STANDARDIZATION AND PHARMACOLOGICAL SCREENING OF ANTI ULCER, ANTI SPASMODIC, AND HAEMATINIC ACTIVITES OF SIDDHA FORMULATION OF *LAVANA DRAVAGAM (*LD*)*

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **" Standardization and Pharmacological screening of Anti-ulcer, anti Spasmodic, and Haematinic Activites of siddha formulation of *Lavana Dravagam (*LD*)*"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. A. Mariappan M.D(S), Ph.D..,** Associate Professor, Department of Gunapadam, National Institute of Siddha, Chennai– 47 and the dissertation has not formed the basis for the award of any Degree, Diploma, Fellowship or other similar title.

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CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **" Standardization and Pharmacological screening of Anti-ulcer, anti Spasmodic, and Haematinic Activites of siddha formulation of *Lavana Dravagam (*LD*)*"** is submitted to The Tamil Nadu Dr. M. G. R. Medical University, Chennai-32 in partial fulfillment of the requirements for the award of degree of M.D (Siddha) is the bonafide and genuine research work done by **Dr. S.JEEVA (Reg. No.321912203)** under my supervision and guidance and the dissertation has not formed the basis for the award of any Degree, Diploma, Associateship, Fellowship or other similar title.

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BONAFIDE CERTIFICATE

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Head of the Department

Signature

The Director

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1. INTRODUCTION:

In Siddha medicine the use of metals and minerals are more predominant in comparison to other Indian traditional medicine systems. In the usage of metals, minerals and other chemicals. The drugs used by the Siddhars could be classified into three groups: Mooligai/Thavaram (herbal product), Thathu (inorganic substances) and Jeevam (animal products). The Thathu drugs are further classified as: 1. Uppu (Salts) (water-soluble inorganic substances or drugs that give out vapor when put into fire), 2. Pashanam (Arsenicals) (drugs not dissolved in water but emit vapor when fired), 3.Ulogam (Heavy metals).

Siddha system of medicine is contributing much to the People healthcare. Siddhars evidently defined classified about 4448 diseases, including Gunmam (ulcer), Pandu (Anaemia), Soothagakkatty (Polypus uteri, internal abscess), Surakkatty (enlargement of spleen).

The sufferers of Anaemia, Gastric ulcer with spasmodic pain are increasing day by day due to lifestyle alteration and is now very common in our clinical practice.

The minaral remedies need a great and deep assessment of their pharmacological activity and safety issues due to the large and growing use of natural-derived substances all over the world, which cannot trust only on the tradition or supposed millenarian beliefs; explanatory and pragmatic studies are useful and complementary in the acquisition of reliable data both for health caregiverand patients . Mineral is the used for prevention and manegement of diseases. It ranges fromtraditional and prevalent medicines of every country tothe use of standardized and titrated Dravagam. Generally, the Traditional System of medicine was having high level of safety and efficacy when compared to the conservative morden medicine system, especially in siddha medicine where formulations are almost completely based on remedies containing active principles at good meditations, or relying on magical-energetic principles. Siddha pharmacopoeia and metiria medica recognized in recent times have imposed more on standardization aspect of the preparation. Starting from preparatory

phase to storage each and individual step involved informulating Siddha formulation has its own qualitycheck evaluations. Bioactive phytocomponents and chemicalcomponents nanoparticles present in preparations like Chenduram have the unique advantage of multiple modes of action. The interaction of using combined phytomedicines and metals are well recognized in traditional medicine like Siddha. Traditional medicine is the ancient healing system of medicine and it has fundamental aspects for drug formulation. Major formulations used in Siddha formulation based on minerals. The minarals are used as parpam, chenthuram, dravagam, infusions, tinctures, and powders [1].

There is a world resurrection in the use of siddha medicines along with a growing scientific interest in them as a source of newdrugs [2].

Among that, Dravagam type is a one of the internal medicine, which is processed by distillation method. The word *Dravagam* means "that dissolves, liquefies". It is also used in the field of medical alchemy. It is known by various names which include *Pugai Neer, Shakthi Neer*, *Dravaga Neer,* etc.., This Dravagam will not deteriorate with lapse of time [3].

In global, Numerous Traditional system of Medicines are involved on basis of their vast Materia medica and it has various forms of Medicines. Conferring to Age, body, gender constitution, nature of disease, the medicine forms are selected by Practitioners. Using various forms of medicine shows helpfulness in metabolism and in Digestion. *Siddha* medicine, which was developed and propounded by earliest supreme spiritual sages called *Siddhars.*

Anaemia is defined as a reduction in haemoglobin level and oxygen carrying capacity below the normal range and is the most common disorder of the blood. It is characterised by a decrease in haemoglobin level to less than 13 g/dL in males or 12 g/dL in females.[4] In

anaemia the rate of production of mature red blood cells entering the blood from the red bone marrow does not keep pace with the rate of haemolysis.[5] Iron is the main constituent of haemoglobin, which is responsible for transporting oxygen, and of myoglobin in muscles and is part of many enzymes concerned with cellular processes, respiration, and cell division.[6] Low haemoglobin (Hb) levels result in a corresponding decrease in the oxygen carrying capacity of blood[7] and other parameters such as total red blood cell (RBC) count, packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and MCH concentration (MCHC).[5,7,8]

.

Anaemia is the most commen nutritional deficiency disorder in the world. WHO defines anaemia is the condition in which the HB content of blood is lower than normal as a result of deficiency of one or more essential nutrients[9]. WHO has estimated that more than 2 billion people worldwide suffering from anaemia with 50% attributed to iron deficiency[10]. 44% of adolescent girls are affected by anaemia in the rural areas in Tamilnadu. Among these 2.1% are severe and 6.3% are moderate and 36.5% are mild [11].

Gastric ulcer is produced by an imbalance between gastro duodenal mucosal defence mechanisms and the aggressive factors, particularly gastric acid and pepsin. It is one of the major diseases affecting the human population. About 10% of the population may develop Peptic ulcer in their life time. It affects 9.5% among women and 10.5% among men. Ulceration is reported for high chances of recurrence and mortality [12].

Identifying a novel drug of choice for Anaemia, and Peptic ulcer with spasmodic pain are a challenge to the Researchers. Apart from drug of choice, the factors like the nature of the formulation, its palatability and faster efficacy has to be also considered wisely. In

traditional *Siddha* literature so many preparations are available which are more valuable and clinically very effective. Among those formulations *Lavana Dravagam* is one of the mineral based *Siddha* preparations which is mentioned in the Siddha literature.

The test drug *Lavana Dravagam* mentioned in Siddha text Kannusamy pillai.S, Kannusamiyam ennum vaithiya segaram , page no 158 has been used for Gunmam (ulcer), Pandu (Anaemia), Soothagakkatty (Polypus uteri, internal abscess), Surakkatty (enlargement of spleen)

The ingredients of this drug are *Vediuppu* (Potassium nitrate) Padigaram (Alum) Saaram (Navacharam) (Ammonium Chloride) Kariuppu It possess Anti- ulcer, Anti- spasmodic, Hematinic. But the above trial drug has not so far been evaluated for its Anti- ulcer, Anti- spasmodic, Hematinic. Hence the author has chosen the drug for this study to validate its Standardization, Pharmacological (Anti- ulcer, Anti- spasmodic, Hematinic) and Analytical studies.

From the literature evidence, Biochemical analysis, Acute Toxi evaluation and Pharmacological studies, the drug *Lavana Drvagam* has Antiulcer, anti- spasmodic and Hematinic activity. It is concluded that the drug *Lavana Dravagam* can be used in the management of Gunmam (peptic ulcer) and anemia.

AIM AND OBJECTIVES

2. AIM AND OBJECTIVES

AIM:

Standardization and Pharmacological screening of Anti -ulcer, Anti-spasmodic, and Hematinic Activities of siddha formulation of *LAVANA DRAVAGAM (*LD*)*

OBJECTIVES:

Objectives are surfaced in the below mentioned points,

- Collection of various information relevant to the study from various *Siddha* and Modern literature.
- Identification of the Ingredients.
- Preparation of the test drug as per classical *Siddha* literature.
- Standardization of the prepared test drug *Lavana Dravagam* as per AYUSH Guidelines.
- Physicochemical analysis.
- Biochemical analysis for determining acidic and basic radicals.
- Estimation of elements through instrumental analysis.

Pharmacological activities

Facts to be proved by pharmacological activities include

Pharmacological activities:

- **Anti – ulcer activity**: (Pyloru,s Ligation method) in Wister albino rat
- **Hematinic activity**: (Phenyl Hydrazine Induced method) in Wister albino rat
- **Anti- spasmodic activity: (**Acetylcholine Induced method**)**

MATERIALS AND METHODS

3. MATERIALS AND METHODS

Standard Operation Procedure of *Lavana Dravagam*

Drug selection:

The test drug *Lavana Dravagam* mentioned in Siddha text Kannusamy pillai.S, Kannusamiyam ennum vaithiya segaram , page no 158 has been used for Gunmam (ulcer), Pandu (Anaemia), Soothagakkatty (Polypus uteri, internal abscess), Surakkatty (enlargement of spleen)

TEST DRUG: *LAVANA DRAVAGAM*

INGREDIENTS:

- Vediuppu (Potassium Nitrate) : 6 Edai
- Padigaram (Alum) : 3 Edai
- Saaram (Navacharam) (Ammonium Chloride) : 1 1/2 Edai
- Kariuppu : 1 1/2 Edai

DOSE:
3 to 5 drops
VEHICLE (adjuvant): Water

INDICATION:
Gunmam (ulcer), Pandu (Anaemia), Soothagakkatty (Polypus uteri, internal abscess), Surakkatty (enlargement of spleen).

Procurement of Raw Drugs:[13]

The raw drugs were purchased from a well reputed country shop in Chennai. All the ingredients were purified and the medicine was prepared in the *Gunapadam* laboratory in National Institute of Siddha.

Identification and Authentication of the drug:

The raw drug was authenticated by the Faculty member, Department of Gunapadam, National Institute of Siddha

Purification of the drugs:

All the drugs mentioned here were purified as per the *Siddha* literature.

METHOD OF PURIFICATION:[13]

PURIFICATION OF *VEDIUPPU*:

1.4 kgm *Vediuppu* (Potassium nitrate) was taken. Add 6500 ml of water into it and boil it well. Now add white of 4 hen's egg. The waste materials floated on the top that was immediately removed. Then the above mixture was filtered into another vessel. Then it was dried in the sunlight. Repeat this process again for seven times [13].

PURIFICATION OF *SEENAKARAM*:

The SEENAKARAM (Alum) was dissolved into the water and it was filtered to remove dust. Boil it well till it turns into a semisolid state. Then the mixture was allowed to cool itself. [13].

PURIFICATION OF *NAVASARAM*:

The NAVASARAM (Ammonium chloride) was dissolved in hot water and filtered to remove dust. Then, it was poured in a broad mouthed vessel and kept in the sun light; the salt was form it is preserved along with small quantity of the root of jequirity, which is used to remove nauseating smell, in an airtight container [13].

PURIFICATION OF KARIUPPU:

KARIUPPU (Common salt) was dissolved in pure water or vinegar and filtered. The filtrate was boiled till it reaches semi-solid consistency, then little amount of lemon juice or butter milk was added to it and insolated. The same process was repeated for 10 times to get the purified form[13].

Method of Dravagam Preparation:[13]

The salts were ground well and transferred to the *Valaiyanthiram* made of earthern distillation set up and intensely heated. During the process of heating the salts decompose completely releasing the acidic fumes and then they get condensed at the condenser submerged in cold water and collects at the receiver vessel kept adjacently. Then, it was stored in an air tight glass container [13].

Labelling:

Name of the preparation	-	*Lavana Dravagam*
Date of preparation	-	10.08.2021
Dose	-	3 to 5 drops
Ingredients	-	*Vediuppu, Seenakaram, kariuppu, Navasaram,*
Adjuvant/Vehicle	-	*water*
Indications	-	Gunmam (ulcer), Pandu (Anaemia), Soothagakkatty (Polypus uteri, Internal abscess), Surakkatty (enlargement of spleen)
Date of expiry	-	1 Year from date of manufacturing
Therapeutic administration of drug		
Form of medicine	-	Liquid (Off white)
Route of administration	-	Oral
Dose	-	3to 5drops
Vehicle	-	*water*
Reference	-	Kannusamy pillai.S, Kannusamiyam E nnum vaithiya segaram

INGREDIENTS OF *ASHTA GUNMA DRAVAGAM*

VEDIUPPU

Before purification	After purification
	
	

SEENAKARAM

Before purification	After purification
	
	

NAVACHARAM

Before purification	After purification
	

KARIUPPU

Before purification	**After purification**
	

Method of Dravagam Preparation (VEDIUPPU)	**SEENAKARAM**
	
NAVACHARAM	**KARIUPPU**
	
STEP: 1	STEP : 2
	

STEP : 3	STEP : 4
	

STEP : 5

LAVANA DRAVAGAM

4. REVIEW OF LITERATURE

4.1. GUNAPADAM REVIEW:

KARIUPPU(SODIUM CHLORIDE):[13]

- Tamil : Uppu
- Sanskrit : Lavana; SamudraLavana
- English : Common Salt:
- Hindi :Namak
- Malayalam : Uppu
- Telugu:Upu

SYNONYMS:-

- Sotruppu
- Kadaluppu
- Veettuppu
- Ilavanam
- Samudra Lavanam

SOURCE:

Sodium chloride is found in nature forming 2.5 p.c of the water in the ocean. Commonsalt is being cultivated in the eastern coast of Tamil Nadu in the following places: Cheyyur, Choonambedu, Marakkanam, Athirampattinam, Arumuganeri and Tuticorin.

PREPARATION:

Sodium chloride is obtained by lixiviation of saline soil or by evaporation of brinesprings or sea water.

CHARACTER:

Salt occurs as transparent cubes or small brownish-white crystalline grains, odourless,of saline taste and neutral reaction, soluble in water, insoluble in alcohol and chloroform. It has white, pale or ash color according to the cultivated land.

GENERAL CHARACTERSTICS:

"அளத்திலுறை நல்லுப் பனல்வாதம் மற்றுந்
களத்துநோய் தன்னைக் களையுங் - கிளைத்தகப
ஆசுடைய வல்லைநோய் அஷ்டகுன்ம மும்போக்குங்
காசினியுள் மாதே கழறு "

Pitha Vatham, Lymphadenitis, Tumor, Kabam, Liver Disorders, Eight Types of Gastric Ulcer, Indigestion, Distended Abdomen, Vaayu and Retention of urine will be cured.Appetite will also be increased.

Common salt is an ingredient of our body and keeps the globulin of the blood in solution. The salt of the sea water contains a small proportion of iodine, which renders it essential for the human being as a preventive of goiter and other glandular enlargements. It excites thirst and thus assists absorption of liquid food. It decreases the secretion of mucous and promotes absorption of effused products. It is eliminated in the urine.

METHODS OF PURIFICATION[13]:

Method 1.

1. KARIUPPU (Sodium chloride) - 35 gm.
2. Red Indian water lily juice (Nymphaea odorata) - 210 gm
3. Black water Lily (Monochoria hastaefolia) - 210 gm
4. Rice washed water

Sodium chloride is kept soaked in red Indian water lily juice in the sun shade from morning to evening for 6 days. Everyday fresh juice should be added. It is then insolated fortwo days without adding juice and dried. The same process is repeated with the black water lily juice and rice washed water; finally it is preserved for use.

Method 2.

KARIUPPU (Common salt) - 1 part

Vinegar (or) Pure water - 7 parts

KARIUPPU (Common salt) is dissolved in pure water or vinegar and filtered. The filtrate is boiled till it reaches semi-solid consistency, then little amount of lemon juice or butter milk is addedto it and insolated. The same process is repeated for 10 times to get the purified form.

Method 3.

KARIUPPU (Common salt) is dissolved in plantain stem juice and filtered. The filtrate is boiled till itreaches semi-solid consistency and little quantity of lemon juice is added and then insolated toget it purified.

Method 4.

KARIUPPU (Common salt) is dissolved in sea water or rain water and filtered. The filtrate is boiledtill it reaches semi consistency state. It is dried in day light and it attains the solid state as purified salt.

ACTION:

- Stomachic
- Laxative
- Emetic
- Antiseptic
- Antiperiodic
- Anthelmintic
- Deobstruent

MEDICINAL USES:[13]

- In fevers, dyspepsia and bilious diarrhea in children it is given with benefit.
- A powder made up of common salt, ajowan, omum seeds, long pepper, ginger and chebulic myrobalan is useful in doses of 20 to 60 grains twice a day as gastric stimulant and carminative.
- It is said to work miracles in anemia, gastric ulcer, catarrh, neuritis, neurasthenia and all cases of debility.
- In neuralgic headache it may be used as a snuff.
- It relieves hemoptysis and migraine.
- About a pound of powdered common salt enclosed in a loose bag heated over a fore and applied for 20 to 30 minutes at a time relieves gastralgia or dyspeptic colic.
- Salt water (1 in 30) or sea bathing is recommended for the cure of various skin infections, rheumatic and muscular pains and sprains etc..,
- As an enema it relieves flatulence and colic, destrous and brings away worms fromthe large bowels and prevents the paraoxysmal attack of epilepsy.
- One percent solution of it is a topical application to stop bleeding from wounds and a wash or a snuff in the cold and catarrh of the nostrils in ozonea and a gargle in chronic diseases of the pharynx and larynx.
- The salt is triturated with water and applied on the site of the poisonous bite to reduce the poison.
- The salt is dissolved in water and instilled as drops to minimize the poisonous effect of the scorpion bite.
- One teaspoon salt is dissolved in 546 ml. of hot water and gargled to reduce inflammation of throat and gingivitis.
- It is used to give fomentation for swelling and pain. The salt (35gm) is bundled ina cloth and dipped in boiling oil and applied over the swelling when it is warm.
- An isotonic solution of sodium chloride in sterile water is given as intravenous infusion in case of severe diarrhea, with dehydration.

- If the salt is placed and heated at the pricked sites of the pile and thorn, the toxicitywill be cured.
- Equal ratio of salt and tamarind are dissolved in water and boiled and the mixtureis taken in semi-solid consistency and applied over the swelling and sprain by which hematoma will subside.
- The salt is also used as one of the ingredients in tooth powders.
- Insects entered in the ear and anus will come out on spraying the salt water.
- Dissolved salt water is given through the rectum to remove the worms in the largeintestine.
- The salt is also used as a preservative for fish, mutton and vegetables.
- The salt is dissolved in water and given for the silver.

VEDIUPPU (Potassium nitrate) [13, 15]

Synonyms

- *Padairaasan,*
- *Inangan,*
- *Poonathan,*
- *Boomi koormai,*
- *Navachaara mithru,*
- *Pottiluppu*

Vernacular names

- Tamil: *vediyuppu*
- Sanskrit: *surakshara*
- Telugu: *surekaramu*
- Kannada: *patluppu*
- Malayalam: *vediyuppu*
- Hindi: *sarakalmi*
- English: Salt petre

Source

It occurs extensively in Bengal, Punjab, naturally as an efflorescence on the soil; but the nitre obtained in the bazaars is generally impure.

Organoleptic characters

Appearance : white thin rods

Synthetic Preparation

Crude salt is placed in a mud pot. Water is added into it and mixed well and a straw is placed inside the pot and filtered. The filtrated mixture is heated to get the salt.

The potassium nitrate salt is used for the preparation of explosives. It is also used for cooling alcohol and to polish the gold ornaments.

General characteristics of Vediuppu:

"சூதக வாயுவொடு சோணிதத்தின் வாதமும்போம்
வாதவலி குன்மமிவை மாறுங்காண் -மீதாங்
கொடிய வயிறிழியுங் கோழைகப மேகும்
வெடியுப்புத் தன்னை விளம்பு".

This cures *Gunmam, Kabham, Vatham, Sobai, Sonitham,Soothaga vayu, Peruvayuru.*

Action

- Refrigerant
- Demulcent
- Astringent
- Diuretic

Dosage for salt: 650mg- 1300mg.

Purification

- 1.4 Kgm *Vediuppu* (Potassium nitrate) was taken. Add 6500 ml of water into it and boil it well. Now add white of 4 hen's egg. The waste materials floated on the top and it was immediately removed. Then the above mixture was filtered into another vessel. Then it was dried in the sunlight. Repeat this process again for seven times
- Potassium nitrate -1 part, Sea water or water -2 parts are taken. The salt is finely powdered and dissolved in water. The clear fluid is poured into an iron pot and heated till a semi- solid consistency is obtained. This is then poured in a copper pot and placed in a cool place now the salt will form , the salt is taken out and dissolved in 2 parts of water and heated as mentioned above, this process is repeated for 5 to 7 times to get it purified.

Properties and Uses [13,15]

- Potassium nitrate salt has got demulcent, diuretic, and diaphoretic properties.
  This should be given by dissolving in large quantities of water.
- The salt is also useful in the treatment of eight types of *gunmam*, uterous fibroids, anorexia, urinary tract infections, dysuria, strangury, ascites, menopaused disorders, abdominal distention and asthma. It improves fertility in women.

- The salt is also effective in fever, swellings, rheumatic disorders, haemorrhage, gonorrhoea, eyes disease, and sore throat.
- For medical use, the earth containing the crude salt is dissolved in water, strained and recrystallized by boiling and evaporation. It is also obtained from collections of the saline earth after the rains, from the land inundated during the rains and from mud heaps, mud buildings, and other places on which it is formed and then subjected to a process of solution and filtration through a crude mud filter.
- The impure nitre is known as *Dhoah* and contains about 45 to 75 percent of the actual salt, the remainder being sulphate and chloride of sodium and insoluble matter. It is again dissolved and crystallized before it is sent, under the name of *Shora kalmi* (refined) to the bazaar for sale while it is further recrystallized in Calcutta and elsewhere before being sold for use.
- Potassium nitrate in solution is a refrigerant, efficient, diuretic and diaphoretic.

- It acts on the vascular system and thus reduce the frequency of the pulse.

- Given in the solid form or in concentrated solution it acts as irritant.

- In weak solutions a quart thin warm rice *conjee* it is an excellent refrigerant drink in fevers with hot and dry skin, parched tongue with great thirst and scanty and high coloured urine. It may also be sweetened with Honey or sugar candy or tamarind or lime juice may be added to improve the flavour if desired.
- It is useful also in the early stages of dropsy, in cases of smallpox, measles, influenza, catarrh, and gonorrhoea, acute rheumatism, bleeding from the lungs, stomach, uterus or other internal organs attended by fever.
- In colic, a powder containing nitre, black pepper and *sanchala* salt in equal parts is recommend to be given in doses of 10 grains in lime juice and in bronchitis in children above 5 years, a powder composed of nitre 5. Sulphate of iron, ammonium chloride and sulphur is recommend to be given.

- A compound preparation known as *Laghu sanka Dravagam*, which smells strongly of nitrous fumes and which is made of country nitre, alum, *yavakshara,* ammonium chloride, borax and vit salt and *gandhaga vadiuppu* , soda carbonas, ferrous sulphate, copper sulphate and black salt, all powdered and distilled, is recommend for the relief of all liver complaints by *vaidyas.*

- In gonorrhoea a mixture of nitre in a wine glasses full of decoction of *abelmoschus esculantus* twice or thrice a day is a nice remedy.

- A powder made of equal parts of salt petre, cardamom, cubebs, soap stone, olibanum, and curcuma longa.

- To relieve scalding and retention of urine, also suppression or scantiness of urine,

- A confection made of nitre, cinnamon, *chebulic myrobalan* and iris pseudocorus, cardamoms and sugar is used in chronic gonorrhoea and gleet.

- In obstinate cases of leucorrhoea a combination of nitre and alum is recommend to be taken thrice daily.

- In the early stages of inflammatory sore throat a small piece of nitre allowed to dissolve slowly in the mouth is a successful popular remedy.

- In asthma, in chronic bronchitis and other spasmodic cough, inhalation of the fumes of burning nitre papers, previously soaked in saturated solution of the nitrate and dried Datura gives great relief.

- Solution of nitre is a good topical application for bruises and abrasions and for the cure of freckles.

- Locally nitre is employed for the relief of headache and delirium in fevers in the form of a cold and agreeable lotion for the head, made by dissolving nitre and sal ammoniac in a big bottle full of water; this is applied by constant relays of freshly wetted clothes.
- In acute rheumatism, strong solution of nitre forms a more soothing application to the swollen and painful joints; cloths saturated with it should be kept constantly applied; the case which it affords is often very great. Also internally it may be given in doses 40 grains gradually increased to 60, 90 up to 120 grains twice daily, vehicle being half a pint of warm rice *conjee*. The quantity of nitre may be diminished as the severity of the symptoms subsides.

SIDDHA FORMULATIONS USING *VEDIUPPU* AS INGREDIENT

1. **Abaraga Chendhuram** [18]

   Dose : 100-150 mg

   Adjuvant : Butter

   Indications : Neer ezhivu, Madhumegam.

2. **Uloga mandura chendhuram** [17]

   Dose : 130 mg

   Adjuvant : Ghee, Butter

   Indications : Neer kattu, Neer erichal, Neer surukku

3. **Gandhaga sudar thylam** [19]

   Dose : 260-390 mg

   Adjuvant : Ilaneer

   Indications : Neer Kattu

4. **Kalamega Narayana Chendhuram**[20]

   Dose : 130-260 mg

   Adjuvant : Ghee, Butter

   Indications : Neer Adaippu, Moolam, Suram

5. **Vediuppu Chunnam**[13]

   Dose : Thuvarai Alavu

   Adjuvant : Ilaneer

   Indications : Kalladaippu, Sadhaiadaippu, Neer Kattu

6. **Gunma kudori** [18]

   Dose : 488mg

   Adjuvant : Ghee

   Indications : Kalladaippu, Sadhaiadaippu, Neer Kattu, Neer Adaippu

7. Sanga Dravagam [21]

Dose : 1 drop

Indications : Marbu vazhi, Gunma vazhi

8. Thalaga kattu [13]

Dose : Ezhaithu bd

Adjuvant : Hotwater

Indication : Iya suram, Sanni

9. Thalaga Parpam [22]

Dose : 15-30mg

Adjuvant : Palm Jaggery

Indications : Azhal suram, Erumal, Vazhi.

10. Nandhi mezhugu [18]

Dose : 60-300mg

Adjuvant : Palm jaggery

Indications : Puttru, Skin disorders

11. Navauppu mezhugu [18]

Dose : 65-130mg

Adjuvant : Palm jaggery

Indications : Megam, vazhi gunmam, Neerkovai

12. Naga Chendhuram [13]

Dose : 65-130mg

Adjuvant : Honey, Ghee

Indications : Vellai. Peruvairu, Gunmam

13. Notchi Thylam [18]

Dose : 15ml

Adjuvant : Hotwater

Indications : Erumal, Elaippu

14. Panchalavana parpam [18]

Dose : 65-200mg

Adjuvant : Ghee

Indications : Gunmam, Kazhichal

15. Poora kattu [13]

Dose : Ezhaithu bd

Adjuvant : Hotwater

Indications : Vazhi, Suram, Dryness of mouth.

SEENAKARAM- Alum (Aluminium potassium sulphate)[13,15,16]

Synonyms

- *Cheenam*
- *Padigi*
- *Padikaram*

Vernacular names

- Tamil: *padikaaram*
- Sanskrit: *sphatika*
- Telugu, Kannada: *padikaaram*
- Hindi: *phatkari*

Aluminium sulphate is a chemical compound with the formula $(AlO_2)_4$ .It is soluble in water and is mainly used as a coagulation agent in the purification if drinking water and waste water treatment plants, and also in paper manufacturing.

Source

This is available in nature and found in combination with certain special form of clay in places such as Nepal, Kathiyawar, Punjab and Bihar. The alum is separated from the clay. It is also found with peroxide of iron in silajit. As found in the bazaars it is often mixed with impurities;it may be rendered fit for medical purposes by dissolving it in boiling water, straining the solution and evaporating it so as to obtain crystals, which should be preserved for use.

Organoleptic characters

Appearance **:** Colourless, transparent crystal like appearance

Taste **:** Sweetish astringent, sour

Potency **:** Heat

Division **:** Pungent

Actions:

- Astringent
- Diuretic
- Haemostatic
- Antispasmodic
- Styptic
- Antiseptic
- Anti-spasmodic

Dosage

650 mg to 1.3 gm.

General characteristics:

"சீனமெனுங் காரமது சீறிவரு பல்லரணை
ஆனைக்கால் கண்ணோய் அனிலமொடு-மாநிலத்தில்
துன்மாங் கிசம்வாயு தோலாத உள்ளழலை
குன்மமிவை போக்குமெனக் கூறு".

It cures gingivitis, eye diseases, ophthalmic, elephantiasis, vayu, tumour, sense of heat, gastric ulcer, hypertension, haemorrhage, dysentery, diarrhoea, children vomiting, and whooping cough with expectorant, pharyngitis, menorrhagia and gonorrhoea.

Purification of *Seenakaram*

The Alum was dissolved into the water and it was filtered. Boil it well till it turns into a semisolid state. Then the mixture was cooled to collect the purified form.

Medicinal Uses [13, 15]

- Alum is dissolved in 1 ounce of water and on washing it controls Eye diseases.
- Alum dissolved in water is used as a mouth wash and for washing ulcers.
- A cloth is soak in alum water is applied over the cut injuries, to arrest bleeding.
- Alum, acacia catechu and bark of Cinnamomum zeylanica are powdered and mixed with honey, give to diarrhoea which is due to tuberculosis.
- Alum with rose water controls cough with asthma
- Alum is dissolved in distillate of bishop's weed theneer and administrated in whooping cough to control effectively.
- Alum with honey will control vomiting due to chronic hiccups and whooping cough.
- For snake bite, alum is administrated with buttermilk.
- Alum with sugar helps in severe head injury.
- Alum with sugar syrup for guinea worm infection.
- In leucorrhoea with bleeding, alum is giving with adathoda leaf juice.
- Boiling alum in milk and filter, that effective in the management of excessive menstrual bleeding and in treatment of toxic fever and haemorrhoid.
- Alum topical application with water for bleeding of nasal, penis and teeth.
- Alum powder used in aloe gel to get juice of it.
- It is useful in leucorrhoea, haematuria, haemoptysis, menorrhagia, gastric and intestinal catarrh and other haemorrhage; in fluxes of the respiratory passages with profuse ropy mucous phlegm; in chronic diarrhoea and dysentery and in atomic discharges generally.
- In chronic diarrhoea, a mixture of alum, laudanum and acorus root, given thrice daily is useful.
- In the diarrhoea preceding cholera and in the diarrhoea of phthisis, a compound powder of alum, catechu and cinnamon mixed with honey is given in repeated doses.
- It is useful also in strangury and vomiting in small doses.
- In narcotic poisoning in children it is a good and efficient antidote.
- In whooping cough, after the first or acute stage has passed, alum in doses of 2 to 4 grains according to age of the child, given twice or thrice a day, in the form of powder or in the solution in omam water.
- For asthma and cough alum in rose water is given twice a day.

- Persons bitten by serpents are made to drink buttermilk or water mixed with good alum powder.
- In obstinate cases of malaria desiccated alum with some aromatic compound powder to disguise the taste given 2 hours before the expected rigoin r with only a teaspoonful of water has given very satisfactory results.
- In injuries which result in concussion of the brain or spinal cord or in severe sprains or fractures the first thing given is alum with sugar.
- In croup mixed with honey or syrup is an excellent emetic.
- In obstinate hiccup, alum is giving to induce vomiting and stop hiccups.
- If the powder is taken with very little water, that will induce vomiting.
- In frequently repeated doses of alum relieves lead colic by precipitating soluble salts of lead.
- Alum with juice of *Adathoda vasica* works wonderfully in certain forms of leucorrhoea, especially when the flow is tingled with blood.
- In haemorrhages from kidneys, uterus and other internal organs alum with or without opium is given with benefit, but not when much fever is present.
- Alum whey or lime whey prepared by boiling for 10 min, powdered alum in a pint of milk and strained is beneficial in doses in menorrhagia and bleeding piles.
- Externally, alum forms one of the ingredients of some hair dyes and hair lotions.
- Locally applied it checks sweats in the armpits, groins and soles of the feet.
- Weak solution is used as a lotion to ulcers and it is used in relaxed or ulcerative sore throat, aphonia, atony of the larynx, spongy or bleeding gums, loose teeth, ulcers of the mouth and tongue, fissures of the tongue in consumption, in excessive salivation.
- It is locally applied in diphtheria, croup and pharyngitis; as a collyrium, it is used in chronic and purulent ophthalmic, chronic conjunctivitis, generally in what is known as country sore eyes, especially among children.
- The solution may be used also as a nasal spray if the lesion is higher up in the nose.
- A lotion made of alum and borax with water is useful in weeping eczema.
- A powder composed of alum and catechu is an application to swollen gums and in toothache.

SIDDHA FORMULATIONS USING *SEENAKARAM* AS INGREDIENT

1. **Padikalinga Chendhuram**[18]

   Dose : 0.5 -1 gm

   Adjuvant : Ghee, Butter

   Indications : Kazhichal, Perumbadu

2. **Karuvanga Parpam** [13]

   Dose : 30-60 mg

   Adjuvant : Ghee, Butter,milk

   Indications : Kabham, Erumal, Azhal

3. **Peranda Parpam** (13)

   Dose : 130-260mg

   Adjuvant : Ginger juice

   Indications : Azhal, Biramai

4. **Jalamanjari**[21]

   Dose : 1-2gm

   Adjuvant : Ilaneer, Mullanki Saaru, Sombu Theneer

   Indications : Neer Adaippu, Neer Erichal, Neer Surukku, Kalladaippu, Neer Arugal

5. **Nandhi mezhugu** [18]

   Dose : 60-300mg

   Adjuvant : Palm jaggery

   Indications : Puttru, Skin disorders

6. **Padikara Parpam**(13)

   Dose : 130-520mg

   Adjuvant : Butter

   Indications : Neer Erichal, Neer Adaippu

7. Padikara Chendooram [18]

Dose : 200-400 mg

Adjuvant : Butter, ghee

Indications : Dysentry, blood stained dysentery, and menhorrhagia.

8. Kalamega Narayana Chendhuram [20]

Dose : 130-260mg

Adjuvant : Ghee, Butter

Indications : Neer Adaippu, Moolam, Suram

9. Sanga Dravagam [13]

Dose : 1 drop

Indications : Marbu vazhi, Gunma vazhi

10. Padikara Neer[13]

Indications : Oral wash, wound wash

11. Ayakandha Chendhuram [18]

Dose : 65-130mg

Adjuvant : Ghee, Honey

Indications : Sobai, Paandu

NAVACHARAM (Ammoni chloridum or Ammonium Sal ammoniac) [13,15,16]

Synonyms

- *Istigai,*
- *Salligai,*
- *Sooligai,*
- *Padu*

This is available in small quantities in brick stone furnace. This is also obtained by sublimation of coal, salt and dung ashes of camel.

Vernacular names

- Tamil: *Navacharam*
- English: Sal Ammoniac
- Arab: *Armina*
- Ben: *Navasagara, Nishadal*
- Hindi: *Navasadara*
- Guj & Mah: *Navasagar*
- Burm: *Lovas, Zarasa*

Organoleptic characters

Appearance	**:** Solid in state, fibre in nature and so it is hard to powder
Colour	**:** White or grey colour.
Taste	**:** Bitter, sour, urine smell.
Potency	**:** Heat
Division	**:** Pungent
Solubility	**:** Dissoluble in water and alcohol

Synthetic preparation of Ammonium chloride (13,15,16)

The sand, available at the places where animals and human beings defecate, is collected and placed in a pot. To one part of the sand, four parts of the urine is added, the clear liquid obtained is taken out. Camphor, alum and potassium nitrate are powdered and burnt and added to 1300 liters of the liquid. This mixture is poured in another pot and the pot is covered and subjected to sublimation. Ammonium chloride settles as a sublimate.

Purification and Detoxification

- The Ammonium chloride was dissolved in hot water and filtered to remove dust. Then, it was poured in a broad mouthed vessel and kept in the sun light; the salt was formed in a purified form it is preserved along with small quantity of the root of jequirity, which is used to remove nauseating smell, in an airtight container
- It is dissolved in cow's urine and filtered. The filtered is boiled and keep undisturbed to get purified form.

Action

- Tonic : In a small doses given for a long period, improves the body strength.
- Stimulant : if given in high doses.
- Expectorant
- Diaphoretic : It acts on the lymphatic channel and glands.
- Diuretic
- Rubifacient
- Pitha neutralizer

General Properties:

"குன்மம் குடற்சூலை கொல்லும் மகோதரத்தை
வன்மையுறு கல்லடைப்பை மாற்றுங்காண்- சன்மக்
கவிச்சுமுத் தோடங் கனவாத நீக்கும்
நவச்சார மாதே நவில்"

Abdominal pain, distended abdomen, urinary calculus, bad odour in the skin, sinusitis, amenorrhoea, whooping cough, intermittent fever, three humours, indigestion, hepatomegaly, hepatitis, splenomegaly, rhinitis, tuberculosis, haematemesis, facial paralysis.

Dosage:

325 mg to 975 mg, if given in high doses it may produces diarrhea.

Medicinal Uses [13, 15]

- Ammonium chloride is dissolved in water and give 4 times a day.
- The salt may be taken in the root decoction of Indian sarasaparila (Hemidesmus indicus) for chronic arthritis, disease of tooth, chest pain and for tiredness due to excessive work.
- The salt dissolved in camphorated water and administrated twice daily for the disease like flatulency, pain and swelling in the uterus, bilious vomiting and headache.
- The ammonium chloride is dissolved in the root decoction of jequirity and given to the old ae patients who are suffering from chronic cough in the doses of 4 to 5 times. The salt may be added to 500 ml of boiled rice –gruel and may be taken in little by little for treatment of leucorrhoea, blood disorder, chronic dysentery, bronchitis, and diseases of stomach and urinary bladder.
- Ammonium chloride is dissolved in alcohol and rose water mixture. A cloth is soaked in this solution and applied over the mammary gland.

  Indication: Suppression of the secretion of the breast milk, breast enlargement

  Abscess in the breast and ulcer in the nipple
- The salt dissolved in the decoction of Hygrophila auriculta may act as a diuretic and may be effective in the treatment of jaundice, liver enlargement splenomegaly.
- Ammonium chloride and potassium nitrate solution may be used for pain in the eye and excessive lacrimation.
- Ammonium chloride is dissolved in water. A cloth is soaked in the solution and applied over the disease affected part.

Indications:

Hydrocele, wound, sprain, swelling, hepatitis, abdominal tumour, an Inflammation of the lymphatic gland etc.,

- It is used in the preparation of philosopher's liquid.
- Ammonium chloride is used in galvanizing, in dyeing and calico-printing and in the manufacture of Leclanche cells and dry batteries. It is employed as a soldering flux, and in electroplating.

- In medicine, the salt is used as an expectorant, diaphoretic and diuretic, and in inhalations. It has marked stimulation action on the mucous membranes, increasing their secretions useful is cases of hepatic abscess, chronic hepatic congestion and in dropsy connected with the liver and ovarian disease; in cirrhosis and in jaundice from catarrh of the bile ducts.
- For hepatitis, sal – ammoniac mixed with absinthium (worm wood), rubbed well in a mortar with a little water and given in a single dose will give relief.
- In gastric catarrh in biliousness with coated tongue, foetid breath, flatulence etc., in bronchial and visual catarrh, in chronic pharyngitis with glary mucous secretions and whooping cough it is valuable, combined with liquid extract of glycyrrhiza or syrup of country liquorice and with a few grains of powdered cinnamon, in case of whooping cough. In amenorrhoea, dysmenorrhoea, gleet , leucorrhoea, chronic dysentery and other similar chronic discharge from lungs, stomach and other internal organs it is given dissolved in *conjee* water in wine glassesful doses every second and third hour, "In hysteria, nervousness, jaundice and other liver complaints and gastric catarrh , doses of 0-20 grains three times daily are beneficial.
- It is often prescribes as a stimulating expectorant in chronic bronchitis and in pneumonia in the stage of resolution"- Chopra.
- In various forms of neuralgia, in chronic liver disease, organic or functional, in rheumatic affections of the face etc., it is given in infusion of Indian Sarsaparilla; in intermittent fever, in sick or nervous headaches, acute alcoholism and in delirium tremens its action is very marked, given dissolved in camphor julep.
- In dropsy due to liver disease and in that following fevers, it is administrated with infusion of moringa or decoction of Astercantha. As an alternative it acts by slowly modifying the nutrition

  of the tissues; it is a useful agent in chronic inflammatory disease of the glands such as thyroid body, liver, and spleen and in induration of the uterus, ovaries and the prostate and externally for fomentation in the form of a lotion.
- In urinary disease chiefly where the urine is full of lithates. It is very useful.

- *Externally,* its solution combined with nitre is a nice cooling and stimulant application to the head in headache, "sprains, rheumatism, lumbago, sciatica", mania and apoplexy. And for inflamed erysipelas and hernia tumours; in inflamed hydrocele, indolent tumours, in enlarged glands, in mammary abscess occurring after confinement and abscess in other parts of the body before formation of matter, in chronic skin diseases and as a dressing for bruises and blows on the eye.
- For milk abscess it is used as lotion with arrack and rose water.
- Mixed with sulphide of arsenic, it is used as an application to scorpion bites.
- As an inhalation in affection of the air passages its vapours produced by heating a drachm of it on a dish are useful.
- Ammonium chloride is recommended for local application in cases of cataract.
- The salt is generally not used as fertilizer, as it is likely to increase the total chlorine content of the soil when other fertilizers like potassium chloride are also employed. In other cases it is as effective as the sulphate, but it is slightly more expensive. A fertilizer grade of synthetic ammonium chloride contains N, 24 per cent. Ammonium chloride is more effective for grain crops than for root crops. When applied to barley, the grains contain a lower percentage of nitrogen than when ammonium sulphate is used, which raises its malting and money value.
- Ammonium chloride is usually produced by passing ammonia gas into hydrochloric acid, or by neutralizing ammonia Cal liquor with hydrochloric acid. The salt is purified by crystallization from water, or by sublimation. A very pure product is obtained by mixing gaseous ammonia and hydrogen chloride diluted with hydrogen maintaining the temperature at 230-310 degrees.

SIDDHA FORMULATIONS USING *NAVACHARAM* AS INGREDIENT

1. Navasara aakraanam [13]

Dose : 5- 10gms
Adjuvant : Water
Indications : Vomiting, Liver and Lund related diseases.

2. Navasara kuzhambu [13]

Dose : 130mg
Adjuvant : Lemon
Indications : Constipation, ascites, diuretic

3. Navasara Ennai [13]

Adjuvant : Neermulli
Indications : Constipation, ascites, eczema, anaemia

4. Navasara Chendhuram [13]

Dose : 488mg
Adjuvant : Honey
Indications : Ulcer, Gastritis, Weakness

5. Navasara kattu [13]

Dose : Panaedai
Adjuvant : Honey
Indications : Vellai, Neer surukku, Sathaiadaippu

6. Navauppu mezhugu [18]

Dose : 65-130mg
Adjuvant : Palm jaggery
Indications : Megam, vazhi gunmam, Neerkovai

7. Sanga Dravagam [13]

Dose : 1 drop
Indications : Marbu vazhi, Gunma vazhi

8. Ayakandha Chendhuram [18]

Dose : 65-130mg
Adjuvant : Ghee, Honey
Indications : Sobai, Paandu

9. Gandhaga sudar thylam [19]

Dose : 260-390mg
Adjuvant : Ilaneer
Indications : Neer Kattu

10. Thanga uram [13]

Dose : 130-260mg
Adjuvant : Honey
Indications : Genital disease

11. Visha Kuzhambu [18]

Dose : 50-100mg
Indications : Vanthi, Bethi

12. Ayaveera Chendhuram [13]

Dose : 50-100mg
Adjuvant : Honey, Palm jaggery
Indications : Soolai, Keel vayu

13. Gunma kudori [18]

Dose : 488mg
Adjuvant : Ghee
Indications : Kalladaippu, Sadhaiadaippu, Neer Kattu, Neer Adaippu

14. Kalamega Narayana Chendhuram [20]

Dose : 130-260mg
Adjuvant : Ghee, Butter
Indications : Neer Adaippu, Moolam, Suram

CHEMICAL REVIEW

4.2 Chemical review:[22,23,24,25]

Name: Alum [22]

Molecular formula : ALKO8S2

- Synonyms: Potassium alum
  - Aluminium potassium sulfate
  - Potash alum
  - Potassium aluminum sulfate

Molecular weight: 258.21g/mole

Physical description: Large,Transparent crystals or crystalline: odorless

Colour/ Form: White/ powder

Taste: astringent

Boiling point: 200 ^{o} c

Melting point: 92.5 ^{o} c

Solubility:

- 1g/7.5 ml at 25 ^{o} c,
- Freely soluble in water.
- Insoluble in ethanol.

Density: 1.725

Stability/Shelf life:

Stable at ambient temperature.

When kept long time at 60-65 C losses a H_2O which is reabsorbed on exposureto air.

pH: Between 3.0 and 4.0 (10% solution)

Dielectric constant: 3.8

Pharmacology and Biochemistry:[22,25]

The presence of potash alum reduces swollen mucous membranes that result from inflammation of the nasal, gastrointestinal and urinary passage as well as in the presence of excessive secretions. The induction of the coagulation cascade will also stop bleeding.

Absorption:

Potassium alum is found in its dodecahydrate form that produces a very large molecule. This large molecule when ingested, the aluminium salts are rapidly solubilized in the stomach and then they can generate aluminium hydroxide or poorly absorbed basic aluminium salts.

Route of elimination:

When potassium alum is absorbed, the kidney is responsible for the elimination of the major portion of the absorbed dose. From the excretion, 0.1 – 0.3% of the absorbed dose is eliminated via the urine.

Volume of distribution:

The distribution of aluminium salts in the body is influenced by increased concentrations of parathyroid hormone.

Clearance:

Renal clearance of aluminium is approximately 5-10% of the excretion of urea or creatinine. **The reduced clearance of aluminium compounds is due to high protein binding.**

Metabolism / Metabolites:

Potassium alum does not go through the metabolic pathway. When ingested or absorbed, it will get rapidly dissolved and it will form ions that will later generate other salt derivatives.

Biological half-life:

4.5 hours when administered instantaneously.

POTASSIUM NITRATE:[23]

Name: potassium nitrate

Molecular formula : KNO3

Synonyms:

- Salt peter
- Nitre
- Nitrate of potash
- Vickite
- Nitric acid

Molecular weight: 258.21g/mole

Colour/ Form: White to dirty grey

Rhombic to trigonal crystals

Taste: pungent

Boiling point: 400 ^{o} c

Melting point: 337 ^{o} c

Solubility:

- 1g/ 2.8ml water at about 25 ^{o} c,
- soluble in water and glycerol.
- Insoluble in ethanol.

Density: 1.725

Stability/Shelf life:

Stable at ambient temperature.

When kept long time at 60-65 C losses a H_2O which is reabsorbed on exposureto air.

pH: Between : 4.5 – 8.5 (5% solution)

Dielectric constant: 5

Pharmacology and biochemistry:

Potassium ions are believed to disturb the synapse between nerve cells, thus decreasing the nerve excitation and associated pain. Potassium ions have demonstrated in animal studies to act directly on the nerves and to reduce sensory activity.

Absorption:

It is established that nitrate is quickly and almost entirely absorbed from the proximal and small intestine subsequent to digestion, with little if any absorption from the stomach and lower intestine. The vast majority of intestinal K^+ absorption occurs in the small intestine; the contribution of the normal colon to net K^+ absorption and secretion is trivial.

SODIUM CHLORIDE: [24]

Name : Sodium Chloride

Molecular formula : NaCl or ClNa

Synonyms:

- Salt
- Halite
- Table salt
- Common salt
- Saline

Molecular weight : 58.44 g/mol

Physical description:

Sodium chloride appears as a white crystalline solid

Color: colorless, transparent crystals or white crystallite powder.

Taste: salty

Boiling point: 1465 ^{o}c

Melting point: 800.7 ^{o}c

Solubility: 36.0g/100g of water at about 25 ^{o}c

Density: 2.165

Vapour pressure: 1mm Hg at 1589 ^{o} F

Viscosity : viscosity of saturated aqueous = 1.9mPa-s solution

Corrosivity: corrosive to base metals.

Ph : 6.7to 7.3

Surface tension: 110mN/m at 850 ^{o}c/ molten sodium chloride

AMMONIUM CHLORIDE:[25]

Name : ammonium chloride

Molecular formula :NH4 CL orCIH4 N

Synonyms:

- Salmiac
- Sal ammoniac
- Ammonium muriate
- Sal ammonia
- Ammonium chloride

Molecular weight: 53.49g/mol

Physical description:

It is a crystalline solid. It is soluble in water (3%). Strongly endothermic, sublimes without melting.

- **Colour / Form:** Colorless crystals or crystallite masses or white; granular powder.
- **Odor**: Odorless
- **Taste:** Cooling; Saline

Boiling point: **338 ºC (sublimes)**

Melting point: 39.5 g/100 g of water at about 25 ºC

350 (sublimes)

Solubility: Soluble in liquid ammonia.

Density: 1.53

Vapour Pressure: 1 mm Hg at 321 ^{o}F

Stability / Shelf life: May volatize and condense on cool surface.

Corrosivity: At fire temperature, it corrodes metals.

pH: 5.0 – 5.5 (5% aqueous solution)

Refractive index: 1.642

Pharmacology and Biochemistry:

Systemic acidifier. In liver, ammonium chloride is converted into urea with the liberation of hydrogen ions (which lowers the pH) and chloride.

Bio-necessity:

Ammonium is an endogenous substance that serves as a major role in the maintenance of the acid-base balance

4.3. PHARMACEUTICAL REVIEW:

Concept and Terminology [31,32,33]:-

Dravagam means an acid. They are all acidic liquid preparation obtained by a process of destructive distillation of salts and alkalies of mineral origin with or without any addition of fluid in a peculiar distillation set up called "*Valaai Iyanthiram*". Dravagam is a mineral quintessence dispersed in water.

Apparatus for distillation:- [47]

The still consists of a basal receptacle to contain the drugs and a cover with an exhaust tube which is conveniently bent to drain the distillate into the bottle. A cupular reservoir is provided at the region where the exhaust leaves the lid portion.

The receptacle of the retort is an earthen pot. The cupular reservoir over the lid is filled with cold water during distillation and it serves as a sort of crude type condenser. This crude device could be replaced by a good condenser in the form of a water jacket around the exhaust tube. This cold water should be circulated continuously through the condenser during distillation.

Principle:-

The process of Dravagam follows the principle of destructive distillation. It is explained as the chemical process of the decomposition of unprocessed material by heating it to a high temperature in the absence of air or in the presence of limited amounts of oxygen or other reagents, catalysts or solvents such as steam.

DRAVAGA VALAIYANTHIRAM

Process of Preparation:- [47]

The raw drugs are powdered and put into the still for distillation. The lid is then tightly sealed with muddy cloth to prevent vapours from escaping. The cupular condenser is placed over the lid, sealed and dried. Heat is applied to the drug mixture and the distillate is collected in a large bottle and mixed well to ensure uniform concentration of the medicine because the first distillate is much concentrated as compared to that collected at the end of the process when the drugs are depleted of the medicinal properties. Continuous water current should be maintained in the condenser. When the cupular condenser is used, water is replaced by cold water as and when it becomes warmed up. The vessel or bottle in which the distillateis collected is also placed in trough containing cold water.

The end of the process of preparation is marked by the escape of dark fumes from the exhaust. Further attempts to heat and collect the remnants of condensate should not be made once this phenomenon is noticed.

Characteristics of Dravagam [34]:-

- Unique dosage forms.
- Highly concentrated. So minimal dosage is required for producing more effect.
- Easy administrable route.
- More potent.
- Palatable.
- It exhibits a higher rate of bioavailability. This is due to its large surface Area and high dissolution.
- More stable.
- Long shelf life and flexibility.
- It increases the saliva, bile, pancreatic juice and decreases gastric juice.
- Act as a catalyst, potency enhancer
- Used in alchemy.
- Should be administered carefully.
- Contact with eyes and skin should be avoided.

5. STANDARDIZATION

5.1BIOCHEMICAL ANALYSIS:-

Biochemical Analysis – *Lavana Dravagam TABLE: 1*

S.no	Experiment	Observation	Inference
1.	Physical Appearance of extract	Off white colour	
2.	**Solubility:** A 2ml of the sample was shaken well with distilled water.	Completely soluble	**Absence of Silicate**
3.	**Action of Heat :** The sample was taken in a dry test tube and heated gently at first and then strong	White fumes evolved No brown flumes	**Presence of Carbonate** **Absence of Nitrate**
4.	**Flame Test :** The sample was mixed with conc Hcl in a watch glass an introduced into non- luminous part of the Bunsen flame	No Bluish green flame	**Absence of Copper**
5.	**Ash Test : A filter paper was soaked into the mixture of drug sample and diluted cobalt nitrate solution and introduced into the Bunsen flame and ignited**	**No appearance of yellow color flame**	**Absence of Sodium**

Preparation of Extract:

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

TABLE : 2

I. TEST FOR ACID RADICALS			
1.	**Test for sulphate:** To 2 ml of the drug sample added 2 ml of 4% dil ammonium oxalate solution.	Cloudy appearance formed	**Presence of Sulphate**
2.	**Test for Chloride :** To 2 ml of the sample 2 ml dil Hcl was added until the effervescence ceases off.	Cloudy appearance formed	**Presence of Chloride**
3.	**Test For Phosphate:** 2 ml of the sample was treated with 2 ml of dil. Ammonium molybdate solution and 2 ml of con.Hno3.	No cloudy yellow appearance present	**Absence of Phosphate**
4.	**Test For Carbonate:** 2 ml of the sample was treated with 2 ml of dil.magnesium sulphate solution.	No Cloudy appearance present	**Absence of Carbonate**
5.	**Test For Nitrate:** 1 ml of sample was heated with copper turning and con.H_2So_4 and viewed the test tube vertically down.	No brown gas evolved	**Absence of Nitrate**
6.	**Test For Sulphide:** 1 ml of the drug sample is treated with 2ml of conc Hcl.	No rotten egg smelling gas was evolved.	**Absence of Sulphide**
7.	**Test For Fluoride and Oxalate:** 2ml of the sample was added with 2 ml dil.acetic acid and 2ml dil.calcium chloride solution and heated.	No cloudy appearance.	**Absence of Fluoride and Oxalate**
8.	**Test For Nitrite:** 3 drops of the sample was placed on a filter paper, on that 2	Nocharacteristic	**Absence of nitrite**

	drops of dil.aceticacid and 2 drops of dil.Benzidine solution was placed.	changes were noted	
9.	**Test For Borate:** **Sample was made into paste by using dil.sulphuric acid and alcohol (95%) and introduced into blue flame.**	**No appearance of bluish green color.**	**Absence of Borate**

TABLE 3 :

II Test For Basic Radicals			
1.	**Test For Lead:** 2 ml of the sample was added with 2ml of dil. Potassium iodine solution.	No yellow precipitate was obtained.	**Absence of Lead**
2.	**Test For Copper:** Sample was made into paste with conc.HCl in a watch glass and introduced into the non-luminous part of the flame.	No blue color appeared	**Absence of Copper**
3.	**Test For Aluminum:** To the 2 ml of sample dil.sodium hydroxide was added in 5 drops excess.	yellow color appearance	**Presence of Aluminium**
4.	**Test For Iron** To 2 ml of sample, added 2 ml of dil.ammonium thiocyanate solution. To 2 ml of sample 2 ml thiocyanate solution and 2ml of con.Hno_3 was added.	Mild red colour appear Blood red color appeared.	**Presence of Iron** **Presence of Iron**
5.	**Test For Zinc:** To 2 ml of sample dil.sodium, hydroxide solution was added in 5drops excess and dil.ammonium chloride was added.	White precipitate was formed	**Presence of Zinc**
6.	**Test For Calcium:** 2 ml of sample was added with 2 ml of 4% dil.ammonium oxalate solution.	Cloudy appearance with precipitate is obtained.	**Absence of Calcium**
7.	**Test For Magnesium:** To 2 ml of sample dil.sodium hydroxide solution was added in 5 drops to excess	White precipitate was obtained	**Absence of Magnesium**

8.	**Test For Ammonium:** To 2 ml of sample 1 ml of Nesslers reagent and excess of dil.sodium hydroxide solution were added.	Brown color was appeared.	**Presence of Ammonium**
9.	**Test For Potassium:** Sample was treated with 2 ml of dil.sodium nitrate solution and then treated with 2 ml of dil.cobalt nitrate in 30% dil.glacial acetic acid.	Yellow precipitate was obtained.	**Presence of Potassium**
10.	**Test For Sodium:** Sample was made into paste by using HCl and introduced into the blue flame of Bunsen burner	Yellow colour flame evolved.	**Presence of Sodium**
11.	**Test For Mercury:** 2 ml of the Sample was treated with 2 ml of dil.sodium hydroxide solution.	No yellow precipitate was obtained.	**Absence of Mercury**
12.	**Test For Arsenic:** **2 ml of the sample was treated with 2 ml of dil.sodium hydroxide solution.**	**No brownish red precipitate was obtained.**	**Absence of Arsenic**

INSTRUMENTAL ANALYSIS

5.2. INSTRUMENTAL ANALYSIS:

FT-IR (Fourier Transform Infra-Red) [26]

The Fourier Transform Infrared Spectroscopy test was carried out for *Lavana Dravagam* as per the standard procedure. The experimental procedure was done Bureau Veritas, Chennai.

DEFINITION:

FTIR offers quantitative and qualitative analysis for organic and inorganic samples. Fourier Transform Infrared Spectroscopy (FTIR) identifies chemical bonds in a molecule by producing an infrared absorption spectrum. The spectra produce a profile of the sample, a distinctive molecular fingerprint that can be used to screen and scan samples for many different components. FTIR is an effective analytical instrument for detecting functional groups.

DESCRIPTION:

The Perkin elmer spectrum FTIR instrument consists of globar and mercury vapour lamp as sources, an interferometer chamber comprising of KBr and mylar beam splitters followed by a sample chamber and detector. Entire region of 400-4500 cm-1 is covered by this instrument. The spectrometer works under purged conditions. Solid samples are dispersed in KBr or polyethylene pellets depending on the region of interest. This instrument has a typical resolution of 1.0cm -1cm. signal averaging, signal enhancement, base line correction and other spectral manipulations are possible.

The interference pattern obtained from a two beam interferometer as the path difference between the two beams is altered, when Fourier transformed, gives rise to the spectrum. The transformation of the interferogram into spectrum is carried out mathematically with a dedicated on line computer.

APPLICATIONS:

Quantitative Scans, Qualitative Scans x Solids, Liquids, Gases

- Organic Samples, Inorganic Samples
- Unknown Identification
- Impurities Screening
- Formulation
- Pharmaceuticals.

IMAGES

FTIR Instrument

INSTRUMENT DETAILS

Model : Spectrum one: FT-IR Spectrometer

Scan Range : MIR 450-4000 cm-1

Resolution : 1.0 cm-1

Sample required : 50 mg, solid or liquid.

Sample preparation:

Solid : KBr or nujol mull method

Liquid : cal / TIBr cells

Gas : Gas cells.

For Solid sample[26]

KBr method:

The sample was grounded using an agate motor and pestle to give a very fine powder. The finely powder sample was mixed with about 100 mg dried potassium bromide salt. The mixture was then pressed under hydraulic press using a die to yield a transparent disc (measure about 13mm diameter and 0.3 mm in thickness) through which the beam of spectrometer passed.

Infrared spectrum is useful in identifying the functional groups like –OH, -CN, -NH2, etc. also quantitative estimation is possible in certain cases for chemical, pharmaceuticals, petroleum products etc. resins from industries, water and rubber samples can be analysed. Blood and food materials can also be analysed.[27]

Measurements techniques:

The procedure for recording the %T or %A is as follows:

1. Air is first scanned for the reference and stored. The sample is then recorded and finally the ratio of the sample and reference data is computed to give required %T or %A at various frequencies.

2. Study of substances with strong absorbance bands and weak absorbance bands as well as possible.

3. Small amount of samples are sufficient.

4. High resolution is obtained.

Procedure:

Typically, 1.5 mg of protein, dissolved in the buffer used for its purification, were centrifuged in a 30K centric on micro concentrator (a micron) at 3000 g at 4ºc until a volume of approximately 40AI.

1. Then, 300AI of 20 Mm buffer, prepared in H2O or 2H2O, PH or P2H 7.2, were added and the sample concentrated again. The P2H value corresponds to the PH.

2. Meter reading +0.4. The concentration and dilution procedure was repeated several times in order to completely replace the original buffer with this buffer.

3. The washings took 24h, which is the time of contact of the protein with the $2H_2O$.

4. Medium prior FT-IR analysis, in the last washing, the protein was concentrated to fine a volume of approximately 40 AI and used for the infrared measurements.

5. The concentrated protein sample was placed in CaF2 windows and a 6 Am tin spacer or a 25Am Teflon spacer for the experiments in H2O or 2H2O, respectively. FT-IR spectra were recorded by means of a Perkin – Elmer – spectrum – 1 FT-IR spectrometer using a deuterated triglycine sulfate detector.

6. At least 24 h before, and during data acquit ion, the spectrometer were continuously purged with dry air at a dew point of 40ºc. Spectra of buffers and samples were acquired at 2cm 1 resolution under the same scanning and temperature conditions. In the thermal denaturation experiments, the temperature was raised in 5ºc steps from 20 to 95ºc.

7. Before spectrum acquition, samples were maintained at the desired temperature for the time necessary for the stabilization of temperature inside the cell (6min). Spectra were collected and processed using the SPECTRUM software from PerkinElmer. Correct subtraction of H2O was judged to yield an approximately flat baseline at 1900-1400 cm-1, and subtraction of 2H2O was adjusted to the removal of the 2H2O bending absorption close to 1220cm-1.

For scanning.

1. The sample is grounded using an agate mortar and pestle to give a very fine powder.

2. The finely powder sample is then mixed with about 100mg dried KBr salt.

3. The mixture is then pressed under hydraulic press using a die to yield a transparent disc and measure about 13mm diameter and 0.3 mm in thickness.

Nujol mull method:

1. The sample is ground using an agate mortar and pestle to give a very fine powder.

2. A small amount is then mixed with nujol oil to give a paste and this paste is then applied between two sodium chloride plates.

3. The plates are then placed in the instrument sample holder ready for scanning.

For Liquid sample:

i) Making a sandwich:

To prepare a liquid sample to IR analysis, firstly place a drop of the liquid on the face of a highly polished salt plate(such as NaCl, AgCl or KBr), then place a second plate on top of the first plate so as to spread the liquid in a thin layer between the plates, and clamps the plates together. Finally wipe off the liquid out of the edge of plate. Then mount the sandwich plate onto the sample holder. After finishing experiment, clean the plates with isopropanol and return them to the desiccators.

Precaution:

Volatile liquid can't be analyse with this method, because it will evaporate while its spectrum is being obtained. If the liquid sample is toxic or smelly, this procedure is not applicable. In addition, NaCl and KBr are dissolved into water and thus they can't be used for aqueous samples. [28]

ii) Using a liquid cell:

The thermo Nicolet demountable pathlength cell is designed for liquid sample. Assemble the cell in regular manner. Then need to use a syringe to fill the liquid into the cell. Finally seal the cell.

Applications:

It is the preferred method of infrared spectroscopy. FT-IR is an important and more advanced technique. It is used to identify the functional group, to determine the quality and consistency of the sample material and can determine the amount of compounds present in the sample. It is an excellent tool for quantitative analysis.

In FT-IR infrared is passed from a source through a sample. This infrared is absorbed by the sample according to the chemical properties and some are transmitted. The spectrum that appears denotes the molecular absorption and transmission. It forms the molecular fingerprint of the sample. Like the finger print there is no two unique molecular structures producing the same infrared spectrum. It is recorded as the wavelength and the peaks seen in the spectrum indicates the amount of material present.

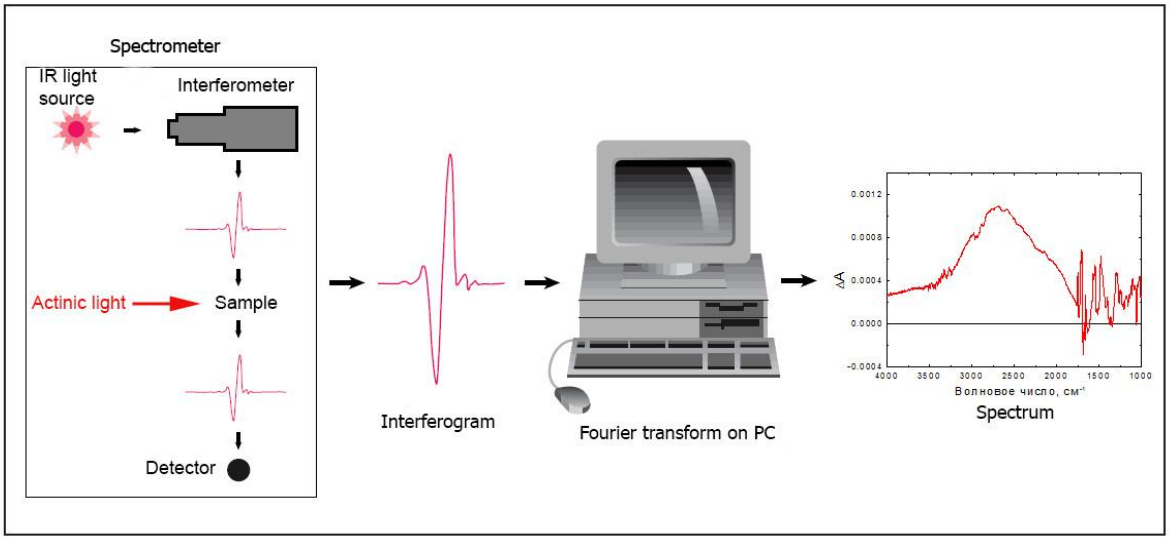
FT-IR is the most advanced and the major advantage is its

- ❖ Speed
- ❖ Sensitivity
- ❖ Mechanical Simplicity
- ❖ Internally Calibrated.

Analytical capabilities:

1. Identifies chemical bond functional groups by the absorption of infrared radiation which excites vibrational modes in the bond.
2. Especially capable of identifying the chemical bonds of organic materials.
3. Detects and identifies organic contaminants.
4. Identifies water, phosphates, sulphates, nitrates, nitrites, and ammonium ions.

Detection limits vary greatly, but are sometimes $<10^{13}$ bonds/cm^3 or sometimes sub monolayer. Useful with solids, liquids, or gases.



FTIR Mechanism

ELEMENTAL ANALYSIS

INDUCTIVELY COUPLED PLASMA OPTICAL EMISSIOS SPECTROMETRY (ICP-OES)[29]

ICP-OES is a trace level elemental analysis that uses the emission spectra of a sample to identify and qualify the elements present. The experimental procedure was done at SCRI, Chennai-106.

Introduction

The element composition of a sample is often an important part of the information needed to assess its properties. Hence there is a need for scientific instrumentation like ICP-OES which plays a pivotal role in the determination of these elements. ICP-OES is widely employed for the estimation of metals and metalloids at trace, minor and major concentration.

Principle

In this technique, the high temperature plasma source atomizes the sample and excites the atoms resulting in emission of photons. The atoms of each element in the sample emit specific wavelength of light. The emission spectrum from the plasma is dispersed by an optical spectrometer, so that intension of the individual wavelength can be measured. The number of photos emitted is directly proportional to the concentration of the element. The photos may be detected either sequentially or simultaneously. Quantitative analysis is achieved by measuring the intensity of these specific wavelength and after performing the calibration using known standards. Identifying the presence of emission at the wavelength characteristic of the element of interest obtaining quantitative information i.e how much of an element is in sample can be accomplished using plots of emission intensity versus concentration called calibration curves.

ICP-OES Operating conditions

Rf frequency 40 M Hz

Range 165-782nm

Detection time up to ppm level using SCD detector

Sample preparation – Microwave Digestion

- Weight 0.25 g of test sample and transfer into a liner provided with instrument.
- Slowly add 9ml of Nitric acid or Sulphuric acid such that no piece of sample sticks on the slide.
- Mix thoroughly and allow reacting for few minutes.

- Place the liner in the vessel jacket.
- Close the screw cap hand- tight in clockwise direction.
- Seal the vessel and placed in the rotor fixed in microwave.
- Set temperature to 180°C for 5 minutes, hold at 180°C for least 10 minutes.
- Allow the vessels to cool down to a vessel interior temperature below 60°C and to a vessel surface temperature (IR) below 50°C before removing the rotor.
- The digested sample was made up to 100ml with Millipore water.
- If visible insoluble particles exist, solution could be filtered through whatmann filter paper.
- Transfer the digested solution into plastic containers and label them properly.

ICP-OES Instrument

Identification by FTIR [29]

Infrared spectroscopy (IR) is proved to be a powerful analytical technique to identify the compounds present in the given mixture of samples. *Lavana Dravagam* was subjected to identification of the inorganic and halide compounds present in it.

Instrument details:-

A JASCO FT-IR 460 PLUS spectrometer (Pike Technologies, Madison, USA)equipped with a pyroelectric DLATGS detector was used.

Procedure:-

FT-IR spectroscopy using KBr-pressed disk technique was conducted. 0.50 ml of PLD and 100 mg of potassium bromide were weighed and grounded in an agate mortar and pressed for 2 minutes at 10 tones/cm^2 to form a semitransparent pellet which lets light to be transmitted to the detector. The pellet was placed in the IR beam using the sample transmission holder. Three measurements were carried out in the transmission mode. Spectra Manager II spectroscopy software developed by JASCO ensures spectral acquisition and processing.

ORGANOLEPTIC CHARACTERS

5.3 .Organoleptic Characters:

STANDARDISATION: TABLE 4:

S. NO	
1.	Color
2.	Odour
3.	Ph
4.	Specific gravity @ 25 degree C
5.	Boiling point
6.	Refractive index
7.	Viscosity
8.	Total acidity
9.	• POTASIUM, • ALUminium, • sulphur, • sodium, • boron, • iron, • copper, • strontium
10.	Heavy metals- Hg, As, Pb, Cd
11.	Pesticide residue (organo phosphorus, organo chlorine, pyrethroids)
12.	Microbial contamination a. total bacterial contamination b. total fungal contamination
13.	Specific pathogen E.coli, Salmonella spp., s.aureus, pseudomonas aeruginosa
14.	Aflatoxins (B1, B2,G1, G2)

1.DESCRIPTION:

Organoleptic Characters:

Organoleptic evaluation means the study of drugs using organs of senses. It refers to the methods of analysis like color, odor, taste, size, shape and special features such as touch, texture, etc. Organoleptic analysis represents the simplest, yet the most humane form of analysis.

2. Color:

It is determined using naked eyes by taking the test drug *Lavana Dravagam* in a test tube and placing it in a white background under white tube light.

3. Odor:

The test drug L*avana Dravagam* was smelled by an individual 2 times with an interval of 2 minutes in order to nullify the effect of previous smelling.

4. Determination of pH:

The pH value of an aqueous liquid may be defined as the common logarithm of the reciprocal of the hydrogen ion concentration expressed in grams per litre. The pH value of a liquid is determined potentiometrically by means of the glass, electrode and a suitable pH meter.

It was determined by taking 5 ml of *Lavana Dravagam* in a 100ml beaker and50 ml of distilled water is added to it and stirred. After 30 min, it was then applied into pHmeter as standard buffer solution of 4.0, 7.9, and 9.2. The test is repeated four times and the average is noted.

5. Determination of specific gravity:

The specific gravity of a liquid is the weight of a given volume of the liquid at 25ºC (unless otherwise specified) compared with the weight of an equal volume of water at the same temperature, all weight being taken in air.

The specific gravity of test drug *Lavana Dravagam* was calculated by dividing the weight of the drug contained in the pycnometer by the weight of water contained being both determined at 25ºC.

6. Determination of Boiling point:

The boiling point of a liquid may be defined as the temperature at which the vapour pressure of the liquid is equal to the atmospheric pressure exerted upon the liquid surface.

7. Determination of Refractive index:

The refractive index (n) of a substance with reference to air is the ratio of the sine of the angle of incidence to the sine of the angle of refraction of a beam of light passing from air into the substance.

The refractive index of test drug *Lavana Dravagam* was identified using refractometer with D line of sodium light at 25^{o}C.

8. Determination of Viscosity:

Measurement of viscosity involves the determination of the time required for a given volume of liquid to flow through a capillary.

Viscosity determination were been carried out using Ostwald viscometers. The test drug *Lavana Dravagam* 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.

9. Determination of Total acidity:

Total acidity is the measure of the total number of hydrogen ions present in a substance in the form of fixed and volatile acids.

About 10 ml of the test drug *Lavana Dravagam* was taken in a suitable titration flask and dissolved in 75 ml of carbon dioxide free water. It was titrated against standard sodium hydroxide solution using 4-6 drops of phenolphthalein indicator till pink colour persists for 10 seconds.

Total acidity as formic acid (%) by weight is calculated.

RESULTS:

The results were noted in Table no.5

10. Test for Heavy metals:

Impurity profiling of a drug plays an important role in standardization. The impurities may be of organic or inorganic in nature. The inorganic impurities comprise of some metal ions, which may be sometimes led to potential toxic effects rather than producing self-toxicity. So, instruments like ICP-OES are used to monitor the levels of heavy metals like mercury, arsenic, lead, cadmium, etc.., It gives the results of concentration of heavy metals up to ppm to ppb levels.

Instrument details:

Agilent ICP-OES 5100 VDV instrument used with the following operation conditions: a RF power 1.2 kW, a plasma gas flow rate 12 L min^{-1}, and a nebulizer gas flow rate 0.70 L min^{-1}.

Procedure:

About 0.5 mL of sample L*avana Dravagam* was taken into theTeflon microwave digestion vessel and add 1 mL of ultrapure nitric acid to digest about 45minutes using Anton Paar microwave digestion unit. After that the sample is made up to a50 mL standard measuring flask. The calibration standard solution is prepared for 0.1 µg/mL to 10 µg/mL by using ultrapure nitric acid and blank also. The samples are introduced into the plasma using nebulizer and spray chamber for the analysis of the elements.

RESULTS:

The results were noted in Table no.6

11. Determination of Pesticide residue:

The determination of pesticide residue for the test drug *Lavana Dravagam* was evaluated using the instrument Gas Chromatography Mass Spectrometry (GCMS)

RESULTS:

The results were noted in Table no.5

12. Tests for Microbial contamination and Specific pathogen:

The procedures recommended for analysis of microbial load as per the guideline (WHO, 2007).

Microbial contaminant study:

The test sample *Lavana Dravagam* was dissolved in water and diluted with phosphate buffer at pH 7.3. Test for microorganisms like E. coli, Pseudomonas aeruginosa, Staphylococcus aureus and Salmonella Sp. in the test sample were studied.

Total viable aerobic Count (TVC):

TVC of LD was observed using series dilution method. In these method 12 tubes containing 9-10 ml of soybean-caseing digest medium was taken. 1 ml of LD solution was added to all the tubes and incubated at 30-35° C for 72 hrs. Microorganisms producedwere determined.

Total bacterial count:

To a Petri dish one ml of LD solution and 15 ml of liquefied casein soybean digest agar was added and incubated at 30-35° C for 72 hours. Bacteria produced were counted.

Total fungal count:

One ml of DLD and 15 ml of antibiotics was added in a petri dish and incubated at 20-25° C for 120 hrs. Fungi count produced were counted.

E. coli:

A small amount of the homogenized lactose broth was prepared and 1 ml of DLD solution in 100 ml of Mac Conkey broth was added and incubated at 43-45° C for 1 ½ to 2 days (18-24 hours). Then it was observed.

Staphylococcus aureus:

A subculture with Baired-Parker agar was prepared and 1 ml of DLD solution was added and incubated at 35-37° C for 24 - 48 hours. Then it was observed.

RESULTS:

The results were noted in Table no.7

13. TEST FOR AFLATOXINS:

The procedures recommended for the detection of Aflatoxin as per WHO (2007).

Instrument Details:

Name of the Instrument: High performance Liquid Chromatography (HPLC)

Procedure:

The sample was processed as per procedures for HPLC.

RESULTS:

The results were noted in Table no.8

TABLE 5:

Description					
Description		**Lavana Dravagam**			
S.No	**Test Parameter**	**Inst. Used**	**Method**	**Requirement**	**Result**
Test Details :					
1.	**General Parameters**				
a.	Odour	NA	Organoleptic		**Characteristics**
b.	Colour	Visual	Visual		**Yellow**
2.	**Chemical Parameters**				
a.	Specific gravity at 25°C	Chemically	API		**1.1358**
b.	Refractive index	Refractometer	API		**1.369**
c.	Test for sulphur	Chemically	In house method		**Present**
d.	Iron (mg)	ICPOES	ITC/STP/F/INST/0 08		**14.98**
e.	Copper (mg)	ICPOES	ITC/STP/F/INST/0 08		**0.01**
f.	Total acidity(% by mass) as Formic acid	Chemically	API		**9.13%**
g.	**Viscosity**	**Brookfield Viscometer**	**In house method**		**1.08**

TABLE 6:

4.	**Heavy metals**				
a.	Lead (as Pb) (ppm)	ICPOES	ITC/STP/F/INST/0 08	NMT-10	**BLQ(LOQ:0.5)**
b.	Arsenic (as As) (ppm)	ICPOES	ITC/STP/F/INST/0 08	NMT-3	**BLQ(LOQ:0.5)**
c.	Mercury (as Hg) (ppm)	ICPOES	ITC/STP/F/INST/0 08	NMT-1	**BLQ(LOQ:0.5)**
d.	**Cadmium (as Cd) (ppm)**	**ICPOES**	**ITC/STP/F/INST/0 08**	**NMT-0.300**	**BLQ(LOQ:0.25)**

TABLE 7:

	Microbiological Tests				
a.	Total viable aerobic count,cfu/gm	Microbiological	API	Max.-100000	<10
b.	Total fungal count, cfu/gm	Microbiological	API	Max.-1000	<10
c.	E.coli/gm	Microbiological	API	Absent	Absent
d.	Salmonella/gm	Microbiological	API	Absent	Absent
e.	S.aureus/gm	Microbiological	API	Absent	Absent
f.	P.aeruginosa/gm	Microbiological	API	Absent	Absent

TABLE 8:

6.	**Aflatoxin**				
a.	Aflatoxin B1+B2+G1+G2(ppm)	HPLC	STP/ITC/AY/003	NMT 5	BLQ (LOQ:0.0005)

TABLE 9:

7.	**Minerals**				
a.	Potassium (mg)	ICPOES	ITC/STP/F/INST/0 08		**102.03**
b.	sodium (mg)	ICPOES	ITC/STP/F/INST/0 08		**49.36**
c.	Aluminium(mg)	ICPOES	ITC/STP/F/INST/0 08		**33.83**
d.	**Strontium(mg)**	**ICPOES**	**ITC/STP/F/INST/0 08**		**0.06**

Analysis for specific Pathogens in Lavana Dravagam: TABLE 10:

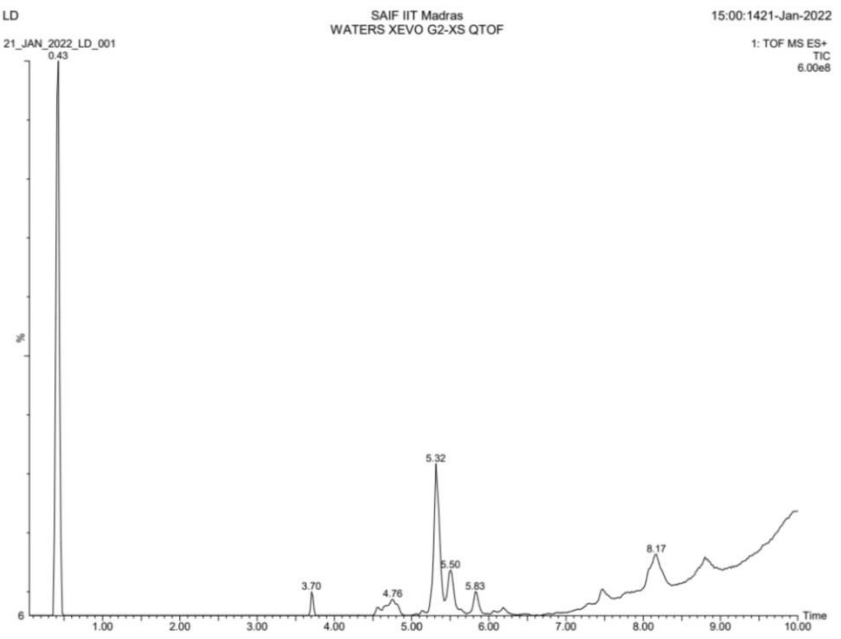
S.NO	PARAMETERS	REFERENCELIMITS AS PER WHO (2007)	RESULTS	REMARKS
1.	Enterobacteriaceae	10^3	Absent	**Within permissible limits**
2.	Escherichia coli	10	Absent	
3.	Salmonella Spp	Absent	Absent	
4.	**Staphylococcus aureus**	**Absent**	**Absent**	

Biochemical Analysis:-

It showed the presence of Sulphate, chloride, aluminium, iron, zinc, ammonium, sodium, potassium.

5.4.Microbial Load and Heavy Metal Analysis:-

On evaluating the microbial load, *Lavana Dravagam* was free from microbes and pathogens. In instrumental analysis for heavy metals, there was no presence of any heavy metals. It indicates that the drug is non-toxic and free from any contamination.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8.17
5.50
3.70
4.76
5.83
%
6
Time
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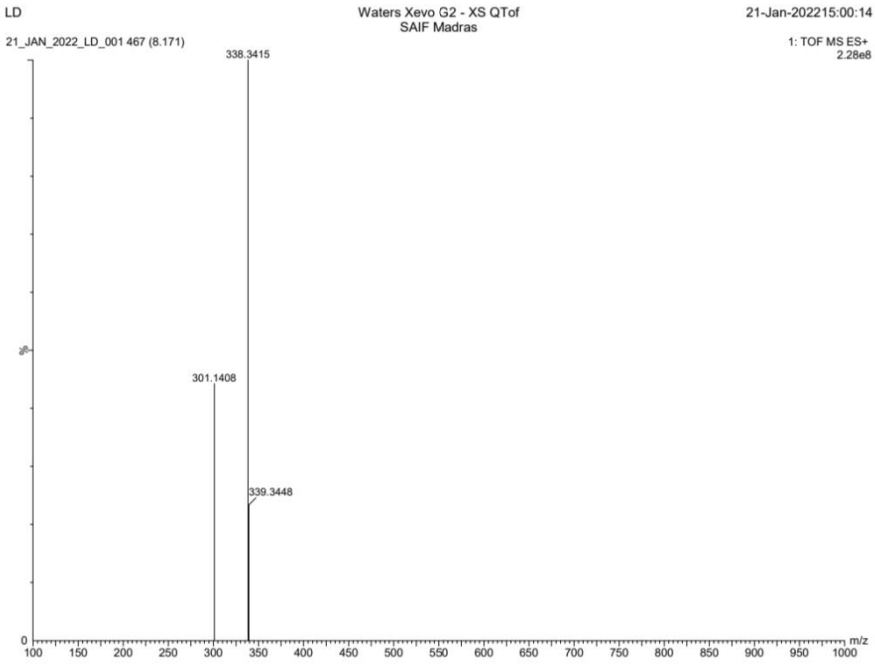
10.00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%
0
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900
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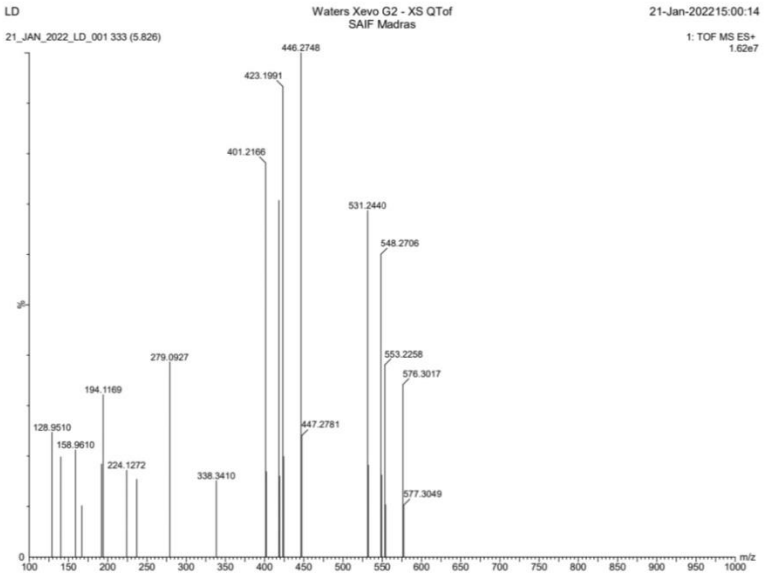
1000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447.2781
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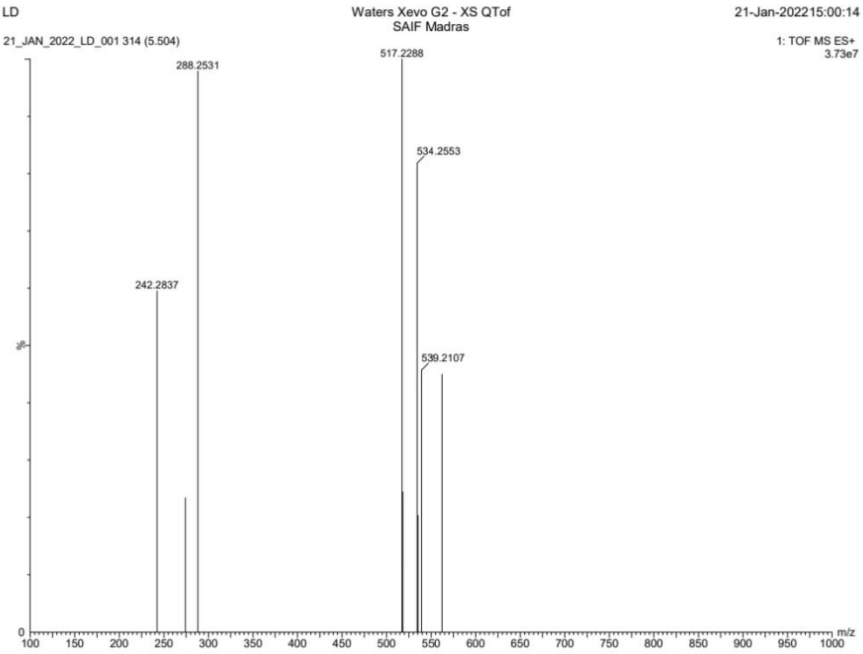
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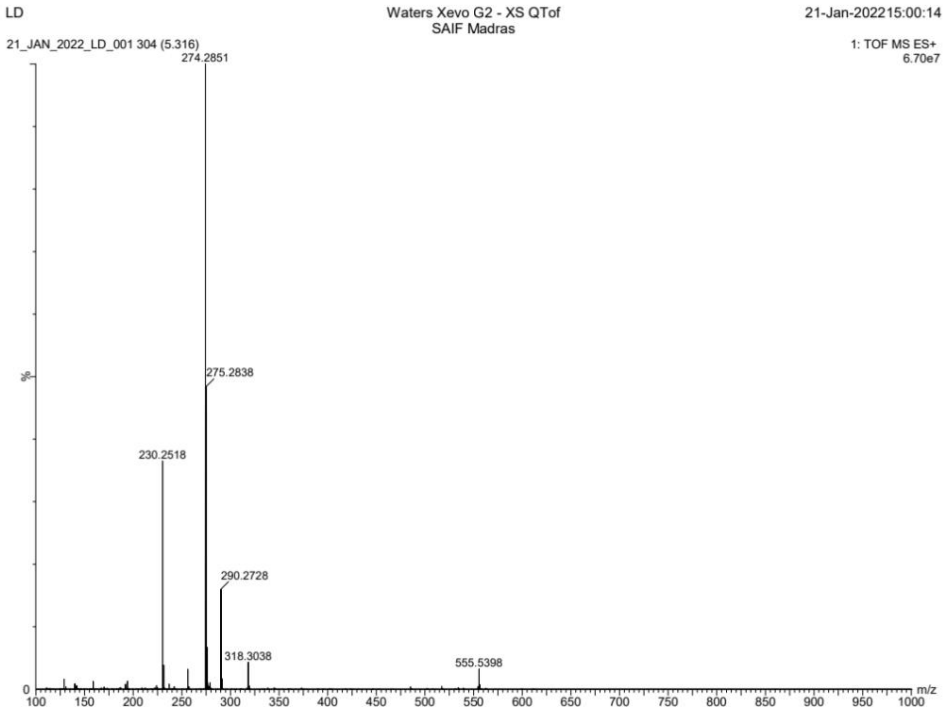
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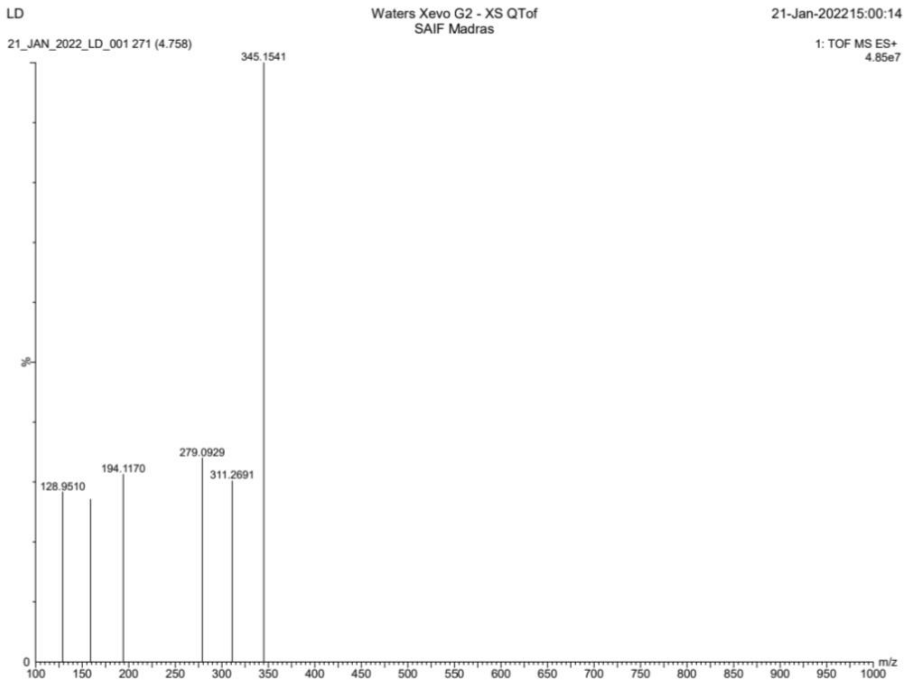
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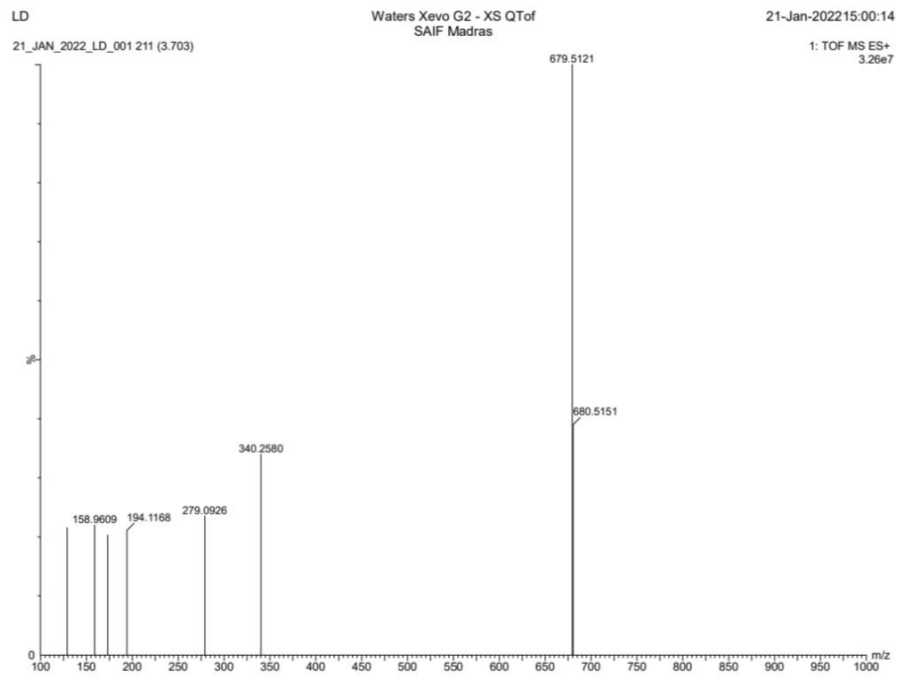
m/z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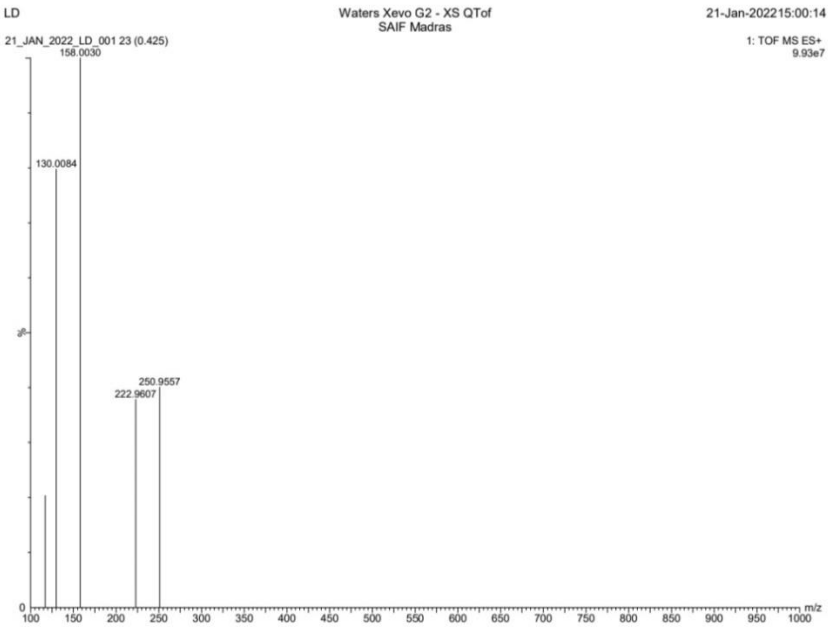
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222.9607
%
0
100 150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950 1000
m/z

6.TOXICITY STUDY

INTRODUCTION:

Toxicity testing is paramount in the screening of newly developed drugs before it can be used on humans. But in case of traditional system of medicines, the drugs are time proven and no such toxicological evidence has been provided. Though it is widely used by humans, according to the context of WHO International Drug Perspective, safety of a drug is more important than its efficacy. Hence the toxicity studies were conducted based on the Organisation for Economic Co-Operation and Development (OECD) guidelines. The essence of toxicity testing is not just to check how safe a test substance is; but to characterize the possible toxic effects it can produce.

Need for toxicity study:

- Assurance of safety, quality and efficacy of Indian System of Medicines (ISM) is very much needed in current scenario.
- It is an initial and essential step, which will strengthen the acceptance of Siddha medicines by scientific community.
- There is a lack in information about toxicity and adverse effects of Siddha formulations.
- Hence, the present study was carried out to ensure the safety of *Lavana Dravagam* in rodents.

Plan of work:

The following study was carried out on *Lavana Dravagam.*

- Acute Oral toxicity Study - OECD 423

6.1 ACUTE ORAL TOXICITY STUDY (OECD – 423):

INTRODUCTION:

- The acute toxic class method is a stepwise procedure with the use of 3 animals of a single sex per step, preferably females.
- Depending on the mortality and/or the moribund status of the animals, on average 2-4 steps may be necessary to allow judgments on the acute toxicity of the test substance.
- This procedure is reproducible, uses very few animals and is able to rank substances in similar manner to the other acute toxicity testing methods.
- The acute toxic class method is based on biometric evaluations with fixed doses, adequately separated to enable a substance to be ranked for classification purposes and hazard assessment.
- In principle, the method is not intended to allow the calculation of a precise LD 50, but does allow for the determination of defined exposure ranges where lethality is expected since death of a proportion of the animals is still the major endpoint of this test.
- The method allows for the determination of an LD 50 value only when at least two doses result in mortality higher than 0% and lower than 100%.
- The use of a selection of pre-defined doses, regardless of test substance, with classification explicitly tied to number of animals observed in different states improves the opportunity for laboratory-to-laboratory reporting consistency and repeatability.

Principle of the Test:

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

- no further testing is needed
- dosing of three additional animals, with the same dose

Description of the method:

Selection of Animal Species:

- The preferred rodent species is the Wistar albino rat. Normally females are used. This is because literature surveys of conventional LD 50 tests show that, although there is a little difference in sensitivity between the sexes with females more sensitive when compared to male rats.
- Healthy young adult animals of commonly used laboratory strains should be employed.
- Females should be nulliparous and non-pregnant.
- Each animal, at the commencement of its dosing, should be between 6 to 8 weeks old and the weight (150-200 grams) should fall in an interval within +20 % of the mean weight of any previously dosed animals.

Housing and Feeding Conditions:

- Animals were housed under standard laboratory conditions.
- They were maintained in a ventilated room. The temperature in the room should be 22° C (± 3°C).
- The relative humidity should be at least 30% and not exceed 70% other than during room cleaning it should be 50%-60%.
- Lighting should be artificial; it is maintained as 12h light/dark cycle.
- Animals were kept in a clean polypropylene cage.
- Rats were fed with standard pellet diet and water *ad libitum*.
- Animals may be group-caged by dose, but the number of animals per cage must not interfere with clear observations of each animal.

Preparation of animals:

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

Test Animals and Test Conditions:

Sexually mature Female Wistar albino rats (150-200 grams) were obtained from TANUVAS, Madhavaram, Chennai. All the animals were kept under standard environmental condition (22±3°C). The animals had free access to water and standard pellet diet.

Preparation for Acute Toxicity Studies:

Rats were deprived of food overnight (but not water 16-18 h) prior to administration of *Lavana Dravagam.*

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

IAEC approval Number	**:**	NIS/IAEC-1/03/30092020/03
Test Substance	**:**	*Lavana Dravagam*
Animal Source	**:**	TANUVAS, Madhavaram, Chennai.
Animals	**:**	Wistar Albino Rats
Sex	**:**	Female (3+3)
Age	**:**	6-8 weeks
Body Weight on Day 0	**:**	160-200 gm.
Acclimatization	**:**	Seven days prior to dosing.
Veterinary examination	**:**	Prior and at the end of the acclimatization period.
Identification of animals	**:**	By cage number, animal number and individual marking by using Picric acid.
Number Of Animals	**:**	3 Female/group
Route Of Administration	**:**	Oral
Water	**:**	Aqua guard potable water in polypropylene cages
Housing & Environment	**:**	The animals were housed in Polypropylene cages provided with bedding of husk.
Housing temperature	**:**	Between 22°C±3°C.
Relative humidity	**:**	Between 30% and 70%
Air changes	**:**	10 to 15 per hour
Dark and light cycle	**:**	12:12 hours.
Duration of the study	**:**	14 Days

Administration of Doses:

Lavana Dravagam was suspended in water and administered to the groups ofwistar albino rats in a single oral dose by gavage using a feeding needle. The control groupreceived an equal volume of the vehicle i.e., Water. Animals were fasted 12 hours prior todosing. Following the period of fasting, the animals were weighed and then the test substance was administered. Three Female animals were used for each group. The dose level of 2 ml/kg body weight was administered. After the substance has been administered, food was withheld for further 3 - 4 hours. The principles of laboratory animal care were followed. Observations were made and recorded systematically and continuously as per theguideline after substance administration. The visual observations included skin changes, mobility and aggressiveness, sensitivity to sound and pain, as well as respiratory movements. Finally, the number of survivors was noted after 24 hours and these animals were then monitored for further 14 days and observations were made daily. The toxicological effect was assessed on the basis of mortality.

Limit test

Number of animals and dose levels:

- The limit test is primarily used in situations where the experimenter has information indicating that the test material is likely to be nontoxic, i.e., having toxicity only above regulatory limit doses.
- Information about the toxicity of the test material can be gained from knowledge about similar tested compounds or similar tested mixtures or products, taking into consideration the identity and percentage of components known to be of toxicological significance.
- A limit test at one dose level of 2000 mg/kg body weight can be carried out with three animals per step.
- If the test substance-related mortality was not produced in the experimented animals, further testing at the next lower level need not be carried out.

Observations:

Animals are observed individually after dosing at least once during the first 30 minutes, periodically during the first 24 hours, with special attention given during the first 4 hours and daily thereafter, for a total of 14 days, except where they need to be removed from the study and humanely killed for animal welfare reasons or are found dead. It should be determined by the toxic reactions, time of onset and length of recovery period and may thus be extended when considered necessary. The times at which signs of toxicity appear and disappear are important, especially if there is a tendency for toxic signs to be delayed. All observations are systematically recorded with individual records being maintained for each animal.

a. Cage-side observation:

These include changes in skin and fur, eyes and mucous membranes and also respiratory, circulatory, autonomic and central nervous systems, somatic motor activity and behaviour patterns. Attention should be directed to observations of tremors, convulsions, salivation, diarrhoea, lethargy, sleep and coma.

b. Behaviour:

The animals will be observed closely for behaviour in the first four hours which includes abnormal gait, aggressiveness, exophthalmos, ptosis, akinesia, catalepsy, convulsions, excitation, head twitches, lacrimation, loss of corneal reflex, loss of traction, piloerection, reactivity of touch, salivation, scratching, sedation, chewing, head movements, sniffing, Straub, tremor and writhes, diarrhoea, leathery, sleep and coma.

c. Food and water Consumption:

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

d. Body Weight:

Individual weight of animals was determined before the test substance was administered and weights will be recorded at day 1, 7, and 14 of the study. Weight changes were calculated and recorded. At the end of the test, surviving animals were weighed and humanely killed.

e. Mortality

Animals will be observed intensively at 1/2, 1, 2, 4, and 24 hours following drug administration on day 1 of the experiment and daily twice thereafter for 14 days.

f. Gross necropsy

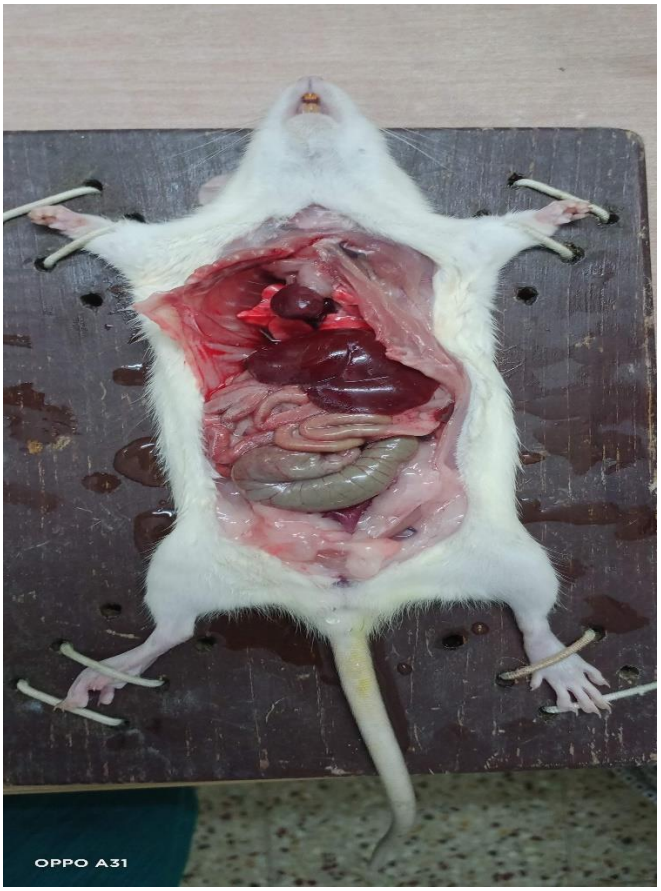
All animals (including those which die during the test period are removed from the study) will be subjected to gross necropsy. Gross necropsy includes examination of the external surface of the body, all orifices, cranial, thoracic and abdominal cavities and their contents, brain, eye, thymus, lungs, heart, spleen. liver, kidneys, adrenals, testes and uterus of all animals.

RESULTS:

The results were noted in Table no.11

CAGE-SIDE OBSERVATION

ACUTE TOXI STUDY:



7. PHARMACOLOGICAL STUDIES:

7.1 ANTI-ULCER ACTIVITY

Aim:

To study the Anti – Ulcer activity of *Lavana Dravagam* in Wistar albino ratsby Pylorus Ligation method.

Materials and Methods:

IAEC Number	**:**	NIS/IAEC-1/03/30092020/03.
Test Substance	**:**	*Lavana Dravagam*.
Animal Source	**:**	TANUVAS, Madhavaram, Chennai.
Animals	**:**	Wistar Albino Rats
Sex	**:**	Male - 12 and Female - 12
Age	**:**	6-8 weeks.
Body Weight	**:**	160-200 gm.
Acclimatization	**:**	14 days prior to dosing.
Veterinary examination	**:**	Prior and at the end of the acclimatization period.
Identification of animals	**:**	By cage number, animal number and individual marking by using Picric acid
Diet	**:**	Pelleted feed.
Water	**:**	Aqua guard potable water in polypropylene Bottles
Housing & Environment	**:**	The animals were housed in Polypropylene cages provided with bedding of husk.

Housing temperature	**:**	between 22°C±3°C.
Relative humidity	**:**	between 30% and 70%,
Air changes	**:**	10 to 15 per hour
Dark and light cycle	**:**	12:12 hours.
Duration	**:**	7 days.

Experimental design:

Pylorus ligated gastric ulcers in rat models were used for evaluation of anti – ulcer activity of *Lavana Dravagam*. Animals were divided into four groups, each group containing six animals as shown in Table no 11.

a. Grouping of Animals

Group I (control): received only distilled water.

Group II (Standard): received Omeprazole (50mg/kg b.w; p.o).

Group III (Test group 1): received *Lavana Dravagam* (0.02 ml/kg b.w, p.o.).

Group IV (Test group 2): received *Lavana Dravagam* (0.03 ml/kg b.w, p.o)**.**

Table no.11: Grouping of animals

S.NO	GROUPS	TREATMENT	NO.OF ANIMALS (EITHER MALE OR FEMALE)
1.	Group – I	Control	**6**
2.	Group – II	Treated with dose 1 of test drug(0.01ml/kg/p.o) and receive omeprazole	**6**
3.	Group - III	Treated with dose 2 of test drug(0.02ml/kg/p.o)	**6**
4,	Group – IV	Treated with standard drug ranitidine(0.03/kg p.o)	**6**
		Total no. of animals	**24**

*LD- *LAVANA DRAVAGAM*

b. Methodology:

Wistar albino rats weighing 160-200 grams were selected and fasted for 24 hours with water *ad libitum*. Under anaesthesia, a one-inch midline abdominal incision was made below the xiphoid process. Pyloric end of stomach was ligated without damaging its blood supply and the stomach was replaced. Then the test compound was given orally. After 4 hours, the rats were sacrificed and stomachs were dissected out. Contents of the stomach were drained into a graduated centrifuge tube and subjected to analysis for volume, pH. Stomach was opened along the greater curvature, pinned on a cork plate and its inner surface was examined.

Ulcer index (UI):

The ulcer index is calculated by the formula

$$UI = UN + US + UP \times 10^{-1}$$

Where,

UI is Ulcer Index

UN is Average number of ulcers per animal

US is Average number of severity score

UP is Percentage of animals with ulcers

Gastric volume and pH:

Gastric juice was collected from the rats. The gastric juice thus collected was centrifuged and the volume of gastric juice as well as the pH of gastric juice was noted.

Results:

The results were noted in Table no.14 and 15.

7.2 **HEMATINIC ACTIVITY**

Aim:

To study the hematinic activity activity of *Lavana Dravagam* in Wistar albino rats by Phenyl Hydrazine induced method.

Experimental design:

Phenyl Hydrazine induced in rats were used in the evaluation of hematinic activity of *Lavana Dravagam.* Animals were divided into four groups, each group containing six animals as shown in Table no.12

a.Grouping of animals

Group I (control): received only distilled water.

Group II (Standard): Received oral single dose of hematinic syrup (0.01ml/kg/p.o)

Group III (Test group 1): Phenyl Hydrazine +Received LD* Dose I (0.02ml/kg/p.o)

Group IV (Test group 2): Phenyl Hydrazine+ Received LD* Dose II(0.03ml/kg/p.o)

Table no.12: Grouping of animals

S.NO	GROUPS	TREATMENT	NO.OF ANIMALS (EITHER MALE OR FEMALE)
1.	Group – I	Control	**6**
2.	Group – II	Test Drug control -Received oral single dose of hematinic syrup (0.01ml/kg/p.o)	**6**
3.	Group – III	Phenyl Hydrazine +Received LD* Dose I (0.02ml/kg/p.o)	**6**
4,	Group – V	Phenyl Hydrazine+ Received LD* Dose II(0.03ml/kg/p.o)	**6**
		Total no. of animals	**24**

*LD- *LAVANA DRAVAGAM*

b.Methodology:

Evaluated for its haematinic activity in phenyl hydrazine (single dose of 10 mg/kg per oral for 8 days) induced anaemia. Wistar rats were grouped into six (n=6). Groups I served as normal control and disease control groups, respectively. Group II received the standard drug (haematinic suspension 2 mL/kg). GroupsIII, IV received the formulated oral indiffusible mixture of *Lavana Dravagam*at a dose of 0.02ml to 0.03ml/kg, respectively

Results:

The results were noted in Table no. 21,22

7.3 ANTI-SPASMODIC ACTIVITY

Aim:

To study the Anti- Spasmodic activity of *Lavana Dravagam* in isolated rat's ileum **Acetylcholine Induced** method.

Materials and Methods:

IAEC Number	**:**	NCP/IAEC/2021-22/12.
Test Substance	**:**	*Lavana Dravagam.*
Animal Source	**:**	Kerala Veterinary and Animal Sciences, Mannuthy, Kerala.
Animals	**:**	Wistar albino rat.
Sex	**:**	Male – 1
Body Weight	**:**	180 - 200gms.
Acclimatization	**:**	14 days prior to dosing.
Veterinary examination	**:**	Prior and at the end of the acclimatization period.
Identification of animals	**:**	By cage number, animal number and individual marking by using Picric acid
Diet	**:**	Pelleted feed.
Water	**:**	Aqua guard potable water in polypropylene Bottles
Housing & Environment	**:**	The animals were housed in Polypropylene cages provided with bedding of husk.
Housing temperature	**:**	between 22°C±3°C.
Air changes	**:**	10 to 15 per hour
Dark and light cycle	**:**	12:12 hours.
Duration	**:**	1 day.

Methodology:

Overnight fasted adult male Wistar rat weighing 180-200 g was used for the study.Wistar albino rat was sacrificed with excess Pentobarbitone sodium and abdomen was cut open and the right flexure, i.e., the subhepatic region of the colon where the ascending colon turns to become transverse colon was disscected and isolated. The isolatedcolon was mounted for tension recording and allowed to equilibrate for 45 minutes in 30 ml organ bath containing aerated normal Tyrode solution (NaCl, KCl, $CaCl_2$, $MgCl_2.H_2O$, $NaHCO_3$, NaH_2PO_4, and Glucose; pH 7.4), and the samples were maintained at 37 °C andbubbled with air. The mechanical response of the colon was recorded with frontal lever using various concentration of acetylcholine until to get sub-maximal responses. The isolated colon was incubated for 45 minutes with test compound. After 45 minutes, responseof the colon was recorded with same concentration of acetylcholine as mentioned above inthe presence of test compounds.

Results:

The results were noted in Table: 17

8. RESULT

ACUTE ORAL TOXICITY STUDY OF LAVANA DRAVAGAM:

Table11: Behavioral signs of Acute oral toxicity:

S.NO	BESERVATION	CONTROL GROUP	TEST GROUP (2 ml/kg b.wt)
1	Body Weight	Normal	Normal
2	Assessments Of Posture	Normal	Normal
3	Signs Of Convulsions	Normal	Normal
4	Ptosis	Normal	Normal
5	Stupor Reaction	Normal	Normal
6	Salivation	Normal	Normal
7	Change In Skin Color	Normal color	Normal color
8	Piloerection	Normal	Normal
9	Defecation	Normal	Normal
10	Sensitivity Response	Normal	Normal
11	Locomotion	Normal	Normal
12	Muscle Gripness	Normal	Normal
13	Rearing	Normal	Normal
14	Urination	Normal	Normal

Table 12 : Home Cage Activity

S.NO	FUNCTIONAL AND BEHAVIOURAL OBSERVATION	CONTROL GROUP	TEST GROUP (2 ml/kg b.wt)
1.	Body Position	Normal	Normal
2.	Respiration	Normal	Normal
3.	Clonic Involuntary Movement	Normal	Normal
4.	Tonic Involuntary Movement	Normal	Normal
5.	Palpebral Closure	Normal	Normal
6.	Approach Response	Normal	Normal
7.	Touch Response	Normal	Normal
8.	Pinna Reflex	Normal	Normal
9.	Tail Pinch Response	Normal	Normal

Table 13 : Hand Held Observation

S.NO	FUNCTIONAL AND BEHAVIOURAL OBSERVATION	CONTROL GROUP	TEST GROUP (2 ml/kg b.wt)
1.	Reactivity	Normal	Normal
2.	Handling	Normal	Normal
3.	Palpebral Closure	Normal	Normal behavior
4.	Lacrimation	Normal	Normal
5.	Salivation	Normal	Normal behavior
6.	Piloerection	Normal	Normal
7.	Pupillary Reflex	Normal	Normal
8.	Abdominal Tone	Normal	Normal
9.	Limb Tone	Normal	Normal

RESULTS:

The results of Acute Toxicity Study of *Lavana Dravagam* were shown on Tables 11, 12 and 13. *Lavana Dravagam* didn't show any change in general behavior, home cage activity, hand held behaviors and did not produce any toxic symptoms and during the 24 hours of oral administration and 14 days of observation. From the dose administered in acute toxicity study, the three doses 0.5, 1 and 2 ml/kg.

PHARMACOLOGICAL ACTIVITY RESULT

Antispasmodic activity of Lavana Dravagam

Animals

Wistar albino rats weighing between 180-200 g was used for the study. The animals was obtained from animal house of Kerala Veterinary and Animal Science University, Kerala, Mannuthy. On arrival, the animal was placed in the animal house of Nandha College of Pharmacy for acclimatization in a stainless cage with dried grass bedding. Animals were housed at a temperature of 24 ± 2ºC and relative humidity of 30–70 %. A 12:12 light: dark cycle was followed. All animals were allowed free access to water and fed with standard commercial pelleted rat chaw (Hindustan Lever Ltd, Mumbai). All the experimental procedures and protocols used in this study were reviewed by the Institutional Animal Ethics Committee (688/PO/Re/S/02/CPCSEA) and were in accordance with the guidelines of the IAEC (Proposal number NCP/IAEC/2021-22/12)

Antispasmodic Activity of Lavana Dravagam

Overnight fasted adult male Wistar rat weighing 180-200 g was used for the study. was mounted as previously described [Kulkarni *et al*,. 1998]. Wistar albino rat was sacrificed with excess Pentobarbitone sodium and abdomen was cut open and the right flexure, i.e., the subhepatic region of the colon where the ascending colon turns to become transverse colon was disscected and isolated. The isolated colon was mounted for tension recording and allowed to equilibrate for 45 minutes in 30 ml organ bath containing aerated normal Tyrode solution (NaCl, KCl, $CaCl_2$, $MgCl_2.H_2O$, $NaHCO_3$, NaH_2PO_4, and Glucose; pH 7.4), and the samples were maintained at 37 °C and bubbled with air. The mechanical response of the colon was recorded with frontal lever using various concentration of acetylcholine until to get sub-maximal responses. The isolated colon was incubated for 45 minutes with test compound. After 45 minutes, response of the colon was recorded with same concentration of acetylcholine as mentioned above in the presence of test compounds.

RESULT

Effect of *Lavana Dravagam* on Acetylcholine Induced Contractions in Isolated Rat Colon

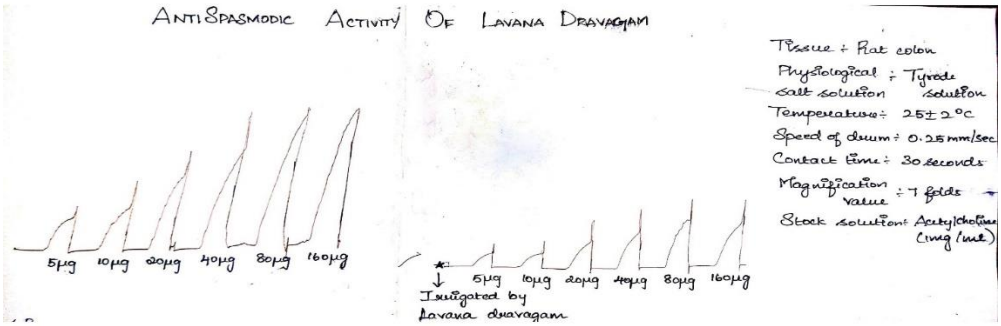
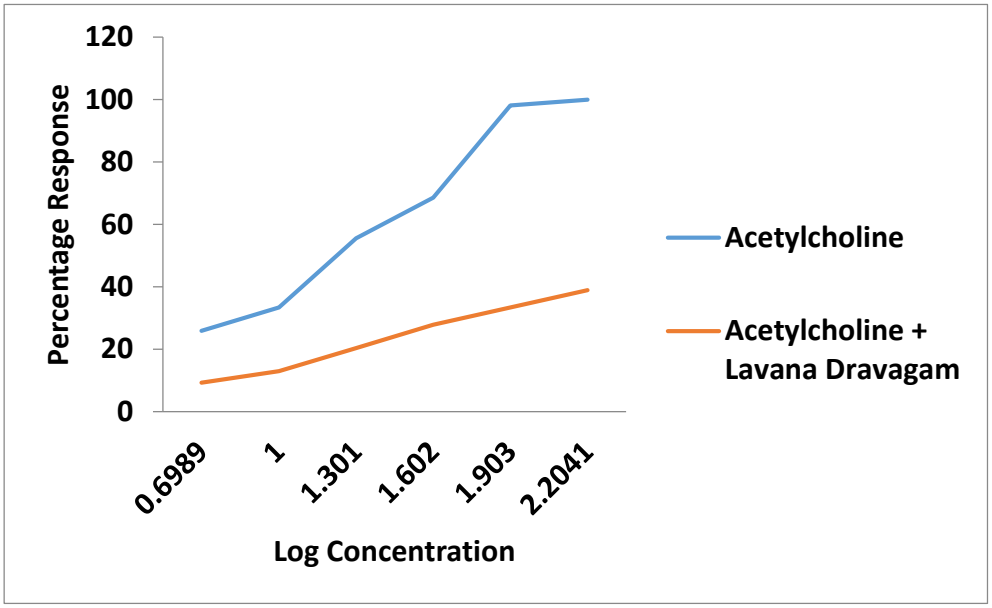


Table 17. Effect of *Lavana Dravagam* on Acetylcholine Induced Contractions in Isolated Rat Colon

S.No	Concentration of Acetylcholine (µg)	Log Concentration	Acetylcholine		Acetylcholine + *Lavana Dravagam*	
			Response (mm)	Percentage Contraction	Response (mm)	Percentage Contraction
1	5	0.6989	14	25.93	5	9.26
2	10	1.000	18	33.33	7	12.96
3	20	1.3010	30	55.56	11	20.37
4	40	1.6020	37	68.52	15	27.78
5	80	1.9030	53	98.15	18	33.33
6	160	2.2041	54	100	21	38.89

Graph 1. Effect of *Lavana Dravagam* on Acetylcholine Induced Contractions in Isolated Rat Colon



Effect of *Lavana Dravagam* on Acetylcholine Induced Contractions in Isolated Rat Colon was studied for its antispasmodic activity and log dose response curve was plotted and the results were showed in table I and Graph 1. The concentration response curve of acetylcholine was recorded, in the presence and absence of *Lavana Dravagam* using rat colon. Acetylcholine binds with cholinergic (Muscarnic) receptor present in rat colon and showed contractions in dose dependent manner. Acetylcholine in the presence of *Lavana Dravagam* showed mild contractions of colon, which may be due to blocked of muscarinic receptor. The above inhibition of muscarinic receptor by *Lavana Dravagam* indicates its antispasmodic activity.

ANTI- ULCER:

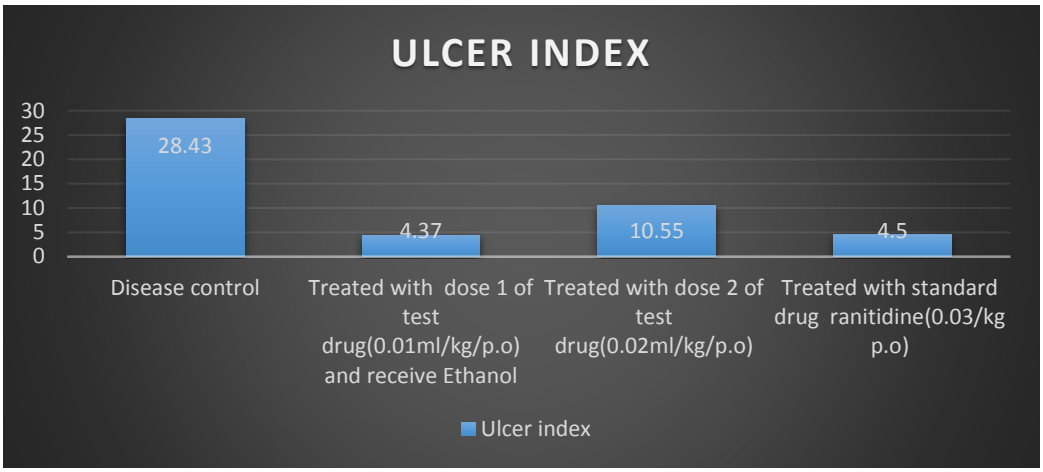
ANTI ULCER ACTIVITY OF *LAVANA DRAVAGAM* ON PYLORUS LIGATED ULCER MODEL IN RATS

Effect of *Lavana* Dravagam(LD) on Ulcer Index and % Protection in Pylorus Ligated Shay Rat Ulcer Model TABLE 18:

GROUPS	DRUG TREATMENT (p.o)	Ulcer index	% PROTECTION
Group – I	Control	28.43 ± 1.66	-
Group – II	Treated with dose 1 of test drug(0.01ml/kg/p.o) and receive Ethanol	4.37± 0.26***	**84.62**
Group – III	Treated with dose 2 of test drug(0.02ml/kg/p.o)	10.55± 1.20***	**62.88**
Group – IV	**Treated with standard drug ranitidine(0.03/kg p.o)**	**5.63± 0.23*** **	**80.18**

Values are expressed as Mean □ Standard Deviation (n=6) with one way ANOVA followed by Dunnett's test. *P<0.05, **P<0.01 and ***P<0.001 Vs Disease Control

Anti - Ulcer Activity - Mean Value of Ulcer Index in DiseaseControl and Lavana Dravagam(LD) Treated Groups of Rats:

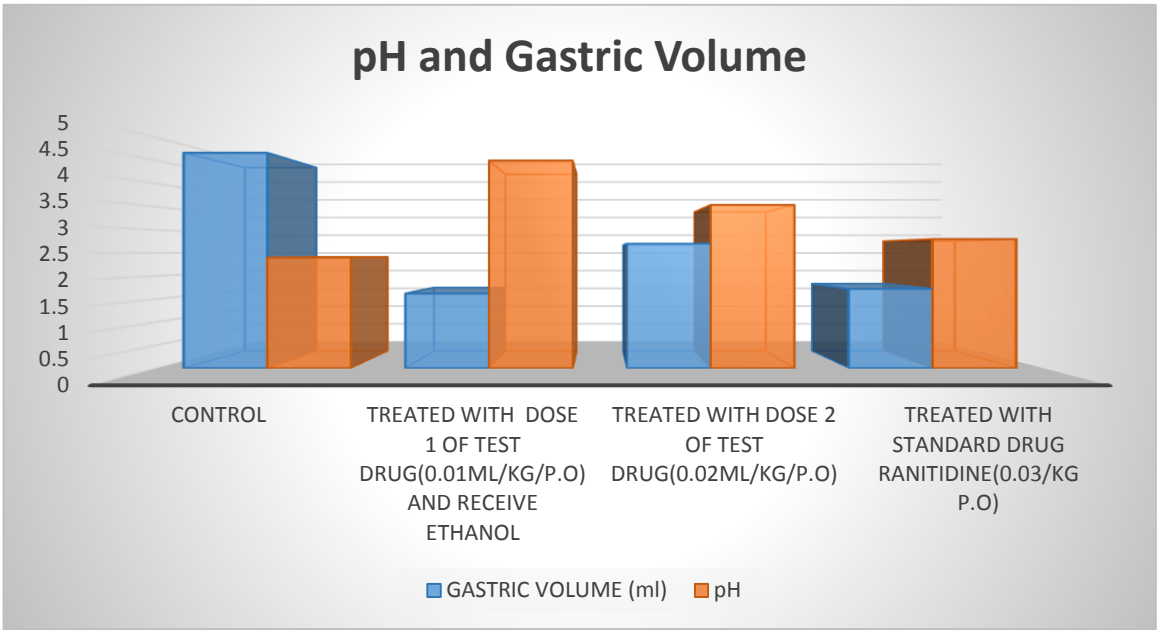


Effect of Lavana Dravagam(LD) on pH and GastricVolume in Pylorus Ligated Shay Rat Ulcer Model TABLE 19:

GROUPS	DRUG TREATMENT (p.o)	GASTRIC VOLUME (ml)	Ph
Group – I	Control	4.67± 0.23	**2.40± 0.20**
Group – II	Treated with dose 1 of test drug(0.01ml/kg/p.o) and receive Ethanol	1.62± 0.02***	**4.50± 0.22****
Group – III	Treated with dose 2 of test drug(0.02ml/kg/p.o)	2.70± 0.20**	**3.54± 0.12***
Group – IV	**Treated with standard drug ranitidine(0.03/ kg p.o)**	**1.72± 0.04*****	**4.70± 0.24****

Values are expressed as Mean □ Standard Deviation (n=6) with one way ANOVA followed by Dunnett's test. *P<0.05, **P<0.01 and ***P<0.001 Vs Disease Control

Anti - Ulcer Activity - Mean Value of Gastric Volume and pHin Disease Control and *Lavana* Dravagam(LD)Treated Groups of Rats

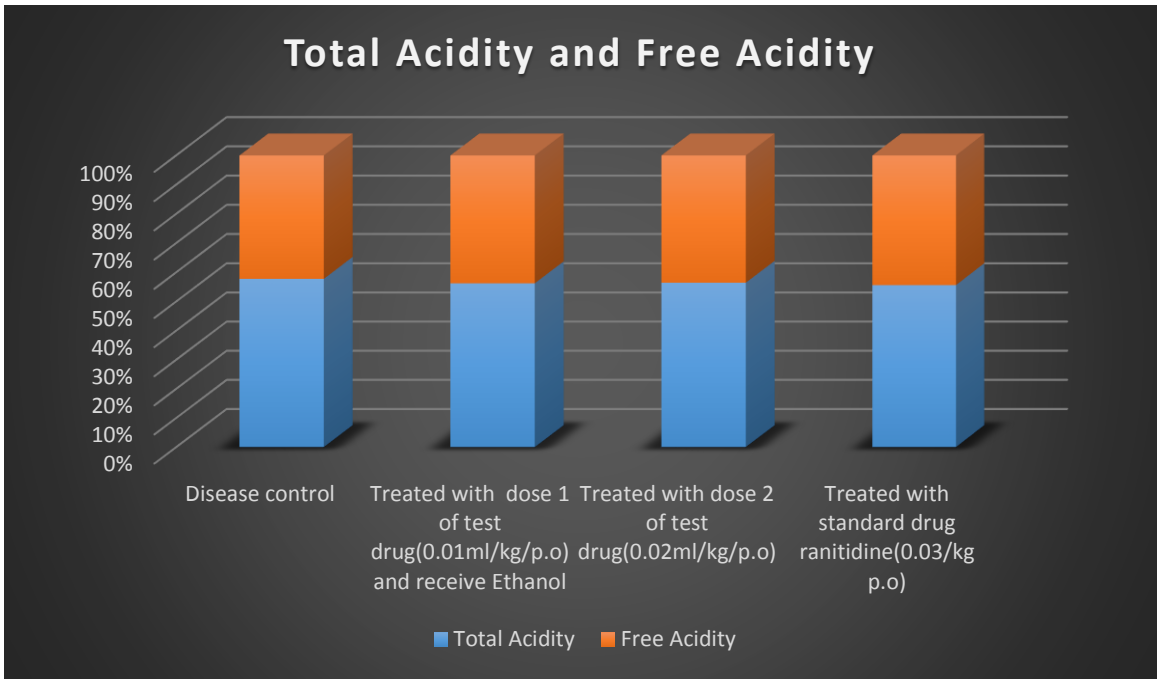


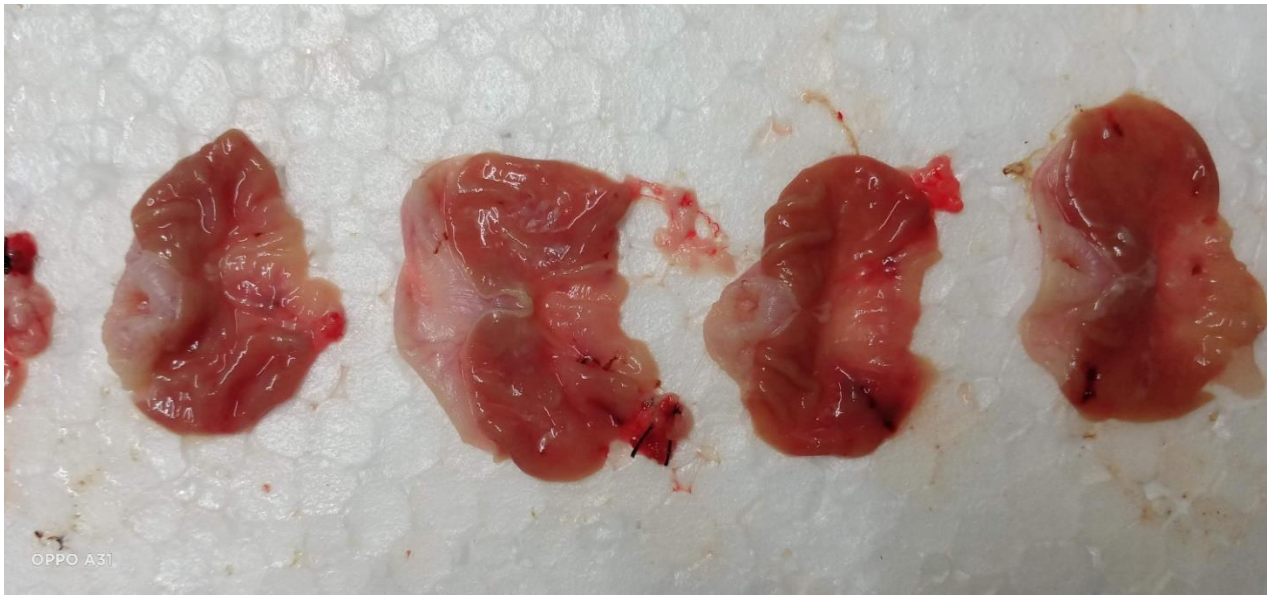
Effect of Lavana Dravagam(LD) on Total Acidity andFree Acidity in Pylorus Ligated Shay Rat Ulcer Model TABLE : 20

GROUPS	DRUG TREATMENT (p.o)	TOTAL ACIDITY	FREE ACIDITY
Group – I	Control	85.63± 2.77	**62.58± 1.11**
Group – II	Treated with dose 1 of test drug(0.01ml/kg/p.o) and receive Ethanol	36.78± 1.98***	**28.61± 2.03*** **
Group - III	Treated with dose 2 of test drug(0.02ml/kg/p.o)	56.22± 2.55**	**43.40± 1.20***
Group – IV	**Treated with standard drug ranitidine(0.03 /kg p.o)**	**39.42± 2.62*** **	**31.45± 1.70*** **

Values are expressed as Mean □ Standard Deviation (n=6) with one way ANOVA followed by Dunnett's test. *P<0.05, **P<0.01 and ***P<0.001 Vs Disease Control.

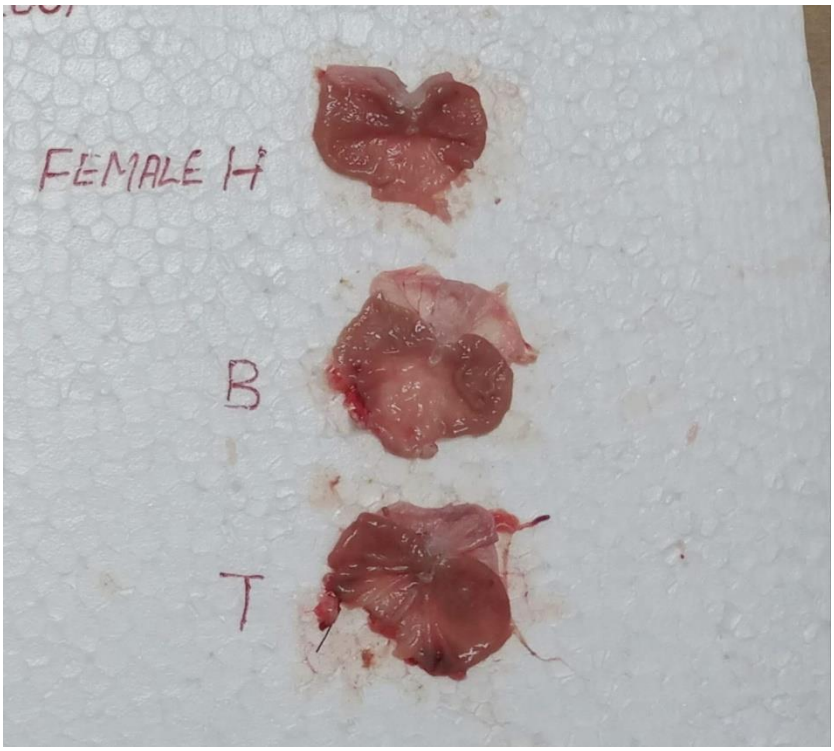
Anti - Ulcer Activity - Mean Value of Total Acidity and Free Acidityin Disease Control and Lavana Dravagam(LD) Treated Groups of Rats





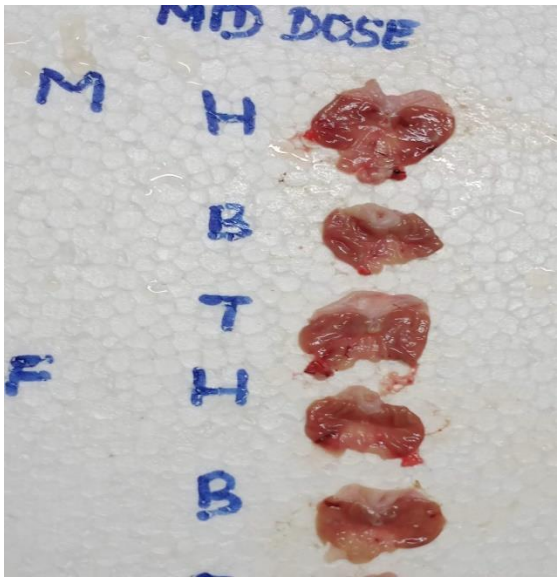
CONTROL GROUP

ANTI-ULCER ACTIVITY

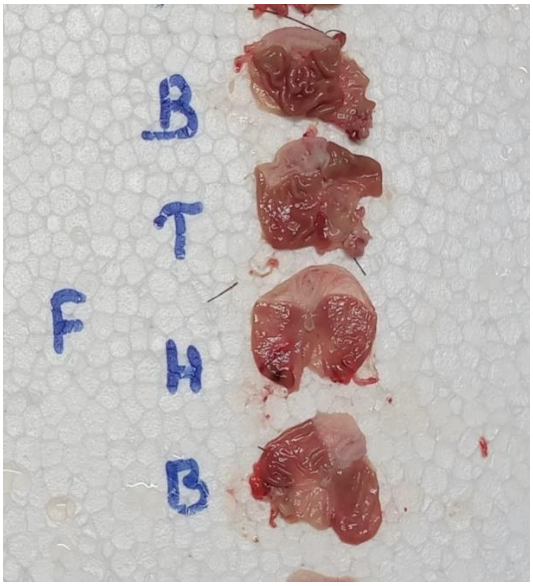


ANTI-ULCER ACTIVITY **STANDARD GROUP**

a



TEST DOSE I



TEST DOSE II

RESULTS:-

- The Anti-Ulcer property of the test drug *Lavana Dravagam* (LD) was studied using Pylorus ligation rat ulcer models.
- The rats were ligated at the pyloric end under anaesthesia after 1 hour of drug administration. Then the rats were sacrificed after 4 hours. The stomach was dissected and the gastric contents were collected for further determination of pH, Gastric volume, Total acidity and Free acidity.
- Table 19 shows the effect of test drug LD on Ulcer Index and Percentage Protection of ulcers in Pylorus ligated rats. From the values it is clear that the ulcer index was reduced and it is extremely significant (P<0.001) in Test Dose IIof LD (0.03/kg p.o) when compared to the disease control group of rats. The percentage protection is also extremely significant when compared to the standard drug.
- Table 20 shows the gastric volume and pH of the gastric juices collected from the ligated stomach. The gastric volume was significantly reduced (P<0.001) when compared to the disease control group and the pH was also increased significantly (P<0.01) in Test Dose II of LD (0.03/kg p.o) group of rats when compared to the disease control group.
- While analyzing the total and free acidity there was a significant (P<0.001) decreasein acidity of the Test dose II of LD (0.03/kg p.o) treated groups when compared to the disease control groups.

After Pylorus ligatio

HEMATINIC ACTIVITY

Hematological findings of Hb concentration (g/dl), RBC count (million cells/c.mm) and PCV, MCV, MCH, MCHC after 8 days treatment with Phenyl hydrazine

TABLE 21:

Blood parameter	Group-I (Anaemia control)	Group-II (Standard)	Group-III **(0.02ml/kg/p.o)**	Group-IV **(0.03ml/kg/p.o)**
Hb (g/dl)	09.7±0.24**	10.26±0.31**	10.77±0.64**	11.49±0.35**
PCV	37.74±2.31**	38.16±2.75**	40.12±1.83*	42.11±2.24
RBC ($\times 10^6$/ml)	4.48±0.21**	4.59±0.37**	4.50±0.23**	4.72±0.19*
MCV(fl)	83.34±3.2	87.40±3.58*	81.45±0.10**	80.14±3.14
MCH (pg)	25.26±1.28	31.22±2.48**	28.16±1.61*	30.20±1.10**
MCHC (g/dl)	33.10±0.3	31.08±2.21	35.01±0.23	36.60±1.45

Effect of Hb concentration (g/dl), RBC count (million cells/c.mm) and PCV, MCV, MCH, MCHC after 8 days treatment with Phenyl hydrazine

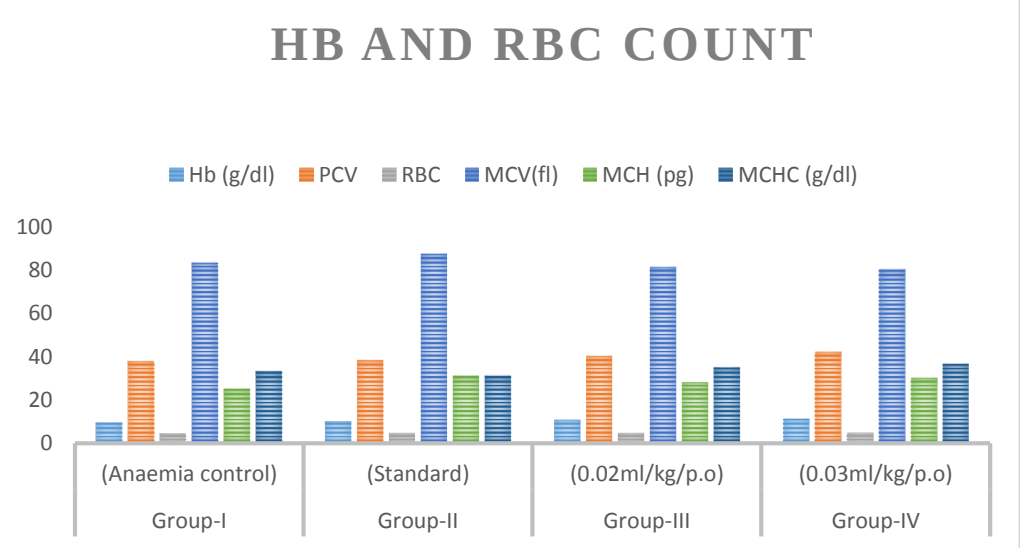


TABLE 22:

Haematological findings of Hb concentration (g/dl), RBC count (million cells/c.mm) and PCV, MCV, MCH, MCHC after 8 days treatment with *Lavana Dravagam*

Blood parameter	Group-I (Anaemia control)	Group-II (Standard)	Group-III (AGD-0.5ml/kg)	Group-IV (AGD-1 ml/kg)
Hb (g/dl)	11.2±1.5	12.45±1.41**	11.98±0.46	12.47±1.24
PCV	39.41±2.5	48.25±2.31**	45.23±2.21	46.34±2.3
RBC ($\times 10^6$/ml)	4.24±0.51	6.43±1.01**	5.15±0.27	5.33±0.12
MCV(fl)	72.45±2.41	75.37±2.51	76.12±1.5	74.42±2.50
MCH (pg)	28.11±1.45	22.60±1.32*	22.23±1.4*	23.01±1.3
MCHC (g/dl)	32.11±1.14	32.14±1.3	28.67±1.7	29.66±1.3

Effect of Hb concentration (g/dl), RBC count (million cells/c.mm) and PCV, MCV, MCH, MCHC after 8 days treatment with *Lavana Dravagam*

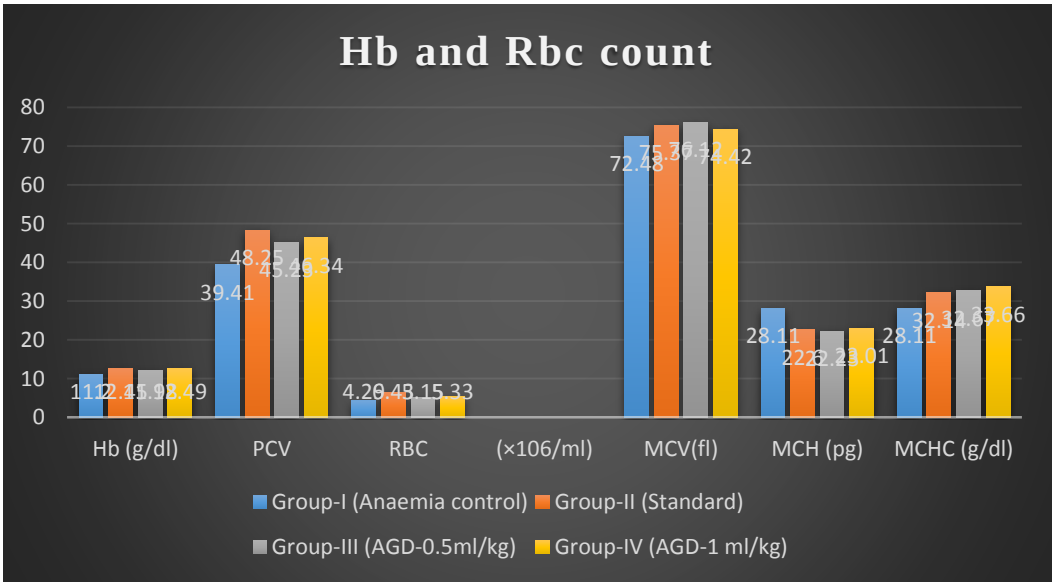
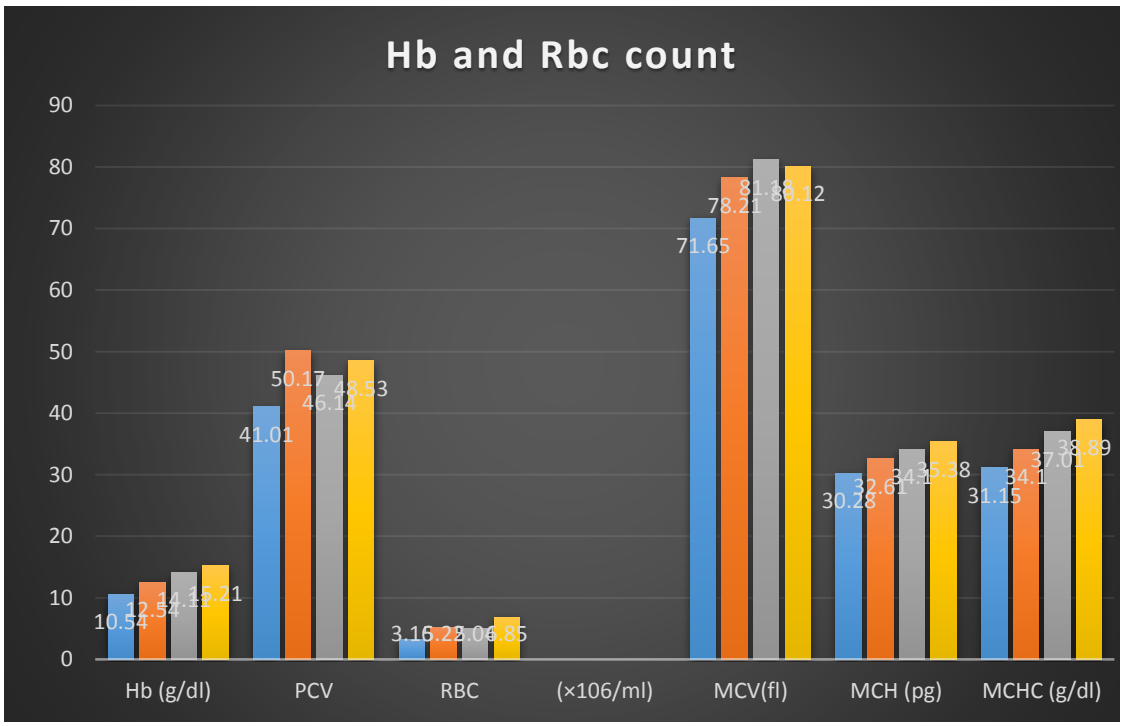


TABLE :23 **Hematological findings of Hb concentration (g/dl), RBC count (million cells/c.mm) and PCV, MCV, MCH, MCHC after 15 days treatment with *Lavana Dravagam***

Blood parameter	Group-II (Anaemia control)	Group-III (Standard)	Group-IV (AGD-0.5ml/kg)	Group-V (AGD-1 ml/kg)
Hb (g/dl)	10.54±1.14	12.54±1.25**	14.11±0.65*	15.21±0.57**
PCV	41.01±1.76	50.17±1.82**	46.14±2.03	48.53±2.1
RBC ($\times 10^6$/ml)	3.16±0.52	5.22±0.53**	5.04±0.37	6.85±0.33*
MCV(fl)	71.65±2.83	78.21±2.47**	81.18±2.41	80.12±1.62**
MCH (pg)	32.28±2.27	29.61±2.26**	30.10±1.47	28.38±1.73
MCHC (g/dl)	31.15±1.37	34.1±3.03	33.01±1.35	33.89±0.65

Effect of Hb concentration (g/dl), RBC count (million cells/c.mm) and PCV, MCV, MCH, MCHC after 15 days treatment with *Lavana Dravagam:*



RESULTS OF HEMATINIC ACTIVITY O*F LAVANA DRAVAGAM* (LD) IN WISTAR ALBINO RATS

This study aimed to evaluate the effect of *Lavana Dravagam* on the haemolytic anaemia induced by phenyl hydrazine in albino rats. There was a significant ($P<0.05$) increase in the mean Hb concentration recorded for rats in the test group 0.02ml/kg of *Lavana Dravagam* relative to that observed in the control group.

After one week of treatment, the mean total red blood cell count of rats in each of the *Lavana Dravagam* test groups (5.18 ± 0.25, $5.15\pm0.27 \times 10^6\mu L$) were observed and compared with those in the control group ($4.24\pm0.51\times 10^6\mu L$), but these difference were not significant ($P<0.05$). There was an increase in the PCV of rats in all the *Lavana Dravagam* treatment groups relative that of the rats in the control group. The increase was significant ($P<0.05$) for rats in high dose group, compared with control group. There was a slight increase observed in the mean MCV values of rats in all drug treated groups but it was not statistically significant compared to control group.

Rats in low dosed test group were observed to have decrease mean MCH value of rats in all test groups.

After 15 days treatment with *Lavana Dravagam* significantly increased almost all parameters towards normal. Hb level was 14.11 ± 0.65, for female rats 15.21 ± 0.57 g/dl for male rats respectively in 0.03 ml/kg *Lavana Dravagam* treated group. The mean RBC and Hb concentration of rats were increased, especially for rats administered the higher doses. Mean MCV values were also increased.

9. DISCUSSION:

The test drug *Lavana Dravagam* was selected from a text Kannukamy ennum vaithiya segaram. It was subjected to various studies based on the evidences like Literature collection, Physiochemical analysis, Biochemical Analysis, Instrumental Analysis, Toxicological Studies and Pharmacological activity. Acute oral toxicity studies were conducted to confirm the safety of the test drug and further Anti-ulcer activity, Hematinic activity and Antispasmodic activity were carried out to evaluate the therapeutic efficacy in anemia and Gastric ulcer.

LITERATURE REVIEW:-

The literature review was carried out in three phases like Gunapadam aspects to know about the evidences in ancient Siddha Texts; Mineralogical aspects to know physical properties and finally chemical.

DRUG ANALYSIS:-

Organoleptic Evaluation:-

- The drug *Lavana Dravagam* is a clear aqueous, non-viscous distillate. It is light lemon yellow in color with bitter and salty taste. It is odorless.
- The analysis of pH showed the acidic nature of *Lavana Dravagam*.
- These standards are also supporting the traditional quality parameters.

Biochemical Analysis:-

It showed the presence of Sulphate, Chloride, Aluminium, Ammonium, Potassium and Sodium. Iron, zinc.

Microbial Load and Heavy Metal Analysis:-

On evaluating the microbial load, *Lavana Dravagam* was free from microbes and pathogens. In instrumental analysis for heavy metals, there was no presence of any heavy metals. It indicates that the drug is non-toxic and free from any contamination.

Identification by FTIR:-

On FTIR analysis, the peaks indicated the presence of inorganic salts like potassium,sodium, boron, aluminum and halide compounds like chloride, sulfate and nitrate.

TOXICITY STUDIES:-

Acute Oral Toxicity Study:-

Lavana Dravagam was subjected to acute oral toxicity study with a dose of 2ml/kg b.wt. It didn't produce any toxic signs, changes in general and functional behaviorand mortality during the study. There were also no abnormal changes in body weight and necropsy findings of the treated group of rats. This ensures that the dosage given was below the toxic limit and confirms the safety of drug. Based on this dosage, further sub- acute and pharmacological activities were carried out.

PHARMACOLOGICAL ACTIVITY:

The test drug *Lavana Dravagam* mentioned in Siddha text Kannusamiyam ennum vaithiya segaram , page no 158 has been used for Gunmam (ulcer), Pandu (Anaemia), Soothagakkatty (Polypus uteri, internal abscess), Surakkatty (enlargement of spleen). The ingredients of this drug are *Vediuppu* **(Potassium nitrate)** Padigaram (Alum)

Saaram (Navacharam) (Ammonium Chloride) Kariuppu It possess Anti- ulcer, Anti-spasmodic, Hematinic. But the above trial drug has not so far been evaluated for its Anti-ulcer, Anti- spasmodic, Hematinic. Hence the author has chosen the drug for this study to validate its Standardization, Pharmacological (Anti- ulcer, Anti- spasmodic, Hematinic) and Analytical studies.

Anti- spasmodic activity:

Wistar albino rat was sacrificed with excess Pentobarbitone sodium and abdomen was cut open and the right flexure, i.e., the subhepatic region of the colon where the ascending colon turns to become transverse colon was disscected and isolated. The isolated colon was mounted for tension recording and allowed to equilibrate for 45 minutes in 30 ml organ bath containing aerated normal Tyrode solution (NaCl, KCl, $CaCl_2$, $MgCl_2.H_2O$, $NaHCO_3$, NaH_2PO_4, and Glucose; pH 7.4), and the samples were maintained at 37 °C and bubbled with air. The mechanical response of the colon was recorded with frontal lever using various concentration of acetylcholine until to get sub-maximal responses. The isolated colon was incubated for 45 minutes with test compound. After 45 minutes, response of the colon was recorded with same concentration of acetylcholine as mentioned above in the presence of test compounds. The concentration response curve of acetylcholine was recorded, in the presence and absence of *Lavana Dravagam* using rat

colon. Acetylcholine binds with cholinergic (Muscarnic) receptor present in rat colon and showed contractions in dose dependent manner. Acetylcholine in the presence of *Lavana Dravagam* showed mild contractions of colon, which may be due to blocked of muscarinic receptor. The above inhibition of muscarinic receptor by *Lavana Dravagam* indicates its antispasmodic activity.

Haematinic activity :

evaluated for its haematinic activity in phenylhydrazine (single dose of 10 mg/kg per oral for 8 days) induced anaemia. Wistar rats were grouped into six (n=6). Groups I served as normal control and disease control groups, respectively. Group II received the standard drug (haematinic suspension 2 mL/kg). GroupsIII, IV received the formulated oral indiffusible mixture of *Lavana Dravagam*at a dose of 0.02ml to 0.03ml/kg, respectively.

Anti- ulcer:

The present study was carried out to investigate the anti-ulcer effect of LD (0.02ml/kg, p.o and 0.03 ml/kg, p.o) in gastric ulcer. The study was carried out using pyloric ligation induced gastric ulcer in albino rats. The anti-ulcer activity of LD (0.02ml/kg, p.o and 0.03 ml/kg, p.o, for 7 days) was compared with standard drug (omeprazole 100 mg/kg, p.o). The parameters like gastric volume, pH, total acidity, free acidity, ulcer index and percentage ulcer protection were studied using this pyloric ligation method. In pyloric ligation model, there was a significant decrease in the ulcer index, gastric volume, total and free acidity in the LD treated groups. There was a significant increase in the percentage protection of gastric ulcers and pH of the gastric juice in LD treated groups when compared to the disease control groups.

10. SUMMARY:

It was indicated for *Lavana Dravagam* mentioned in Siddha text Kannusamiyam ennum vaithiya segaram , page no 158 has been used for Gunmam (ulcer), Pandu (Anaemia), Soothagakkatty (Polypus uteri, internal abscess), Surakkatty (enlargement of spleen) Hence, it is studied for Anti-Ulcer, Hematanic activity and Anti Spasmodic activity in animal models.

The literature for the ingredients of drug was done in order to reveal the uniqueness of drug. It was carried out in three aspect. Siddha aspect and Mineralogical aspect and Chemical aspect. After literature review, the drug was exposed to standardization. As a preliminary step, the drug was subjected to Physicochemical and Biochemical analysis, FTIR and Instrumental analysis was done by ICP – OES.

After collecting adequate data on standardization of the drug, it was subjected to acute toxi evaluation to ensure safety of the drug. It was done by following OECD guidelines 423 (Acute Oral Toxicity)

After assuring the safety of test drug, pharmacological studies were carried out for Anti-Ulcer activity, Hematinic activity and Anti-Spasmodic activity in animal models to explore its therapeutic efficacy.

The results of these study showed that the test drug has potent activity against anemia gatric ulcer and spasmodic pain. Thus, the drug *Lavana Dravagam (LD)* has significant medicinal values and it can be a very good drug of choice for proceeding with clinical trials in future.

11. CONCLUSION:

From the literature evidence, Biochemical analysis, Acute Toxi evaluation and Pharmacological studies, the drug *Lavana Drvagam* has Antiulcer, anti-spasmodic and Hematinic activity. It is concluded that the drug *Lavana Dravagam* can be used in the management of Gunmam (peptic ulcer) and Pandu anemia. *Lavana Dravagam* is a poly mineral siddha formulation obtained by distillation process as mentioned in the text named kannusay ennum vaithiya segaram. Based on the above studies, it is evident that the drug *Lavana Dravagam* is safe and therapeutically effective. Further clinical studies can be done to bring it as effective drug for diseases of Pandu (anemia) and Gunmam (gastric ulcer).

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Institutional Animal Ethics Committee (IAEC)

NATIONAL INSTITUTE OF SIDDHA
(An autonomous body under Ministry of AYUSH, Govt. of India)
Tambaram Sanatorium, Chennai 6000 47.

CERTIFICATE

This is to certify that the project proposal No. **NIS/IAEC-1/ 03/30092020/03** entitled "Standardization and Pharmacological screening of Anti-ulcer, Anti-spasmodic, and Hematinic Activities of Siddha formulation of *LAVANA DRAVAGAM (*LD*)*" submitted by **Dr.S.Jeeva** has been approved/recommended by the IAEC of National Institute of Siddha in its meeting held on 30.09.2020 and **30 Rats (Female 18 + Male 12)** have been sanctioned under this.

Authorized by	**Name**	**Signature /Date**
Chairperson	Prof.Dr.R.Meenakumari	30/9/2020
Main Nominee of CPCSEA	Prof.Dr.Geetha Ramesh	30/9/2020
Member Secretary	Dr.B.R.Senthilkumar	30 Sep 2020

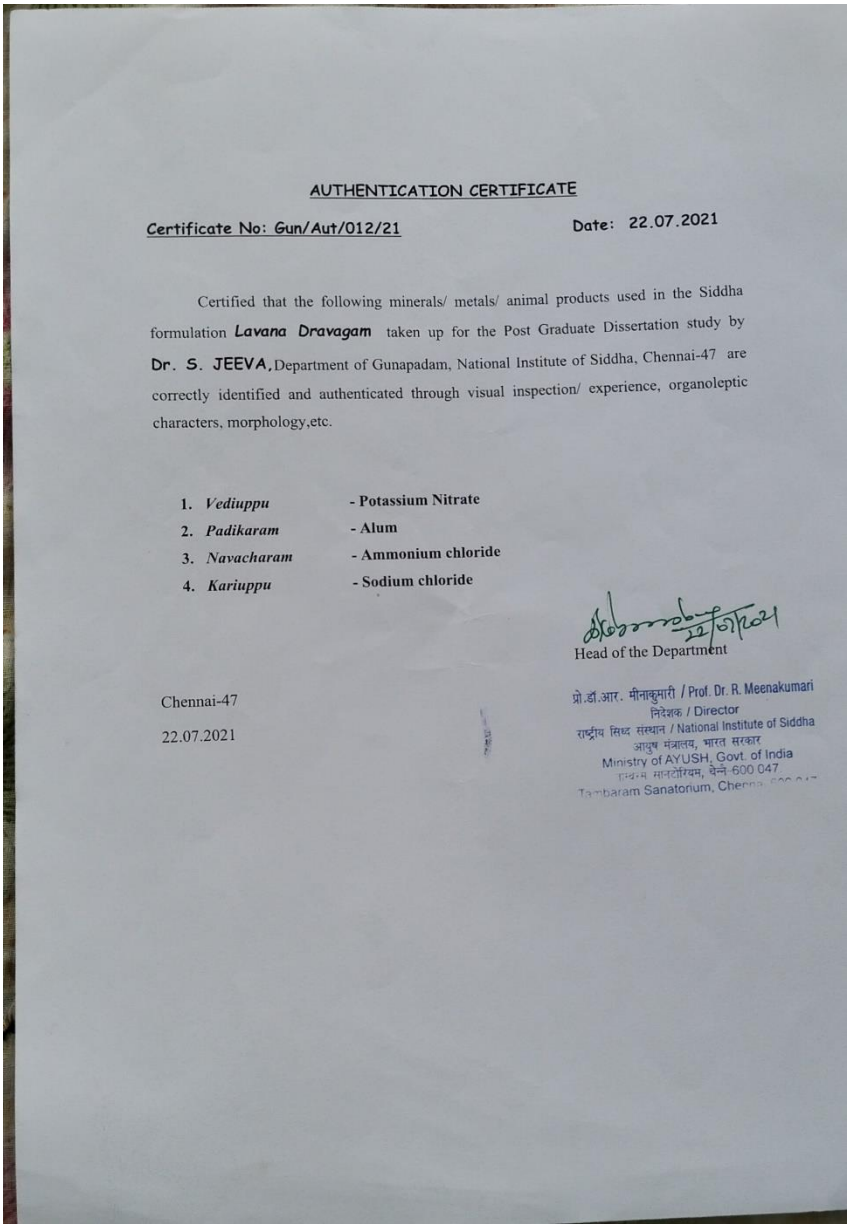
NANDHA COLLEGE OF PHARMACY, ERODE - 52
Committee for the Purpose of control and Supervision of Experiments on Animals (CPCSEA)
Institutional Animal Ethics Committee (IAEC)
Reg No: 688 /PO/Re/S/02/CPCSEA

CERTIFICATE

This is to certify that the project **Proposal No: NCP/IAEC/2021-22/12** entitled **"Standardization and Pharmacological screening of Anti-spasmodic activity of siddha formulation of Lavana Dravagam (LD)"** submitted by Dr./Mr./Ms. **S. Jeeva** has been approved/recommended by the IAEC of Nandha College of Pharmacy in its meeting held on 12/08/2021 and **Wistar Albino Rat: 1** (Number and Species of animals) have been sanctioned under this.

Authorized by	Name	Signature	Date
Chairperson	Dr. T. Sivakumar		12/8/21
Main Nominee of CPCSEA	Dr. C. Gunasekaran		12/8/21
Member Secretary	Dr. S. Sengottuvelu		12/8/21

Nandha College of Pharmacy Erode-52



AUTHENTICATION CERTIFICATE

Certificate No: Gun/Aut/012/21 **Date: 22.07.2021**

Certified that the following minerals/ metals/ animal products used in the Siddha formulation ***Lavana Dravagam*** taken up for the Post Graduate Dissertation study by **Dr. S. JEEVA,** Department of Gunapadam, National Institute of Siddha, Chennai-47 are correctly identified and authenticated through visual inspection/ experience, organoleptic characters, morphology,etc.

1. ***Vediuppu*** - **Potassium Nitrate**
2. ***Padikaram*** - **Alum**
3. ***Navacharam*** - **Ammonium chloride**
4. ***Kariuppu*** - **Sodium chloride**

22/07/2021

Head of the Department

Chennai-47

22.07.2021

प्रो.डॉ.आर. मीनाकुमारी / Prof. Dr. R. Meenakumari
निदेशक / Director
राष्ट्रीय सिद्ध संस्थान / National Institute of Siddha
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National Institute of Siddha

10/12/2021

Forwarded by Head of the Department
प्रो.डॉ.आर. मीनाकुमारी / Prof. Dr. R. Meenakumari
निदेशक / Director
राष्ट्रीय सिद्ध संस्थान / National Institute of Siddha
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The Tamil Nadu Dr.M.G.R. Medical University

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

This certificate is awarded to Dr. JEEVA.S

for participating as Resource Person / Delegate in the 34th Workshop on

"How To Do a Good Dissertation & Publish? (Research Methodology and Biostatistics)"

(Virtual mode) for AYUSH Post - Graduates & Researchers organized by the

Department of Siddha, The Tamil Nadu Dr.M.G.R. Medical University

from 26 - 07 - 2021 to 30 - 07 - 2021.

Dr.N. KABILAN
PROFESSOR & HEAD, DEPT. OF SIDDHA

Dr.M.B. ASWATH NARAYANAN
REGISTRAR

Dr.SUDHA SESHAYYAN
VICE-CHANCELLOR

NATIONAL INSTITUTE OF SIDDHA
Ministry of AYUSH, Government of India
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CERTIFICATE

Workshop on
Basic Research Techniques & Practices of Laboratory Animal Care

24 - 28 February, 2020

This is to certify that ..... Dr. S. Jeeva .....

has participated as Trainee in the Workshop on Basic Research Techniques & Practices of Laboratory Animal Care on 24 - 28 February, 2020 at National Institute of Siddha, Chennai - 47.

Dr.V.Suba	Dr.B.R.Senthilkumar	Prof.Dr.R.Meenakumari
Organising Secretary	Co - Ordinator	Chairperson / Director