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Research Article

A LITERARY REVIEW OFTHE CONTENTS OF THULASI ENNAI (PEDIATRIC SIDDHA FORMULATION) IN THE MANAGEMENT OF PEDIATRIC BRONCHIAL ASTHMA

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ABSTRACT

Objectives: The purpose of this review article is focused on the photochemical constituents and therapeutic potential of Thulasi Ennai to combat pediatric bronchial asthma.

Methods: The electronic databases such as Google Scholar, Medline/PubMed, Web of Science, Science Direct, Scopus and Directory of Open Access Journals (DOAJ), and reference lists have been looked to identify publications pertinent to the individual herbs of Thulasi Ennai.

Results: The pharmacological effects of the herbs found in Thulasi Ennai possess anti-asthmatic, anti-inflammatory, antibacterial, antiviral, and other pharmacological effects relevant to the management of bronchial asthma.

Conclusion: The present review concluded the safety of the Thulasi Ennai in preclinical studies. Further, clinical studies of Thulasi Ennai would need to be performed in humans to assess the efficacy of Thulasi Ennai.

Keywords: Bronchial asthma, Thulasi Ennai, Polyherbal formulation, Pediatric Siddha formulation.

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INTRODUCTION

Bronchial asthma is a chronic inflammatory disease characterized by inflammation of the respiratory tract, accompanied by excess production of mucus leading to bronchial hyper activity to specific and non-specific stimuli. In children, asthmatic exacerbations are predominantly caused by respiratory viral infections, aeroallergen appears in seasonal patterns, indoor air pollution, and also environmental factors [1-3]. The Global Asthma Report has reported that approximately 334 million people worldwide suffer from asthma and being the major public health problem among children [4-6]. Even though there is an availability of standardized therapeutics in the management of asthma, patients seek herbal medicine for alternative drug of choice to manage the disease. According to the World Health Organization (WHO), about 80% of the population in developing countries use herbal medicine to meet their primary health-care needs [7-8].

Siddha system of medicine is one such ancient traditional system of India which is practiced mostly in its Southern part for treating various diseases including chronic conditions [9]. Siddha system comes under the AYUSH (Ayurveda, Yoga and Naturopathy, Unani, Siddha, and Homeopathy) system of India. In 2003, department of AYUSH was formed under aegis of Ministry of Health and Family Welfare, Government of India [10]. Siddha system of medicine includes herbal products, inorganic substances, and animal products, leading to different formulations such as Parpam, chendooram, and chunam prepared by the process of calcination [11].

Thulasi Ennai is a Siddha polyherbal formulation comprises of ten herbal ingredients specifically prescribed to manage pediatric bronchial asthma. Thulasi Ennai is an oil-based medication recommended with the dosage of 5 ml in the morning for the age group 6–12 years as per Siddha pediatric literature. The safety profile of Thulasi Ennai was demonstrated in preclinical studies [12,13]. The present review focuses on the remedial capacity of the ingredients of Thulasi Ennai to combat bronchial asthma in children.

METHODS

The literature search was conducted in electronic databases such as Google Scholar, Medline/PubMed, Web of Science, Science Direct, Scopus, and Directory of Open Access Journals (DOAJ), using terms pediatric asthma, Thulasi Ennai and herbal preparation. This review includes the articles relevant to the morphology and distribution, chemical constituents, and pharmacological action of individual ingredients of Thulsi Ennai. Mostly, the articles published in English are reviewed. Articles published in languages other than English, and duplicate publications were excluded from the study.

RESULTS AND DISCUSSION

The ingredients of Thulasi Ennai and their therapeutic uses specified in the Siddha literature are presented in Table 1.

Ocimum tenuiflorum L.

O. tenuiflorum belongs to the family Lamiaceae and is commonly called Tulsi. In Siddha literature, it is commonly used in herbal formulations, particularly prescribed for respiratory diseases. It is widely distributed throughout the South-east Asian tropics [15]. The morphological feature of the leaves is ovate with petioles, up to 5 cm long, slightly toothed. Phytochemical qualitative analysis revealed the presence of flavonoids, tannins, saponins, alkaloids, anthraquinones, and reducing sugars [16]. Essential oil of this plant contains major constituents of camphor, eugenol, methyl eugenol, eucalyptol, β-elemene, and β-caryophyllene [17]. The studies proved the pharmacological properties such as anti-asthmatic, anti-bacterial, antimicrobial activity, anti-inflammatory, and antioxidant [16,18-22]. Recently, the plant has proven its antiviral activity against HSV (Herpes Simplex Virus), H9N2 (Influenza A virus), NDV (Newcastle Disease Virus) BHV (Bovine herpes virus), etc. [23].

Platostoma menthoides (L.) A.J. Paton

Platostoma menthoides (L.) A.J. Paton (Synonym: *Geniosporum prostratum* (L.) Benth, it is an aromatic annual herb belonging to

Table 1: Thulasi Ennai with their therapeutic effects in Siddha literature

S. No.	Scientific Name	Part used	Therapeutic uses in siddha literature [14]
1.	*Ocimum tenuiflorum* L.	Leaves	Bronchial asthma, cough, anthelmintic, fever, expectorant, and vomiting.
2.	*Platostoma menthoides* (L.) A.J. Paton	Leaves	Fever, expectorant, indigestion, and ulcer.
3.	*Ocimum americanum* L.	Leaves	Expectorant, cough, fever, sinusitis, asthma, indigestion, and stomachic.
4.	*Artemisia nilagirica* (C.B.Clarke) Pamp.	Leaves	Expectorant, stomach pain, anthelminthic, fever, ulcer, and head ache.
5.	*Aegle marmelos* (L.) Correa	Leaves	Fever, digestion, stomachic, laxative, vomiting, aphrodisiac, vomiting, and jaundice.
6.	*Allium sativum* L.	Fruit	Bronchial asthma, stomachic, expectorant, anthelminthic, cough, sinusitis, diarrhea, and piles.
7.	*Zingiber officinale* Roscoe	Rhizome	Bronchial asthma, anemia, cough, dyspepsia, digestive, diarrhea, fever, heartburns, peptic ulcer, and sinusitis.
8.	*Piper nigrum* L.	Fruit	Bronchial asthma, stimulant, expectorant, cough, anemia, indigestion, ear diseases, and jaundice.
9.	*Piper longum* L.	Fruit	Bronchial asthma, anemia, cough, indigestion, and anthelminthic.
10.	*Ricinus communis* L.	oil	Bronchial asthma, cough, laxative, and leucorrhoea.

the family Lamiaceae [24]. It is traditionally used in various systems of Indian medicine to manage fever, malaise, indigestion, and also as an expectorant. The main components of essential oil include β-caryophyllene, limonene, bornyl formate, α-humulene, caryophyllene oxide, sesquiterpene hydrocarbons, monoterpene hydrocarbons, oxygenated monoterpenes, and oxygenated sesquiterpenes [25]. The pharmacological activity of the plant has anti-asthmatic and antioxidant properties [26,27].

***Ocimum americanum* L.**

Ocimum americanum L., syn. O. canum Sims. "Hoary basil" is an annual herbaceous plant widespread in Asia and Africa. It is an aromatic plant with an erect stem, the first leaf with seven distinct veins, mid-vein reaches to apex. Conventionally, it was named that has Nai thulasi, the decoction of the leaf extract is used to treat diabetes, diarrhea, piles, constipation, infections, and dysentery [28]. The chemical composition of *Ocimum americanum* L. includes phytochemicals (phenol, alkaloids, quinones, glycosides, flavonoids, amino acids, tannins, proteins, carbohydrates, and saponin), flavonoids (dihydroxy-tetramethoxy (iso) flavone, dodecanedioic acid, eriodictyol, feruloylhexose isomers, feruloylhexose isomer 2, isoquercitrin, and jasmonic acid), and fatty acids (stearidonic, α-linolenic, linoleic acid, palmitic, oleic, stearic, and arachidic acids) present in the leaf extract of the plant [29,30]. Pharmacological properties include anti-inflammatory, antioxidant, antibacterial, and antimicrobial activities [31-34].

***Artemisia nilagirica* (C.B. Clarke) Pamp.**

Artemisia nilagirica (C.B.Clarke) Pamp. is a perennial herb found mainly in the hilly regions of India. The plant commonly known as Indian wormwood or mugwort belongs to the family Asteraceae [35]. Leaves are alternate, large, ovate, and lobbed, and ash-grey or white tomentose beneath, uppermost part of the leaves in the plant is smaller and lanceolate [36]. The chemical constituents present in the essential oil of *Artemisia nilagirica* (C.B.Clarke) Pamp. include (monoterpenoids, sesquiterpenoids, α-thujone, β-thujone, germacrene D, 4-terpineol, β-caryophyllene, camphene, borneol, caryophyllene oxide, camphor, monoterpene hydrocarbon, sesquiterpene hydrocarbon, monoterpene alcohol, sesquiterpene oxide, and sesquiterpene alcohol), and phytochemicals (tannins, flavonoid, alkaloids, saponins, coumarins, and phenols [37-39]. The plant has pharmacological effects of anti-asthmatic, anti-inflammatory, antimicrobial, antibacterial, and antioxidant [40-43]. Conventionally, the plant used in the treatment for epilepsy, diuretic, anti-inflammatory, and nervous disorders.

***Aegle marmelos* (L.) Correa**

Aegle marmelos (L.) is commonly known as wood apple or Bael belonging to the family Rutaceae. It is native to Northern India and found throughout South Asia. The tree has been considered sacred and planted in temples of Hindu Gods Shiva. Leaves are alternate, oval, pointed, and shallowly toothed leaflets [44]. In Siddha system of medicine, it is used to treat diarrhea, dysentery, indigestion, myalgia, ulcers, fever, anemia, nausea, vomiting, inflammations, eye disorders, and hemorroids. The active phytochemical constituents of *A.marmelos* include marmenol, marmin, marmelosin, marmelide, psoralen, alloimperatorin, rutaretin, scopoletin, aegelin, marmelin, fagarine, limonene, anhydromarmelin, marmesin, a-phellandrene, betulinic acid, imperatorin, marmelosin, luvangentin and auroptene [45,46]. The leaf extract contains flavonoids, alcohols, aldehydes, aromatic compounds, fatty acid methyl esters, terpenoids, phenols, and steroids. The pharmacological activities include antihistamine, antimicrobial, anti-inflammatory, analgesic, antipyretic, and antibacterial properties [47-50].

***Allium sativum* L.**

Garlic (*Allium sativum* L.) is an annual aromatic herbaceous annual spice, belonging to the amaryllidaceae family. Conventionally, it has been used as one of the main ingredients in South Indian food. In Siddha medicines, it is used to treat gastritis, inflammations, tonsillitis, cough, bronchial asthma, myalgia, otalgia, diarrhea, and wounds. The chemical constituents in the bulbs of *Allium sativum* include organosulfur compounds (allicin[S-(2-propenyl)-2-propene-1-sulfinothioate], alliin (S-allyl-L-cysteine sulfoxide), thiosulfinates), phytochemicals (E-ajoene, Z-ajoene), thiosulfinates (allicin), vinyldithiins (2-vinyl-(4H)-1,3-dithiin, 3-vinyl-(4H)-1,2-dithiin), sulfides (diallyl disulfide (DADS), diallyl trisulfide (DATS)), phenolic compounds (β - resorcylic acid, followed by pyrogallol, gallic acid, rutin, protocatechuic acid, and quercetin), alkaloids, saponins, tannins, polysaccharides along with numerous vitamins, minerals, trace elements (germanium and selenium), flavonoids like quercetin and enzymes like (alliinase, peroxidase, and myrosinase) that are present [51-53]. The previous studies had proven the pharmacological activities such as anti-asthmatic, antioxidant, antimicrobial, antibacterial, antiviral and anti-inflammatory [54-59].

***Zingiber officinale* Roscoe**

Zingiber officinale Roscoe, commonly known as ginger, belongs to the family zingiberaceae, widely consumed as a spice and traditionally used as herbal medicine to manage abdominal disorders [60]. Ginger is a herbaceous, rhizomatous, perennial, and 2 or 3 feet in height,

the stems are erect and oblique, laterally compressed rhizomes are 7–15 cm long and 1–1.5 cm broad. The bioactive components such as (6)-Gingerol, (8)-gingerol, and (6)-shogaol possess anti-asthmatic activity [61]. The phenolic compounds in ginger are mainly gingerols, shogaols, and paradols. Polyphenols are (quercetin, zingerone, gingerenone-A, and 6-dehydrogingerdione) terpene components (β-bisabolene, α-curcumene, zingiberene, α-farnesene, and β-sesquiphellandrene [62,63]. Phytochemical analysis of the crude extract contains alkaloids, saponins, tannins, glycosides, flavonoids, and terpenoids. In Siddha system of medicine, fresh ginger juice is used as an adjuvant for Siddha medicine especially prescribed for respiratory and abdominal disorders. The pharmacological properties of ginger include anti-asthmatic, antimicrobial, antioxidant, antiviral, antibacterial, and anti-inflammatory [64-68]. Ginger reduces allergic airway inflammation by suppression of Th2 mediated immune response in respiratory disorders [69].

***Piper nigrum* L.**

Piper nigrum is a perennial shrub, belonging to the piperaceae family commonly named as black pepper. It is native to South India and is extensively cultivated throughout tropical regions of the world. It is considered as the King of spices due to its huge trade share in the international market [70]. The chemical constituent in *Piper nigrum* includes piperine, piperic acid, piperlonguminine, pellitorine, piperolein B, piperamide, piperettine, and (-)-kusunokinin, secondary metabolites (alkaloids, glycosides, terpenoids, steroids, flavonoids, tannins, and anthraquinones, caryophyllene, and sabinene) [71,72]. Terpenes are (β-caryophyllene, 3-carene, limonene, α-pinene and β-pinene) [73].

Table 2: Thulasi Ennai polyherbal formulation

S. No.	Ingredients	Major phytoconstituents	Pharmacological activity relevant to bronchial asthma.
1.	*Ocimum tenuiflorum* L.	Essential oil (camphor, eugenol, methyl eugenol, eucalyptol, β-elemene, and β-caryophyllene), phytochemicals (flavonoids, tannins, saponins, alkaloids, anthraquinones, and reducing sugars).	Anti-asthmatic, anti-bacterial, antimicrobial activity, and anti-inflammatory.
2.	*Platostoma menthoides* (L.) A.J. Paton	Essential oil contains β-caryophyllene, limonene, bornyl formate, α-humulene, caryophyllene oxide, sesquiterpene hydrocarbons, monoterpene hydrocarbons, oxygenated monoterpenes, and oxygenated sesquiterpenes.	Anti-asthmatic and antioxidant
3.	*Ocimum americanum* L.	Phytochemicals (phenol, alkaloids, quinones, glycosides, flavonoids, amino acids, tannins, proteins, carbohydrate, and saponin), flavonoids (Dihydroxy-tetramethoxy (iso) flavone, dodecanedioic acid, eriodictyol, feruloylhexose isomers, feruloylhexose isomer 2, isoquercitrin, and jasmonic acid, fatty acids (stearidonic, α-linolenic, linoleic acid, palmitic, oleic, stearic, and arachidic acids)	Anti-inflammatory, antioxidant, antibacterial, and antimicrobial
4.	*Artemisia nilagirica* (C.B. Clarke) Pamp.	Essential oil contains (monoterpenoids, sesquiterpenoids, α-thujone, β-thujone, germacrene D, 4-terpineol, β-caryophyllene, camphene, borneol caryophyllene oxide, camphor, monoterpene hydrocarbon, sesquiterpene hydrocarbon, monoterpene alcohol, sesquiterpene oxide, and sesquiterpene alcohol), phytochemicals (tannins, flavonoid, alkaloids, saponins, coumarins, and phenols.	Anti-asthmatic, anti -inflammatory, antimicrobial antibacterial, and antioxidant
5.	*Aegle marmelos* (L.) Correa	Phytoconstituents mainly marmenol, marmin, marmelosin, marmelide, psoralen, alloimperatorin, rutaretin, scopoletin, aegelin, marmelin, fagarine, limonene, anhydromarmelin, marmesin, a-phellandrene, betulinic acid, imperatorin, marmelosin, luvangentin, and auroptene.	Antihistamine, antimicrobial, anti-inflammatory, analgesic, antipyretic, and antibacterial.
6.	*Allium sativum* L.	Organosulfur compounds (allicin[S-(2-propenyl)-2-propene-1-sulfinothioate], alliin (S-allyl-L-cysteine sulfoxide), thiosulfinates), phytochemicals including sulfur containing compounds (E-ajoene, Z-ajoene), thiosulfinates (allicin), vinyldithiins (2-vinyl-(4H)-1,3-dithiin, 3-vinyl-(4H)-1,2-dithiin), sulfides (diallyl disulfide (DADS), diallyl trisulfide (DATS)), phenolic compounds (β - resorcylic acid, followed by pyrogallol, gallic acid, rutin, protocatechuic acid, and quercetin), alkaloids, saponins, tannins, and polysaccharides along with numerous vitamins, minerals, and trace elements (germanium and selenium)	Anti-asthmatic, antioxidant, antimicrobial, antibacterial, antiviral, and anti-inflammatory.
7.	*Zingiber officinale* Roscoe	(6)-Gingerol, (8)-gingerol, and (6)-shogaol, phenolic compounds in ginger are mainly gingerols, shogaols, and paradols. polyphenols (gingerol, 6-gingerol, 8-gingerol and 10- gingerol, quercetin, zingerone, gingerenone-A and 6-dehydrogingerdione), terpene components (β-bisabolene, α-curcumene, zingiberene, α-farnesene, and β-sesquiphellandrene.	Anti-asthmatic, antimicrobial antioxidant, antiviral, antibacterial, and anti-inflammatory
8.	*Piper nigrum* L.	Piperine, piperic acid, piperlonguminine, pellitorine, piperolein B, piperamide, piperettine and (-)-kusunokinin, secondary metabolites, including alkaloids, glycosides, terpenoids, steroids, flavonoids, tannins, and anthraquinones, terpenes are β-caryophyllene, 3-carene, limonene, α-pinene, and β-pinene.	Anti-asthmatic, anti -inflammatory, bronchodilation, antimicrobial, antioxidant, antiviral, and antitussive activity.
9.	*Piper longum* L.	Alkaloid (piperine) phytochemicals (pipyahyine, piperlongumamides A-C, piperchabamide B, 3β, 4α-dihydroxy-1-(3-phenylpropanoyl)-piperidine-2-one and (2E, 4E,14Z)-6-hydroxyl-N-isobutyleicosa-2,4,14-trienamide, flavonoid (catechin, epicatechin, quercetin, myricetin, kaempferol, apigenin, luteolin, and naringenin).	Anti-asthmatic, antimicrobial, anti-inflammatory, antibacterial, antiviral, and antioxidant.
10.	*Ricinus communis* L.	Phytochemicals (kaempferol-3-O and kaempferol-3-O- β -D-glucopyranoside, ingenol), triterpenoids (lupeol, β- and α-amyrin, quercetin and gallic acid, athujone, camphor and beta thujone, ricin, epicatechin, gentisic acid, catechin, kaempferol-3-*O*- β -D- glucopyranoside, and quercetin-3-*O*-β-monoterpenoids, fatty acid (ricinoleic acid, stearic, palmitic, oleic acid, and linoleic acid), triglyceride (triricinolein), and phytosterols (β-sitosterol, 4-desmethylsterols).	Antimicrobial, antibacterial, and antioxidant.

The pharmacological experiments have demonstrated that *Piper nigrum* exhibited anti-asthmatic, anti-inflammatory, bronchodilation, antimicrobial, antioxidant, antiviral, and antitussive activity [74-80].

***Piper longum* L.**

Piper longum L. is a perennial climbing shrub widely distributed throughout tropical regions of India. The fruits are fleshy spikes with 2.5–3.5cm long and 5mm thick, oblong, blunt, and blackish green. The mature spikes are collected and dried for commercial and medicinal purposes [81]. In Siddha system of medicine, the dried fruit is used as the main ingredient to manage respiratory tract diseases. The fruit contains alkaloid (piperine), phytochemicals (pipyahyine, piperlongumamides A-C, piperchabamide B, 3β, 4α-dihydroxy-1-(3-phenylpropanoyl)-piperidine-2-one and (2E, 4E,14Z)-6-hydroxyl-N-isobutyleicosa-2,4,14-trienamide, and flavonoid (catechin, epicatechin, quercetin, myricetin, kaempferol, apigenin, luteolin, and naringenin) [82,83]. The pharmacological activities are proven as anti-asthmatic, antimicrobial, anti-inflammatory, antibacterial, antiviral, and antioxidant properties [79,84-88].

***Ricinus communis* L.**

Ricinus communis L. (Castor bean) is a perennial shrub, belonging to the Euphorbiaceae family. It is widely distributed throughout the tropical and temperate regions of the world [89]. The seeds contain 50% of fixed oil used commercially for chemical industry and international trade [90]. The chemical composition of castor oil is mainly composed of fatty acids and neutral lipids (triglycerides). Phytochemicals constituents revealed the presence of (kaempferol-3-O and kaempferol-3-O- β -D-glucopyranoside, ingenol), triterpenoids (lupeol, β- and α -amyrin, quercetin and gallic acid, athujone, camphor and beta thujone, ricin, epicatechin, gentisic acid, catechin, kaempferol-3-*O*- β -D- glucopyranoside and quercetin-3-*O*-β-monoterpenoids, fatty acid (ricinoleic acid, stearic, palmitic, oleic acid, and linoleic acid), triglyceride (triricinolein), and phytosterols (β-sitosterol, 4-desmethylsterols) [91,92]. The pharmacological properties of *Ricinus communis* are antimicrobial, antibacterial, antioxidant, and laxative [93-96] (Table 2).

CONCLUSION

The present review concluded that Thulasi Ennai may help to manage bronchial asthma in children. The ingredients of Thulasi Ennai mentioned in the Siddha literature exhibited pharmacological actions such as anti-asthmatic, anti-inflammatory, antibacterial, antiviraland, and antimicrobial properties. In addition, safety profile of Thulasi Ennai demonstrated in preclinical studies. Clinical studies of Thulasi Ennai would need to be performed in humans to assess the efficacy of Thulasi Ennai.

AUTHORS' CONTRIBUTIONS

Dr. S. Sonitha has contributed to the preparation of this review and drafting of the manuscript Dr. S. Mathu kumar, Dr. P. Sathiyarajeswaran and Dr. M. S. Shree devi contributed equally in the revisions and finalization of manuscript.

CONFLICT OF INTEREST

There is no conflict of interest

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