THERAPEUTIC EFFECT OF SIDDHA POLYHERBAL FORMULATION ATHIMATHURA CHOORANAM FOR THE MANAGEMENT OF RESPIRATORY DISORDERS

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Abstract

Siddha system of medicine is one of the indigenous system of medicine practised in India. The Siddhars who are the exponents of this system classified the diseases on the basis of three humours *Vatha, Pitha, Kaba* and signs and symptoms. All the Siddha drugs are natural products obtained from herbs, metals, minerals and animal kingdom which are given by the Siddhar's spiritual knowledge to this society. Siddha sastric preparation *Athimathura chooranam* is a poly herbo mineral formulation and it is the safe and efficacious medicine used traditionally for the treatment of Respiratory illness. This review describes the chemical constituents, pharmacological and therapeutic uses of its ingredients thereby substantiating the traditional claims of Athimathura chooranam under scientific evidence.

Keywords: *Athimathura chooranam, Kanam,* Anti-inflammatory activity, Antipyretic activity, Antihistaminic activity.

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1. INTRODUCTION

The major cause of morbididty and mortality in developing countries are due to respiratory diseases. Upper respiratory tract infections comprises 87.5% of total acute respiratory infections morbidity. Data suggest that children could suffer from 7 to 8 episodes of upper respiratory tract infections per year until they are 5 years of age, when their immune status reaches adult level.[3] Respiratory diseases such as asthma and Chronic obstructive pulmonary disease (COPD) are one of the major causes of human mortality [5][6].Chronic obstructive pulmonary disease (COPD) is the fourth leading cause of mortality world wide and an important cause of global burden of disease.1 The traditional Siddha system of medicine (SSM) has herbal, mineral and also drugs of animal origin. It is practiced mostly in its southern part for treating various diseases including even chronic conditions.[1][2]. According to Siddha system, Kanam is referred to as group of respiratory disorders pertaining to both upper and lower respiratory tract infections [4]

Though several drugs such as steroids, β2-agonists, anticholinergics and phosphodiesterase (PDE) inhibitors have been used for temporary relief, they offer cheifly symptomatic and transient relief [8]. Moreover, their adverse effects such as deficiency in bone mineral density [7][8], cardiovascular effects [9], osteoporosis and osteonecrosis [10][11], risk of cataract [12] demands the need of new alternative approach. In the present review, we

have taken a preliminary effort to unveil the therapeutic action of the Siddha herbal formulation *Athimathura Chooranam* against respiratory diseases.

2. MATERIALS AND METHODS

An extensive survey of literature analysis was performed using traditional texts containing the ingredients of *Athimathra Chooranam* as well as from modern scientific journals using various scientific platforms and databases such as Pumed, Embase, Google scholar etc.
Literature analysis of study drug

Preparation of *Athimathura Chooranam*
The following are the ingredients of *Athimathura Chooranam*

S.No	Botanical Name	Tamil Name	Quantity
1	Glycyrrhiza glabra	*Athimathuram*	35gm
2	Elettaria cardomomum	*Elam*	35gm
3	Cinnamomum verum	*Lavangapattai*	35gm
4	Michelia champaga	*Chanpaga mokku*	35gm
5	Costus speciosus	*Kottam*	35gm
6	Zingiber officinale	*Chukku*	35gm
7	cuminum cyminum	*Nar seeragam*	35gm
8	Cyperus rotandus	*Koraikizhangu*	35gm
9	Sugar	*Sarkarai*	280gm

Preparation
The above ingredients are to be purified according to Siddha literature and fried in an iron pan until they turn to golden brown colour. Then the drugs are ground to fine powder and filtered in a mesh cloth. Finally equal quantity of sweet candy powder is added with the ingredients and stored in clean , dry and airtight container. The drug dosage 1.25-1.5 grams which may vary according to ag and honey can be used as adjuvant. The above formulation has been indicated for respiratory disorders especially in pediatric age groups.

Trihumoral theory and Siddha pharmacodynamics of Athimathura Chooranam

S.No	Ingredients	Suvai	Veeriyam	Action
1.	*Athimaduram* (*Glycyrrhiza glabra*)	Sweet	Cold property	Emollient, Demulcent, Mild expectorant, Laxative, Tonic
2.	*Elam* (*Elettaria cardomomum*)	Pungent	Hot property	Stimulant, Carminative, Stomachic
3.	*Lavangapattai* (*Cinnamom verum*)	Sweet & Pungent	Cold property	Stimulant, Carmenative, Aphrodisiac
4.	*Shanbagam* (*Michelia champaca*)	Bitter	Hot property	Demulcent, Tonic, Carmenative, Stomachic
5	*Kottam* *(Costus speciosus)*	Bitter	Hot property	Stomachic, Expectorant, Tonic, Stimulant, Diaphoretic
6	*Chukku* (Zingiber officinale)	Pungent	Hot property	Carminative, Stomachic, Sialogogue, Digestive, Stimulant, Rubefacient

7	*Nar seeragam* (cuminum cyminum)	Pungent, Sweet	Cold property	Carminative, Stimulant, Stomachic, Astringent
8	*Koraikizhangu* (Cyperus rotandus)	Pungent	Hot property	Astringent, Tonic, Stimulant,Diuretic Diaphoretic, Demulcent, Emmenagogue, Vermifuge

Trihumoural action

Athimathuram reduces the increased *Pitham* and dissolves the solidified mucous caused by *Iyam*. *Elam* pacifies *Azhal* thereby reducing cough, mucous in chest and throat infections. *Lavangapattai* removes the cough and asthma causing the body to cool down. *Shanbagam* reduces *Veppam* treating fever and nasal congestion. [13]

Pharmacological Actions Of Ingredients Of Athimathura Chooranam

Glycyrrhiza Glabra

Botanical information

G. glabra is a typical herbaceous perennial with a height of 1 m and pinnate leaves that range in length from 7 to 15 cm. The fruit is an oblong legume with a length of 2 to 3 cm and contains numerous seeds. The flowers are purple to pale white blue and are placed in a hermaphrodite inflorescence.

Due to a root-level symbiosis with bacteria from the genus Rhizobium, G. glabra can fix nitrogen and is suited for both sandy and clay soils, however it prefers wet soils. The most used component is the root, whereas the leaves are regarded as agrochemical waste.[14]

Generally it has been traditionally used for the treatment of ssthma, tonsillitis, sore throat, hyperdipsia, flatulence, epilepsy, fever, sexual debility, paralysis, coughs, stomach ulcers, heartburn, colic, swellings, rheumatism, skin diseases, acidity, leucorrhea, bleeding, hemorrhagic diseases, and jaundice[14].

Phytoconstituents

Glycyrrhiza glabra roots contain several active compounds including flavonoids, such as liquirtin, rhamnoliquirilin, liquiritigenin, prenyllicoflavone A, glucoliquiritin apioside, 1-metho-xyphaseolin, shinpterocarpin, shinflavanone, licopyranocoumarin, glisoflavone, licoarylcoumarin, coumarin-GU-12 and saponin. TPharmacologically, G. glabra and the major components of it have actions that are antibacterial, antiparasitic, antiviral, antitussive, immune-stimulating, antioxidant, anti-inflammatory, and anticancer.[14].

Uses in respiratory disorders

The tonic and expectorant properties of Glycyrrhiza glabra's roots make them beneficial for treating hyperdipsia, cough, bronchitis, and pharyngitis. [15] Glycyrrhiza glabra Linn which contains the ingredients glycyrrhizin, 18-glycyrrhetinic acid, and liquiditigenin, has anti-allergic properties that help relieve Ig E-induced allergic illnesses including dermatitis and asthma. [14] Gastric mucus production is stimulated by the semi-synthetic chemical carbenoxolone, which is produced from glycyrrhiza. The demulcent properties of licorice are a result of glycyrrhizin. Liquiritin apioside, an active ingredient found in liquorice's methanolic extract, prevents capsaicin-induced coughing. [14]

Antimicrobial activity

Licochalcone E, which is found in G. glabra, may be employed in the chemical synthesis of new anti-S. aureus compounds, therefore lowering toxin production in methicillin-sensitive and methicillin-resistant S. aureus. One of liquorice's most potent components, liqueritigenin, has shown that it can protect human lung cells (A549) against haemolysin-mediated damage by reducing the formation of haemolysin. Similar antibacterial action against S. aureus has been demonstrated by glabrin and glycyrrhetinic acid. G. glabra's ability to combat Mycobacterium tuberculosis shows that glabridin, not hispaglabridin B, is the active ingredient in this process. Licoisoflavone and

licochalcone A were previously recognised as the antitubercular phenolic compounds. [16]

Antifungal activity
The methanolic extract of liquorice has fungicidal action against Arthrinium sacchari and Chaetomium funicola, according to G. glabra's antifungal activity, and glabridin was identified as the active ingredient responsible for the results. Liquiritigenin, liquiritin, licochalcone A, and glabridin, crude methanolic extract of G. glabra is prone to having antifungal action against Aspergillus niger and Candida albicans. The compounds licoflavanone and glabridin have therapeutic promise against C. albicans oral infections. [16]

Anti-viral activity
Glycyrrhizin, which impacts cellular signalling pathways including protein kinase C, casein kinase II, and transcription factors like activator protein 1 and nuclear factor Kb, was tested for its antiviral effectiveness against the severe acute respiratory syndrome virus. Furthermore, inducible nitric oxide synthase expression and nitric oxide production in macrophages are upregulated by glycyrrhizin and its aglycone, 18-glycyrrhetinic acid. [16]

Glycyrrhetinic acid-containing oral liquorice formulations are used to treat viral diseases such viral hepatitis and the common cold. Roots of G. glabra have been shown to contain triterpenoid saponins that have antiviral action. Thus, in hen embryos, these saponins prevent the development of influenza A virus. [14]

Elettaria Cardomomum
Botanical information
Elettaria cardamomum (L.), a perennial herbaceous plant that belongs to the Zingiberaceae family, with leaves that are lance-shaped, acuminate, and 30-35 cm long and broad. [17][18]

Phytoconstituents
Polyphenolic substances such gallic acid, tannic acid, caffeic acid, and 4.5-dicaffeoyl quinic acid have been found in cardamom extract. Epicatechin, vanillin, p-coumaric acid, trans-ferulic acid, and ellagic acid are all found in cardamom ethanol extract. Essential oil of cardamom capsules possess predominantly monoterpene constituents, such as 1,8- cineole, α-pinene, α-terpineol, linalool, linalyl acetate and nerolidol and the ester constituent α-terpinyl acetate, all of which have therapeutic benefits including antioxidant, anticancer, antidiabetic, anti-inflammatory, antifungal, antiviral and gastroprotective activities. According to recent findings, cardamom's flavonoids, terpenoids, anthocyanins, alkaloids, and other phenolic compounds are utilised to treat conditions related to the heart, lungs, kidneys, and blood vessels.[19]

Traditionally it is used in the treatment of asthma, teeth and gum infections, digestive and kidney disorders, cataracts, cardiac disorders, nausea, and diarrhoea, bronchitis, carminative, cold, cough, congestion of lungs, diuretic, kidney disorders, teeth and gum infections, urinary and pulmonary tuberculosis and irritation of eyelids, bladder infections, constipation, stomach ache, and dysentery in children are among the conditions it is traditionally used to treat. It is also used in the production of some plant -based hand creams and soaps.[17].

Uses in Pediatric respiratory disorders.
Due to their apneic effects, 1,8-cineole-rich essential oils like Elettaria cardamomum (cardamom) shouldn't be used on children under the age of ten. In the treatment of respiratory diseases like asthma, 1,8-cineole has anti-inflammatory effects on the airways. This is because corticosteroid medication is being reduced as a result of the suppression of cytokines via the arachidonic acid route. [20]

Uses in respiratory disorders-
The seeds can be used to treat hyperdipsia, halitosis, asthma, and bronchitis. Strong diuretic, stomachic, carminative, fragrant, and stimulating. The essential oil found in the seeds is what gives them their qualities. [18]

Using a biochemical experiment, the preventive effect of E. cardamom against pan masala-induced lung injury in male Swiss mice was assessed. In the pan masala treated mice, cardamom therapy resulted in minor lung congestion and practically no medullary haemorrhage. Furthermore, when the treatment groups were exposed to just cardamom during amelioration, enzymatic activity drastically

reduced and the levels practically reached the control [17]

A poor immune system is one of the primary causes of COVID-19 sequelae such pneumonia, asthma, and death in infected individuals, according to studies on SARS-CoV and COVID-19. A number of respiratory disorders with symptoms like COVID-19 have been found to be improved by the anti-inflammatory and immunostimulating characteristics of Elettaria cardamom. The juice prepared from cardamom (Elettaria cardamomum), cinnamon (Cinnamomum verum), and other components including bay leaves, cumin, black pepper, and clove was taken orally and its vapour was inhaled for symptoms like sore throat, dry cough, loss of taste or smell, diarrhoea, weariness, etc.[21]

Bronchodilatory action

Given its well-known pharmaceutical usage for treating asthma, cardamom prevented mice under anaesthesia from experiencing bronchospasm that was induced by carbachol. In isolated tracheal tissues, the cardamom crude extract relaxed contractions brought on by K + and carbachol. The inhibitory activity of cardamom crude extract against the two spasmogens suggests a general tracheaorelaxant action, mediated by a mechanism akin to a Ca++channel blocker. Since Ca++ antagonists are known to be useful in treating asthma, the existence of such activity as seen in this study may help to explain why cardamom is used as a medication to treat hyperactive airways. Due to the flavonoids' well-known bronchodilator properties, cardamom's inclusion of this class of chemicals is believed to contribute to the herb's ability to relax the airways.[22]

Antimicrobial activity

Cardamom plant essential oil extract has antibacterial properties and inhibits certain significant pathogenic pathogens, including *Escherichia coli, Staphylococcus aureus, and Bacillus cereus*. The cardamom plant's fruit and seeds were efficient against *Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, Fusobacterium nucleatum, and Prevotella intermedia* bacteria. After researching the cardamom plant's antibacterial and antifungal properties, it was found that the essential oil, as well as the oleoresins of methanol, ethanol, chloroform, and diethyl ether, had a broad range of antimicrobial activity against *Aspergillus terreus, Fusarium graminearum, Penicillium purpurogenum, and Penicillium madriti* fungi strains, as well as various gram positive *S. aureus and B. cereus* and negative *E. coli and Salmonella typhi* bacterial strains. As a consequence of these research, it is evident that the cardamom plant's essential oil extract and other extracts have a potent antibacterial impact on gramme positive and gramme negative bacteria and fungal strains. *S. aureus* being the most susceptible strain to the cardamom seed extract.[23]

The primary chemical component of *Elettaria cardamom* essential oil, 1,8-cineole monoterpene, exhibits antibacterial action against respiratory tract diseases. Effective antibacterial and antifungal effects against S. aureus, P. aeruginosa, S. pneumoniae, and C. albicans have been demonstrated. Staphylococcus aureus, a bacterium linked to respiratory tract infections, has been treated with a combination of antibiotics (Ciprofloxacin, Amoxicillin) and *Elettaria cardamomum* essential oil.[20]

Antiviral activity

A number of RNA (ssRNA/dsRNA) and DNA (ssDNA/dsDNA) viruses were resistant to the antiviral effects of Elettaria cardamomum. [21]

Cinnamomum Verum

Botanical information

The tropical evergreen shrub Cinnamomum zeylanicum has thick, smooth, reddish-brown bark and can reach heights of 6 to 8 metres. Glabrous, ovate and lanceolate, hard and coriaceous are the characteristics of the opposite or sub-opposite leaves [24]

Phytoconstituents

A number of resinous substances, including cinnamaldehyde, cinnamate, cinnamic acid, and several essential oils, may be found in cinnamon. Chemical elements are extracted from the plant's bark, leaves, fruits, buds, and stalks. Eugenol is mostly prevalent in cinnamon leaves, however methyl, ethyl cinnamate, and -ylangene are also detected in the leaf oil. In addition, the bark oil and root-bark oil of

cinnamon contained benzyl benzoate and terpinen-4-ol, respectively. Cinnzeylamine and Cinnzeylanol, two new compounds, were found in the dry bark of C. zeylanicum. P-cymene and eugenol were found in the oil of C. zeylanicum leaves after analysis.[24]

General traditional uses
Its wood is used to create plywood, cabinets, furniture, and other items. One of the most popular spices is true cinnamon, which is produced from the bark of the Cinnamomum verum tree. Among other things, cinnamon possesses antifungal, antibacterial, antitermitic, larvicidal, nematicidal, and insecticidal properties. The Vata and Pitta forces in the body are balanced by this plant. It lessens the discomfort of menstruation. According to a research, drinking a cup of warm cinnamon water every day can help women get temporary relief from menstrual pain. [24]

Uses in respiratory disorders
Cinnamomum verum soothes headaches, flu, the common cold, and sore throats. It functions as an expectorant and also possesses antitubercular qualities. To treat cough and influenza, Cinnamomum zeylanica essential oil is utilised.[24]

Anti allergic activity
The bark of *Cinnamomum verum* has an anti-allergic and expectorant effect and is helpful for halitosis, asthma, and bronchitis. Anorexia, inflammations, abdominal discomfort, toothaches, and tubercular ulcers can all benefit from cinnamon oil's stomachic, carminative, emmenagogue, and styptic properties.[25]

Antiviral activity
Cinnamomum verum along with a number of other plants (*Zingiber officinale, Piper nigrum, Psidium guajava, Azadirachta indica, and Nigella sativa*), shows potent antiviral responses against a variety of RNA and DNA viruses, according to research on the antiviral properties of plants.[21]

Anti-oxidant activity-
By using DPPH free radical scavenging, essential oils used to treat respiratory infections have some level of antioxidant activity. The essential oils may have an additional antibacterial impact, treating the infection holistically. C. zeylanicum has shown the most potent antioxidant action when combined.[20]

Antimicrobial Activity
Numerous studies have found Cinnamomum zeylanicum to be a well-researched antibacterial agent due to its potent hydrophobic properties. Using the broth method, the antimicrobial effects of the essential oils of Cuminum cyminum, Amomum subulatum, and Syzygium aromaticum against Salmonella typhi, Salmonella para-typhoid, Escherichia coli, Staphylococcus aurens, Bacillus licheniformis, and Pseudomonas fluorescens were examined. C. zeylanicum was found The findings showed that petroleum ether extract had the maximum sensitivity against Bacillus subtilis, whereas ethyl acetate had significant antibacterial effect against Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa. Compared to other essential oils, cinnamon essential oil has a stronger antibacterial effect.[24]

The essential oil Cinnamomum zeylanicum was found to have the most antibacterial properties against the bacterium S. pneumoniae, which causes lower respiratory tract infections. The biomarker for the essential oil C. zeylanicum, which exhibits the highest level of antibacterial activity against M. tuberculosis and K. pneumonia, was discovered to be the chemical molecule eugenol. The antibacterial activity of essential oils against Candida albicans has been noted when tested against respiratory fungal infections.[20]

Michelia Champaca
Botanical information
The Michelia champaca tree, which belongs to the Magnoliaceae family, is a tall, attractive, evergreen tree with a straight trunk, climbing branches, spreading branches, and a closed head. It is a medium-sized tree that is approximately 50 cm tall.[26]

Phytoconstituents
Triterpenoids, steroids, fatty acids with sesquiterpene lactones, alkaloids, flavonoids, tannins, and saponins have been found in the leaves, stems, and roots of M. champaca, according to phytochemical research on stem bark. Liriodenine, parthenolide, and guaianolides are found in M. champaca.

Polyphenolic compounds, such as gallic acid, have also been found in the stem bark, as have quercetin in the stem bark and leaves of the plant. Bark also includes resin, tannin, mucilage, starch, sugar, volatile, essential, and fixed oils. [26]

General traditional uses

The stem bark has historically been used to cure eye conditions, inflammation, antidotes for scorpion and snake venoms, cough, and gonorrhoea. It is frequently used as a diuretic and to treat stomach ulcers in conventional medicine. Additionally helpful are rheumatism, gout, ophthalmia, and cephalalgia. It has historically been used to treat parasite infections, astringents, diuretics, cooling properties, and diseases brought on by vitiated blood. It is also used as a febrifuge and for other conditions such as fever, colic, leprosy, postpartum protection. The Siddha medical system employs M. champaca flower oil to alleviate swollen joints. [26]

Uses in respiratory disorders-

The shrub is cultivated close to churches and temples because of its fragrant blossoms. These are used to treat the bilious condition in rheumatism (Uuani) as a stimulant and expectorant. Gastritis, fever, and cough are all treated with stem bark, whereas inflammation, constipation, and dysmenorrhea are all treated with root bark. [14] It was also discovered that M. alba, a hybrid of Magnolia champaca (L.), might reduce coughing and alleviate expectorants and bronchitis.[27]

The ethanolic extract of Michelia champaca (MC) was tested pharmacologically using mouse models of milk-induced leukocytosis and eosinophilia, rat models of compound 48/80-induced mast cell degranulation, and rat models of egg albumin-induced passive paw anaphylaxis. MC significantly reduced the amount of paw edoema in rats, significantly protected mast cells, and significantly inhibited the total number of eosinophils and leukocyte count in mice. These findings imply that MC may be a promising therapeutic agent in the treatment of asthma, possibly as a result of its anti-stress, mast cell stabilising, and anti-inflammatory properties.[28]

Traditional applications of *M. champaca* include treating bronchitis, coughing, and expectoration. Similar to verapamil, its aqueous-ethanolic extract showed relaxant effects on carbachol (1 mol/L)- and high K+-induced tracheal contractions. Carbachol is a member of the cholinergic drug family and acts on Gq-coupled muscarinic M3 receptors, facilitating signal transduction for the release of intracellular calcium ions from calcium reserves and inducing contraction through several routes. [29]

By inhibiting the Gq linked muscarinic M3 receptor and blocking the signal transduction of the muscarinic receptor pathway of the contractile response, *M. champaca* causes bronchodilation. The impact of Ca2+ channel blocking is demonstrated by the relaxation of high K+-induced contraction. Therefore, the Ca2+ channel blocking mechanism is presumably how the relaxant consequence was seen. The Ca2+ channel inhibitors are crucial in reducing airway hyperactivity, and evidence of this action can support the plant's traditional usage in disorders of the airways[29]

Antifungal activity

A plant extract can prevent the growth of fungi demonstrated by the bioactive content of the chemicals formed from secondary metabolites can be categorised as an antifungal. The potential of Michelia champaca L. as a fungicide has long been recognised. Rhizoctonia solani's mycelia, which cause root rot in beans (Phaseolus vulgaris), were able to develop at a lesser rate when the yellow-flowered M. champaca plant extract was applied. High antifungal activity was demonstrated by M. champaca crude extract against the mould Candida albicans. The pathogenic Curvularia lunata was able to develop in seeds with an inhibitory diameter zone of 15 mm in the presence of M. champaca plant root extract[30]

Antiviral activity

The plant Michelia champaca contains phenols and triterpenoids, which have antiviral and anti-inflammatory properties. The common symptoms of a viral infection include coughing, runny noses, and shortness of breath when feverish. One of the inflammatory mediators employed by the body in coronavirus defence is

ACE2. In Silico, the plant's ligands Taraxerol, Taraxeron, Ferulic Acid, and Gallic Acid were utilised to bind the protein ACE2. The analysis's finding is that COVID 19 has completely enabled disease prevention and treatment in the Michelia Champaca plant.[31]

Anti-microbial activity:
With methanolic extract of the leaves, seeds, stem, root bark, stem, and root heartwood, *M. champaca* has anti-microbial activity. Activity is enhanced following fractionation (petrol, dichloromethane, ethyl acetate, butanol). All fractions of stem bark and the dichloromethane fraction of root bark exhibit broad-spectrum antibacterial activity as a result of fractionation. Additionally, it has antifungal properties. The active component in plants that confers antibacterial action is liriodenine.[26]

Anti-Cancer activity:
Liriodenine, a substance isolated from Michelia champaca branches, exhibits anti-cancer properties. On MDA-MB-231 human breast cancer cells and A549 human lung adenocarcinoma cells, it exhibits maximal inhibitory activity (20 μm in 48 hrs). [26].

Costus Speciosus
Botanical information:
Spiral ginger or Crepe ginger belongs to the family Zingiberaceae of order Zingiberales. This plant shows similarities with other Zingiberaceae members in their floral characters and inflorescences.[32]. However, it can be distinguished from other members of the family Zingiberaceae because of the presence of remarkable spiral stems and spiral phyllotaxy. [33] *Costus speciosus* (Koen) Sm. (*Zingiberaceae*) is an ornamental erect, rhizomatous, perennial succulent herb, up to 2.7 m high, with tuberous rootstock.[34]

Phytoconstituents:
Spiral ginger plant shows diverse pharmacological effects due to presence of variety of bioactive phytochemicals, but the compounds like diosgenins, costunolides, eremanthin, and arbusculin are highly specific that exhibit effective antidiabetic, anticancerous, and antioxidative properties through different mechanismSeeds of the plant produce oil which shows the prevalence of some saturated fatty acids such as myristic acid, stearic acid, behenic acid, palmitic acid, and monounsaturated fatty acid like oleic acid (monounsaturated omega-9 fatty acid), gadoleic acid, and polyunsaturated fatty acid include linoleic acid (polyunsaturated omega-6 fatty acid) [36]

Traditonally, the roots and rhizomes of the plant have been reported to be used against disorders like rheumatism, anemia, bronchitis, skin diseases, constipation, jaundice, flatulence, asthma, helminthiasis, leprosy, pneumonia, dropsy, inflammation, hiccough, fever, and some urinary diseases in which urination is accompanied by the sensation of burning. [37] Various other properties of the rhizomes show that they are strongly laxative in effect (purgative), astringent, depurative, anthelmintic, tonic, acrid, febrifuge, expectorant and are also believed to improve digestion[38]. The juice made up of the rhizomes of *C. speciosus* is used to cure leprosy and also for abortion [39] and it is known to provide a cooling effect and thus used in headaches [34] The sap of young leaves and stems is used in eye and ear infections, [40] catarrhal fever, cold and cough, and also against snake bites [39]

Because of the presence of diosgenin, this plant is given the name "insulin plant." Diosgenin along with an important sesquiterpene, costunolide, performs significantly high antioxidant, anticancer, and antidiabetic activities. In addition, *C. speciosus* extract, along with other herbs, has been used in the patented process for anti-inflammatory and analgesic preparation by Khamar [41] with patent number WO-02/085394 by World Intellectual Property Organization under Patent Cooperation Treaty.

Uses in respiratory disorders:
C. speciosus exhibited a variety of in vitro anti-TB activity against *M. tuberculosis* H37Rv. Based on their MIC and MBC values, the most active partitions were n-hexane partitions of *C. speciosus* (stem and flower) and *T. coronaria* (leaf), with promising MIC of 100 μg/mL and MBC of 200 μg/mL. These results indicate that these partitions could contain the highest amount of bioactive constituents. The other partition that possessed good anti-TB activity

with MIC of 200 µg/mL was *C. speciosus* chloroform and *C. citratus* n-hexane.[42]

Antifungal:
Various antifungal compounds such as saponin (B and C) and tigogenin have been investigated against fungi *Botrytis cinerea, Curvularia sp., Alternaria sp., Sclerotinia sclerotiorum, Fusarium lini, Curvularia lunata, Scopulariopsis sp., Epidermophyton floccosum, Trichophyton spp., Magnaporthe grisea,* and *Aspergillus niger.* Furthermore, the antifungal activity of *Costus speciosus* can also be evinced through the research work done by Sulakshna and Rani [43] where it has been observed that the diameter of the inhibition zone of different fungi increases as the concentration of the prepared stock solutions (with 0.5-2 mg of plant extract) made by using dimethyl sulfoxide, DMSO as solvent, was increased.[44]

Anthelmintic:
Methanolic and aqueous extract of the *C. speciosus'* aerial parts has been studied against one of the most common and widely spread worms *Pheretima posthuma* (adult earthworm). [45] Also, comparative studies were done using the conventional antiworm medication, Albendazole, which is reported to cause paralysis and death of the worm by causing expulsion of the worms as the conductance of the chloride ion gets increased in the membrane of the muscles of the worm and thus there occurs flaccid paralysis due to reduction in excitability and hyperpolarization in the muscles. Through these studies, the traditional claims of anthelminthic potential of *C. speciosus* have been proved as the aqueous and the methanolic extract showed greater potency against the worm than the standard drug, albendazole.[46]

Antibacterial:
The rhizomes and leaves of *C. speciosus* are known to possess a wide variety of compounds that have antibacterial properties. In vitro studies were performed by Sulakshana and Rani [43] against bacteria such as *Staphylococcus aureus, Salmonella, Bacillus subtilis, Shigella, Klebsiella pneumoniae, Pseudomonas,* and *Escherichia coli* using aqueous, hexane, and methanolic extracts of *C. speciosus*. [40] By employing the disc diffusion method, another evaluative study was conducted by Arunprasath and Gomathinayagam [47] using the methanolic and hexane extracts of *C. speciosus* and proved the antibacterial potential of the plant against *Bacillus subtilis, Shigella sp., Escherichia coli, and Staphylococcus aureus.* It is believed that the alkaloids such diosgenin might be responsible for such antibacterial properties exhibited by the plant.
[48]

Antiinflammatory:
Costus speciosus has been used by traditional folk for ages to treat various inflammatory disorders like bronchitis, fever, rheumatism, and headache. Bioactive components like diosgenin and costunolide have been exploited against various inflammatory diseases as they are known to potentially inhibit the activity of tumor necrosis factor-alpha (TNF-α), a cytokine, which is released in response to infection as an alarm for other immune reactions to occur and leads to the inflammation of the concerned tissues or cells and it was observed that there was an inhibitory or suppressive effect on the virus and the activity of diosgenin was found similar to the MTX (methotrexate), a commonly used immune system suppressant.[49]

Uses in Pediatrics:
A pilot study revealed significant efficacy of the use of aqueous extract of *C. speciosus* rhizome in adult and pediatric patients suffering from acute pharyngitis and tonsillitis. [50]

Zingiber Officinale
Botanical information
Ginger (*Zingiber officinale* Roscoe), which belongs to the Zingiberaceae family and the *Zingiber* genus, has been commonly consumed as a spice and an herbal medicine for a long time. [51] Ginger root is used to attenuate and treat several common diseases, such as headaches, colds, nausea, and emesis.[52]

Phytoconstituents
Ginger is abundant in active constituents, such as phenolic and terpene compounds[53]. The phenolic compounds in ginger are mainly gingerols, shogaols, and paradols. In fresh ginger, gingerols are the major polyphenols,

such as 6-gingerol, 8-gingerol, and 10-gingerol. With heat treatment or long-time storage, gingerols can be transformed into corresponding shogaols. After hydrogenation, shogaols can be transformed into paradols. [54] There are also many other phenolic compounds in ginger, such as quercetin, zingerone, gingerenone-A, and 6-dehydrogingerdione.[55] . Moreover, there are several terpene components in ginger, such as β-bisabolene, α-curcumene, zingiberene, α-farnesene, and β-sesquiphellandrene, which are considered to be the main constituents of ginger essential oils.[56]. Besides these, polysaccharides, lipids, organic acids, and raw fibers are also present in ginger [53][56]

Traditionally, Ginger root is used to attenuate and treat several common diseases, such as headaches, colds, nausea, and emesis. Many bioactive compounds in ginger have been identified, such as phenolic and terpene compounds. The phenolic compounds are mainly gingerols, shogaols, and paradols, which account for the various bioactivities of ginger. [54] In recent years, ginger has been found to possess biological activities, such as antioxidant,[57]. anti-inflammatory [58] antimicrobial [59] and anticancer [60] activities.

Uses in respiratory disorders.
Ginger and its bioactive compounds have exhibited bronchodilating activity and antihyperactivity in several studies. [61] Ginger and its bioactive constituents, including 6-gingerol, 8-gingerol, 6-shogaol, citral, and eucalyptol, have protective effects against respiratory disorders, at least mediating them through the induction of relaxation in airway smooth muscle and the attenuation of airway resistance and inflammation. In results from guinea pig and human tracheas models, 6-gingerol, 8-gingerol, and 6-shogaol could lead to the rapid relaxation of precontracted airway smooth muscle. The nebulization of 8-gingerol attenuated airway resistance via a reduction in Ca^{2+} influx in mice[62]

Antioxidant
Dried ginger exhibited the strongest antioxidant activity, because the number of phenolic compounds was 5.2-, 1.1-, and 2.4-fold higher than that of fresh, stir-fried, and carbonized ginger, respectively. [63]

Anti-inflammatory
A series of studies showed that ginger and its active constituents possessed anti-inflammatory activity, which could protect against inflammation-related diseases such as colitis.[58][64]. The anti-inflammatory effects were mainly related to phoshatidylinositol-3-kinase (PI3K), protein kinase B (Akt), and the nuclear factor kappa light chain-enhancer of activated B cells (NF-κB) [65] The above studies found that ginger and its bioactive compounds, such as 10-gingerol, 6-shogaol, and 6-dehydrogingerdione, exhibited protective effects against AD and PD. The antioxidant and anti-inflammatory activities of ginger contributed to neuroprotection.[66]

Antimicrobial activity
In recent years, ginger has been reported to show antibacterial, antifungal, and antiviral activities[67][68]. Biofilm formation is an important part of infection and antimicrobial resistance. One result found that ginger inhibited the growth of a multidrug-resistant strain of *Pseudomonas aeruginosa* by affecting membrane integrity and inhibiting biofilm formation. [69] An in vitro study revealed that gingerenone-A and 6-shogaol exhibited an inhibitory effect on *Staphylococcus aureus* by inhibiting the activity of 6-hydroxymethyl-7, 8-dihydropterin pyrophosphokinase in the pathogen. [71] Ginger essential oil had efficacy in suppressing the growth of *Aspergillus flavus* as well as aflatoxin and ergosterol production. [72] Fresh ginger was found to inhibit plaque formation induced by human respiratory syncytial virus (HRSV) in respiratory tract cell lines. Ginger was effective in blocking viral attachment and internalization. [73]

Uses in Pediatric
Oral administration of ginger is effective and safe at improving vomiting in children with AGE. [74]

Cuminum Cyminum
Botanical information
Cumin (*Cuminum cyminum* L.) is an annual plant that is not only one of the most popular seed species but also one of the oldest and most

cultivated aromatic and herbaceous natural products with numerous medicinal, nutraceutical, and pharmaceutical properties.[75]. *Cuminum cyminum* belonging to the family Apaiaceae, are one of the earliest cultivated herbs in Asia, Africa and Europe. Cumin and caraway seeds from *Cu. cyminum* and *Ca. carvi*, respectively, have remained popular as culinary spices and are also overwhelmingly used in folklore therapy since antiquity in diverse geographical areas. [76]
It is native to and cultivated extensively in several places, mainly in arid and semi-arid climates, such as China, Egypt, Saudi Arabia, and the Mediterranean, as well as India and Iran. However, the largest consumer of cumin seed in the world is India while China is the largest exporter and producer. [75]

Phytoconstituents
A diverse array of compounds have been revealed in essential oils, oleoresins and seeds of carum and caraway that have grown in diverse agro-climate locations. Majority of such compounds are monoterpene hydrocarbons, oxygenated monoterpenes, oxygenated sesquiterpenes, saturated and unsaturated fatty acids, aldehydes, ketones and esters[76] The other components which occur in caraway seed are fatty acids, triacylglycerols, polysaccharides, and lignin. [77] From these studies, it has emerged that the major compounds occurring in caraway are carvacrol, carvone, α-pinene, limonene, γ-terpinene, linalool, carvenone, and *p*-cymene, whereas the major compounds occurring in cumin are cuminaldehyde, limonene, α- and β-pinene, 1,8-cineole, *o*- and *p*-cymene, α- and γ-terpinene, safranal and linalool.

The cumin and caraway oils exhibited high antioxidant activity which has been attributed largely to the presence of monoterpene alcohols, linalool, carvacrol, anethole and estragol, flavonoids and other polyphenolic compounds. [79] [80]

General traditional uses
Cumin as well as caraway seeds are prominently considered carminative, eupeptic, antispasmodic, astringent and used in the treatment of mild digestive disorders, diarrhea, dyspepsia, flatulence, morning sickness, colic, dyspeptic headache and bloating, and are said to promote the assimilation of other herbs and to improve liver function. They have also been used in bronchopulmonary disorders and as a cough remedy, as well as an analgesic. Caraway water finds use as a vehicle for pediatric medicines. As a mixture with alcohol and castor oil, it has been used for the treatment of scabies[81] Aqueous and solvent derived extracts of cumin increased amylase, protease, lipase and phytase activities.[82] . The antiradical profile of cumin has been proposed as the underlying mechanism for their multifaceted pharmacological properties such as antimicrobial, antidiabetic, anticarcinogenic/antimutagenic, antistress, antiulcerogenic, etc. as outlined in the succeeding sections.

Numerous investigations have revealed a potential antimicrobial activity of cumin and caraway products (oils as well as their aqueous and solvent derived extracts). This antibacterial action was assessed against a range of useful and pathogenic gram-positive and gram-negative bacterial strains. [83] The ability of caraway oils to inhibit the growth of fungi and bacteria is attributed to carvone, limonene and linalool, whereas limnonene, eugenol, -pinene and some other minor constituents have been suggested to contribute to the antimicrobial activity of cumin oil.

Many studies have related the anticarcinogenic actions of cumin to their potential apoptotic, antimutagenic and antiproliferative properties. The apoptotic activities of caraway ethanol extract are reported against several human cancer leukemia cell lines. [85] Cumin added to a hypercholesterolemic diet decreased serum and liver cholesterol in rats. [86] Cumin significantly reduced the blood glucose and inhibited glycosylated hemoglobin, creatinine, blood urea nitrogen and improved serum insulin and glycogen (liver Cumin seed has potential as an anti-allergic functional food[87] and skeletal muscle) content and hyperglycemic peak. [88]

Uses in respiratory disorders.
A study suggested that cumin essential oil (CuEO) exerted anti-inflammatory effects in lipopolysaccharide- (LPS-)stimulated RAW 264.7 cells via inhibition of NF-*κ*B and mitogen-activated protein kinases ERK and

JNK signaling; the chemical could be used as a source of anti-inflammatory agents as well as dietary complement for health promotion[89]. NF-kB is a critical transcription factor for the production of many inflammatory cytokines. It is activated in the airway epithelium of human asthmatics and in mice after allergic stimulation. [90] Therefore the reduction of NFkB reduces the Airway obstruction caused by various inflammatory responses.

Cyperus Rotundus

Botanical information

The nutgrass, *Cyperus rotundus* L. (Family: Cyperaceae), is a colonial, perennial herb considered to have originated in India 2000 years ago and widely used in Ayurveda to treat several ailments. *Cyperus rotundus* L, also known as purple nutsedge or nutgrass or java grass. It is the third largest family of monocotyledonous plants [91]

Phytoconstituents

The major chemical constituents in the rhizome of *C. rotundus* are α-cyperolone, β-cyperone, ρ-cymol, calcium, camphene, copaene, cyperene, cyperenone, cyperol, cyperolone, caryophyllene, cyperotundone, d-copadiene, d-epoxyguaiene, isocyperol, isokobusone, kobusone, limonene, linoleic-acid, linolenic-acid, mustakone, myristic acid, oleanolic acid, oleic acid, β-pinene, patchoulenone, rotundene, rotundenol, rotundone, α-rotunol, β-rotunol, β-selinene, selinatriene, sitosterol, stearic acid, sugeonol, and sugetriol. [92] [93]

General traditional uses

Studies indicated that the rhizomes of *C. rotundus* are used as traditional folk medicine for the treatment of stomach and bowel disorders and inflammatory diseases in Asian countries[94]. Clinical trials and animal research support the use of the plant as an analgesic, anti-arthritic, antibacterial, anticancer, anti-candida, anti-convulsant, anti-diabetic, anti-emetic, anti-histaminic, anti-inflammatory, anti-malarial, anti-obesity, anti-pyretic, anti-spastic, gastroprotective, hypotensive, sedative, and tranquilizing agent [95] Studies on the ethnobotanical use of *C. rotundus* showed that the rhizomes were used to treat aging, apoptosis, atherosclerosis, cancer, cystitis, epilepsy, genotoxicity, hirutism, nociception and prostatitis disorders[96] . It is reported that the tuber part of *C. rotundus* is used for the treatment of dysmenorrheal and menstrual irregularities from ancient times [97]

Uses in respiratory disorders

The compound *α*-cyperone, one of the main phytochemicals found in *C. rotundus* oil, was found to inhibit lipopolysaccharide- (LPS-) stimulated inflammatory response in a murine BV-2 microglial cell line, by activating Akt (protein kinase B)/nuclear factor-E2-related factor (Nrf)-2/heme oxygenase- (HO-) 1 and suppressing the nuclear factor kappa light chain enhancer of the activated B cell (NF-*κ*B) pathway. [98]

Another study using methanol extracts from *C. rotundus* rhizomes revealed that cyperalin A has high anti-inflammatory activity through inhibition of prostaglandin E2 (PGE-2), cyclooxygenase-2 (COX-2), and arachidonate 5-lipoxygenase (LOX-5) and that sugetriol triacetate, another compound of biological interest in *C. rotundus*, presented a similar effect on PGE-2, COX-2, and LOX-5 enzymes.[99]. *α*-Cyperone revealed to suppress the inflammatory response in lipopolysaccharide- (LPS-) induced acute lung injury in mice, through inhibiting the growth of inflammatory cells along with cytokines and downregulating the NF-*κ*B and NLR family pyrin domain containing 3 (NLRP3) signalling pathways.[100]. Thus by inhibiting the inflammatory enzymes, the plant extract reduces inflammation in the lungs, thereby facilitating in respiratory ailments. The antimycobacterial activity of *C. rotundus* extracts, evaluated on multidrug-resistant strains of *Mycobacterium tuberculosis*, also revealed to be prominent. [101]

Uses in Pediatric

Musta is one of the remedy that is comprised of cyperus rotundus in the treatment of diarrhea described by Acharyas. [102] Musta kwatha (*C. rotundus*) with honey can be used as effective remedy for childhood diarrhea. [103]

3. CONCLUSION

The present literature review on Athimathura Chooranam reveals the various

pharmacological and therapeutic dynamics of its ingredients. The scientific exploration of its active ingredients reveal the multimodal action of this single formulation such as antiinflammatory, antimicrobial, antiallergic, bronchodilator actions which pertain to respiratory illness. Apart from these specific actions it also has the ability to modulate the immune system and act as antioxidant which promotes the drug to be as a prophylactic drug to prevent frequent episodes and exacerbations of respiratory illness in adults and also in pediatric age groups.Further preclinical and clinical studies are warranted in the near future to scientifically re-confirm its traditional claims

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