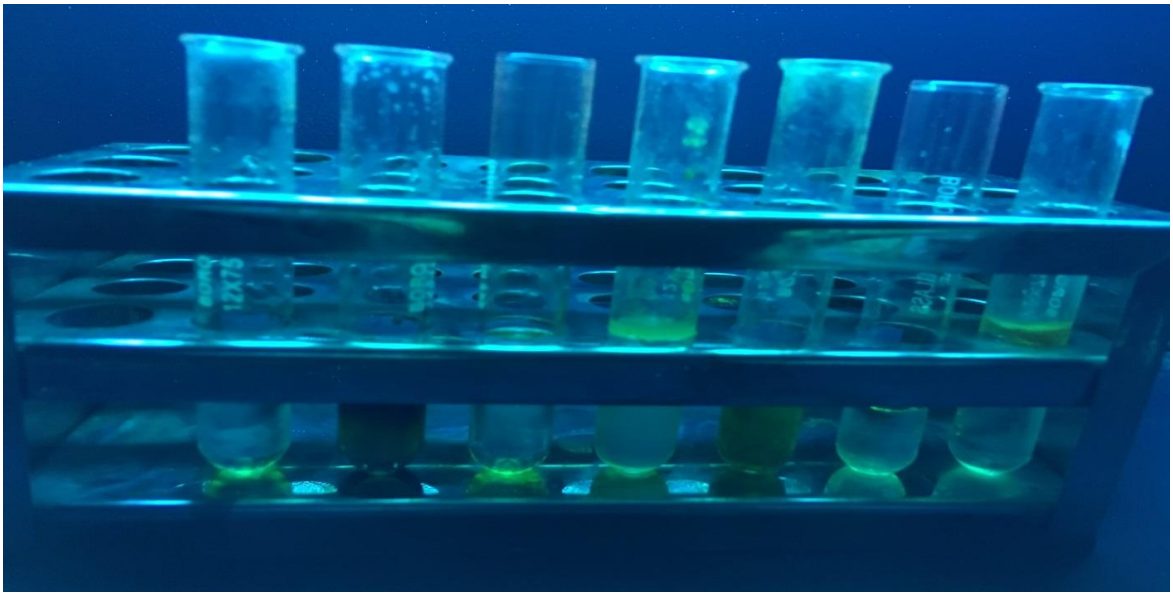


D. Fluorescence analysis in dried powder

Visible light



Short UV- light (254 nm)



Long UV- light (365 nm)

Table-7: Fluorescence analysis in dried powder

S.No	Experiment	Visible light	Short UV – Light 254 nm	Long UV – Light 365 nm
1.	Sample + Conc. Hcl	Mild yellowish	Mild yellow Florescent	Yellowish
2.	Sample + Conc. Sulphuric Acid	Greenish brown	Greenish brown	Crimson red
3.	Sample + Conc. Nitric acid	Lime Yellow	Mild Florescent yellow	Crimson brown
4.	Sample + Sodium hydroxide in water	Creamy white	Pale yellowish white	Pale yellow
5.	Sample + Ferric chloride	Reddish orange	Florescent green	Reddish brown
6.	Sample + glacial acetic acid	Turbid white	Milky white	Pale Yellow
7.	Sample + Water	White	Milky white	Pale yellow

E. HEAVY METAL ANALYSIS

Table-8: Heavy metal analysis on Silvisha Usidham

Name of the heavy metal	Absorption max A max	Result analysis	Maximum limit
Mercury	253.7nm	BDL	1ppm
Lead	217.0nm	0.010ppm	10ppm
Arsenic	193.7nm	BDL	3ppm
Cadmium	228.8nm	BDL	0.3ppm

BDL- Below Detection Limit

Inference

- Results of the present investigation has clearly shows that the sample SU has no traces of Mercury, Arsenic and Cadmium and hence it was considered that these heavy metals was absent in the sample SU.
- The reported heavy metal lead seems very low (0.010 ppm) when compare to the allowed recommended limit of 10 ppm.

F. Test for Specific Pathogen

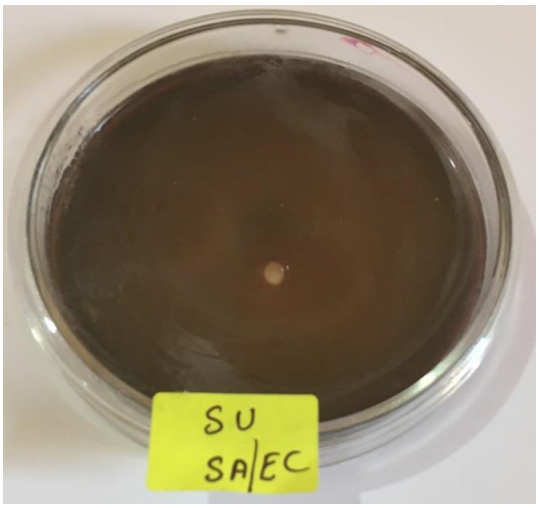
Table-9: Specfic Pathogen test on Silvisha Usidham

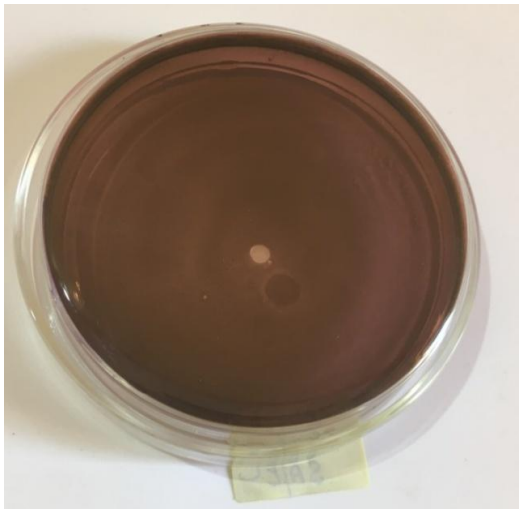
Organism	Specification	Result	Method
E-coli	Absent	Absent	As per AYUSH specification
Salmonella	Absent	Absent	
Staphylococcus aureus	Absent	Absent	
Pseudomonas aeruginosa	Absent	Absent	

Result

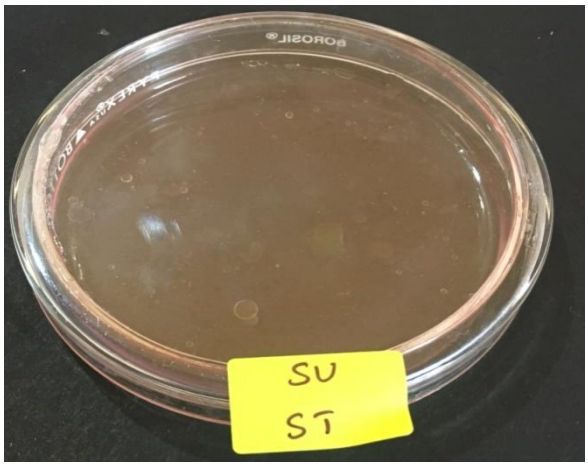
No growth / colonies were observed in any of the plates inoculated with the Silvisha Usidham.

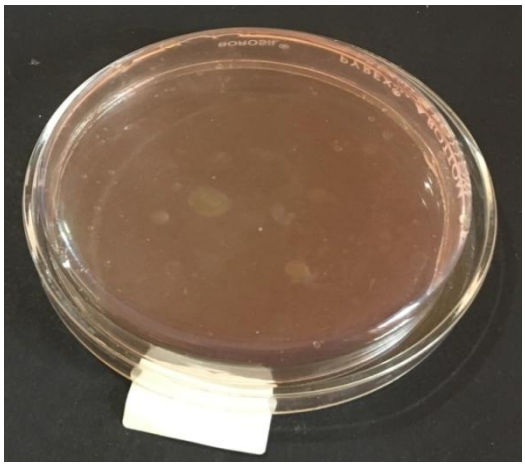
Culture plate with E-coli and Salmonella specific medium



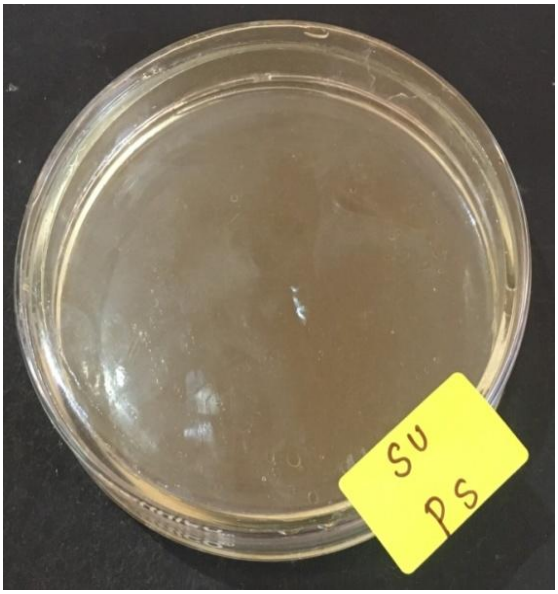


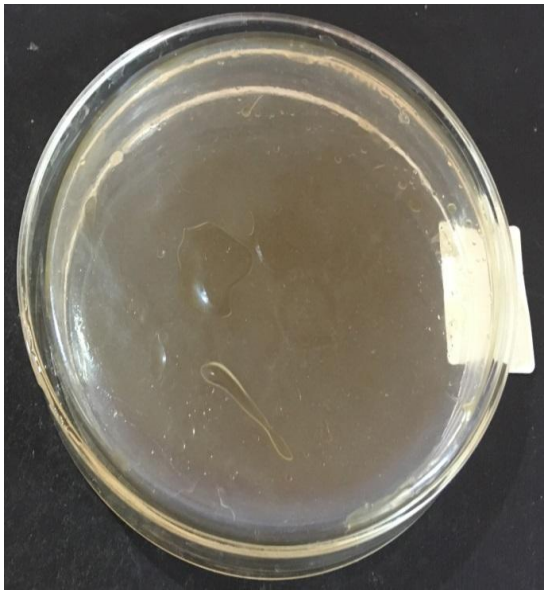
Culture plate with Staphylococcus Aureus specific medium





Culture plate with Pseudomonas Aeruginosa specific medium





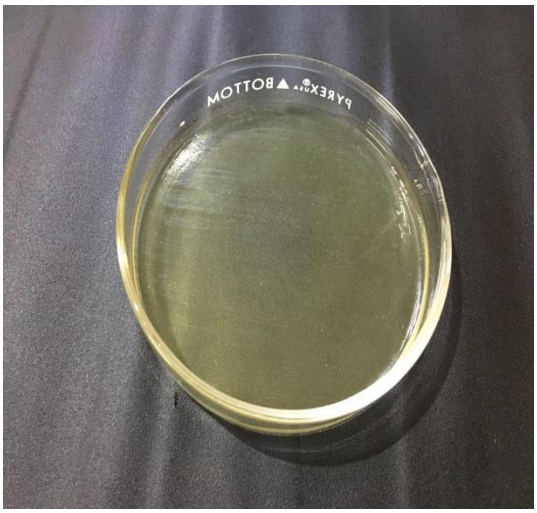
G . STERILITY TEST BY POUR PLATE METHOD

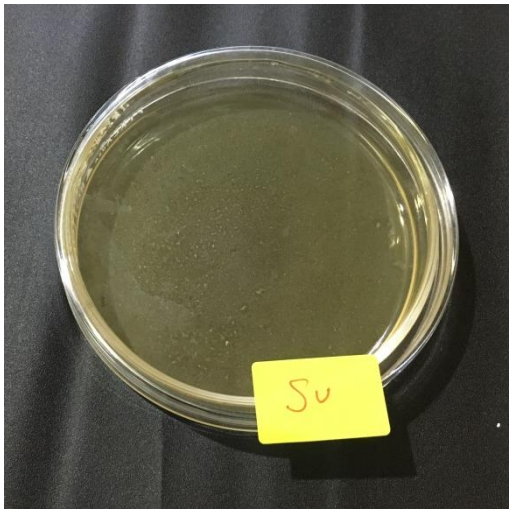
Table-10: Sterilty test by pour plate method

Test	Result	Specification	As per AYUSH/WHO
Total Bacterial Count	Absent	NMT 10^5CFU/g	As per AYUSH specification
Total Fungal Count	Absent	NMT 10^3CFU/g	

Result

No growth / colonies were observed in any of the plates inoculates with the Silvisha Usidham.





H. AFLATOXIN REPORT

Table-11: Aflatoxin test on Silvisha Usidham

AFLATOXIN	SAMPLE SU	AYUSH Specification
B1	Not Detected-Absent	0.5ppm
B2	Not Detected-Absent	0.1ppm
G1	Not Detected-Absent	0.5ppm
G2	Not Detected-Absent	0.1ppm

Result:

The results shows that there was no spots were been identified in the Silvisha Usidham loaded TCL plate when compare to the standard indicates that the Silvisha Usidham were free from AflatoxinB1, Aflatoxin B2, Aflatoxin G1, Aflatoxin G2.

I. Pesticide Residue

Table-12: Test for pesticide residue on Silvisha Usidham

Pesticide Residue **I.Organo chlorine Pesticides**	**Sample SU**	**AYUSH Limit (mg/kg)**
Alpha BHC	BQL	0.1mg/kg
Beta BHC	BQL	0.1mg/kg
Gamma BHC	BQL	0.1mg/kg
Delta BHC	BQL	0.1mg/kg
DDT	BQL	1mg/kg
Endosulphan	BQL	3mg/kg
II. organo Phosphorus Pesticides		
Malathion	BQL	1mg/kg
Chlorpyriphos	BQL	0.2mg/kg
Dichlorovos	BQL	1mg/kg
III.Pyrethroid		
Cypermethrin	0.2mg/kg	1mg/kg

BQL-Below quantification Limit.

Result:

The results showed that there were no traces of pesticides residue such as organo chlorine and organo phosphorus pesticides such as Organo chlorine and Organo phosphorus Pesticides in the sample SU. Further Silvisha Usidham shows the presence of Cypermethrin belongs to Pyrethroid type of pesticides at the concentration of 0.2 mg/kg which was low compare the AYUSH prescribed limit of 1mg/kg

J. HPTLC REPORT:

Table-13: HPTLC finger printing analysis of the Silvisha Usidham

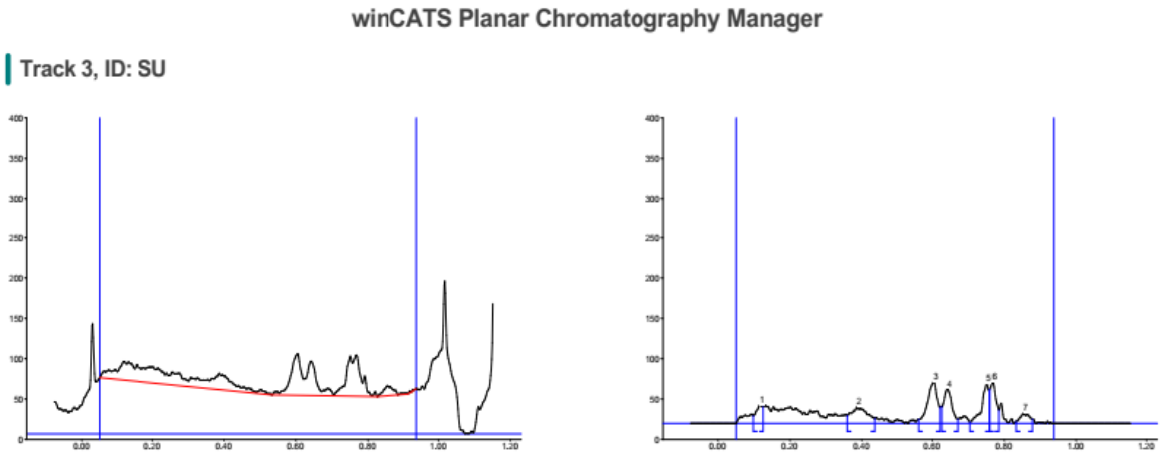
Peak	Start Rf	Start Height	Max Rf	Max Height	Max%	End Rf	End Height	Area	Area %
1.	0.10	9.7	0.12	22.8	9.10	0.13	20.3	333.6	7.45
2.	0.36	9.9	0.39	20.2	8.06	0.44	6.4	694.8	15.51
3.	0.56	5.3	0.61	51.6	20.61	0.62	20.3	1074.4	23.98
4.	0.63	20.9	0.64	42.6	17.05	0.67	5.3	749.1	16.72
5.	0.71	1.8	0.75	49.6	19.84	0.76	41.1	743.0	16.58
6.	0.67	42.6	0.77	51.1	20.44	0.79	16.4	638.8	14.26
7.	0.84	2.8	0.86	12.3	4.90	0.88	5.4	247.2	5.52

RESULT:

HPTLC finger printing analysis of the Silvisha Usidham reveals the presence of seven prominent peaks corresponds to presence of seven versatile phytocomponents present within it. Rf value of the peaks ranges from 0.10 to 0.84.Further the peak 3 occupies the major percentage of area of 23.98% which denotes the abundant existence of such compound .Followed by this peak 4 and 5 occupies the percentage area of 16.72 and 16.58%.

TLC Analysis at 254 nm **TLC Analysis at 366 nm**

HPTLC finger printing of Sample SU



K. PHARMACOLOGICAL ACTIVITY:

In-vitro Anti-Inflammatory Activity by Protein (Albumin) denaturation Assay

FINAL RESULT

Concentration in µg/ml	Absorbance
Control	0.981 ± 0.008
SU 100	0.926 ± 0.020
SU 200	0.86 ± 0.01
SU 300	0.796 ± 0.0057
SU 400	0.733 ± 0.015
SU 500	0.68 ± 0.026
Diclofenac sodium (100 µg)	0.023 ± 0.024

Each value represents the mean ± SD. N=3

Concentration in µg/ml	Percentage Inhibition of Protein Denaturation
SU 100	3.64 ± 1.152
SU 200	10.44 ± 0.767
SU 300	16.89 ± 1.06
SU 400	23.35 ± 1.409
SU 500	28.79 ± 2.389
Diclofenac sodium (100 µg)	95.69 ± 2.349

Each value represents the mean ± SD. N=3

Result Analysis

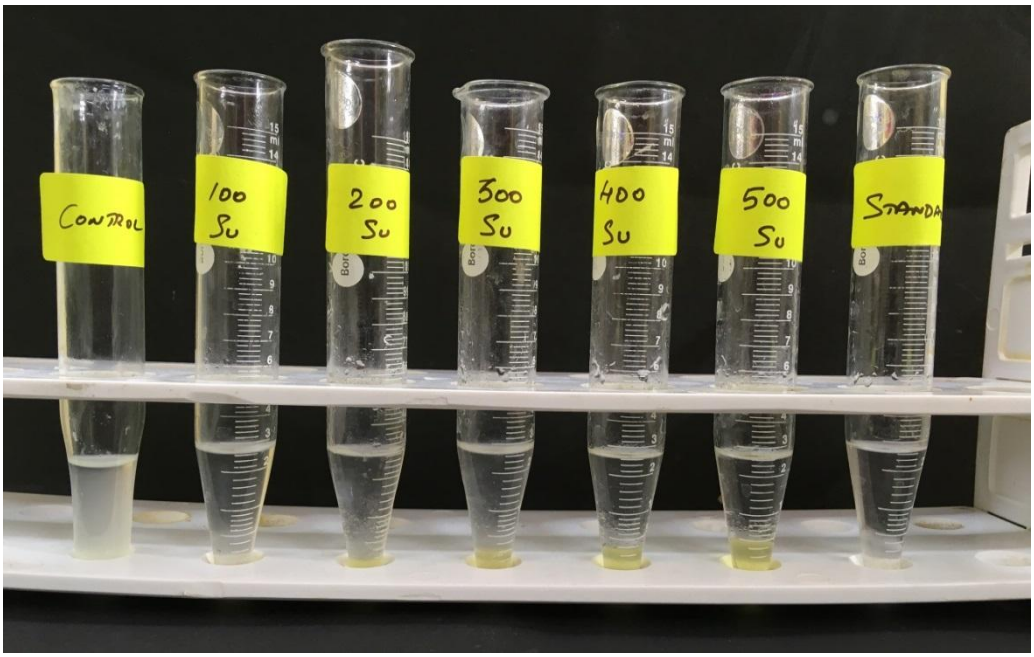
The result obtained from the present clearly indicates that the test drug SU was effective in inhibiting heat induced albumin denaturation. Maximum percentage inhibition of about 28.79 % was observed at 500 µg/ml when compare to that of the

Diclofenac sodium, a standard anti-inflammatory agent with the maximum inhibition 95.69 % at the concentration of 100 µg/ml.

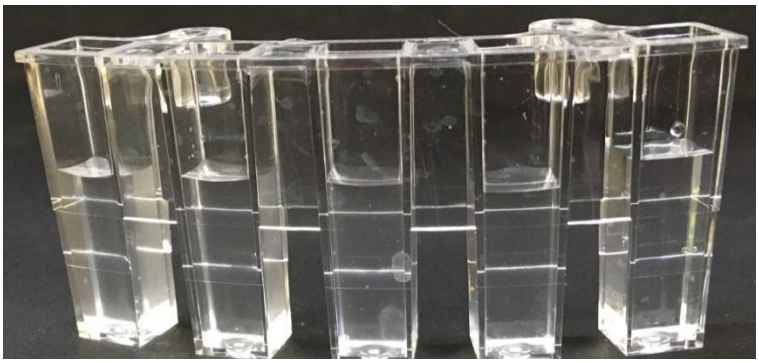
Conclusion

From the result of the study it was concluded that the test drug SU possess convincing anti-inflammatory property in protein denaturation assay.

Preparation of Test and control

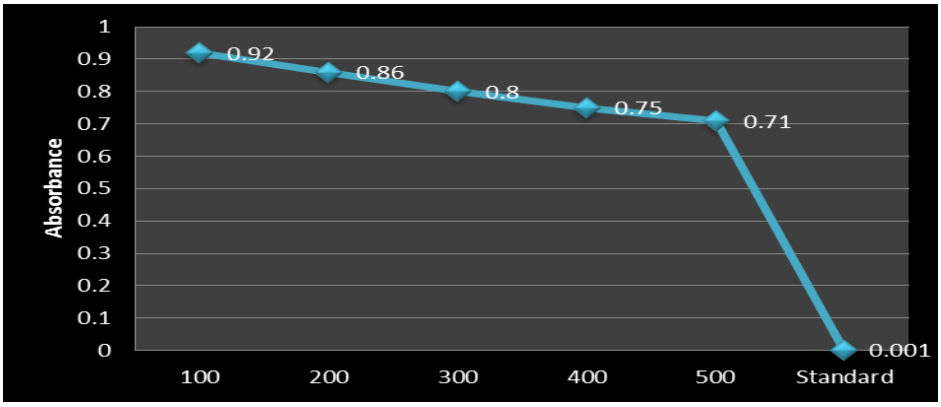


Absorbance of reaction mixture – Test Sample

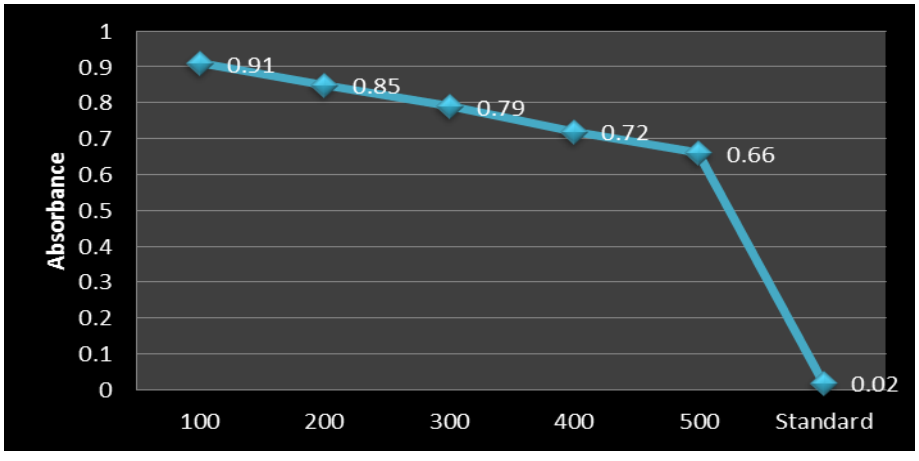


Absorbance of reaction mixture – Control and Standard

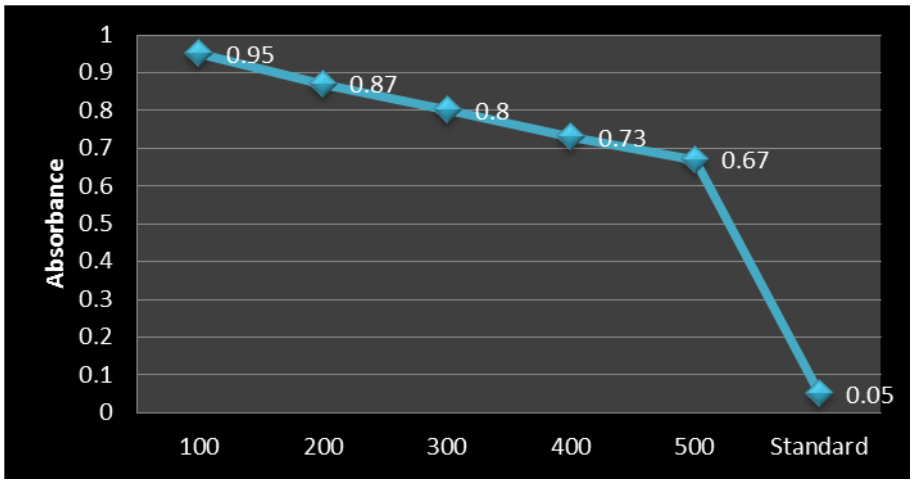
Absorbance Range of test and standard at Trial 1



Absorbance Range of test and standard at Trial 2



Absorbance Range of test and standard at Trial 3



L. ACUTE TOXICITY STUDY

Table-14: Behavioral Signs of Acute Toxicity Study of Silvisha Usidham

Parameters	30 mints		4 hrs		24 hrs		1st week		2nd week	
	C	T	C	T	C	T	C	T	C	T
Skin & Fur	N	N	N	N	N	N	N	N	N	N
Mucous Membrane	N	N	N	N	N	N	N	N	N	N
Respiratory rate	N	N	N	N	N	N	N	N	N	N
Heart rate	N	N	N	N	N	N	N	N	N	N
Salivation & Lacrimation	N	N	N	N	N	N	N	N	N	N
Lethargy	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
Piloerection	N	N	N	N	N	N	N	N	N	N
Urinary incontinence	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
Defecation	N	N	N	N	N	N	N	N	N	N
Sleep & Gait	N	N	N	N	N	N	N	N	N	N
Tremors &Convulsion	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL
Mortality	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL	NIL

N – Normal, C – control, T- Test Group

All the data were summarized in the form of revealed that there was no abnormal signs and behavioural changes in all animals at the dose level of 5,000 mg/kg body weight administered orally, during the study period.

There was no mortality observed after dosing of Silvisha Usidham upto 5000mg/kg body weight during the study period of 14 days. This indicates that the LD50 of Silvisha Usidham is more than 5000mg/kg b.wt.

There were no changes in skin and fur, eyes and mucous membranes of all animals. The eating, drinking habit, sleep pattern, locomotion were normal in all animals and no changes in body weight as compared to control group.

At the end of the 14 the day, necropsy was performed and there was no abnormality seen in test groups as compared to control group during the examination.

Clinical studies

30 Patients with confirmed diagnosis of Puzhuvettu with satisfying the inclusion criteria were enrolled after obtaining written informed consent and were to receive Silvisha Usidham with dosage of 2-4ml BID and Puzhuvettu Thylam external for 45 days.

Results were observed with respect to the following criteria:

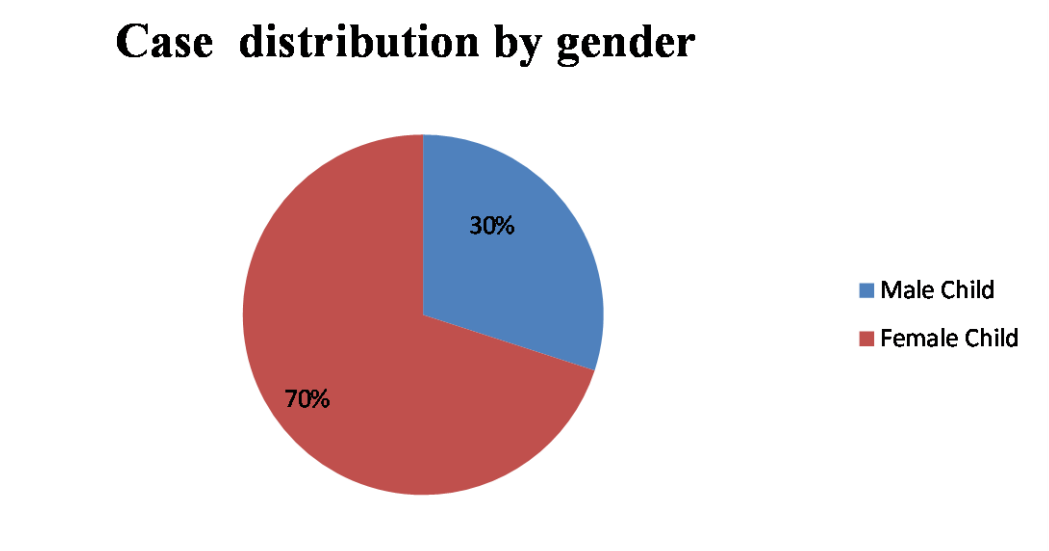
1. Sex distribution
2. Age distribution
3. Parent's socio economic status
4. Duration of illness
5. Diet
6. Family History
7. Habit
8. Nilam
9. Kaalam distribution
10. Yakkai
11. Gunam
12. Uyirthathukal.
13. Udarthathukkal
14. Envagai thervugal
15. Neikuri
16. Area affected
17. SALT Score

.

1. GENDER DISTRIBUTIONS:

Table-15: Distributions of patient with Puzhuvettu according to Gender

SI.NO	Sex	No of Cases	Percentage
1.	Male child	9	30
2.	Female child	21	70

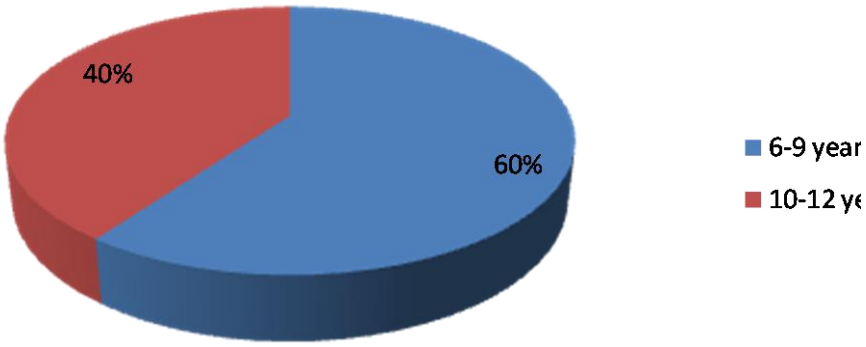


Inference:

Out of 30 patient 30% were male children and 50% were female children (Table15)

Table-16: Distribution of Patients with Puzhuvettu according to Age

S.NO	Age	No of Cases	Percentage
1.	6-9 years	18	60
2.	10-12 years	12	40

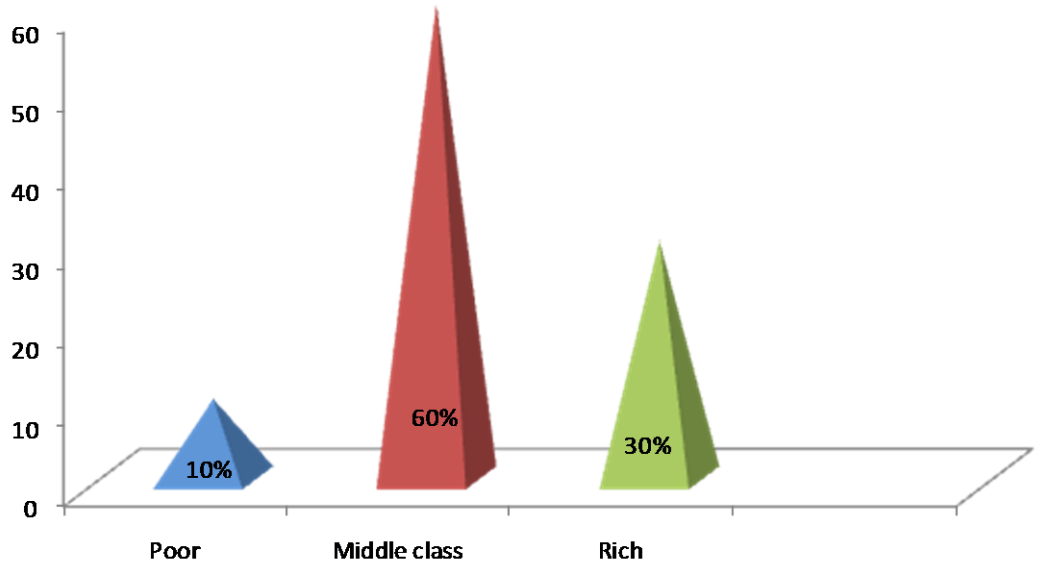


Inference:

Out of 30 patients, 60% of cases were 6-9 years, 40% were 10-12 years. (Table16)

Table-17: Distribution of patients with Puzhuvettu according to Socio-economic status

S.NO	Socio-economic status	No of cases	Percentage
1.	Poor	3	10%
2.	Middle class	18	60%
3.	Rich	9	30%

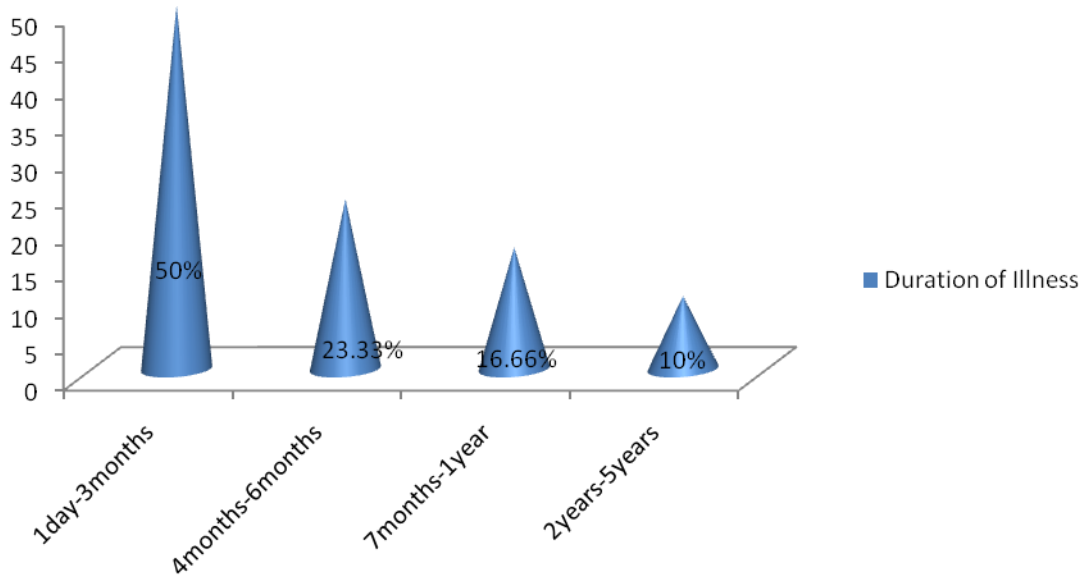


Inference:

About 10% Patients were under lower income group, 60% Patients were under middle income group and 30% patients were under high income group. The high incidences were in middle income group.

Table-18: Distribution of patient with Puzhuvettu according to Duration of Illness

S.NO	Duration	No of cases	Percentage
1.	1Day-3Months	15	50%
2.	4Months-6Months	7	23.33%
3.	7Months-1Year	5	16.66%
4.	2Year-5Year	3	10%

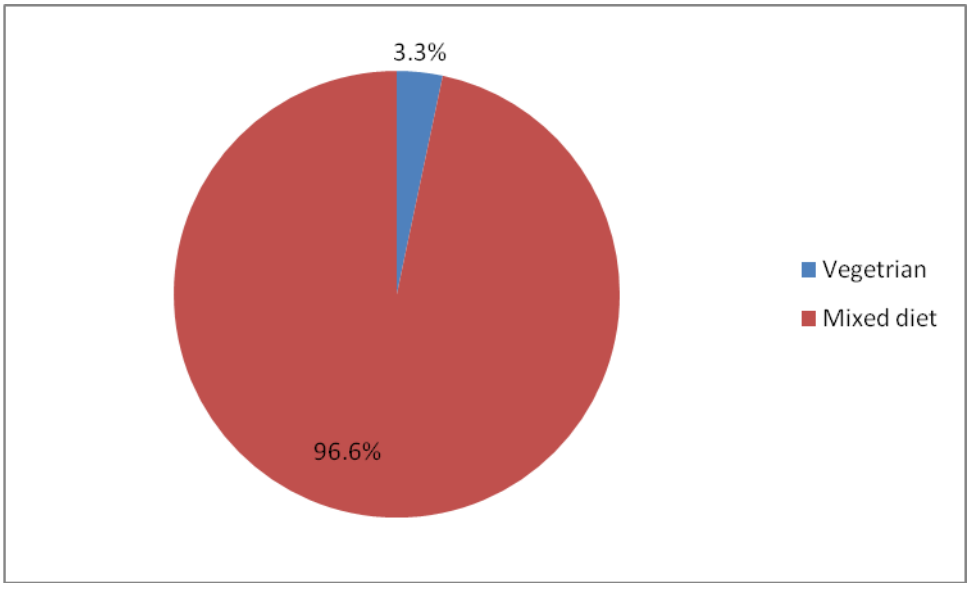


Inference:

According to duration of the illness, high incidence of case (50%) was noted in 1day-3months duration, 23.33% cases noted in 4months-6months duration, 16.66% cases noted in 7months-1year duration and 10% cases were noted in 2years-5years duration.

Table-19: Distribution of patients with Puzhuvettu according to Diet reference

S.NO	FOOD HABIT	No of Cases	Percentage
1.	Vegetarian	1	3.3%
2.	Mixed	29	96.6%

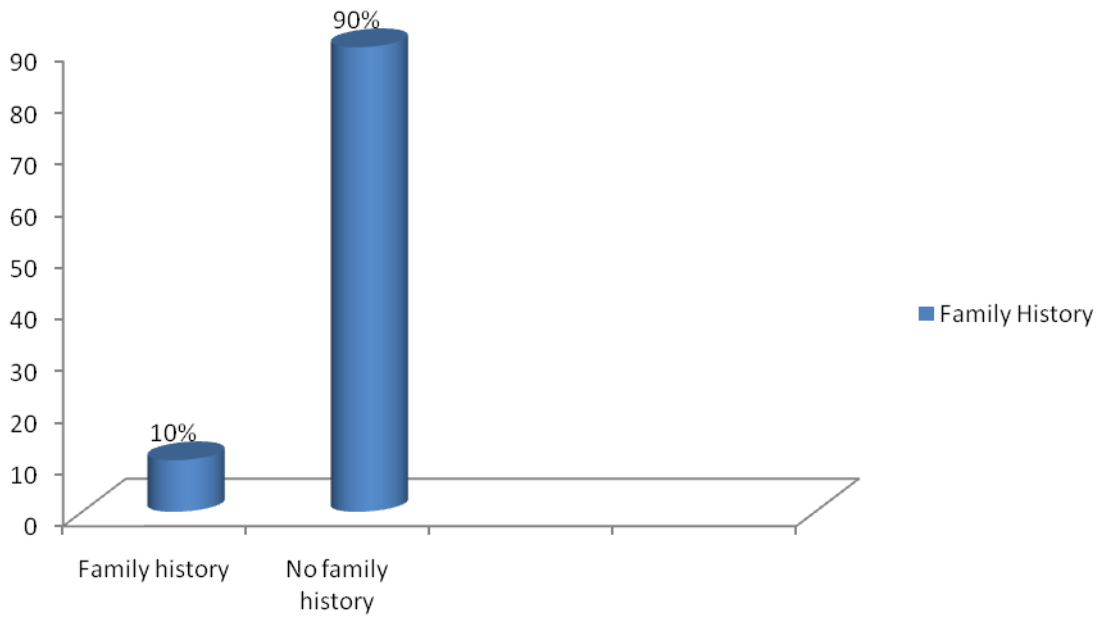


Inference:

According to diet, high incidence of cases (96.6%) was noted in mixed diet and in Vegetarian c 3.33% cases were noted.

Table-20: Distribution of patients of Puzhuvettu according to Family history

S.NO	History	No of cases	Percentage
1.	Family history	3	10
2.	No Family history	27	90

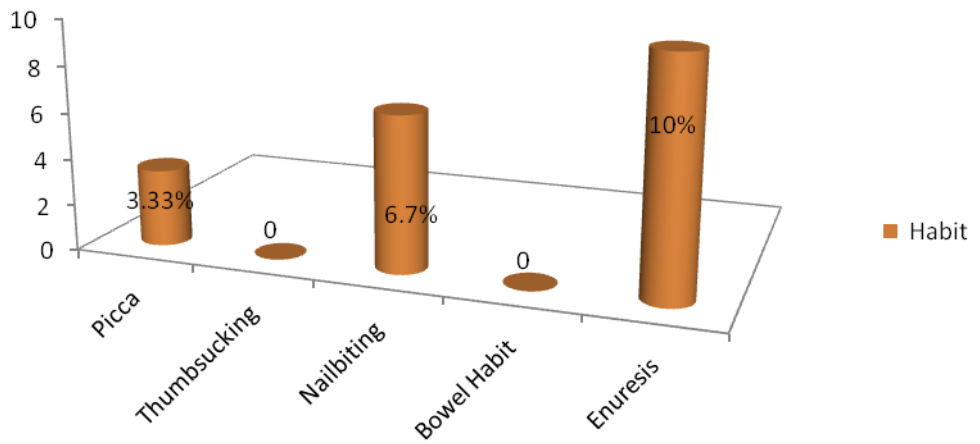


Inference:

According to Family history 10% case were reported as known family history and 90% cases were reported as no relevant family history.

Table-21: Distribution of patients of Puzhuvettu according to Habit

S.NO	Habit	No of patient	Percentage
1.	Pica	1	3.33
2.	Thumb sucking	0	0
3.	Nail biting	2	6.7
4.	Bowel Habit	0	0
5.	Enuresis	3	10

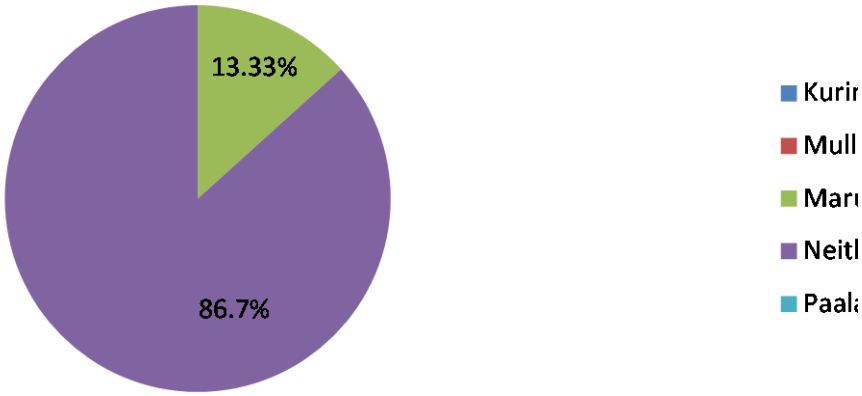


Inference:

Out of 30 cases, 3.33% cases were reported as Pica, 6.7% cases reported as nail biting and 10% cases were reported as Enuresis.

Table-22: Distribution of Patients with Puzhuvettu according to Nilam

S.NO	Nilam	No of cases	Percentage
1.	Kurinji	0	0
2.	Mullai	0	0
3.	Marutham	4	13.33
4.	Neithal	26	86.66
5.	Paalai	0	0

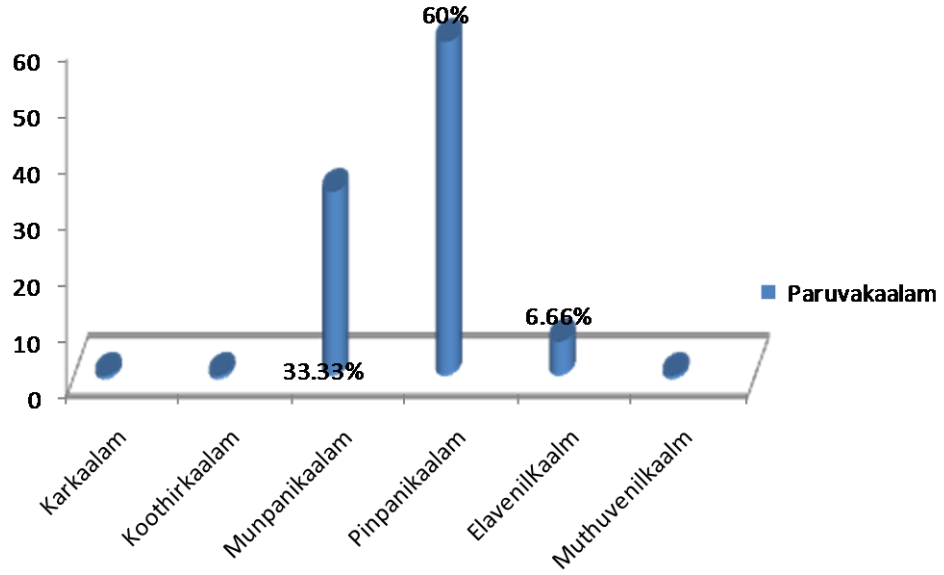


Inference:

Out of 30 cases, 86.7% of cases from Neithal nilam and 13.33% of cases from Marutham nilam. (Table 22)

Table-23: Distribution of Patients with Puzhuvettu according to Paruvakalam

S.NO	Paruvakaalam	No of cases	Percentage
1.	Karkaalam (Avani, Pratasi)	0	0
2.	Koothirkaalam (Iyppasi, Karthigai)	0	0
3.	Munpani (Markazhi, Thai)	10	33.33
4.	Pinpani (Masi- Panguni)	18	60
5.	Elavenil (chitirai, Vaigasi)	2	6.66
6.	Mudhuvenil (Aani, Aadi)	0	0

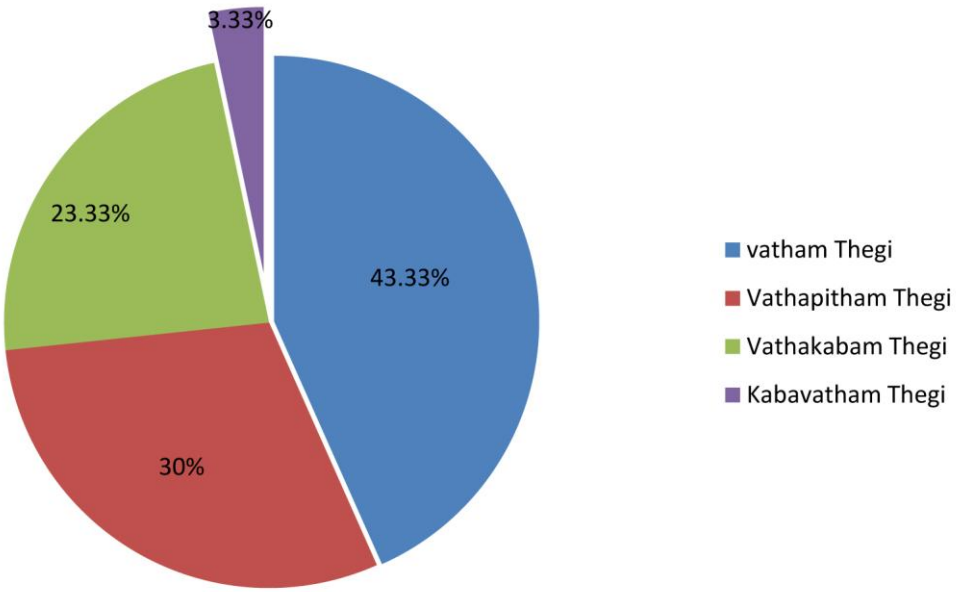


Inference:

According to paruvakaalam, high incidence of cases (60%) were reported in Pinpanikaalam, 33.33% cases were from Munpanikaalam and 6.66% cases were from Elavenil kaalam. (Table 23)

Table-24: Distribution of Patients with Puzhuvettu according to Yakkai

S.NO	Yakkai	No. of cases	Percentage
1.	Vatham	13	43.33
2.	Vathapitham	9	30
3	Vathakabam	7	23.33
4.	Kabavatham	1	3.33

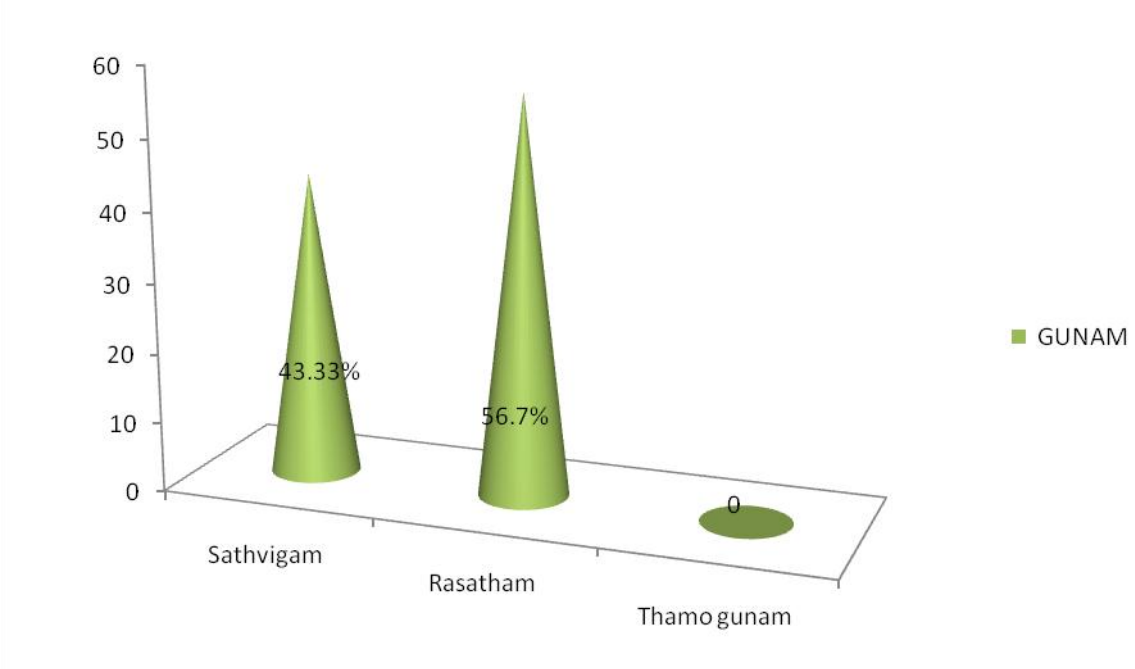


Inference:

Out of 30 cases, 43.33% cases were reported as vathathegi, 30% cases were reported as Vathapitha thegi, 23.33% cases were reported as Vathakaba thegi and 3.33 % cases were reported as Kabavatha thegi.(Table24)

Table-25: Distribution of Patients with Puzhuvettu according to Gunam

S.NO	Gunam	No of patients	Percentage
1.	Sathuvam	13	43.33
2.	Rasatham	17	56.7
3.	Thamo	0	0



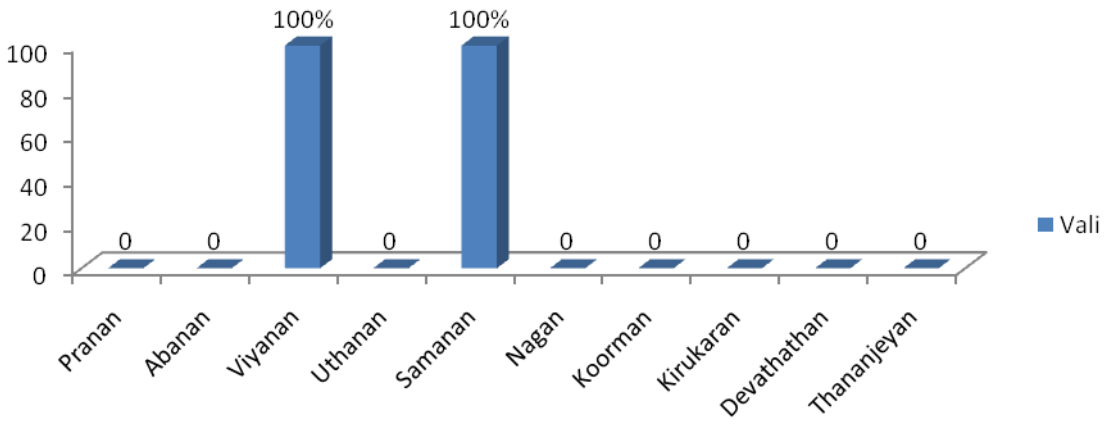
Inference:

According to gunam, 43.33% cases were reported as Sathvigam and 56.7% cases were reported in Rasatha gunam. (Table 25)

Table-26: Distribution of Patients with Puzhuvettu according to Uyirthathukkal

VALI :

S.NO	Vatham	No of cases	Percentage
1.	Pranam	0	0
2.	Abanan	0	0
3.	Viyanan	30	100
4.	Udhanan	0	0
5.	Samanan	30	100
6.	Naagam	0	0
7.	Koorman	0	0
8.	Kirukaran	0	0
9.	Devathathan	0	0
10.	Thananjeyan	0	0

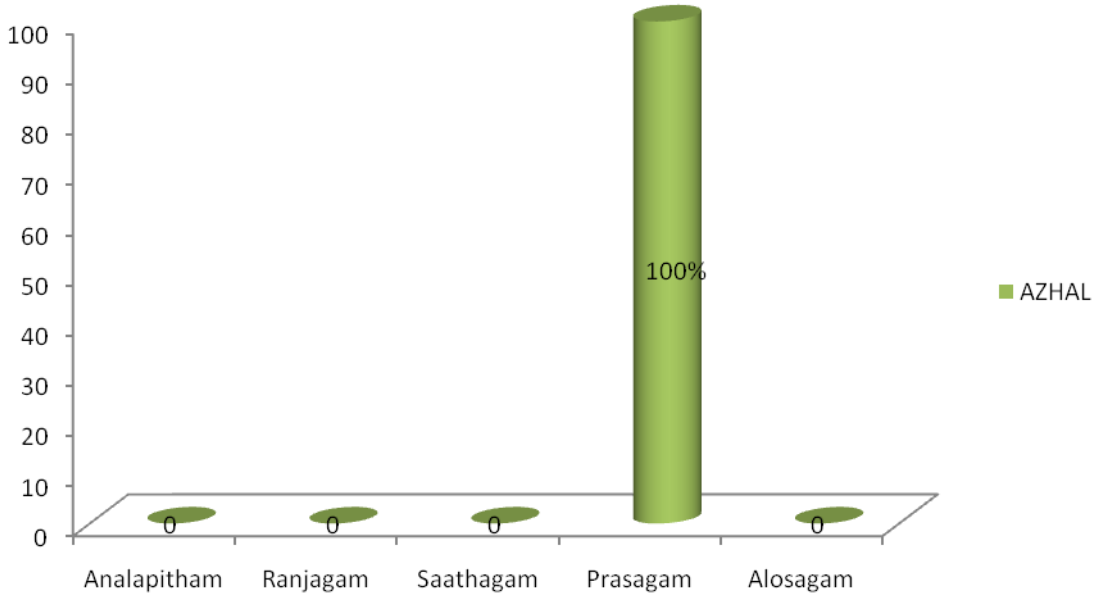


Inference:

According to Vali, derangement of Viyanan and Samanan was 100% affected.

Table-27: Distribution of Patients with Puzhuvettu according to Azhal

S.NO	AZHAL	No of cases	Percentage
1.	Analapitham	0	0
2.	Ranjagam	0	0
3.	Saathagam	0	0
4.	Prasagam	30	100
5.	Alosagam	0	0

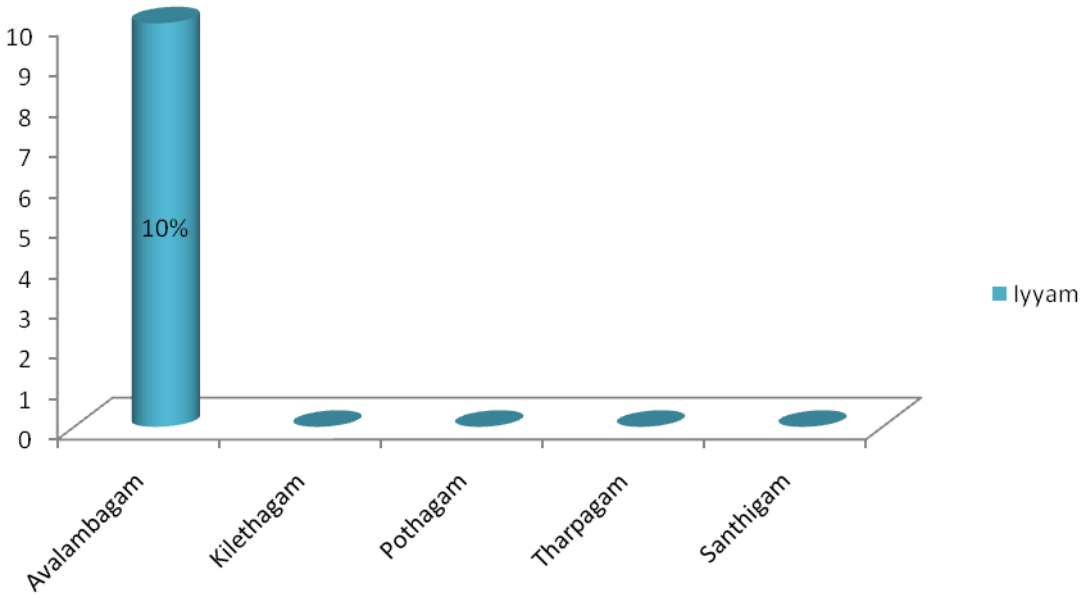


Inference:

According to Azhal, Derangement of Prasagam was deranged in 100%.

Table-28: Distribution of Patients with Puzhuvettu according to Iyyam

S.NO	Iyyam	No of cases	Percentage
1.	Avalambagam	3	10
2.	Kilethagam	0	0
3.	Pothagam	0	0
4.	Tharpagam	0	0
5.	Santhigam	0	0

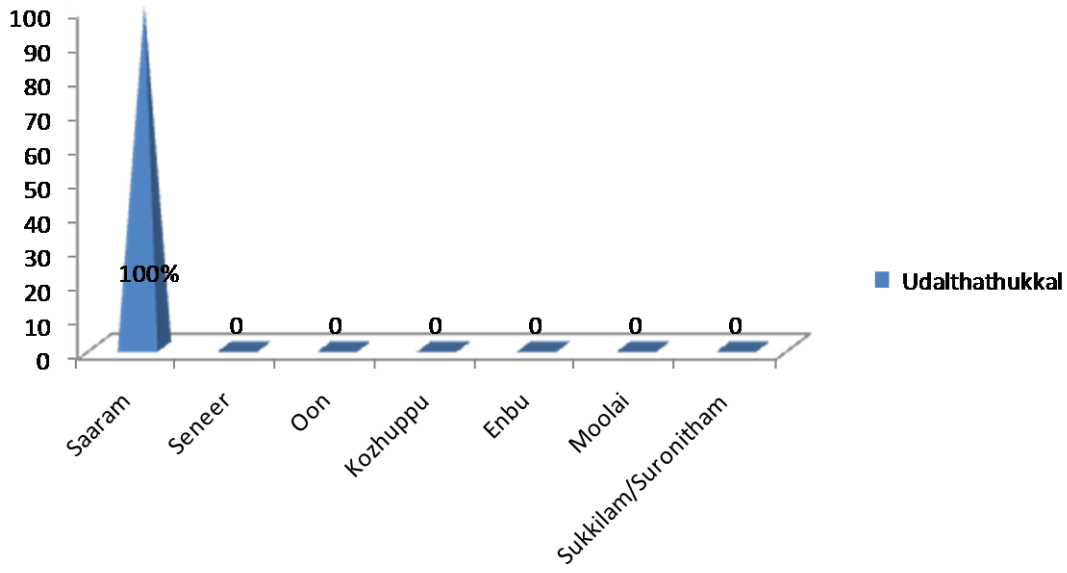


Inference:

Out of 30 cases derangement of Avalambagam was 10%.

Table-29: Distribution of Patients with Puzhuvettu according derangement of Udarthathukal

S.NO	Udarthathukkal	No of cases	Percentage
1.	Saaram	30	100
2.	Seneer	0	0
3.	Oon	0	0
4.	Kozhuppu	0	0
5.	Enbu	0	0
6.	Moolai	0	0
7.	Sukkilam/Suronitham	0	0

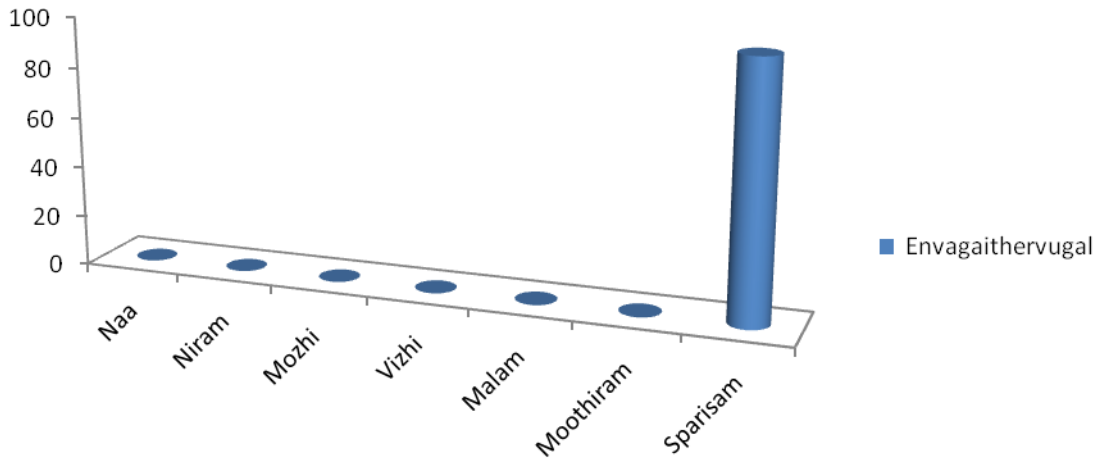


Inference:

According to Udarthathukkal Saram was affected in 100% of cases.

Table-30: Distribution of Patients with Puzhuvettu according to Envagaithervugal

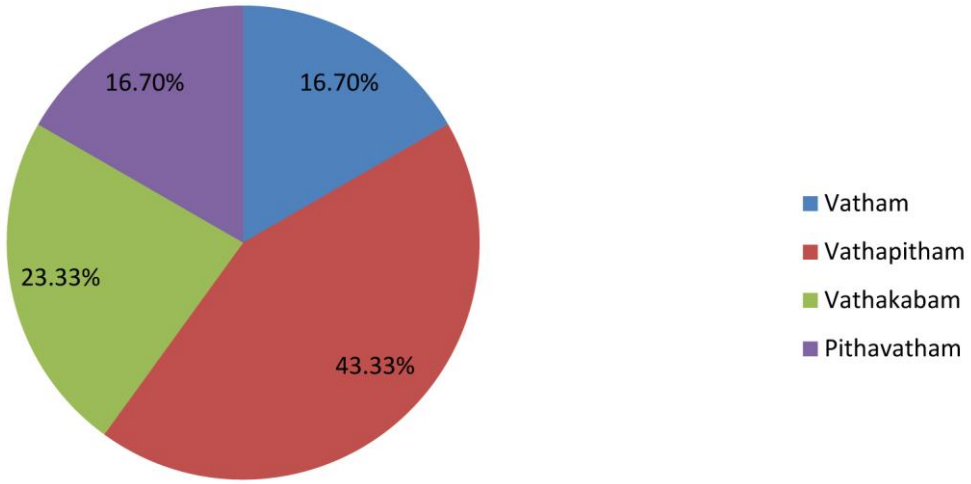
S.NO	Envagaithervugal	No of cases	Percentage
1.	Naa	0	0
2.	Niram	0	0
3.	Mozhi	0	0
4.	Vizhi	0	0
5.	Sparisam	30	100
6.	Malam	0	0
7.	Moothiram	0	0
8.	Naadi- Vatham Vathapitham Vathakabam Pithavatham	5 13 7 5	16.7 43.33 23.33 16.7



Inference:

Out of 30 cases, 100% of cases were affected in Sparisam.

Naadi:

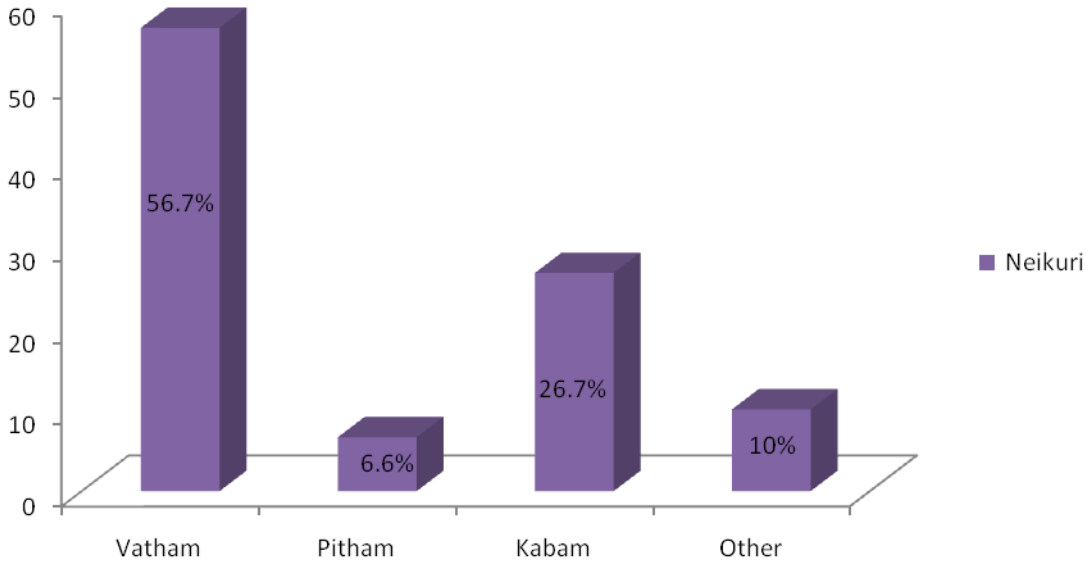


Inference:

In Naadi, Vatham was observed in16.7% of cases,Vathapitham was observed in 43.33% of cases, Vathakabam was observed in 23.33%of cases and Pithavatham was observed in 16.75% of cases. (Table 16)

Table-31: Distribution of Patients with Puzhuvettu according to observation of Neikuri Analysis

S.NO	Neikuri reference	No of cases	Percentage
1.	Vatham	17	56.7
2.	Pitham	2	6.6
3.	Kabam	8	26.7
4.	Other	3	10

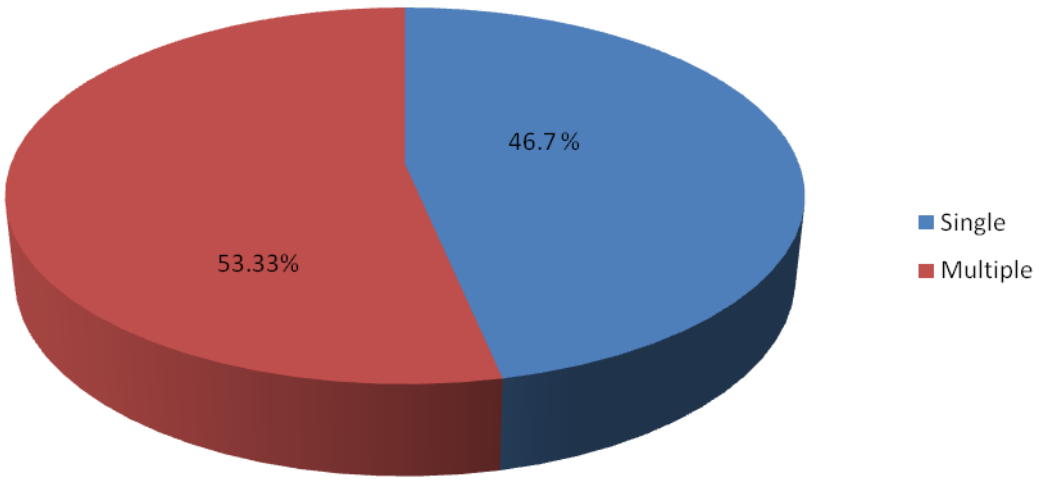


Inference:

According to Neikuri,Vatha neer was observed in 56.7% of cases, Pitha neer was observed in 6.6% of cases, Kaba neer was observed in 26.7% of cases and 10% cases was observed in Others.

Table-32: Distribution of Patients with Puzhuvettu according to Area affected

S.NO	Area affected	No of cases	Percentage
1.	Single	14	46.7
2.	Multiple	16	53.33



Inference:

According to area affected out of 30 cases 46.7% was affected by Single area and 53.33% was affected by multiple areas.

Table-33: Distribution of Patients with Puzhuvettu according to SALT Score

S. NO	SALT Score	Before treatment		After Treatment	
		(No of cases)	Percentage	(No of cases)	Percentage
1.	1-5	9	30%	17	56.7%
2.	6-10	13	43.33%	9	30%
3.	11-15	4	13.33%	2	6.7%
4.	16-20	1	3.33%	1	3.3%
5.	21-25	1	3.33%	0	-
6.	26-30	1	3.33%	0	-
7.	31-35	0	-	1	3.3%
8.	36-40	1	3.33%	0	-

SALT score-Severity of Alopecia Tool score: Grade I Slightly improvement barely noticeable (upto25%), Grade II Moderate improvement noticeable (25-50%), Grade III Obvious improvement (51-75%), Grade IV Marked improvement (>75%)

Table-34: Grading according to SALT score

S. No	SALT SCORE	IMPROVEMENT
1.	1-5	Obvious
2.	6-20	Moderate
3.	21-40	Slight

Inference:

Out of 30 cases, 56.7% of cases has obvious improvement, moderate in 40% of cases and 3.33% of case were slight improvement. These results were based on the Clinical improvements observed by Salt score.

STATISTICAL ANALYSIS OF SALT SCORE:

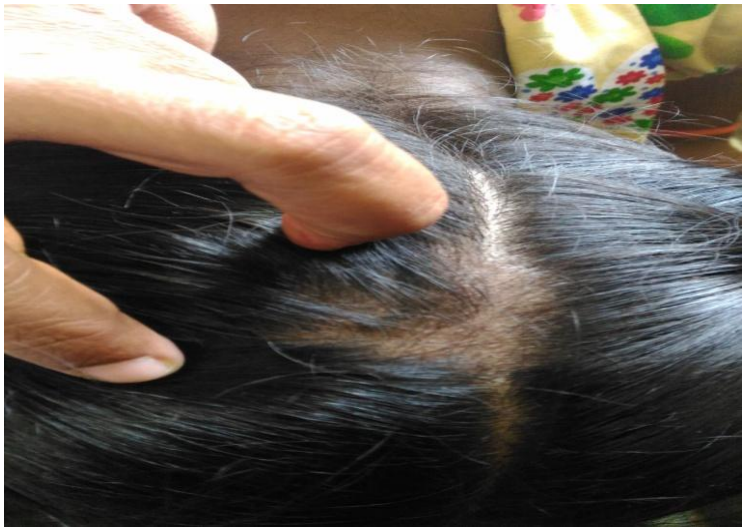
SALT SCORE No of Patients	**Mean ± Std Dev**	**Std error**	**Significance (t value, p value)**
Before (30)	9.4 ± 7.62	1.39	T=7.942,P< 0.0001
After (30)	6.2 ± 6.2	1.13	

There is considerable significant difference between before and after treatment in the SALT score of Puzhuvettu (Alopecia areata).9.4± 7.62 and 6.2± 6.2, P < 0.0001. The difference in mean reduction of SALT score was statistically significant.

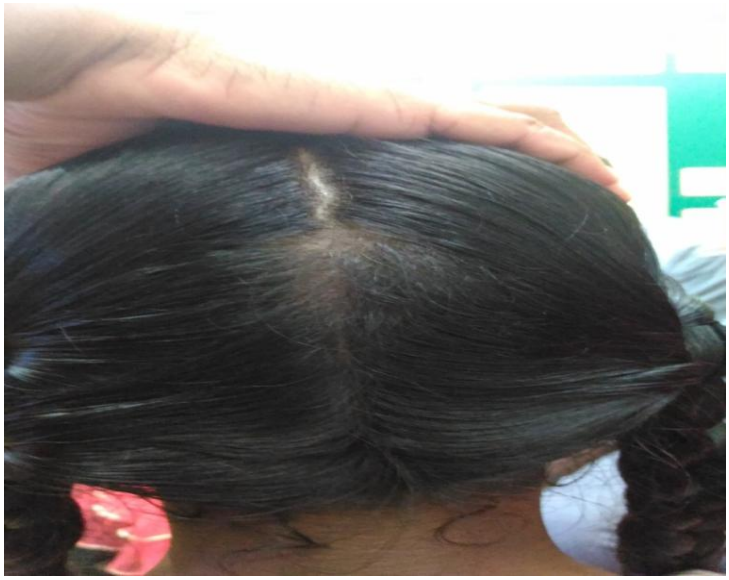
OP NO: I83043

AGE/SEX-6/FC

BEFORE TREATMENT



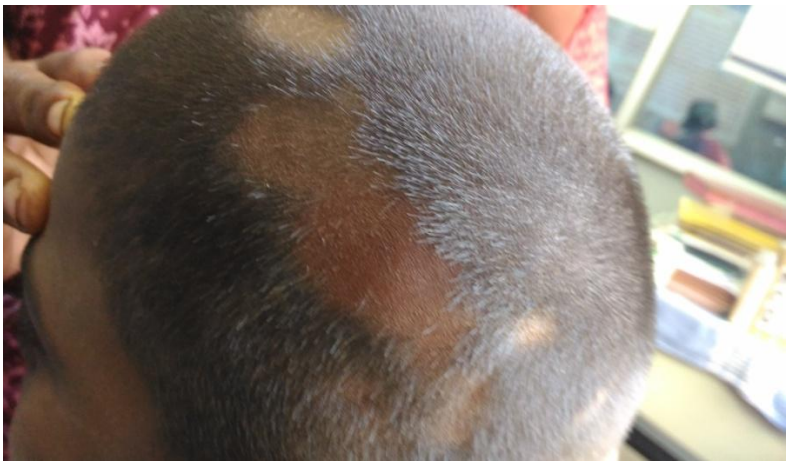
AFTER TREATMENT



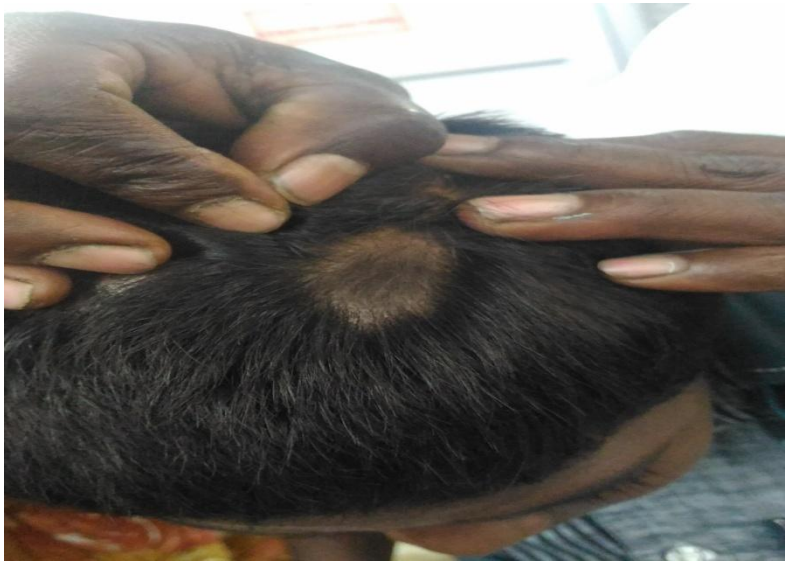
OP NO: J05415

AGE/SEX-9/MC

BEFORE TREATMENT



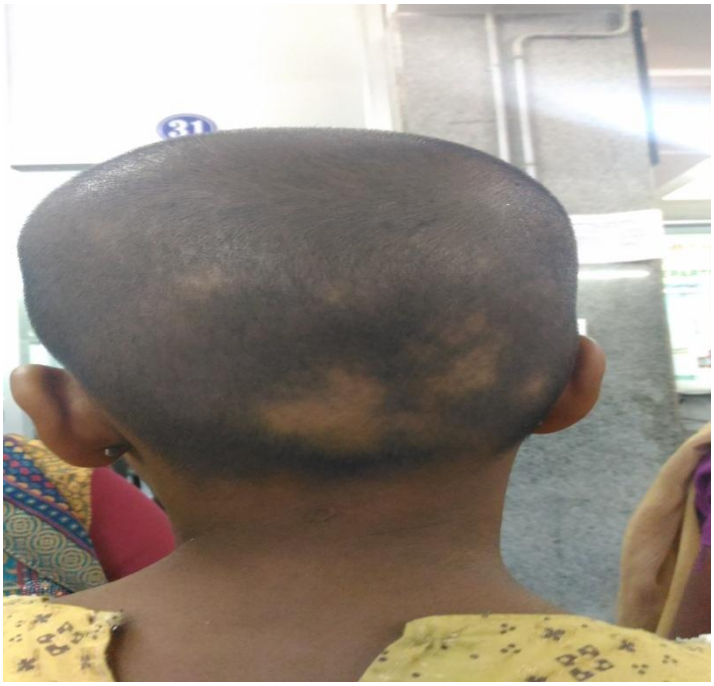
AFTER TREATMENT



OP NO: K09836

AGE/SEX-7/FC

BEFORE TREATMENT



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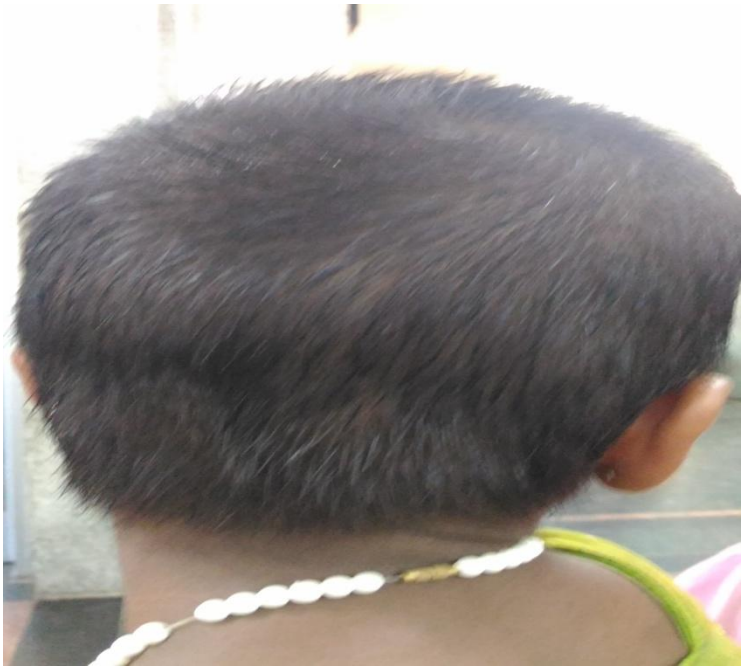

6. DISCUSSION

Puzhuvettu is a one of the commonest skin disease in childhood. Puzhuvettu resembles alopecia areata in modern literature. The disease is characterized by Patchy hair loss in scalp region, itching, non- scarring, well circumscribed loss of hair, atopy with exclamation mark hair, associated with nail pitting and ridges.

In the present study, thirty cases were treated in the outpatient department, according to clinical features mentioned in textbook of Sirappu Maruthuvam. The Diagnosis is based on clinical observation. The diagnosis were confirmed and treated with the drug "Silvisha Usidham" and "Puzhuvettu Thylam" and clearly observed.

The Drugs which are mentioned in Siddha literature for the management of Puzhuvettu were selected and the study is conducted after the proposal was screened by the screening committee of National Institute of Siddha and the trial was also approved by the Institutional Ethical Committee (NIS/IEC/2016/11-20/14.10.2016).The trial was registered in Clinical trial registry of India (CTRI Reg No :CTRI/2018/01/011311).

The trail drugs were prepared by the author in the Gunapadam Practical laboratory of National Institute of Siddha, after getting proper authentication of raw drugs from the Medicinal botany department at NIS, Chennai-47.The trail drug was prepared by the standard operating procedure as mentioned in the protocol.

The Biochemical analysis of drugs was performed in biochemistry lab of NIS and it showed the presence of silicate, sulphate, carbonate, iron, ammonium, starch and alkaloid.

In acute toxicity study carried out as per WHO guideline there was no yreatment related death of significance of toxicity developed in albino rats at dosage level 5000mg/kg/b.wt Throughout the study period no change in behavioural pattern, food and water intake,no gross pathological changes have been seen in the internal organs of both control and treated groups. Thus the LD50 value was found to be greater than 5000mg/kg/b.wt.

The Physiocochemical, Phytochemical, heavy metal analysis, Pesticide residue, Specific pathogen test, Aflotoxin Assay and Pharmacological activity of the drug was done at Noble Research Solution, Chennai.

The Phytochemical analysis of Silvisha Usidham constitutes alkaloid, steroids, Triterpenoids, coumarin and tanin.

HPTLC finger printing analysis of the Silvisha Usidham reveals the presence of seven prominent peaks corresponds to presence of seven versatile phytocomponents present within it. Rf value of the peaks ranges from 0.10 to 0.84.Further the peak 3 occupies the major percentage of area of 23.98% which denotes the abundant existence of such compound .Followed by this peak 4 and 5 occupies the percentage area of 16.72 and 16.58%.

Heavy metal analysis shows that the heavy metals like Lead, Cadmium, Arsenic and Mercury are within the permissible limits.

Analysis of microbial load reveals that the drug does not have any microbial contamination.

The Silvisha Usidham does not show the evidence for the presence of any of the aflatoxins and the Pesticide residue values are within limit.

The Pharmacological studies were done. It revealed that the drug Silvisha Usidham possess Anti-inflammatory activities by In-vitro study.

The Safety of the trial drug usage through biochemical analysis, heavy metal analysis, and toxicity study was also ensured during the study. It revealed the presence of effective minerals.

The patients were recruited for the trial based on inclusion and exclusion criteria and after getting the consent from the patient.30 Patients Were included in this study.

The 30 patients were treated in OPD of Ayothidoss Pandithar Hospital of National Institute of Siddha. Separate proforma was maintained to monitor the clinical signs and symptoms of the disease. Progress chart was also maintained to monitor the clinical symptoms of the disease.

The treatment was aimed at normalizing the deranged thodams and providing relief from symptoms. Before treatment the patients were advised to adapt lifestyle modifications such as oil bath weekly twice and to follow good dietary regimen.

The patients were treated with trial drugs Silvisha Usidham and Puzhuvettu Thylam for 45days.Patients were instructed to take the medicines regularly and advised to follow pathiyam and avoid exposure to allergic substance if any. Patients were asked to visit the hospital every 7^{th} day for 45 days.

After completion of the study, the patients were advised to visit the out-patient ward of department of Kuzhanthai Maruthuvam for further follow up. The results observed during the study period were discussed by the author below.

The study evaluates the effect of “Silvisha Usidham” and “Puzhuvettu Thylam” in relieving the symptoms of Puzhuvettu.

CLINICAL REVIEW

Age:

In the present study, out 30 cases 60% were reported between 6-9 years of age group and 40% of cases were 10-12 years of age group.

Sex:

Out of 30 cases, 30% (9 cases) were male children and 70% (21 cases) were female children. In distribution of sex it was observed that there was high incidence of female children than male children.

Socio-economic status:

About 30 cases, 10% (3cases) were under lower income group, 60% (18cases) cases were under middle income group and 30% (9cases) were under high income group. The highest incidence occurred in middle income group

Seasonal Variation:

Out of 30 cases, 33.33% of cases were reported on Munpani kaalam, 60% of cases were reported on Pinpani kaalam and 6.66% of cases were reported on Elavenil kaalam.

Family History:

Out of 30 cases, 3 (10%) cases were reported as known family history and 27 (90%) cases have no relevant family history.

Food Habit:

According to food habits 3.3% of cases had vegetarian diet and 96.6% of cases had mixed diet. The highest incidence of cases was observed in Mixed diet of food habits.

Duration of Illness:

According to duration of illness 15 (50%) of cases were reported between 1day-3months, 7 (23.33%) of cases were reported between 4months-6months, 5 (16.66%) of cases were reported between 1year-5years. The highest incidence of cases was observed in 1day-3months duration.

Nilam:

Among 30 cases,4 (13.33%) cases were from Marutham nilam and 26 (86.66%) cases were from Neithal nilam.

Vali (Vatham):

Due to the derangement of different vatha the following symptoms occur. Viyanan affected in 100% cases and causes and samanan affected in 100% cases.

Azhal (Pitham):

Due to the derangement of Pitham the following symptoms occur Prasagam was affected 100% and causes

Iyyam (Kabam):

Deranged Avalambagam was affected 10% and causes cough.

Ezhu Udarkattugal:

In Ezhuudalkattugal Saram was affected 100% and causes

Envagai Thervugal:

According to study, Sparisam was affected in 100% of cases

Naadi:

- Vatham was observed in 16.7%
- Vathapitham was observed in 43.33%
- Vathakabam was observed in 23.33%
- Pithavatham was observed in 16.7%

Neerkuri:

Regarding Moothiram, neerkuri showed straw coloured urine in all cases

Neikuri:

In the present study, 56.7% of cases was observed as Vatha neikuri, 6.6% of cases was observed as Pitha neikuri, 26.7% of cases was observed as Kaba neikuri. According to this neikuri, Vatham was dominantly affected.

The trail medicine chosen for the treatment of Puzhuvettu was “Silvisha Usidham” and “Puzhuvettu Thylam”.

The pharmacological studies already reported on the individual drugs also favor its effect in disease of Puzhuvettu (Alopecia areata) as given below. Elarisi have a potent immunomodulator, anti-inflammatory and anti fungal activity. Peyathi, Thippili and sesame oil have anti inflammatory and immunomodulator activity. Avuri have

antioxidant and effect on promoting hair growth. The Phytocemical analysis shows the presence of steroids and Psoralen a chemical constituent present in Ficus hispida.These are more effective in the management of Puzhuvettu.

According to SALT score:

Grading was carried out based on subjective assessment as follows.

- Grade I Slightly improvement barely noticeable (upto25%)
- Grade II Moderate improvement noticeable (25-50%)
- Grade III Obvious improvement (50-75%)
- Grade IV Marked improvement (>75%)

Out of the 30 case, 56.7% of cases were obvious improvement, 40% of cases were moderate improvement and 3.33% were Slight improvement. These results were based on the clinical improvement by SALT score. The results of the study suggest that treatment with Silvisha Usidham and Puzhuvettu thylam has significant improvement in patients of Puzhuvettu.

7. SUMMARY

- The aim of the study was Preclinical and clinical evaluation of Silvisha Usidham (Internal) and Puzhuvettu Thylam (External) for Puzhuvettu (Alopecia areata) in children.
- Before initiating the clinical trial, approval was got from the Institutional Ethical committee of National Institute of Siddha (NIS/IEC/2016/11-20/14.10.2016) for conducting the clinical studies respectively by submitting the well defined protocol and proforma. It was registered prospectively in the Clinical Trail Registry of India (CTRI Reg No :CTRI/2018/01/011311)
- The raw drugs were authenticated by the Assistant professor of medicinal botany and Investigator, Dept. of Gunapadam, NIS, and the trail drug was prepared by the investigator in the Gunapadam lab of National Institute of Siddha as per the standard operating procedure mentioned in the protocol.
- The Phytochemical, physicochemical, heavy metal analysis, specific pathogen test, pesticide residue of the drug Silvisha Usidham were done in Noble Research Solution and the bio chemical qualitative analysis were done in the biochemistry lab of National Institute of Siddha. The biochemical analysis revealed the presence of Alkaloid, starch, silicate, Sulphate, carbonate, Iron and ammonium,.
- The Physicochemical analysis of Silvisha Usidham constitutes alkaloid, steroids, Triterpenoids, coumarin and tanin.
- Heavy metal analysis shows that the heavy metals like Lead, Cadmium, Arsenic and Mercury are within the permissible limits.
- Analysis of microbial load reveals that the drug does not have any microbial contamination.
- The Silvisha Usidham does not show the evidence for the presence of any of the aflatoxins and the Pesticide residue values are within limit.

  The Pharmacological studies were done. It revealed that the drug Silvisha Usidham possess Anti-inflammatory activities by In-vitro study.
- The Children with Puzhuvettu were recruited based on inclusion and exclusion criteria and a detailed study was done. Separate proforma was maintained for each patient along with daily progress chart to monitor the prognosis.
- Before initiating the trial informed consent was obtained from all the parents.

- 2-3ml of Mantha ennai with luke warm water was administered at bedtime.Before starting the treatment to bring the vitiated vatham to normal.
- The patients were treated for a period of 45 days. The trial medicine selected for the treatment was Silvisha Usidham (internal medicine) at the dose of 2-4ml twice a day and Puzhuvettu Thylam (external) for 45 days as per Siddha literature Anuboga vaithiya navaneetham thirattu - Part -10 ,Page no :108.
- Clinical assessment was done during each visit in OPD patients (7 days once) and the data were noted in the prescribed proforma. (Form-IV)
- During the study period there was no event of any adverse reactions were reported owing to the drug or disease.
- Diet restriction was strictly followed during the period of drug administration as well as in re-dieting period as per noted in the dietary advice form .(Form-X)
- The SALT score showed obvious improvement in 56.7%, moderate improvement in 40% and slight improvement in 3.33%. Statistical analysis done for SALT score and it shows that the trail drug Silvisha Usidham (Internal) and Puzhuvettu Thylam (External) is effective and it is consider significant ($p<0.001$).
- Thus the drug is found to be safe and effective in the management of Puzhuvettu.
- The clinical efficacy of the drug was analyzed statistically by Salt score. The observation made during the clinical study showed that the trail drug Silvisha Usidham and Puzhuvettu Thylam was clinically effective.

8. CONCLUSION

It is concluded by this study that Silvisha Usidham (Internal) and Puzhuvettu Thylam (External) is to be safe, efficacious and cost effective potent herbal drug in the treatment of Puzhuvettu. From the SALT score, finally it is concluded that 56.7% of case obvious improvement, 40% of cases moderate improvement and 3.33% of cases slight improvement. Statistical analysis done for SALT score shows that the trial drug Silvisha Usidham (Internal) and Puzhuvettu Thylam (External) is effective and $p<0.0001$ considerable significant. There was no adverse reaction was reported during the trial period. The Clinical Trial conducted in selected patients was satisfactory and the results were encouraging. However a study with large number of patients is required to find out the ideal dose response.

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NATIONAL INSTITUTE OF SIDDHA

AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI – 600 047.

DEPARTMENT OF KUZHANDHAI MARUTHUVAM PRECLINICAL AND CLINICAL EVALUATION OF SILVISHA USIDHAM (INTERNAL) AND PUZHUVETTU THYLAM (EXTERNAL) FOR PUZHUVETTU (ALOPECIA AREATA) IN CHILDREN.

FORM I- SCREENING AND SELECTION FORM

1. S No:	2. OP/ IP No:	3.Name:
4. Age:	5.Gender:	6.Date of Enrollment:
7. Date of completion:	8.Informant:	9.Reliability:

INCLUSION CRETERIA:

Age: between 6-12 years

Sex: Both male and female

Patient who are satisfying minimum of 3 to 4 symptoms	Yes	No
Scattered long hairs within the bald area	☐	☐
Non- scarring	☐	☐
The area of hair loss may tingle or be painful	☐	☐
Hair loss in patches	☐	☐

EXCLUSION CRITERIA:

Scarring alopecia	☐	☐
Alopecia universalis	☐	☐
Alopecia totalis	☐	☐
Vitligo	☐	☐
Atopic dermatitis	☐	☐
Thyroid disease	☐	☐
Down syndrome	☐	☐

CHILDREN ADMITTED TO TRIAL: 1.Yes ☐ 2.No ☐

1. IP ☐ 2.Op ☐

DATE**:** SIGNATURE OF THE INVESTIGATOR:

STATION**:** SIGNATURE OF THE GUIDE:

SIGNATURE OF THE HOD:

NATIONAL INSTITUTE OF SIDDHA

AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI-47

DEPARTMENT OF KUZHANDHAI MARUTHUVAM

FORM-II- CONSENT FORM

CERTIFICATE BY INVESTIGATOR

I certify that I have disclosed all the details about the study in the terms readily understood by the parent/guardian

Signature _____

Name _____

Date _____

CONSENT BY PARENT

I have been informed to my satisfaction, by the attending physician, the purpose of the clinical trial, and the nature of drug treatment and follow-up including the laboratory investigations to be performed to monitor and safeguard my son/daughter body functions.

I am aware of my right to OPT my son/daughter out of the trail at any time during the course of the trail without having to give the reasons for doing so.

I, exercising my free power of choice, hereby give my consent to include my son/daughter as a subject in the Pre-clinical and clinical trial of SILVISHA USIDHA (Internal medicine) PUZHUVETTU THYLAM (External medicine) for "PUZHUVETTU" (Alopecia areata) in children.

The photographs taken in the study will be displayed only in scientific conference for the advancement of medical knowledge.

Date: **Signature** _____

Name _____

Station:

Signature of witness _____

Name _____

NATIONAL INSTITUTE OF SIDDHA AYOTHIDOSS PANDITHAR HOSPITAL

CHENNAI – 600047.

DEPARTMENT OF KUZHANDHAI MARUTHUVAM

PRECLINICAL AND CLINICAL EVALUATION OF SILVISHA USIDHAM (INTERNAL MEDICINE)AND PUZHUVETTU THYLAM (EXTERNAL MEDICINE) FOR PUZHUVETTU(ALOPECIA AREATA) IN CHILDREN.

FORM- III CASE RECORD FORM

Demographic data

OP/IP No.	Visit Date : (__/__/____)
Name :	
Age :	
Gender Male ☐ Female ☐	Date Of Birth : (__/__/____)
Father/ Mother /Guardian Name :	
Fathers Occupation :	
Fathers Monthly Income :	
Religion :	
Socioeconomic Status :	
Patient Informant :	

Postal Address:

Contact No :

1. **Complaints and Duration**

2. **Present illness**

3. **History of Past Illness**

History /Symptoms/Signs	**Yes**	**No**	**If, Yes Details**
Any Similar Complaints	☐	☐	_____
Bronchial Asthma	☐	☐	_____
Hospitalization	☐	☐	_____
Any other	☐	☐	_____

Family History

Any Hereditary/ Familial Disease Yes No

If Yes, Details --------

Immunization History

Proper Immunization given Yes ☐ No ☐

Food habits:

1. Veg ☐ 2. Non-Veg ☐

General assessment

1. Pica ☐ ☐
2. Thumb sucking ☐ ☐
3. Nail biting ☐ ☐
4. Bowel movements ☐ ☐
5. Enuresis ☐ ☐

General Examination

1. Pallor YES ☐ NO ☐
2. Jaundice YES ☐ NO ☐
3. Cyanosis YES ☐ NO ☐
4. Clubbing YES ☐ NO ☐
5. Pedal oedema YES ☐ NO ☐
6. Lymph adenopathy YES ☐ NO ☐

Vital signs:-

1. Pulse rate / mint
2. Heart rate / mint
3. Respiratory Rate / mint
4. Temperature

Anthropometry:-

Height-

Weight-

Examination of systems: Normal Affected

Cardio – Vascular system: ☐ ☐

Gastro intestinal system: ☐ ☐

Central nervous system: ☐ ☐

Genito – urinary system: ☐ ☐

Endocrine system: ☐ ☐

Nilam:-

Kurinji ☐ Mullai ☐ Marutham ☐ Neithal ☐ Paalai ☐

KaalaIyalbu:-

Kaarkalam ☐ Koothirkaalam ☐ Munpanikaalam ☐

Pinpanikaalam ☐ Illavenirkaalam ☐ Muthuvenirkaalam ☐

Yaakai

Vatham ☐ VathaPitham ☐ VathaKabam ☐

Pitham ☐ Pithavatham ☐ PithaKabam ☐

Kabam ☐ KabaVatham ☐ KabaPitham ☐

Gunam

Sathuvam ☐ Rasatham ☐ Thamasam ☐

Pori / Pulangal

	Normal	Affected	Normal	Affected	Remarks
Mei / unarvu	☐	☐	☐	☐	
Vaai / suvai	☐	☐	☐	☐	
Kan / parvai	☐	☐	☐	☐	
Mooku / natram	☐	☐	☐	☐	
Sevi / olli	☐	☐	☐	☐	

Kanmendhirium / Kanmavidayam

	Normal	Affected	Normal	Affected
Remarks	☐	☐	☐	☐
Kai / dhanam	☐	☐	☐	☐
Kaal / ghamanam	☐	☐	☐	☐
Vaai / vaku				
Eruvai / visarkam	☐	☐	☐	☐
Karuvai / anantham	☐	☐	☐	☐

UyirThathukkal

Vali:

	Normal	Affected	Remarks
Pranan	☐	☐	
Abanan	☐	☐	
Viyanan	☐	☐	

Uthanan	☐	☐
Samanan	☐	☐
Nagan	☐	☐
Koorman	☐	☐
Kirukaran	☐	☐
Devathathan	☐	☐
Dhanajeyan	☐	☐

Azhal

	Normal	Affected	Remarks
Analam	☐	☐	
Ranjagam	☐	☐	
Saathagam	☐	☐	
Alosagam	☐	☐	
Prasagam	☐	☐	

Iyyam

	Normal	Affected	Remarks
Avalambagam	☐	☐	
Kilethagam	☐	☐	
Pothagam	☐	☐	
Tharpagam	☐	☐	
Santhigam	☐	☐	

Udalthathukkal

	Normal	Affected	Remarks
Saaram	☐	☐	
Senneer	☐	☐	
Oon	☐	☐	
Kozhuppu	☐	☐	
Enbu	☐	☐	
Moolai	☐	☐	
Sukilam / Suronitham	☐	☐	

EnvagaiThervugal

	Normal	Affected	Remarks
Naa			
Niram	☐	☐	
Thanmai	☐	☐	
Suvai	☐	☐	
Niram	☐	☐	
Mozhi	☐	☐	
Vizhi			
Niram	☐	☐	
Thanmai	☐	☐	
Parvai	☐	☐	

Sparisam ☐ ☐

Malam

Niram Normal ☐ Affected ☐

Nurai Normal ☐ Affected ☐

Elagal Yes ☐ No ☐

Erugal Yes ☐ No ☐

Moothiram

Neerkuri: Niram Normal ☐ Affected ☐

Edai Normal ☐ Affected ☐

Nurai Normal ☐ Affected ☐

Manam Normal ☐ Affected ☐

EnjalNeikuri Normal ☐ Affected ☐

Neikuri:

Vatham ☐

Pitham ☐

Kabam ☐

Others ☐

<u>Naadi:</u>

<u>ThaniNadi</u>

Vadham ☐ Pitham ☐ Kabam ☐

ThonthaNadi

Vathapitham ☐ Pitha vatham ☐ Pitha kabam ☐ Kabapitham ☐

ThodaNadi

Vatha kabam ☐ Kaba vatham ☐

Mukkutra Nadi

Diagnosis:

DRUGS ISSUED: _____

Date : _____

Station: _____

Date: _____

Signature of principle investigator

NATIONAL INSTITUTE OF SIDDHA

AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI – 600 047.

DEPARTMENT OF KUZHANDHAI MARUTHUVAM

PRECLINICAL AND CLINICAL EVALUATION OF SILVISHA USIDHAM (INTERNAL MEDICINE) AND PUZHUVETTU THYLAM (EXTERNAL MEDICINE) FOR PUZHUVETTU (ALOPECIA AREATA) IN CHILDREN.

1. S No: 2. OP/ IP No: 3.Name:

4. Age: 5.Gender: 6.Date of Enrollment:

7. Date of completion: 8.Informant: 9.Reliability:

CLINICAL ASSESSMENT FORM-IV

SEVERITY OF ALOPECIA TOOL SCORE (SALT Score)

DAYS	**SCALP SURFACE AREA MEASUREMENT**				**SALT SCORE**
	VERTEX AREA 40% (0.4)	RIGHT PROFILE AREA 18% (0.18)	LEFT PROFILE AREA 18% (0.18)	POSTERIOR ASPECT OF SCALP AREA 24% (0.24)	
0^{th} day					
7^{th} day					
14^{th} day					
21^{st} day					
28^{th} day					
35^{th} day					
45^{th} day					

Date: Signature of Principle Investigator

Station:

Signature of Lecturer: Signature of HOD:

NATIONAL INSTITUTE OF SIDDHA

AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI – 600 047.

DEPARTMENT OF KUZHANDHAI MARUTHUVAM

PRECLINICAL AND CLINICAL EVALUATION OF SILVISHA USIDHAM (INTERNAL) AND PUZHUVETTU THYLAM (EXTERNAL) FOR PUZHUVETTU

(ALOPECIA AREATA) IN CHILDREN.

FORM V -DRUG COMPLIANCE FORM

S. NO: --------- OPD/IPD NO: ---------- NAME: ---------- REG NO:

Name of the drug: Silvisha Usidham

Form of the drug: Oil

Administration: Oral route

Dose and Duration: 2-4ml twice daily for 45 days

DAY	DATE	MORNING	NIGHT
1			
2			
3			
4			
5			
6			
7			
8			
9			
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42			
43			
44			
45			

Date: Signature of Principle Investigator

Station:

Signature of Lecturer: Signature of HOD:

NATIONAL INSTITUTE OF SIDDHA

AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI-47

FORM VI-A – PATIENT INFORMATION SHEET

Name of principle investigator:

I Dr.R.D.Indumathi Studying as PG Scholar at National Institute of Siddha, Tambaram Sanatorium is doing a open clinical trial on "**PUZHUVETTU**" (Alopecia areata). Alopecia areata is a most common disease. In this regard, I am in a need to ask you few questions. I will maintain confidentiality of your comments and data obtained. There will be no risk of disclosing your identity and no physical, psychological or professional risk is involved by taking part in this study. Taking part in this study is voluntary. No compensation will be paid to you for taking part in this study.

You have the liberty in choosing to take part in the study or not to take part. You can choose not to answer a specific question. You may be benefited if you take part in the study. Moreover, taking part in the study may be of benefit to the community, as it may help us to understand the problem of defaulters and potential solutions.

If you agree to be a participant in this study, you will be included in the study primarily by signing the consent form and then you will be given the internal medicine "**SILVISHA USIDHAM**" (2-4ml) and **PUZHUVETTU THYLAM** (External Medicine) for 45 days.

The information I am collecting in this study will remain between you and myself. I will ask you few questions through a questionnaire. The questionnaire will take approximately 20 minutes of your time.

If you wish to find out more about this study before taking part, you can ask me all the questions you want or contact me (Dr.R.D.INDUMATHI) through 9092765785, PG scholar National Institute of Siddha, Chennai-47.

You can also contact the Member-secretary of Ethics committee, National Institute Siddha, Chennai 600047, Tel no: 91-44-22380789, for rights and participation in the study.

Name: Signature:

Date:

தேசிய சித்த மருத்துவ நிறுவனம்

அயோத்திதாச பண்டிதர் மருத்துவமனை சென்னை-47

குழந்தை மருத்துவத்துறை

பரிகரிப்புத் திறனைக் கண்டறியும் மருத்துவ ஆய்வு

ஒப்புதல் படிவம்

ஆய்வாளரால் சான்றளிக்கப்பட்டது.

நான் இந்த மருத்துவ ஆய்வை குறித்த அனைத்து விபரங்களையும் நோயாளியின் பெற்றோருக்கு புரியும் வகையில் எடுத்துரைத்தேன் என உறுதி அளிக்கிறேன்.

தேதி: **கையொப்பம்:**

இடம்: **பெயர்:**

நோயாளியின் பெற்றோர் ஒப்புதல் படிவம்

என்னிடம் இந்த மருத்துவ ஆய்வின் காரணத்தையும்,மருந்தின் தன்மை மற்றும் மருத்துவ வழிமுறைப் பற்றியும், இந்த மருத்துவத்தை தொடர்ந்து எனது குழந்தையின் உடல் இயக்கத்தைக் கண்காணிக்கவும்,அதனைத் பாதுகாக்க பயன்படும் மருத்துவ ஆய்வுக்கூடப் பரிசோதனைகள் பற்றியும் திருப்தி அளிக்கும் வகையில் ஆய்வு மருத்துவரால் விளக்கிக் கூறப்பட்டது.

நான் இந்த மருத்துவ ஆய்வின் போது காரணம் எதுவும் கூறாமல் எப்போது வேண்டுமானாலும் என் குழந்தையை விடுவித்துக் கொள்ளும் உரிமையை தெரிந்திருக்கிறேன்.

நான் என்னுடைய சுதந்திரமாக தேர்வு செய்யும் உரிமையைக் கொண்டு புழுவெட்டு நோய்க்கான சில்விஷ உசிதம் (உள்மருந்து) மற்றும் புழுவெட்டு தைலம்(வெளிமருந்து) பரிகரிப்புத் திறனை கண்டறியும் மருத்துவ ஆய்வுக்கு எனது குழந்தையை உட்படுத்த ஒப்புதல் அளிக்கிறேன்.

தேதி: **பெற்றோர் பெயர் :**

இடம்: **கையொப்பம்:**

சாட்சிக்காரர் பெயர்:

கையொப்பம்:

NATIONAL INSTITUTE OF SIDDHA

AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI – 600 047.

DEPARTMENT OF KUZHANDHAI MARUTHUVAM

PRECLINICAL AND CLINICAL EVALUATION OF SILVISHA USIDHAM (INTERNAL) AND PUZHUVETTU THYLAM (EXTERNAL) FOR PUZHUVETTU (ALOPECIA AREATA) IN CHILDREN.

Principle Investigator: Dr.R.D.INDUMATHI

1. S.I No:	2. OP/ IP No:	3.Name:
4. Age:	5.Gender:	6.Date of Enrollment:
7. Date of completion:	8.Informant:	9.Reliablity:

FORM-VI WITHDRAWAL FORM

10. DATE OF TRIAL COMMENCEMENT: ……...

11. DATE OF WITHDRAWAL FROM TRIAL: ……..

12.REASONS FOR WITHDRAWAL:

Long absence at reporting:	Yes/ No
Irregular treatment:	Yes/ No
Shift of locality:	Yes/No
Increase in severity of symptoms:	Yes/No
Development of severe adverse drug reactions:	Yes/No
Development of adverse event:	Yes/No

(If YES, give the details of adverse reaction in Adverse Reaction Form / Pharmaco Vigilance Form)

Date:

Station:

Signature of the Investigator:

Signature of the Guide: Signature of the HOD

1. Patient / consumer identification (please complete or tick boxes below as appropriate)

NATIONAL PHARMACOVIGILANCE PROGRAMME FOR SIDDHA DRUGS

Reporting Form for Suspected Adverse Reactions to Siddha

Please note: i. All consumers / patients and reporters information will remain confidential.

ii. It is requested to report all suspected reactions to the concerned, even if it does not have complete data, as soon as possible.

Peripheral Center code: State:

<table>
<tr><td>Name</td><td>Father name</td><td rowspan="2">Patient / Record No.</td></tr>
<tr><td>Ethnicity</td><td>Occupation</td></tr>
<tr><td colspan="2" rowspan="2">Address
Village / Town
Post / Via
District / State</td><td>Date of Birth / Age:</td></tr>
<tr><td>Sex: M / F
Weight :
Degam:</td></tr>
</table>

2. Description of the suspected Adverse Reactions (please complete boxes below)

Date and time of initial observation		Season:
Description of reaction		Geographical area:

3. List of all medicines / Formulations including drugs of other systems used by the patient during the reporting period:

Medicine	Daily dose	Route of administration & Vehicle - Adjuvant	Date		Diagnosis for which medicine taken
			Starting	Stopped	
Siddha					
Any other system of medicines					

4. Brief details of the Siddha Medicine which seems to be toxic :

Details	Drug – 1	Drug – 2	Drug - 3
a) Name of the medicine			
b) Manufacturing unit and batch No. and date			
c) Expiry date			
d) Purchased and obtained from			
e) Composition of the formulation / Part of the drug used			

b) Dietary Restrictions if any

c) Whether the drug is consumed under institutionally qualified medical supervision or used as self medication.

d) Any other relevant information.

5. Treatment provided for adverse reaction:

6. The result of the adverse reaction / side effect / untoward effects (please complete the boxes below)

Recovered:	**Not recovered:**	**Unknown:**	**Fatal:**	**If Fatal** **Date of death:**
Severe: Yes / No.	Reaction abated after drug stopped or dose reduced:			
	Reaction reappeared after re introduction:			
Was the patient admitted to hospital? If yes, give name and address of hospital				

7. Any laboratory investigations done to evaluate other possibilities? If Yes specify:

8. Whether the patient is suffering with any chronic disorders?

Hepatic Renal Cardiac Diabetes Malnutrition

Any Others

9. H/O previous allergies / Drug reactions:

10. Other illness (please describe):

11. Identification of the reporter:

Type (please tick): Nurse / Doctor / Pharmacist / Health worker / Patient / Attendant / Manufacturer / Distributor / Supplier / Any others (please specify)
Name:
Address:
Telephone / E – mail if any :

Signature of the reporter: **Date:**

Please send the completed form to:

Name & address of the RRC-ASU / PPC-ASU

The Director

National Institute of Siddha,

(Pharmacovigilance Regional Centre For Siddha Medicine),

Tambaram Sanatorium, Chennai-600 047.

☏ (O) 044-22381314 Fax : 044 – 22381314

Website : www.nischennai.org

Email: nischennaisiddha@yahoo.co.in

* *

This filled-in ADR report may be sent within one month of observation /occurrence of ADR

	Who Can Report?
What to Report?	⇒ Any Health care professionals like Siddha Doctors / Nurses / Siddha Pharmacists / Patients etc.
Confidentiality	⇒ All reactions, Drug interactions,
	⇒ The patient's identity will be held in strict confidence and protected to the fullest extent. ⇒ Submission of report will be taken up for remedial measures only not for legal claim

Date:

Station:

Signature of the Investigator:

Signature of the Lecturer: Signature of the HOD

NATIONAL INSTITUTE OF SIDDHA

AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI – 600 047.

POST GRADUATE DEPARTMENT OF KUZHANDHAI MARUTHUVAM

PRECLINICAL AND CLINICAL EVALUATION OF SILVISHA USIDHAM (INTERNAL) AND PUZHUVETTU THYLAM (EXTERNAL) FOR PUZHUVETTU (ALOPECIA AREATA) IN CHILDREN.

FORM IX - DIETARY ADVICE FORM

✓ THINGS TO TAKE	× THINGS TO AVOID
Non animal source of protein (Grain, Nuts and Seeds)	Animal fat (meat)
Foods that are high in calcium (Soya products, nuts, nut milks)	Acidic foods
Healthy fats (Olive oil, Walnuts, Canola oil)	Milk and Dry Products
Fresh fruits and Vegetables	Refined food like Bakery items
Vitamin B rich foods (Nuts, Carrots)	Oily and greasy food

மருத்துவ அறிவுரை மற்றும் உணவு அறிவுரை-கடைப்பிடிக்க:

- ✓ **உணவில்மிளகு,இஞ்சி,சுக்கு,மஞ்சள்அதிகமாகசேர்க்கவும்.**
- ✓ **பசும்பாலில்பனங்கற்கண்டு,ஏலக்காய்இட்டுகாய்ச்சிதரவும்.**
- ✓ **பப்பாளி,கொய்யா,சப்போட்டா,மாதுளைபோன்றபழவகைகளைகாலைஅல்லதுமதியவேளையில்தரவும்.**
- ✓ **காய்கறிகீரைவகைகளைதினமும்உணவில்சேர்க்கவும்**
- ✓ **மிதமானசுடுநீரில்குளிப்பாட்டவும்**

தவிர்க்க:

- × **தூசி, ஒட்டடை,மாசுபடிந்தசூழலைதவிர்க்கவும்**
- × **குளிர்ந்தகாற்று,குளிர்சாதனபெட்டிஉணவுகளைதவிர்க்கவும்.**
- × **செயற்கைஇனிப்புதிண்பண்டங்களானமிட்டாய்,கிரீம்சேர்ந்தகேக்,பிஸ்கட்டுகளைநீக்கவும்.**
- × **உணவுஉண்டபின்குளிப்பாட்டுவதைதவிர்க்கவும்.**
- × **மாமிசஉணவில்பிராய்லர்கோழியைதவிர்க்கவும்.**

NATIONAL INSTITUTE OF SIDDHA,

AYOTHIDOSS PANDITHAR HOSPITAL, CHENNAI-600047.

DEPARTMENT OF KUZHANDHAI MARUTHUVAM

PRECLINICAL AND CLINICAL EVALUATION OF SILVISHA USIDHAM (INTERNAL) AND PUZHUVETTU THYLAM (EXTERNAL) FOR PUZHUVETTU (ALOPECIA AREATA) IN CHILDREN.

FORM-X ASSENT FORM

I, _____understand that my parents (mom and dad)/guardian have/has given permission (said it's okay) for me to take part in a project about done by _____.

I am taking part because I want to. I have been told that I can stop at any time I want to and nothing will happen to me if I want to stop.

_____

Signature

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

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

This Certificate is awarded to Dr/~~Mr/Mrs~~.....R..D.:...INDHUMATHI.....

For participating as ~~Resource Person~~ / Delegate in the Twenty second Workshop on

"RESEARCH METHODOLOGY & BIOSTATISTICS"

*For **AYUSH Post Graduates & Researchers***

Organized by the Department of Siddha

The Tamil Nadu Dr. M.G.R. Medical University From 06th to 10th June 2016.

Dr.N.KABILAN, M.D.(S)
PROF & HEAD
DEPT.OF SIDDHA

Prof. **Dr.S.PUSHKALA,** M.D.,
REGISTRAR (FAC)

Prof. **Dr.S.GEETHALAKSHMI,** M.D., Ph.D.,
VICE CHANCELLOR

NATIONAL INSTITUTE OF SIDDHA- राष्ट्रीय सिद्ध संसथान
Ministry of AYUSH- आयुष मंत्रालय
GOVERNMENT OF INDIA-भारत सरकार
TAMBARAM SANATORIUM, CHENNAI -600 047 -ताम्बरम सनटोरियमचेन्नई -600 047
फ़ोन\Tele : 044-22411611 फैक्स\Fax : 22381314
ईमेल: nischennaisiddha@yahoo.co.in वेब :www.nischennai.org

F.No.NIS/6-20/IEC/15-16 Dt: 14.10.2016

CERTIFICATE

Address of Ethics Committee: National Institute of Siddha, Tambaram Sanatorium, Chennai-600047, Tamil Nadu, India	
Principal Investigator: Dr. R.D.Indumathi – I year, Dept.of Kuzhanthai Maruthuvam	
Protocol Title:- Preclinical and Clinical Evaluation of Silvisha Usidham (Internal) and Puzhuvettu Thylam (External) for Puzhuvettu (Alopecia Areata) in Children.	
Documents filed	1) Protocol, 2) Data Collection forms
Clinical trial Protocol (others – Specify)	**Yes-(M.D-Dissertation)**
Informed consent documents	**Yes**
Any other documents	-
Date of IEC approval & its number	**NIS/IEC/2016/11-20/ 14.10.2016**

We approve the trial to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study.

(Dr.V.Subramanian)
Chairman

(Prof.Dr.V.Banumathi)
Member Secretary

NATIONAL INSTITUTE OF SIDDHA ★ CHENNAI 600 047

CERTIFICATE

This is certify that the project title Preclinical and clinical evaluation of Silvisha Usidham (Internal) and Puzhuvettu thylam (external) for puzhuvettu (Alopecia areata) in Children **has been approved by the IAEC.** Rats - 20 Nos (10 Male + 10 Female)
Approval No: NIS/IAEC-IV/05/05012017

V. Banumathi

Prof. Dr. V Banumathi MD (s)

Prof. Dr. K. Nachimuthu 7/11/2017

Chairman/Member Secretary IAEC: **CPCSEA nominee:**

Signature with date

Chairman/Member Secretary of IAEC: **CPCSEA nominee:**

(Kindly make sure that minutes of the meeting duly signed by all the participants are maintained by Office)

Name of the PI:

R. D. INDUMATHI

Name of the Department & Institution:

KUZHANTHAI MARUTHUVAM
NATIONAL INSTITUTE OF SIDDHA

NATIONAL INSTITUTE OF SIDDHA

(An Autonomous body under Ministry of AYUSH, Govt. of India)
Tambaram Sanatorium, Chennai- 600 047

Workshop on

"BASIC RESEARCH TECHNIQUES AND PRACTICES INVOLVED IN LABORATORY ANIMAL CARE"

06 -10 February 2017

CERTIFICATE

This is to certify that Dr. R. D. Indumathi has participated as Delegate/~~Resource~~ Person in the workshop on "Basic Research Techniques and Practices involved in Laboratory Animal Care" held on 06-10 February, 2017 at National Institute of Siddha, Chennai-47, Tamilnadu.

Dr. V. Suba
Organizing Secretary

Dr. P. Muthusamy
Veterinary Consultant

Prof. Dr. V. Banumathi
Director / Chairperson

NATIONAL INSTITUTE OF SIDDHA, CHENNAI – 600047

BOTANICAL CERTIFICATE

Certified that the following plant drugs used in the Siddha formulations **"Silvisha Usidham"** (Internal) and **"Puzhuvettu Thylam"** (External) taken up for Post Graduation Dissertation studies by **Dr.R.D.Indumathi** M.D.(S), II year, Department of Kuzhandhai Maruthuvam, 2017, are identified through Visual inspection, Experience, Education & Training, Organoleptic characters, Morphology and Taxonomical methods as

Ficus hispida Linn. f. (Moraceae), Bark
Elettaria cardamomum Maton (Zingiberaceae), Seed
Piper longum Linn. (Piperaceae), Fruit
Sesamum indicum Linn. (Pedaliaceae), Seed oil
Shorea robusta Gaertn.f. (Dipterocarpaceae), Oleo resin
Indigofera tinctoria Linn. (Fabaceae), Leaves
Ricinus communis Linn. (Euphorbiaceae), Seed oil

MEDICINAL BOTANY CHENNAI 600 047

Certificate No: NISMB3022017

Date: 12-06-17

Authorized Signatory
Dr. D. ARAVIND, M.D.(s),M.Sc.,
Assistant Professor
Department of Medicinal Botany
National Institute of Siddha
Chennai - 600 047, INDIA

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We Trust in Quality and Ethics

Noble Research Solutions

We Trust in Quality and ethics

E-mail : nobleresearchsolutions@gmail.com
info@nobleresearchsolutions.com
Contact : 9710437419, Admin : 044 - 42691289

Date: 22.04.2018

To,

Dr.Indumathy
National Institute of Siddha,
Tambaram Sanatorium, Chennai 600047, Tamil Nadu, India.

Project Id: **NRS/AS/0089/01/2018**

This is to certify that Dr.Indumathy from National Institute of Siddha, Tambaram Sanatorium, Chennai, has carried out the following activity at our facility for the trial drug *Silvisha usidham (SU)*

S.No	Study Description	Annexure no
1.	Standardization and Physicochemical Evaluation of study drug *Silvisha usidham (SU)*	I
2.	In-Vitro Anti-Inflammatory activity by Protein denaturation assay for study drug *Silvisha usidham (SU)*	II

Note:

- *Annexures was attached as a separate enclosure along with this report.*

NOBLE RESEARCH SOLUTIONS TAMIL NADU INDIA CHENNAI

For NOBLE RESEARCH SOLUTIONS

Clinical Trial Details (PDF Generation Date :- Tue, 10 Jul 2018 04:54:22 GMT)

CTRI Number	CTRI/2018/01/011311 [Registered on: 12/01/2018] - **Trial Registered Retrospectively**
Last Modified On	11/01/2018
Post Graduate Thesis	Yes
Type of Trial	Interventional
Type of Study	Drug Siddha
Study Design	Other
Public Title of Study	PUZHUVETTU (Alopecia areata) in Children - Silvisha usidham (Internal) and Puzhuvettu thylam (External)
Scientific Title of Study	Preclinical and Clinical evaluation of Silvisha Usidham (Internal) and Puzhuvettu Thylam (External) for Puzhuvettu (Alopecia areata) in Children.

Secondary IDs if Any

Secondary ID	Identifier
NIL	NIL

Details of Principal Investigator or overall Trial Coordinator (multi-center study)

Details of Principal Investigator	
Name	Dr R D Indumathi
Designation	PG Scholar
Affiliation	National Institute of Siddha
Address	National Institute of Siddha Tambaram Sanatorium Chennai 47 National Institute of Siddha Tambaram Sanatorium Chennai 47 Kancheepuram TAMIL NADU 6000047 India
Phone	9092765785
Fax	
Email	indubsms@gmail.com

Details Contact Person (Scientific Query)

Details Contact Person (Scientific Query)	
Name	Dr M Meenakshi sundharam
Designation	Head of the Department
Affiliation	National Institute of Siddha
Address	National Institute of Siddha Tambaram Sanatorium Chennai 47 National Institute of Siddha Tambaram Sanatorium Chennai 47 Kancheepuram TAMIL NADU 6000047 India
Phone	9444214582
Fax	
Email	mmssiddha@rediffmail.com

Details Contact Person (Public Query)

Details Contact Person (Public Query)	
Name	Dr R D Indumathi
Designation	PG Scholar
Affiliation	National Institute of Siddha
Address	Department of Kuzhanthai Maruthuvam National Institute of Siddha Tambaram Sanatorium Kancheepuram Tamil Nadu 600047 India Kancheepuram TAMIL NADU 6000047 India

Phone	9092765785
Fax	
Email	indubsms@gmail.com

Source of Monetary or Material Support

Source of Monetary or Material Support
> Kuzhandai Maruthuvam National Institute of Siddha Ayothidoss pandithar Hospital Tambaram Sanatorium Chennai 47

Primary Sponsor

Primary Sponsor Details	
Name	Ayodhidoss Pandithar Hospital
Address	National Institute of Siddha Tambaram Sanatorium Chennai 47
Type of Sponsor	Research institution and hospital

Details of Secondary Sponsor

Name	Address
NIL	NIL

Countries of Recruitment

List of Countries
India

Sites of Study

Name of Principal Investigator	Name of Site	Site Address	Phone/Fax/Email
R D Indumathi	National Institute of Siddha	Kuzhandai Maruthuvam, Room no 4 National Institute of Siddha Tambaram Sanatorium Chennai Kancheepuram TAMIL NADU	9092765785 indubsms@gmail.com

Details of Ethics Committee

Name of Committee	Approval Status	Date of Approval	Is Independent Ethics Committee?
Institutional Ethical Committee	Approved	14/10/2016	No

Regulatory Clearance Status from DCGI

Status	Date
Not Applicable	No Date Specified

Health Condition / Problems Studied

Health Type	Condition
Patients	Puzhuvettu (Alopecia areata)

Intervention / Comparator Agent

Type	Name	Details
Intervention	Silvisha Usidham Puzhuvettu Thylam	2-4ml of Silvisha Usidham will be orally twice a day for a period of 45days Puzhuvettu Thylam will be apply externally for 45days
Comparator Agent	Silvisha Usidham Puzhuvettu Thylam	2-4ml of Silvisha Usidham will be orally twice a day for a period of 45days Puzhuvettu Thylam will be apply externally for 45days

Inclusion Criteria

Inclusion Criteria	
Age From	6.00 Year(s)
Age To	12.00 Year(s)
Gender	Both
Details	1 Patchy hair loss in the scalp 2 Non Scarring 3 Scattered long hair within bald area 4 Patient who is willing to be admitted in the hospital or willing to

	attend OPD when required 5 Willing to sign the informed and consent form

Exclusion Criteria

Exclusion Criteria	
Details	1 Scarring alopecia 2 Alopecia totalis 3 Alopecia universalis 4 Thyroid disease 5 Atopic dermatitis 6 Vitiligo 7 Pernicious anaemia 8 Down syndrome

Method of Generating Random Sequence	Not Applicable
Method of Concealment	Case Record Numbers
Blinding/Masking	Open Label

Primary Outcome

Outcome	Timepoints
It is mainly assessed by SALT Score	45 days

Secondary Outcome

Outcome	Timepoints
Comparing the improvement of clinical symptoms before and after treatment	45days

Target Sample Size	**Total Sample Size=**30 **Sample Size from India=**30
Phase of Trial	Phase 2
Date of First Enrollment (India)	30/12/2017
Date of First Enrollment (Global)	No Date Specified
Estimated Duration of Trial	**Years=**2 **Months=**0 **Days=**0
Recruitment Status of Trial (Global)	Not Applicable
Recruitment Status of Trial (India)	Open to Recruitment
Publication Details	Not yet
Brief Summary	**It is a single,non randamized open - label trial to determine the efficacy and safety of SILVISHA USIDHAM and PUZHUVETTU THYLAM in patients with PUZHUVETTU (ALOPECIA AREATA).In this trail 30 alopecia areata patients will be recruited and the trail drug (Internal) will be administrated 2-4ml twice a day for a period of 45 days and External drug will be apply for 45days during the study period all the study related data will be recorded and documented in a separate trail master file for each patients. During the trail period if any adverse effect will be noticed and referred to pharmacovigilance dept.in NIS and further management will also be given in NIS OPD and IPD. The entire trail will be monitored by the research monitoring committee of NIS . During this trail all the safety and efficacy parameters will be recorded in the CFR.After the completion of the**

trail all the study related data will be analysed statistically the outcome of this trail will be published in Indian Journal of Medical Research.

INTRODUCTION

AIM AND OBJECTIVE

LITERATURE REVIEW - SIDDHA ASPECT

LITERATURE REVIEW-MODERN ASPECT

MATERIALS AND METHODS

RESULT AND OBSERVATION

DISCUSSION

SUMMARY

BIBILIOGRAPHY

ANNEXURE

CONCLUSION

DRUG REVIEW