Available online on 15.03.2025 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Review Article

A review on therapeutic effect of Siddha classical formulation Seenthil Chooranam.

Dr. J. Jaya Sheeba [1], Dr. K. Sivaranjani [2*], Dr. L. Santhoshkumar [1]

1. Consultant (Siddha), Siddha Clinical Research Unit, Ribandar, Goa

2. Research Officer (Siddha), Siddha Clinical Research Unit, Ribandar, Goa

Article Info:

Article History:

Received 22 Dec 2024
Reviewed 08 Feb 2025
Accepted 02 March 2025
Published 15 March 2025

Cite this article as:

Sheeba JJ, Sivaranjani K, Santhoshkumar L, A review on therapeutic effect of Siddha classical formulation Seenthil Choornam, Journal of Drug Delivery and Therapeutics. 2025; 15(3):151-160 *DOI: http://dx.doi.org/10.22270/jddt.v15i3.7024*

*Address for Correspondence:

Dr. K. Sivaranjani, Research Officer (Siddha), Siddha Clinical Research Unit, Ribandar, Goa

Abstract

Introduction: *Seenthil Chooranam* is a classical Siddha formulation composed of *Tinospora cordifolia, Eclipta prostrata*, and earthworm extract. Traditionally used in *Siddha* medicine, it is known for its diverse therapeutic applications. The modern pharmacological studies on individual ingredients suggest its potential in managing various diseases due to its bioactive compounds, which exhibit multiple medicinal properties.

Objective: The objective of this review is to analyse the pharmacological activities of *Seenthil Chooranam*, evaluate its traditional indications, and examine scientific studies supporting its medicinal applications.

Source of Data Collection: The data for this review was collected from classical Siddha texts, published research articles, pharmacological studies, and scientific databases. Relevant literature on the bioactive compounds and therapeutic applications of *Seenthil Chooranam* and its key ingredients was systematically analysed.

Summary of the Content: *Seenthil Chooranam* is known for its wide range of pharmacological properties, including anti-diabetic, antimicrobial, antioxidant, anti-inflammatory, anti-asthmatic, anti-tumor, immunomodulatory, and wound-healing effects. The active compounds present in its ingredients, such as alkaloids, flavonoids, terpenoids, and bioactive peptides, contribute to its therapeutic potential. It has been traditionally indicated for the treatment of sinusitis, diabetes mellitus, tuberculosis, cough, bronchial asthma, scrotal swelling, alopecia areata, and hair fall. Scientific studies validate its medicinal benefits, supporting its traditional use in managing various diseases.

Conclusion: This review establishes a strong correlation between Siddha textual references and modern pharmacological research, affirming the therapeutic potential of *Seenthil Chooranam*. While scientific evidence supports its medicinal applications, further research is necessary to determine its safety, optimal dosage, and clinical efficacy for widespread therapeutic use. Integrating traditional knowledge with contemporary research could enhance its acceptance in modern medicine.

Keywords: *Seenthil Chooranam, Tinospora cordifolia, Eclipta prostrata*, Earthworm, Chemical constituents, Pharmacological activity.

Introduction:

Siddha medicine is one of the oldest traditional healing systems originating in Tamil Nadu, South India. It is closely related to other systems of traditional Indian medicine but it has its own unique philosophies, practices, and therapeutic approaches. While the Siddha system has been practiced for thousands of years, it continues to be relevant in modern times, especially in India, Sri Lanka & Malaysia. It is recognized as one of the traditional systems of medicine by the Indian & Sri Lankan government, and there are institutions that teach and promote Siddha medicine.

Seenthil chooranam [1] is a classical siddha drug which is mentioned in Siddha text book, Siddha vaithya thirattu. The *Seenthil chooranam* drug review gives sound evidence for its therapeutic action mentioned in literature. The major ingredients of this drug are *Tinospora cordifolia, Eclipta proatata*, Earthworm. This review examines the pharmacological activities of each ingredient, supporting traditional claims, and focuses on literature search within that area. The search was conducted using various sources such as Siddha textbooks, journals, and internet databases.

Objectives:

1. To highlight its pharmacological properties, such as anti-diabetic, antimicrobial, antioxidant, anti-inflammatory, anti-asthmatic, anti-tumor, immunomodulatory, and wound-healing effects.

2. To analyse scientific studies that validate the bioactive components and medicinal applications of *Seenthil Chooranam*.
3. To establish a correlation between traditional Siddha references and contemporary pharmacological research, reinforcing the relevance of *Seenthil Chooranam* in modern medicine.

Data Collection Sources:

The data for this review was collected from classical Siddha texts like *Siddha Vaidya thirattu, Maruthuvam (Pothu), Agasthiyar Paripooranam 400*, published research articles, pharmacological studies, and scientific databases like PubMed, Web of Sciences, Research Gate etc. Relevant literature on the bioactive compounds and therapeutic applications of *Seenthil Chooranam* and its key ingredients were systematically analysed.

Literature Review:

Seenthil Chooranam is a Herbo–animal formulation with its reference *Agathiyar paripooranam-400*[2]. The ingredients of the *Seenthil Chooranam* are given in table1.

Table1

S.No	Tamil Name	Botanical/Zoological Name	Quantity
1.	*Seenthil*	*Tinospora cordifolia*	350 grams
2.	*Karisalai*	*Eclipta prostata*	350 grams
3.	*Poonagam*	*Eudrilus eugeniae*	350 grams
4.	*Paal*	Cow's Milk	Required Quantity

Method of Preparation

The stem of *Seenthil* is washed 21 times with pure water, then dried and mixed with cow's milk, and further dried until all moisture is completely removed. To those 350 grams of *Seenthil* stem, 350 grams of *Karisalai Chooranam* is added. *Poonagam*, when soaked in milk, releases all the soil. It is then dried, ground to powder and washed three more times in milk. After filtration, it is dried until all moisture is completely removed. Finally, 350 grams of *Poonagam Chooranam* is added to the mixture of *Seenthil Chooranam* and *Karisalai Chooranam*.

Dosage:

Verukadi alavu (1250 mg to 1500 mg[3] or a large pinch, as much as can be taken up with tips of thumb and two fingers[4])

Therapeutic Indication:

When taken with ghee cures *Megam* (Diabetes mellitus), *Eelai* (Tuberculosis), *Kasam* (Cough), *Elaippu* (Bronchial asthma), *Andavaayu* (Scrotal swelling), with Honey cures *Peenisam* (Sinusitis), *Naasi Pungal (wound* in the nose), *Kanmma Noigal*, with Sugar cures *Puzhuvettu* (Alopecia areata), *Kan thelivuv* (improves Vision)[1]

Studies on *Seenthil Chooranam*:

Macroscopic study of *Seenthil Chooranam*:

Figure 1: *Seenthil Chooranam*

Table 2: Organoleptic characters of *Seenthil Chooranam*[5]:

Colour	Yellowish Brown
Odour	Aromatic with rotten
Taste	Bitter
Texture	Fine powder
Particle size	Completely pass through sieve no 80

***Microscopical Study of Seenthil Chooranam*[5]:**

When observed under microscope, *Seenthil Chooranam* shows numerous fragments of stone cells embedded with prismatic crystals of calcium oxalate; fragments of thick walled polygonal cork cells in surface view; fragments of bordered pitted vessels; numerous simple, irregularly ovoid or elliptical shaped starch grains with concentric striations having hilum in centre and sometimes compound with 2-4 components measuring 12.2 to 51.8µ in diameter, numerous unicellular, uniseriate, warty, tubercles, pointed with basal in different sizes of trichomes; a few fragments of epidermis with anomocytic, anisocytic stomata and cicatrix; a few fragments of parenchyma cells; a few spherical shaped pollen grains with spines or warty surface; a few fragments of lignified spiral and reticulate vessels; a few fragments of non-lignified septate fibers; a few fragment of thick walled sclereid with narrow lumen and pits; a few fragments of parenchyma and annular vessels; a very few fragments of lamina with veins and vein- islets in surface view and a few entire seta[5]

Physicochemical analysis of *Seenthil Chooranam*[6]

Physicochemical analysis such as Water-soluble ash, Acid insoluble ash, Alcohol soluble extractive values, Water

soluble extractive value and Loss on drying of *Seenthil Chooranam* was studied. Results obtained were given

Table 3: Physicochemical analysis of samples of *Seenthil Chooranam*[6]

Physicochemical Parameters	Values
Water soluble ash	6.70±0.058
Acid insoluble ash	2.90±0.003
Alchol soluble extractive	9.10±0.500
Water soluble extractive	10.20±0.500
Loss on drying at 70°C	9.03±0.500

[Values are mean of three determinations ±SEM]

Phytochemical analysis of *Seenthil Chooranam* indicates the presence of Saponin, Terpenoid, lipids. Biochemical analysis of *Seenthil Chooranam* indicates the presence of calcium, starch, ferrous iron, tannic acid, unsaturated compound, reducing sugar, amino acid. FTIR data of *Seenthil Chooranam* contains alcohols, phenols, alkenes, nitriles, aromatics, alkanes, aromatic amines, alkyl halides, aliphatic amines, alkynes, carboxylic acid[6].

Pharmacological Studies on *Seenthil Chooranam*:

Alpha amylase inhibitory activity*:*

The spectrophotometric assay method was used to find alpha amylase inhibitory activity of *Seenthil Chooranam*. It was observed from the results of the present investigation that the formulation SC shown promising alpha amylase enzyme inhibition potential with the maximum inhibition of about 68.29 ± 7.362 % and the corresponding IC50 is 332.3 ± 52.41 µg /ml. Standard acarbose exhibited significant inhibition in alpha glucosidase enzyme with the maximum inhibition of about 95.96 ± 1.465 % and the corresponding IC50 is 20.61 ± 5.146 µg /ml. In conclusion, this study adds to the growing body of evidence supporting the antidiabetic properties and highlights the need for further research in this area[7].

Antidiabetic activity:

In the present study, alcohol extract of the *Seenthil Chooranam* was assessed for its anti-diabetic activity in Alloxan-induced diabetic rats. The results obtained were recorded. Three doses of alcoholic extract of the powder of *Seenthil Chooranam* were taken to study the hypoglycemic effect in 5 groups of alloxan-induced diabetic rats. It was a placebo-controlled open study where blood sugar levels were recorded daily for 5 weeks. The study showed hypoglycemic effect of the extract in the oral dose range of 100mg/kg to 300mg/ kg body weight of rats. The hypoglycemic effect was comparable to that of established anti-diabetic drug Glibenclamide in the dose of 10mg / Kg. The broad dose range of the extract producing hypoglycemic effect in diabetic rats was an interesting observation, which requires further study[8].

Hepatoprotective

Hepatoprotective activity of *Seenthil Chooranam* was studied in Wistar rats by inducing hepatic damage by administering Carbon tetrachloride (CCl_4). This study reveals that increase in the activity of the serum enzymes SGOT, SGPT and ALP were detected in mouse treated with CCl4 (Group II). However, the activities of these serum enzymes were significantly ($P < 0.001$) lower in rats treated with *Seenthil Chooranam* (Group 3 and 4) than in Group 2. This study confirmed that both the doses of *Seenthil Chooranam* (200 and 400 mg/kg body wt.) significantly improved the liver damage induced by CCl4[9].

Antimicrobial activity

The research assesses the antimicrobial properties of *Seenthil Chooranam*. The aqueous extract demonstrated notable antibacterial effects against *Bacillus subtilis, Enterococcus faecalis, Staphylococcus aureus,* and *Klebsiella pneumonia*, in addition to antifungal effects against *Aspergillus flavus*. These results indicate that *Seenthil Chooranam* may be beneficial in the management of infections, particularly those associated with chronic inflammatory disorders[10].

Antihistamine Activity:

The study evaluates the in-vitro anti-histaminic activity of *Seenthil Chooranam* using an isolated chick ileum preparation. Results indicate a significant reduction in histamine-induced contractions, demonstrating its potential for bronchial asthma management. Biochemical analysis confirmed the presence of sulphates, starch, ferrous iron, amino acids, and unsaturated compounds, supporting its pharmacological efficacy. The study concludes that *Seenthil Chooranam* has promising anti-histaminic properties, warranting further in-vivo investigations[11].

Anti-obesity and Antioxidant Property

The study investigated the anti-lipase and antiradical activities of *Seenthil Chooranam* decoction. The phytochemical constituents were screened, and the decoction showed superior antiradical activity compared to standard ascorbic acid. The decoction also showed the highest percentage of lipase inhibition (82.3%), with coefficients of determination greater than 0.95. The results suggest potential for plant-based pancreatic lipase inhibitors as potential anti-obesity therapeutics[12].

Anti-asthmatic activity

The study evaluated the anti-asthmatic activity of classical Siddha formulation *Seenthil Chooranam* using in-vivo methods. Results showed *Seenthil Chooranam* has potent broncho dilator properties, significant mast cell stabilizing activity, and a dose-dependent decrease in leukocytosis. These findings support *Seenthil Chooranam*'s traditional claims as a potent inhibitor of mast cell degranulation and bronchodilator, potentially aiding asthma management[13].

Toxicity Study

The repeated 90 days oral toxicity study on rats for *Seenthil Chooranam* were conducted. All animals from the treated dose survived throughout the dosing period of 90 days. Animals from treated groups and control group shows overall weight gain throughout the study period of 90 days. The quantity of food taken by the animals from different dose groups and the control group is comparably normal.

The haematological results show no significant changes in the values when compared to control group. The biochemical results revealed that, there were no significant changes in the values of different parameters with that of the control group. But sugar levels were reduced significantly when compared to the control group, other values were within the normal biological and laboratory limits.

At the end of the study gross pathological examination of animals in control group and treated groups did not reveal any abnormalities. The vital organs such as liver, heart, kidneys, lungs and brain from the test group did not reveal any abnormal macroscopic changes. Gross pathological investigation was carried out and histopathology of vital organs revealed normal histological appearance when compared with the control group[14].

Studies on individual ingredients

Tinospora cordifolia

***Chemical constituents of* Tinospora cordifolia**

Tinospora cordifolia contains several essential bioactive constituents categorized into terpenoids, alkaloids, lignans, steroids, and other compounds. The terpenoids include tinosporide, furanolactone diterpene, furanolactone clerodane diterpene, furanoid diterpene, tinoporaside, ecdysterone, makisterone, and various glucosides such as poly acetate and phenylpropene disaccharides. Additional terpenoid components are cordifoliosides A, B, C, D, and E, tinocordioside, cordioside, palmatosides C and F, sesquiterpene glucoside tinocordifolioside, and sesquiterpene tinocordifolin.

The alkaloid group consists of tinosporaine, magnoflorine, berberine, choline, jatrorrhizine, 1,2-substituted pyrrolidine, along with alkaloids like palmatine, bebeerine, tembetarine, and choline.

The lignans present include 3-(4,4-dihydroxy-3-methoxybenzyl)-4-(4-hydroxy-3-methoxybenzyl).
Steroidal compounds such as giloinsterol, β-sitosterol, and 20α-hydroxy ecdysone are also identified. Other significant constituents include giloin, tinosporan acetate, tinosporal acetate, tinosporidine, heptacosanol, octacosanol, sinapic acid, tinospanone, and two phytoecdysone compounds found in immunologically active arabinogalactan[15].

Anti-Diabetic Activity

Tinospora cordifolia's active components, including flavonoids, saponins, cardiac glycosides, tannins, steroids, and alkaloids, have shown potential in treating diabetes mellitus.

The present study assesses the antidiabetic activity of *Tinospora cordifolia* in alloxan-induced diabetic albino rats and compares it with the standard drug glibenclamide. Results indicated that *Tinospora cordifolia* possesses dose-dependent hypoglycemic activity, where at higher doses of 400 mg/kg, it was comparable to glibenclamide. The results suggested that *Tinospora cordifolia* could be a promising therapeutic agent for type 2 diabetes mellitus[16].

The anti-diabetic and hypolipidemic effects of *Tinospora cordifolia* ethanolic extract are examined in a study by Lohitasu et al. in albino rats with diabetes induced by alloxan. The extract demonstrated dose-dependent effects similar to those of glibenclamide, significantly lowering blood glucose and improving lipid profiles. According to the results, *Tinospora cordifolia* may be used therapeutically to manage diabetes by reducing cholesterol and blood sugar levels[17].

Patel et al studied the hypoglycemic effects of the isoquinoline alkaloid-rich fraction (AFTC) of *Tinospora cardifolia* in vitro and in vivo. AFTC and its alkaloids (palmatine, jatrorrhizine, and magnoflorine) demonstrated insulin-mimicking and insulin-secreting properties in pancreatic β-cell lines and rat hepatocytes. In glucose-loaded rats, AFTC significantly reduced serum glucose levels and increased insulin secretion, suggesting its potential role in managing postprandial hyperglycemia. The findings support the traditional use of in diabetes treatment *Tinospora cardifolia*, highlighting its insulinotropic and gluconeogenesis inhibitory mechanisms[18].

Antimicrobial activity

Tinospora cordifolia's antimicrobial activity is assessed in the study by Nayak et al. *Tinospora cordifolia* hydrogel is prepared with various concentrations of Carbopol base. Comparable to amoxicillin, TC1 showed notable antibacterial efficacy against *E. coli* along with spreadability, pH compatibility and superior viscosity among the tested formulations. It is potential as an herbal antimicrobial agent for additional therapeutic research which was highlighted by phytochemical analysis, which attributed its antimicrobial qualities to alkaloids, sterols, glycosides and tannins[19].

Krishnadutt et al evaluates the antimicrobial properties of *Tinospora cordifolia* extracts utilizing ethanol and water as solvents. The ethanolic extract demonstrated enhanced antibacterial activity due to its elevated levels of phenolic compounds and antioxidants, exhibiting the largest inhibition zones against pathogens including *Salmonella typhi, Bacillus cereus, Bacillus subtilis,* and *E. coli.* The minimum inhibitory and bactericidal concentrations for the ethanolic extract were determined to be 62.5 µg/ml. This research highlights the potential of the plant in the development of effective herbal antimicrobials, particularly targeting drug-resistant bacteria[20].

Immunomodulatory Activity

Tinospora cordifolia is well known for its immunomodulatory activity. This research conducted by Gupta *et al* examines the immunomodulatory properties of G1-4A, a polysaccharide sourced from *Tinospora cordifolia*, in managing *Mycobacterium tuberculosis* (MTB) infection. G1-4A boosts macrophage activity, stimulates pro-inflammatory cytokines (such as TNF-α, IFN-γ), and encourages nitric oxide production through the TLR4-MyD88 signaling pathway, which reduces intracellular MTB survival. When G1-4A is combined with isoniazid, it shows improved effectiveness, highlighting its potential role as an adjunct therapy for tuberculosis[21].

This study confirms the immunomodulatory potential of *Tinospora cordifolia* through its aqueous and methanol stem extracts, which enhance immune response by modulating cytokines, nitric oxide, and macrophage activity. The plant extract demonstrated efficacy in experimental models against *Salmonella typhimurium*, viral infections, and immune-related disorders. Key bioactive compounds, including alkaloids, glycosides, and polysaccharides, contribute to its immunostimulatory effects by enhancing phagocytosis, lymphocyte proliferation, and cytokine secretion[22].

Anti-asthmatic Activity

Syed Safiullah Ghori et al. used rat models of histamine-induced bronchospasm and acetylcholine-induced contraction to observe the anti-asthmatic potential of *Tinospora cordifolia* root extract. Significant broncho dilatory, anti-inflammatory, anti-histaminic, mast cell stabilizing, and anticholinergic effects were shown by the ethanolic extract. The extract's traditional use in the treatment of asthma was supported by its comparable efficacy to the standard medication theophylline, especially at 200 mg/kg[23].

The study evaluates the anti-asthmatic activity of *Tinospora cordifolia* leaf extract in acetylcholine and citric acid-induced asthma in rats. The extract exhibited significant bronchodilator and anti-inflammatory effects, reducing asthma symptoms in a dose-dependent manner. Results suggest that *Tinospora cordifolia* could be a potential natural alternative to conventional asthma treatments. *Tinospora cordifolia* leaf extract's ability to prevent acetylcholine and citric acid-induced asthma in rats. According to Deeparani Urolagin et al, the extract demonstrated strong bronchodilator and anti-inflammatory properties, lowering asthma symptoms in a dose-dependent manner[24].

Anti-inflammatory Activity& anti-arthritic activity

Sheena Philip, et al. examined the anti-inflammatory effects of *Tinospora cordifolia* chloroform extract (CETC) in RAW264.7 macrophages and in a rat model of carrageenan-induced paw edema. CETC caused a significant downregulation of inflammatory biomarkers such as COX-2, TNF-α, and iNOS and cytokines like IL-6, IL-1β, and PGE2 without affecting COX-1, reduced p38 MAPK phosphorylation, and retained NF-κB in the cytoplasm. In vivo, CETC resulted in significant edema reduction and was found to contain stigmasterol and β-sitosterol. The extract is promising for developing anti-inflammatory drugs with minimal COX-1 inhibition[25].

The anti-inflammatory and anti-arthritic qualities of a hydro-alcoholic extract of *Tinospora cordifolia* (TCE) were noted in the study by Genu George, the extract downregulated pro-inflammatory mediators (IL-6, TNF-α, PGE2, NO) and suppressed COX-2, iNOS, and VEGF expression via the JAK/STAT pathway in LPS-stimulated macrophages. In a collagen-induced arthritis model, TCE significantly alleviated clinical arthritis symptoms and reduced serum inflammatory cytokines, confirming its potential as a therapeutic agent for rheumatoid arthritis [26].

Tinospora cordifolia extract (TCE) showed anti-arthritic properties in a rat model of RA (Rheumatoid Arthritis). In a rat model of rheumatoid arthritis, Sannegowda et al. examined the anti-arthritic properties of *Tinospora cordifolia* extract (TCE). TCE therapy reduced cartilage, bone damage and inflammation. This effect was mediated by reducing pro-inflammatory cytokines (IL-1β, TNF-α, IL-6, IL-17), IL-17-producing T cells, and chemokines like RANTES. TCE also shifted the balance of bone remodeling mediators, favoring anti-osteoclastic activity[27].

Anti-Oxidant Activity

The antioxidant potential of *Tinospora cordifolia* stem extracts is assessed by Neha Upadhyay et al., which shows a notable 56.35% free radical scavenging activity. Higher phenolic content was correlated with better antioxidant activity in the ethanolic extract when compared to the methanolic extract. According to the research, phenolic compounds support the plant's antioxidative qualities, which may lessen the effects of diseases linked to oxidative stress. These findings support the pharmacological potential of *Tinospora cordifolia* as a natural antioxidant for therapeutic applications[28].

Eclipta prostrata

The chemical constituents of **Eclipta prostrata**

The chemical constituents of *Eclipta prostrata* are distributed across various parts of the plant. The entire plant contains a diverse range of compounds, including alkaloid nicotine, alkanes, ecliptine, coumarin, wedelolactone, stigmasterol, dimethylwedelolactone-7-glucoside, ecliptal, α-formylterthienyl, triterpine, resin, glycosides, reducing sugars, β-sitosterol, flavonoids, triterpene saponin, and eclalbactin, along with α-amyrin, ursolic acid, and oleanolic acid. The roots are rich in thiophenes, heptacosanol, ecliptal, stigmasterol, hentriacontanol, and eclalbactin. The stems primarily contain wedelolactone, while the leaves are composed of stigmasterol and β-terthienylmethanol. The twigs of the plant are characterized by the presence of sterols and ecliptalbine. The seeds contain alkaloids, and the aerial parts are enriched with amyrin and luteolin-7-O-glucoside, showcasing the plant's wide phytochemical diversity[29].

The chemical constituents of the *Eclipta prostrata* include a diverse range of phytochemicals. Among the

coumestans, wedelolactone, demethylwedelolactone, and demethylwedelolactone-7-glucoside are present. Terpenoids and their glycosides comprise eclabasaponins VII–X, which are taraxastane triterpene glycosides, along with eclabasaponins I–VI from the oleanane triterpene glycoside group. Additionally, the plant contains eclabasaponins I–VI (triterpene glycosides), ecliptasaponins C and D (triterpenoid glucosides), and other triterpenoids such as α-amyrin, oleanolic acid, and ursolic acid. The sterol components include stigmasterol, daucosterol, and stigmasterol-3-O-glucoside. Various alkaloids such as verazine, ecliptalbine, and hydroxyverazarine derivatives are also present. The flavonoid profile consists of luteolin-7-glucoside, luteolin, apigenin, and orobol (isoluteolin). Among the sesquiterpene lactones, the plant contains 5-hydroxymethyl-(2,2':5',2")-terthienyl tiglate, 5-hydroxymethyl-(2,2:5,2)-terthienyl agelate, and 5-hydroxymethyl-(2,2:5,2)-terthienyl acetate. The volatile oil fraction is composed of heptadecane, 6,10,14-trimethyl-2-pentadecanone, n-hexadecanoic acid, pentadecane, eudesma-4(14),11-diene, phytol, and octade-9-enoic acid, along with other compounds such as 1,2-benzenedicarboxylic acid di isooctyl ester, (Z, Z)-9,12-octadecadienoic acid, and (Z)-7,11-dimethyl-3-methylene-1,6,10-dodecatriene. Additionally, tetramehyl-1,4,7-cycloundecatriene is found among the volatile constituents. The plant also contains saponins, including eclalbatin (a triterpene saponin) and dasyscyphin C. Polyacetylenic compounds such as α-terthienylmethanol and various polyacetylenes, including polyacetylene-substituted thiophenes, are also significant components. Phenolic acids like protocatechuic acid and 4-hydroxybenzoic acid are detected. Lastly, substituted thiophenes such as 5-hydroxymethyl-(2,2':5',2")-terthienyl tiglate, 5-hydroxymethyl-(2,2':5',2")-terthienyl agelate, and 5-hydroxymethyl-(2,2':5',2")-terthienyl acetate are also present in the plant[30].

Pharmacological activity of *Eclipta prostrata*

Anti-Diabetic Activity

Ampa Raoul et al study shows that leaf extracts from *Eclipta prostrata* can help with diabetes and healing wounds. In their experiments with Wistar rats, they found that the water-based extract lowered high blood sugar in a way that depended on the dose given. They also tested this on rats with type II diabetes caused by streptozotocin and saw good results. Moreover, ointments made from both the water and hydroethanolic extracts helped speed up the healing of wounds, with complete healing happening by day 14. This research backs up the traditional use of *Eclipta prostrata* for managing diabetes and wound care[31].

In a study by Rahman at el it was shown that methanolic extracts from *Eclipta prostrata*, along with a compound called eclalbasaponin II, have benefits for diabetes in rats that were made diabetic using alloxan. When given a dose of 300 mg/kg for the extract and 10 mg/kg for eclalbasaponin II, there was a noticeable drop in blood sugar levels, and importantly, there were no signs of liver damage. Additionally, the extract helped the diabetic rats gain weight and brought down high liver enzyme levels. This research supports the traditional use of *Eclipta prostrata* for managing blood sugar and suggests it could be useful in treating diabetes[32].

Antimicrobial activity

Prabagar et al. studies the antimicrobial potential of aqueous extracts from leaves and whole plants of *Eclipta prostrata*. The extracts exhibited narrow-spectrum antibacterial activity, mainly against *Escherichia coli*, and moderate antifungal activity, especially inhibiting the growth of *Rhizopus* and *Aspergillus*. The result suggests possible therapeutic applications in treating infectious diseases, with alcohol-based extracts offering enhanced antimicrobial activity due to better solubility of bioactive compounds[33]

Anti-inflammatory Activity

The research conducted by Arunachalam et al. investigated the anti-inflammatory effects of methanolic extract from *Eclipta prostrata* in albino Wistar rats. The oral administration of the extract at dosages of 100 and 200 mg/kg resulted in a significant dose-dependent reduction of paw edema induced by carrageenan and egg white, showing results comparable to established anti-inflammatory medications such as indomethacin and cyproheptadine. These results reinforce the traditional application of *Eclipta prostrata* in the treatment of inflammatory disorders and indicate its potential as a natural therapeutic agent[34].

Morel et al observed that methanolic extract of *Eclipta prostrata* MEEP), primarily consisting of wedelolactone (WED) and demethylwedelolactone (DMW), has demonstrated anti-inflammatory effects in acute asthma but its impact on chronic asthma remains unclear. This study investigates MEEP's effects in a chronic ovalbumin (OVA)-induced allergic asthma model in mice. The concentrations of WED and DMW in MEEP were confirmed at 5.12% and 1.04%, respectively. Male Balb/c mice underwent OVA sensitization and were treated with varying doses of MEEP alongside a control group treated with dexamethasone or saline. Observations included bronchial hyperresponsiveness, immune cell counts in bronchoalveolar lavage (BAL), and Th2 cytokine levels, with histological analysis used to assess lung inflammation. Results showed that MEEP treatment significantly reduced bronchial hyperresponsiveness, total and eosinophil counts in BAL, and IL-4 levels, while inhibiting NF-κB activation. Although MEEP at 500 mg/kg diminished IL-5 levels, IL-13 and mucus production remained unchanged. Thus, MEEP alleviated bronchial hyperresponsiveness and lung inflammation in a chronic asthma model, likely through NF-κB inhibition, supporting the traditional use of *Eclipta prostrata* in treating respiratory inflammatory diseases[35].

Anti-oxidant properties

The antioxidant and antiproliferative properties of *Eclipta prostrata* (L.) L. extract was noted by Yang. The ethyl acetate (EtOAc) extract exhibited strong free radical scavenging activity and high phenolic and flavonoid content, contributing to its antioxidant potential. In AGS,

A549 and HT-29 cancer cell lines by inducing apoptosis via modulation of apoptotic gene expression. These findings highlight *Eclipta prostrata* as a promising natural source of anticancer and antioxidant compounds[36].

Hair regenerative activity

Eclipta prostrata L. (EP), was investigated for its hair growth-promoting effects both in vivo and in vitro. In a study done by Keun-hyeun Lee et al involving C57BL/6N mice groups received either a control treatment, topical minoxidil or oral EP at low and high doses for 14 days following depilation to induce hair growth. Observations revealed that EP stimulated anagen phase induction, demonstrated by the formation of the inner root sheath and hair shaft emergence. Molecular analysis showed that EP elevated the expression of fibroblast growth factor 7 (FGF-7) while reducing FGF-5 levels. In human dermal papilla cells, EP similarly increased FGF-7 expression and activated mTOR signaling pathways. These findings suggest that EP effectively promotes hair follicle growth by modulating key growth factors[37].

Earthworm

Chemical constituents of Earthworm

Earthworms contain lumbrofebrine, terrestrolumbrlysin, lumbritin, hypoxanthine and other purines, pyrmidines, choline and guanidine. The fat of earthworm is composed of octade acids, palmitic acids, high-chain unsaturated fatty acids, linear and carbon fatty acids, branched fatty acids, phosphate, cholestrin etc. The yellow chloragenous cells and organs of Lumbricus terrestris contain large amount of carbohydrates, lipid, protein, pigments and some alkaline amino acids. The yellow pigments perhaps consist of riboflavine or its analogues (Anonymous, 1985). The tissues of Pheretima species contain large amount of microelements-Zn 59.1 µg/g, Ca 25.4 µg/g, Fe 1735.5 µg/g, Cr 10.93 µg/g, Mo 0.25 µg/g, Ca 1019.2 µg/g and Mn 1143 µg/g (Zhang, 1988). Those of *Allolobophora caliginosa* contain crude protein 57.96%, crude fat 6.53%, crude ash 21.09%, crude fibre 0.36%, N extract 14.06%. Those of Eisenia foetida contain crude protein 64.61%, crude fat 12.29%, crude ash 10.16%, crude fibre 0.27%, N extract 12.67%. Those of E. rosea contain crude protein 63.71%, crude fat 12.29%, crude ash 10.66% crude fibre 0.21%, N extract 12.67% (Zhang, 1987). The blood and body fluids of Lumbricus terrestris contain small concentration of glucose (0.01-0.05 µg/ml), considerable lipids, including 35.14% neutral fat, 41.74% glucolipid, and 23.12% phosphatide. The neutral fat consists mainly of lauric acid, oleate, myristic acid and decanoic acid.

The fatty acids of the glucolipids are decanoic acid and some short chain fatty acids. The acids of phosphatide are mainly oleate, decanoic, linoleate and behcnic acids. The proportion of unsaturated fatty acids is higher than that of neutral fatty acids and saccharides (Hu, 1980). A peptide substance exists in gut wall of Lumbricus terrestris (Kaloustain, 1986). The dormant species of *Allolobophora caliginosa* contain a protein which can hydrolyze collagen (Kaloustain, 1986). Scientists from Japan, China and Korea isolated the enzymes from earthworm gut and body fluids which can dissolve fibrin.

These enzymes have been developed as innovative medicines to treat cerebral thrombosis and myocardial infarction (Cheng, 1985). Sun (1989) reported a kind of acid antibacterial peptide, a tetra decapeptide, which has produced a disease resistant, nutrient earthworm preparation and which can be used in plant and animal production. There is also an enzyme in the earthworm body tissue, which can dissolve the earthworms after death under certain conditions (Sun, 1997). Some active enzymes occur in the yellow chloragenous cells and organs of Lumbricus terrestris in high concentrations. These include catalase, peroxidase, dismutase, â- D-glucosyl-enzyme, alkaline phosphatase and porphyrin synthetase. The body fluids of Eisenia species contains at least 18 proteins with molecular weights between 1000 and 95,000 Da. (Cheng, 1985)[38].

Pharmocological activity of Earth worm

Antimicrobial activity

Vasanthi K, et al evaluates the antimicrobial activity of earthworm (*Eudrilus eugeniae*) paste against various bacterial and fungal strains. The paste showed strong antibacterial activity against *Staphylococcus aureus* and *Klebsiella pneumoniae*, and notable antifungal activity against *candida albicans*. The value of the minimum inhibitory concentration (MIC) was found to be 200 µl which shows the ability of the paste prepared from earthworm may act as a natural source for the development of new antimicrobial agents[39].

This study by Abhishek Mathur et al demonstrates the antimicrobial activity of earthworm extracts prepared with various solvents. The 95% ethanolic extract exhibited potent antibacterial effects against *Streptococcus pyogenes* and antifungal activity against *Candida albicans*, whereas petroleum ether extract showed maximum efficacy against *Staphylococcus aureus* and *Aspergillus niger*. In contrast, the phosphate buffer extract did not exhibit any antimicrobial activity, thus, indicating that earthworm-derived bioactive compounds have the potential as novel antimicrobial agents[40].

Anti-inflammatory Activity

The anti-inflammatory activity of earthworm extract was investigated in two in vivo models - carrageenan-induced paw odema and a cotton pellet-induced granuloma pouch in rats. The extract showed marked inhibition of acute and chronic inflammation, reducing the biomarkers of oxidative stress (GSH, TBARS, SOD, catalase, etc.) and modulating the levels of pro-inflammatory cytokines (decrease TNF-α; increase IL-10). The findings show that the extract from the earthworm possesses compelling anti-inflammatory and antioxidant activities, like indomethacin[41].

Yang et al show that earthworm extract (EE) protects against silica-induced pulmonary fibrosis via Nrf2-dependent antioxidant, anti-inflammatory, and anti-apoptotic pathways. EE administration enhances lung structure and function, inhibits epithelial-mesenchymal

transition (EMT), and reduces oxidative stress and cytokine production in both in vivo and in vitro models. These findings highlight EE's potential as a therapeutic agent for silicosis, addressing oxidative damage and fibrosis progression[42].

Anti-ulcer and anti-oxidant

A comparative investigation was conducted to assess the anti-ulcerative and antioxidant properties of a paste derived from indigenous earthworms, relative to the standard anti-ulcer medication, ranitidine, using Wistar strain albino rats as subjects. The outcomes of the study indicated that administration of aspirin led to an increase in several gastric parameters, namely gastric juice secretion, total acidity, ulcer index and pH levels, resulting in a reduction of antioxidant levels. The earthworm paste also enhanced pH, decreased gastric juice volume, and reduced ulcer index. The results were more significant in rats given 160 mg/kg paste, suggesting its anti-ulcer and anti-oxidative effects[43].

Wound healing Properties

Miao He, et al studied how the earthworm extract (EE) affects the healing process of deep second-degree burn wounds. The solution of EE was given to mice, and then wound healing rate, time, and more were measured. Results showed better, faster wound healing in the EE group compared to control. EE also promoted skin wound healing by decreasing edema, suppressing fibrosis, activating angiogenesis and epithelial regeneration, inhibiting scar formation, and reducing infection risk, making it a promising healing agent for burn wounds[44].

Anti-tumor activity

Zhenhan et al investigates the antitumor effects of earthworm extract (EE) in mice implanted with S180 sarcoma tumor cells. EE administration significantly reduced tumor size in a dose-dependent manner and promoted apoptosis via Bax/Bcl-2 pathway regulation while lowering lactate dehydrogenase (LDH) levels, a biomarker of tumor invasiveness. These findings suggest EE as a potential natural anticancer agent with immunomodulatory properties and minimal hematological side effects[45].

The study by Burcu Yuksel looks into the antiproliferative and antitumor activities of earthworm extracts, especially those from *Eisenia foetida*, in different models of cancer. The aim is to show that coelomic fluid from earthworm has cytotoxic effects, induces apoptosis, and inhibits the proliferation of cancerous cells due to colon and prostate cancer. The outcome indicated that earthworm-derived bioactive compounds could be potential adjuncts in treating cancer, using a natural, less toxic protocol than those applied in chemotheraphy[46].

Conclusion

Seenthil Chooranam is a classical siddha drug with the combination of *Tinospora cordifolia, Eclipta prostrata and* Earthworm. The therapeutic indications of *Seenthil Chooranam are* Diabetes mellitus, Tuberculosis, Cough, Bronchial asthma, Scrotal swelling, Alopecia areata, Sinusitis etc. The ingredients present in *Seenthil Chooranam* has Anti-diabetic, Anti-microbial, Anti-oxidant, Anti-inflammatory, Anti-asthmatic, Anti-tumor, immunomodulator, hair regenerative and wound & burn healing activities. These activities help to treat the above-mentioned diseases. The review concluded that the drug's pharmacological action and medicinal uses were perfectly matched with each ingredient in the formulation. However, further clinical studies are required to determine its precise mechanisms of action, bioavailability, and long-term safety and efficacy.

Acknowledgement: We acknowledge Prof. Dr. N.J. Muthukumar, Director General, CCRS, Chennai for his constant support and motivation given for writing this article.

Conflict of Interest: None

Funding: None

Source of Support: None

Informed Consent Statement: Not applicable

Ethics Approval: Not applicable

References

1. Kuppusamy Mudaliar K N, Uthamarayan K S, Siddha Vaidya Thirattu, First Edition, Chennai: Dept. of Indian medicine and Homeopathy,1998;217-218

2. Vadivelu Mudaliar M, Murugesa mudaliar K S, Agasthiya Paripooranam 400, First edition, Chennai: Ganesha Printing Press, 1921;98-99

3. Matheshvaran S, Sushma S, Shankar S, Saravanadevi M D, Evaluation of phytochemical, physicochemical and biochemical analysis of Siddha polyherbal formulation Asuwathy chooranam, International Journal of Scientific Development and Research, 2023; 8(6):1773-1783

4. Meaning of Verukkadi available at https://ta.wiktionary.org/wiki/

5. Ushakanthan S, Pharmacognostical study of Seenthil chooranam: A siddha formulation, Journal of Pharmacognosy and Phytochemistry, 2019; 8(4):41-45

6. DLogadevi D, Suguna R, Qualitative and Quantitative analysis of Seenthil Chooranam, International Journal of Advanced Research in Biological Science, 2020; 7(1):102-114

7. Rohini J alias Elavarasi, Jani Antony S, Murugalakahmi R, Menaka R, Anbu N, Alpha Amylase Inhibitory Activity of Siddha Formulation Seenthil Chooranam-In Vitro Study, International Journal of Creative Research Thoughts, 2024; 12(6):840-845

8. Ramanarayana Reddy RV, Raja T A R, Uma Maheshwara Rao K, Evaluation of Antidiabetic Activity of Polyherbal Formulation Seenthil Churnam in Alloxan Induced Diabetic Rats, World Journal of Pharmaceutical Research, 2014; 3(3):4739-4746

9. Dr.Ushakanthan S, Hepatoprotective activity of Seenthil chooranam, European Journal of Biomedical and Pharmaceutical sciences 2021; 8(11): 216-223

10. Sunanna L, Manoharan A, Evaluation of Anti-Microbial Activity of Classical Siddha Medicine Seenthil Chooranam, Asian Journal of Pharmaceutical Research and Development, 2022; 10(3):24-29 https://doi.org/10.22270/ajprd.v10i3.1121

11. Thavalakshmi M, Sindhu M, Sundararajan S, In-Vitro Anti-Histaminic Activity and Qualitative Biochemical Analysis of Seenthil Chooranam - A Siddha Herbo Animal Formulation, International Journal of Science and Research, 2022; 11(5): 1953-1955 https://doi.org/10.21275/MR22527112111

12. Panneerselvam N R, An invtro study on anti-obesity and antiradical activities of siddha medicine seenthil chooranam, International Journal of Botany Studies, 2021; 6(4):983-987

13. Vijayalakshmi A, Suganya M, Giri Pankaj Kumar, Jayakumari S, Shanmugasundaram P, Bronchodilator and Mast Cell Stabilizer Effect of Siddha Formulation Seenthil Chooranam, Research Journal of Pharmacy and Technology, 2017; 10(1):252-256 https://doi.org/10.5958/0974-360X.2017.00052.X

14. Ushakanthan S, Safety Profile of Seenthil Chooranam on Repeated Dose 90 days Oral Toxicity study in Wistar Albino Rats, World Journal of Pharmaceutical Research, 2020; 9(8):101-112

15. Sharma P, Dwivedee BP, Bisht D, Dash AK, Kumar D, The chemical constituents and diverse pharmacological importance of Tinospora cordifolia, Heliyon, 2019; 5(9): e02437 https://doi.org/10.1016/j.heliyon.2019.e02437 PMid:31701036 PMCid:PMC6827274

16. Abhijith L M, Ravi K Sori, Evaluation of antidiabetic activity of Tinospora cordifolia in alloxan induced diabetes in albino wistar rats, International Journal of Basic & Clinical Pharmacology, 2018; 7(7):1382-1386 https://doi.org/10.18203/2319-2003.ijbcp20182686

17. Duppala L, Naga Ravikiran T, Madhulatha A V S, Rajendra Prasad Y, Exploration of Anti-Hyperglycemic and Hypolipidemic Activities of Ethanolic Extract of Tinospora Cordifolia (Willd)Hook Whole Plant Alloxan Induced Diabetic Rats, Journal of Drug Delivery and Therapeutics, 2015; 5(2):94-99 https://doi.org/10.22270/jddt.v5i2.1094

18. Patel M B, Mishra S, Hypoglycemic activity of alkaloidal fraction of Tinospora cordifolia, Phytomedicine:international journal of phytotherapy and phytopharmacology, 2011;18(12):1045-1052 https://doi.org/10.1016/j.phymed.2011.05.006 PMid:21665451

19. Nayak P, Sandeep DS, Mridul, Munavvara, Nafeesa F, Nafeesathu, Pankaj K, Abhishek Kumar, Screening Of Antimicrobial Activity Of Tinospora Cordifolia Hydrogel,Plant Archives, 2020; 20(2):7457-7460

20. Pratihast K, Kumar R, Bharti SK, Comparative antimicrobial activity of ethanolic and aqueous extract of Tinospora cordifolia, The Pharma Innovation Journal, 2019; 8(3):129-136

21. Gupta P K, Chakraborty P, Kumar S, Singh P K, Rajan MGR, Sainis K B, Kulkarni S, G1-4A, a Polysaccharide from Tinospora cordifolia Inhibits the Survival of Mycobacterium tuberculosis by Modulating Host Immune Responses in TLR4 Dependent Manner, PLOS one, 2016;11(5):1-22 https://doi.org/10.1371/journal.pone.0154725 PMid:27148868 PMCid:PMC4858241

22. Mahesh Shivananjappa, Vidya H R, Manasa R, Santosha D U, Shekhara Naik R, Immunomodulatory activity of Tinospora cordifolia, IP Journal of Nutrition, Metabolism and Health Science, 2022; 5(3):103-108 https://doi.org/10.18231/j.ijnmhs.2022.024

23. Ghori SS, Fathima I, Qureshi MS, Tehseen F, Evaluation of Antiasthmatic Activity of Tinospora Cordifolia root extract against ach and citric acid induced Asthmatic rats, Plant Archives, 2022; 20(2):4221-4223

24. Urolagin D, Sheshbee D, Imtiyaz AARM, Panda S, Kashyap A, Anti-asthmatic activity of Tinospora cordifolia leaves extract against ach and citric acid-induced asthma in rats, International Journal of Science and Research Archive, 2024; 12(01):586-595 https://doi.org/10.30574/ijsra.2024.12.1.0829

25. Philip S, Tom G, Vasumathi AV, Evaluation of the anti-inflammatory activity of Tinospora cordifolia (Willd.) Miers chloroform extract - a preclinical study, Journal of pharmacy and pharmacology, 2018; 70(8):1113-1125 https://doi.org/10.1111/jphp.12932 PMid:29770441

26. George G, Shyni GL, Sreelekshmi Mohan, Billu Abraham, Nisha P, Ranjith S, Rajankutty K, Raghu KG, In vitro and in vivo anti-inflammatory and anti-arthritic effect of Tinospora cordifolia via modulation of JAK/STAT pathway, Inflammopharmacology, 2023; 31(2):1009-1025 https://doi.org/10.1007/s10787-023-01155-7 PMid:36840884

27. Sannegowda K M, Venkatesha, S H, Moudgil K D, Tinospora cordifolia inhibits autoimmune arthritis by regulating key immune mediators of inflammation and bone damage, International journal of immunopathology and pharmacology, 2015; 28(4):521-531 https://doi.org/10.1177/0394632015608248 PMid:26467057 PMCid:PMC8082752

28. Upadhyay N, Ganie SA, Agnihotri RK, Sharma R, Studies on Antioxidant Activity and Total Phenolic Content of Tinospora cordifolia (Miers.) Stem Using in Vitro Models, American Journal of Phytomedicine and Clinical Therapeutics, 2013;1(8):617-627

29. Ill-Min Chung, Govindasamy Rajakumar, Ji-Hee Lee, Seung-Hyun Kim, Muthu Thiruvengadam, Ethnopharmacological uses, phytochemistry, biological activities, and biotechnological applications of Eclipta prostrata, Applied microbiology and biotechnology, 2017; 101(13):5247-5257 https://doi.org/10.1007/s00253-017-8363-9 PMid:28623383

30. Tambe Nikhil S, Bondre Kajal A, Chemical Constituents & Therapeutic Uses of Eclipta Prostrata Linn., International Journal For Multidisciplinary Research,2024; 6,(1):1-11 https://doi.org/10.36948/ijfmr.2024.v06i01.12023

31. Raoul A, Jonas MC, Rommelle SMC, Elion Itou De Garde Romaric, Diatewa Martin, Abena Ange Antoine, Antidiabetic and Wounds Healing Activities of Eclipta Prostrata (Asteraceae) Leaves, International Journal of Advanced Research, 2018; 6(12):393-398

32. Rahman MS, Rahman MZ, Begum B, Chowdhury R, Nazrul Islam SK, Rashid MA, Antidiabetic principle from Eclipta prostrata, Latin American Journal of Pharmacy, 2011; 30(8):1656-1660

33. Prabagar S, Nandakumar J, Thuraisingam S, Prabagar J, Investigation of antimicrobial activity of aqueous extracts of Eclipta prostrata, 2020; 11(1):1-6

34. Arunachalam G, Subramanian N, Pazhani G P, Ravichandiran V,Anti-inflammatory activity of methanolic extract of Eclipta prostrata L. (Astearaceae),African Journal of Pharmacy and Pharmacology, 2009; 3(3):097-100

35. Morel, L. J. F., Carmona, F., Guimarães, C. C., Moreira, L. G. Q., Leão, P. D. S., Crevelin, E. J., Batah, S. S., Fabro, A. T., França, S. C., Borges, M. C., & Pereira, A. M. S. (2024). A methanolic extract of Eclipta prostrata (L.) L. decreases inflammation in a murine model of chronic allergic asthma via inhibition of the NF-kappa-B pathway, Journal of ethnopharmacology, 2023; 318(2):116930 https://doi.org/10.1016/j.jep.2023.116930 PMid:37487966

36. Yang J, Kim J S, Kwon Y S, Seong E S, Kim M J, Antioxidant and Antiproliferative Activities of Eclipta prostrata (L.) L. Extract and Isolated Compounds, Molecules (Basel, Switzerland), 2023; 28(21): 7354 https://doi.org/10.3390/molecules28217354 PMid:37959773 PMCid:PMC10650814

37. Keun-Hyeun Lee, Dabin Choi, Seung-Il Jeong, Sang-Jun Kim, Chang Hyun Lee, Hyung-Sik Seo, Han-Sol Jeong, Eclipta prostrata promotes the induction of anagen, sustains the anagen phase through regulation of FGF-7 and FGF-5, Pharmaceutical Biology, 2019; 57(1):105-111 https://doi.org/10.1080/13880209.2018.1561729 PMid:30757935 PMCid:PMC6374973

38. Afreen S, Shaikh A, Therapeutic Uses of Earthworm - A Review, International Journal of Advanced Ayurveda, Yoga, Unani, Siddha and Homeopathy, 2020; 9(1):571-580 https://doi.org/10.23953/cloud.ijaayush.469

39. Vasanthi K, Chairman, K, Ranjitsingh A J A, Antimicrobial activity of earthworm (Eudrilus eugeniae) paste, African Journal of Environmental Science and Technology, 2013; 7(8):789-793 https://doi.org/10.5897/AJEST2013.1455

40. Mathur A, Verma SK, Bhat R, Singh SK, Prakash A, Prasad GBKS, Dua VK, Antimicrobial Activity of Earthworm Extracts, Journal of Chemical and Pharmaceutical Research, 2010; 2(4):364-370

41. Chauhan PS, Tomar J, Prasad GBKS, Agrawal OP, Evaluation of anti-inflammatory activity of earthworm (Eudrilus eugeniae) extract through animal models, International Journal of Advanced Research and Development, 2018; 3(1):283-292

42. Yang J, Wang T, Li Yan, Yao Wenxi, Ji X, Wu Q, Han L, Han R, Yan W, Yuan J, Ni C, Earthworm extract attenuates silica-induced pulmonary fibrosis through Nrf2-dependent mechanisms, Laboratory investigation; a journal of technical methods and pathology, 2016; 96(12):1279-1300 https://doi.org/10.1038/labinvest.2016.101 PMid:27775689

43. Prakash M, Balamurugan M, Parthasarathi K, Gunasekaran G, Cooper E L, Ranganathan, L S, Anti-ulceral and anti-oxidative properties of "earthworm paste" of Lampito mauritii (Kinberg) on Rattus Norvegicus, European review for medical and pharmacological sciences, 2007; 11(1):9-15

44. Miao He, Wen-Qing Xie, Guo Cheng, Wen-Ping Li, Deng-Jie Yu, Hong-Fu Jin, Zhen-Han Deng, Yusheng Li, The therapeutic effects of earthworm extract on deep second-degree burn wound healing, Annals of Palliative Medicine, 2021;10(3):2869-2879 https://doi.org/10.21037/apm-20-2393 PMid:33691441

45. Deng Z, Gao S, Xiao X, Yin N, Ma S, Li W, Li Y, The effect of earthworm extract on mice S180 tumor growth and apoptosis, Biomedicine & Pharmacotherapy, 2019;115(1):108979. https://doi.org/10.1016/j.biopha.2019.108979 PMid:31100538

46. Yuksel B, Özkan AD, A systematic review of antiproliferative and antitumour activity of earthworm extracts, Trakya University Journal of Natural Sciences, 2024; 25(1):111-120 https://doi.org/10.23902/trkjnat.1373797