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Research Article

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

SONITHA S[1]*, MATHU KUMAR S[1], SATHIYA RAJESWARAN P[2], SHREE DEVI MS[2]

[1]Sri Sairam Siddha Medical College and Research Centre, Chennai, Tamil Nadu, India. [2]Central Council for Research in Siddha, Ministry of AYUSH, Chennai, Tamil Nadu, India. Email: sonithakepid@gmail.com

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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.

2011;3:187-93.
28. Bassole HN, Nebie R, Savadogo A, Quattara CT, Barro N, Traore SA. Composition and antimicrobial activities of the leaf and flower essential oil of *Lippia chevalieri* and *Ocimum canum* from Bukina Faso. Afr J Biotechnol 2005;4:1156e-60.
29. Behera S, Babu SM, Ramani YR, Choudhury PK. A comparative study on phytochemical investigation and antioxidant activity of poly herbal mixture of *Ocimum canum* and *Pongamia pinnata* hydro-alcoholic Leaf Extracts. Res J Pharmacogn Phytochem 2012;4:250-61.
30. Zengin G, Ferrante C, Gnapi DE, Sinan KI, Orlando G, Recinella L, *et al*. Comprehensive approaches on the chemical constituents and pharmacological properties of flowers and leaves of American basil (*Ocimum americanum L*). Food Res Int 2019;125:108610. doi: 10.1016/j.foodres.2019.108610, PMID 31554064
31. Yamada AN, Grespan R, Yamada ÁT, Silva EL, Silva-Filho SE, Damião MJ, *et al*. Anti-inflammatory activity of *Ocimum americanum* L. essential oil in experimental model of zymosan-induced arthritis. Am J Chin Med 2013;41:913-26. doi: 10.1142/S0192415X13500614, PMID 23895160
32. Selvi MT, Thirugnanasampandan R, Sundarammal S. Antioxidant and cytotoxic activities of essential oil of *Ocimum canum Sims*. from India. J Saudi Chem Soc 2015;19:97-100. doi: 10.1016/j.jscs.2011.12.026
33. Dhale DA, Birari AR, Dhulgande GS. Preliminary screening of antibacterial and phytochemical studies of *Ocimum americanum* Linn. J Ecobiotechnol 2010;2.
34. Vijayakumar S, Vidhya E, Rajalakshmi S, Kalaiselvi S, Pandiyan P. Antimicrobial activity and phytochemical screening of *Ocimum americanum* L extracts against pathogenic microorganisms. Acta Ecol Sin 2020;40:214-20. doi: 10.1016/j.chnaes.2019.09.001
35. Walter HL, Memory PF, Elvin L. Medical Botany: Plants Affecting Human Health. 2nd ed. Hiboken: Wiley; 2003. p. 345.
36. Suresh J, Mahesh NM, Ahuja J, Santilna KS. Review on *Artemisia nilagirica* (Clarke) pamp. J Biol Act Prod Nat 2011;1:97-104. doi: 10.1080/22311866.2011.10719075
37. Sati SC, Sati N, Ahluwalia V, Walia S, Sati OP. Chemical composition and antifungal activity of *Artemisia* nilagirica essential oil growing in northern hilly areas of India. Nat Prod Res 2013;27:45-8. doi: 10.1080/14786419.2011.650636, PMID 22348279
38. Haider F, Kumar N, Naqvi AA, Bagchi GD. Oil constituents of *Artemisia* nilagirica var. septentrionalis growing at different altitudes. Nat Prod Commun 2010;5:1959-60. doi: 10.1177/1934578X1000501227, PMID 21299131
39. Parameswari P, Devika R. Phytochemical screening of bioactive compounds of *Artemisia* nilagirica (Clarke) pamp. J Chem Pharm Sci 2014;7:351-3.
40. Aparna N, Duraiswamy B. Evaluation of antiasthmatic activity of aerial parts of *Artimisia* nilagirica and seeds of *Sesamum Indicum*. In: 2nd Indian Pharmaceutical Association Studies Congress, Bangalore, Jul 9-11 2009. Bangalore: Indian Pharmaceutical Association; 2009.
41. Parameswari P, Devika R, Vijayaraghavan P. *In vitro* anti-inflammatory and antimicrobial potential of leaf extract from *Artemisia nilagirica* (Clarke) Pamp. Saudi J Biol Sci 2019;26:460-3. doi: 10.1016/j.sjbs.2018.09.005, PMID 30899158
42. Ahameethunisa AR, Hopper W. Antibacterial activity of *Artemisia nilagirica* leaf extracts against clinical and phytopathogenic *bacteria.* BMC Complement Altern Med 2010;10:6. doi: 10.1186/1472-6882-10-6, PMID 20109237
43. Gul MZ, Bhat MY, Maurya R, Qureshi IA, Ghazi IA. *In vitro* evaluation of antioxidant and antiproliferative activities of *Artemisia nilagirica* extracts. Indian J Pharm Sci 2018;79:872-84. doi: 10.4172/pharmaceutical-sciences.1000303
44. Sharma PC, Bhatia V, Bansal N, Sharma A. A review on bael tree. Nat Prod Radiance 2007;6:171-8.
45. Yadav N, Tyagi G, Jangir DK, Mehrotra R. Rapid determination of polyphenol, Vitamins, organic acids and sugars in *Aegle marmelos* using reverse phase-high-performance liquid chromatography. J Pharm Res 2011;4:717-9.
46. Mujeeb F, Bajpai P, Pathak N. Phytochemical evaluation, antimicrobial activity, and determination of bioactive components from leaves of *Aegle marmelos.* BioMed Res Int 2014;2014:497606. doi: 10.1155/2014/497606, PMID 24900969
47. Arul V, Miyazaki S, Dhananjayan R. Mechanisms of the contractile effect of the alcoholic extract of *Aegle marmelos* Corr. On isolated guinea pig ileum and tracheal chain. Phytomedicine 2004;11:679-83. doi: 10.1016/j.phymed.2002.12.001, PMID 15636185
48. Devi M, Devi S, Sharma V, Rana N, Bhatia RK, Bhatt AK. Green synthesis of silver nanoparticles using methanolic fruit extract of *Aegle marmelos* and their antimicrobial potential against human bacterial pathogens. J Trad Complement Med 2020;10:158-65. doi: 10.1016/j.jtcme.2019.04.007, PMID 32257879
49. Arul V, Miyazaki S, Dhananjayan R. Studies on the anti-inflammatory, antipyretic and analgesic properties of the leaves of *Aegle marmelos* Corr. J Ethnopharmacol 2005;96:159-63. doi: 10.1016/j.jep.2004.09.013, PMID 15588665
50. Ezhilarasi AA, Vijaya JJ, Kaviyarasu K, Kennedy LJ, Ramalingam RJ, Al-Lohedan HA. Green synthesis of NiO nanoparticles using *Aegle marmelos* leaf extract for the evaluation of *in-vitro* cytotoxicity, antibacterial and photocatalytic properties. J Photochem Photobiol B 2018;180:39-50. doi: 10.1016/j.jphotobiol.2018.01.023
51. Al-Snafi AE. Pharmacological effects of *Allium* species grown in Iraq. An overview. Int J Pharm Health Care Res 2013;1:132-47.
52. Shang A, Cao SY, Xu XY, Gan RY, Tang GY, Corke H, *et al*. Bioactive compounds and biological functions of garlic (*Allium sativum* L.). Foods 2019;8:246. doi: 10.3390/foods8070246, PMID 31284512
53. Abdelrahman M, Hirata S, Mukae T, Yamada T, Sawada Y, El-Syaed M, *et al*. Comprehensive metabolite profiling in genetic resources of garlic (*Allium sativum L*.) collected from different geographical regions. Molecules 2021;26:1415. doi: 10.3390/molecules26051415, PMID 33807861
54. El-Din MM, Mostafa AM, Abd-Elkader A. Experimental studies on the effect of (Lambda-cyhalothrin) insecticide on lungs and the ameliorating effect of plant extracts (ginseng (*panax ginseng*) and garlic (*Allium sativum* L.) on asthma development in albino rats. BMC Res Notes 2014;7:243.
55. Hsieh CC, Liu KF, Liu PC, Ho YT, Li WS, Peng WH, *et al*. Comparing the protection imparted by different fraction extracts of garlic (*Allium sativum* l.) against der p-induced allergic airway inflammation in mice. Int J Mol Sci 2019;20:4879. doi: 10.3390/ijms20194879, PMID 31581442
56. Cheng H, Huang G. Extraction, characterisation and antioxidant activity of *Allium sativum* polysaccharide. Int J Biol Macromol 2018;114:415-9. doi: 10.1016/j.ijbiomac.2018.03.156, PMID 29596932
57. Viswanathan V, Phadatare AG, Mukne A, Mukne A. Antimycrobacterial and antibacterial activity of *Allium sativum* bulbs. Indian J Pharm Sci 2014;76:256-61. PMID 25035540
58. Rouf R, Uddin SJ, Sarker DK, Islam MT, Ali ES, Shilpi JA, *et al*. Antiviral potential of garlic (*Allium sativum*) and it's organosulfur compounds: A systematic update of preclinical and clinical data. Trends Food Sci Technol 2020;104:219-34. doi: 10.1016/j.tifs.2020.08.006
59. Shao X, Sun C, Tang X, Zhang X, Han D, Liang S, *et al*. Anti-inflammatory and intestinal microbiota modulation properties of Jinxiang garlic (*Allium sativum* L.) polysaccharides toward dextran sodium sulfate-induced colitis. J Agric Food Chem 2020;68:12295-309. doi: 10.1021/acs.jafc.0c04773, PMID 33095019
60. Haniadka R, Saldanha E, Sunita V, Palatty PL, Fayad R, Baliga MS. A review of the gastroprotective effects of ginger (*Zingiber officinale Roscoe*). Food Funct 2013;4:845-55. doi: 10.1039/c3fo30337c, PMID 23612703
61. Townsend EA, Siviski ME, Zhang Y, Xu C, Hoonjan B, Emala CW. Effects of ginger and its constituents on airway smooth muscle relaxation and calcium regulation. Am J Respir Cell Mol Biol 2013;48:157-63. doi: 10.1165/rcmb.2012-0231OC, PMID 23065130
62. Ji K, Fang L, Zhao H, Li Q, Shi Y, Xu C, *et al*. Ginger oleoresin alleviated gamma-ray irradiation-induced reactive oxygen species via the Nrf2 protective response in human mesenchymal stem cells. Oxid Med Cell Longev 2017;2017:1480294. doi: 10.1155/2017/1480294, PMID 29181121
63. Yeh H, Chuang C, Chen H, Wan C, Chen T, Lin L. Bioactive components analysis of two various gingers (*Zingiber officinale Roscoe)* and antioxidant effect of ginger extracts. LWT Food Sci Technol 2014;55:329-34. doi: 10.1016/j.lwt.2013.08.003
64. Kumar NV, Murthy PS, Manjunatha JR, Bettadaiah BK. Synthesis and quorum sensing inhibitory activity of key phenolic compounds of ginger and their derivatives. Food Chem 2014;159:451-7. doi: 10.1016/j.foodchem.2014.03.039, PMID 24767081
65. Nile SH, Park SW. Chromatographic analysis, antioxidant, anti-inflammatory, and xanthine oxidase inhibitory activities of ginger extracts and its reference compounds. Ind Crops Prod 2015;70:238-44. doi: 10.1016/j.indcrop.2015.03.033
66. Chang JS, Wang KC, Yeh CF, Shieh DE, Chiang LC. Fresh ginger (*Zingiber officinale)* has anti-viral activity against human respiratory syncytial virus in human respiratory tract cell lines. J Ethnopharmacol 2013;145:146-51. doi: 10.1016/j.jep.2012.10.043, PMID 23123794
67. Vijaya JJ, Jayaprakash N, Kombaiah K, Kaviyarasu K, Kennedy JL,

Ramalingam JR, *et al*. Bioreduction potentials of dried root of *Zingiber officinale* for a simple green synthesis of silver nanoparticles: Antibacterial studies. J Photochem Photobiol Biol 2017;177:62-8. doi: 10.1016/j.jphotobiol.2017.10.007

68. Zhang M, Viennois E, Prasad M, Zhang Y, Wang L, Zhang Z, *et al*. Edible ginger-derived nanoparticles: A novel therapeutic approach for the prevention and treatment of inflammatory bowel disease and colitis-associated cancer. Biomaterials 2016;101:321-40. doi: 10.1016/j.biomaterials.2016.06.018, PMID 27318094
69. Khan AM, Shahzad M, Asim MB, Imran M, Shabbir A. *Zingiber officinale* ameliorates allergic asthma via suppression of Th2-mediated immune response. Pharm Biol 2015;53:359-67. doi: 10.3109/13880209.2014.920396, PMID 25420680
70. Srinivasan K. Black pepper and its pungent principle-piperine: A review of diverse physiological effects. Crit Rev Food Sci Nutr 2007;47:735-48. doi: 10.1080/10408390601062054, PMID 17987447
71. Singh S, Kapoor IP, Singh G, Schuff C, De Lampasona MP, Catalan CA. Chemistry, antioxidant and antimicrobial potentials of white pepper (*Piper nigrum* L.) essential oil and oleoresins. Proc Natl Acad Sci India Sect Biol Sci 2013;83:357-66. doi: 10.1007/s40011-012-0148-4
72. Nahak G, Sahu RK. Phytochemical evaluation and antioxidant activity of *Piper cubeba* and *Piper nigrum.* J Appl Pharm Sci 2011;1:153-7.
73. Wang M, Chittiboyina A, Parcher J, Ali Z, Ford P, Zhao J, *et al*. *Piper nigrum* oil determination of selected terpenes for quality evaluation. Planta Med 2018;17:84.
74. Bui TT, Piao CH, Song CH, Shin HS, Shon DH, Chai OH. *Piper nigrum* extract ameliorated allergic inflammation through inhibiting Th2/Th17 responses and mast cells activation. Cell Immunol 2017;322:64-73. doi: 10.1016/j.cellimm.2017.10.005, PMID 29066080
75. Ngo QM, Tran PT, Tran MH, Kim JA, Rho SS, Lim CH, *et al*. Alkaloids from *Piper nigrum* exhibit anti-inflammatory activity via activating the Nrf2/HO1 pathway. Phytother Res 2017;31:663-70. doi: 10.1002/ptr.5780, PMID 28185326
76. Rehman A, Mehmood MH, Haneef M, Gilani AH, Ilyas M, Siddiqui BS, *et al*. Potential of black pepper as a functional food for treatment of airways disorders. J Funct Foods 2015;19:126-40. doi: 10.1016/j.jff.2015.09.006
77. Zarai Z, Boujelbene E, Salem NB, Gargouri Y, Sayari A. Antioxidant and antimicrobial activities of various solvent extracts, piperine and piperic acid from *Piper nigrum.* LWT Food Sci Technol 2013;50:634-41. doi: 10.1016/j.lwt.2012.07.036
78. Favre LC, Rolandelli G, Mshicileli N, Vhangani LN, Ferreira C, Van Wyk J, *et al*. Antioxidant and anti-glycation potential of green pepper (*Piper nigrum*): Optimization of β-cyclodextrin-based extraction by response surface methodology. Food Chem 2020;316:126280. doi: 10.1016/j.foodchem.2020.126280, PMID 32058192
79. Priya NC, Kumari PS. Antiviral activities and cytotoxicity assay of seed extracts of *Piper longum* and *Piper nigrum* on human cell lines. Int J Pharm Sci Rev Res 2017;44:197-202.
80. Khawas S, Nosáľová G, Majee SK, Ghosh K, Raja W, Sivová V, *et al*. *In vivo* cough suppressive activity of pectic polysaccharide with arabinogalactan type II side chains of *Piper nigrum* fruits and its synergistic effect with piperine. Int J Biol Macromol 2017;99:335-42. doi: 10.1016/j.ijbiomac.2017.02.093, PMID 28254575
81. Rastogi RP, Mehrotra BN. Compendium of Indian Medicinal Plants. New Delhi: Lucknow and Central Drug Research Institute; 1993.
82. Saraf A, Saraf A. Phytochemical and antimicrobial studies of medicinal plant *Piper longum* linn. Int J Pharm Phytochem Res 2014;6:213-22.
83. Madhu SK, Vijayan VA, Shaukath AK. Bioactivity guided isolation of mosquito larvicide from *Piper longum*. Asian Pac J Trop Med 2011;4:112-6. doi: 10.1016/S1995-7645(11)60048-5, PMID 21771432
84. Kaushik D, Rani R, Kaushik P, Sacher D, Yadav J. *In vivo* and *in vitro* antiasthmatic studies of plant *Piper longum* Linn. Int J Pharmacol 2012;8:192-7. doi: 10.3923/ijp.2012.192.197
85. Shah R, Pathan A, Vaghela H, Ameta SC, Parmar K. Green synthesis and characterization of copper nanoparticles using mixture (*Zingiber officinale, Piper nigrum* and *Piper longum*) extract and its antimicrobial activity. Chem Sci 2019;8:63-9.
86. Guo Z, Xu J, Xia J, Wu Z, Lei J, Yu J. Anti-inflammatory and antitumour activity of various extracts and compounds from the fruits of *Piper longum* Linn. J Pharm Pharmacol 2019;71:1162-71. doi: 10.1111/jphp.13099, PMID 31049982
87. Chauhan N, Uniyal P, Chauhan R, Singh C, Kumar D. *In* vitro antibacterial effects of piper longum fruit extracts on human pathogens and phytochemical analysis. Int J Res Anal Rev 2019:6:232-88.
88. Nakkala JR, Mata R, Sadras SR. The antioxidant and catalytic activities of green synthesized gold nanoparticles from *Piper longum* fruit extract. Process Saf Environ Prot 2016;100:288-94. doi: 10.1016/j.psep.2016.02.007
89. Jeyaseelan EC, Jashothan PT. *In vitro* control of *Staphylococcus aureus* (NCTC 6571) and escherichia coli (ATCC 25922) by *Ricinus communis*. Linn. Asian Pac J Trop Biomed 2012;2:717-21. doi: 10.1016/S2221-1691(12)60216-0, PMID 23570001
90. Patel VR, Dumancas GG, Viswanath LC, Maples R, Subong BJ. Castor oil: Properties, uses, and optimization of processing parameters in commercial production. Lipid Insights 2016;9:1-12. doi: 10.4137/LPI.S40233, PMID 27656091
91. Abdul WM, Hajrah NH, Sabir JM, Al-Garni SM, Sabir MJ, Kabli SA, *et al*. Therapeutic role of *Ricinus communis* L. and its bioactive compounds in disease prevention and treatment. Asian Pac J Trop Med 2018;11:177. doi: 10.4103/1995-7645.228431
92. Omahu OJ, Omale AC. Physicochemical properties and fatty acid composition of castor bean *Ricinus communis* Linn seed oil. Am J Appl Ind Chem 2017;3:1-4.
93. Salles MM, Badaró MM, Arruda CN, Leite VM, Silva CH, Watanabe E, *et al.* Antimicrobial activity of complete denture cleanser solutions based on sodium hypochlorite and *Ricinus communis* Linn a randomized clinical study. J Appl Oral Sci 2015;23:637-42. doi: 10.1590/1678-775720150204, PMID 26814466
94. Al-Mamun MA, Akter Z, Uddin MJ, Ferdaus KM, Hoque KM, Ferdousi Z, *et al*. Characterization and evaluation of antibacterial and antiproliferative activities of crude protein extracts isolated from the seed of *Ricinus communis* Linn in Bangladesh. BMC Complement Altern Med 2016;16:211. doi: 10.1186/s12906-016-1185-y, PMID 27405609
95. Javanshir A, Karimi E, Maragheh AD, Tabrizi MH. The antioxidant and anticancer potential of *Ricinus communis* Linn. Essential oil nanoemulsions. J Food Meas Char 2020;14:1356-65. doi: 10.1007/s11694-020-00385-5
96. Tunaru S, Althoff TF, Nüsing RM, Diener M, Offermanns S. Castor oil induces laxation and uterus contraction via ricinoleic acid activating prostaglandin EP3 receptors. Proc Natl Acad Sci U S A 2012;109:9179-84. doi: 10.1073/pnas.1201627109, PMID 22615395