Review Article

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THE NARRATIVE REVIEW ON SIDDHA POLYHERBAL FORMULATION: GARUDAN KIZHANGU ENNAI

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ABSTRACT

Garudan kizhangu ennai is a polyherbal Siddha formulation widely used for various skin diseases, especially alopecia areata, mentioned in the Siddha literature "Siddha vaidya thirattu". Alopecia areata can be correlated with the term "Puzhuvettu" in the Siddha system of medicine. This is a complex autoimmune condition that causes non-scarring hair loss. Nowadays, the prevalence rate of alopecia is higher among children and adolescents. Hence, this review aims to emphasise the potential role of Garudan kizhangu ennai in managing alopecia areata in Siddha. The ingredients of Garudan kizhangu ennai are briefly explained here in Siddha aspects, actions, chemical constituents and pharmacological aspects. All the above information was collected from various scientific articles and books. The scientific studies explored the ingredients of Garudan kizhangu ennai, predominantly possessing antihistamine, antivenom, antioxidant, antipyretic, anti-inflammatory, analgesic, antimicrobial, antidiabetic, immunomodulatory, and anticancer activities. This review revealed that the Garudan kizhangu ennai could be effective for managing alopecia areata, and further clinical studies will be needed to prove the drug's efficacy.

Keywords: Alopecia areata, Garudan kizhangu ennai, Puzhuvettu, Kollan kovai, Skin diseases, Siddha.

INTRODUCTION

The Siddha system has played an essential role in the medical world. Siddha is an integrated part of the Indian system, which is very potent and unique in nature[1]. Garudan kizhangu ennai is the polyherbal Siddha formulation widely used for various skin diseases, especially alopecia areata. This is mentioned in the literature Siddha vaidya thirattu[2]. Aagasa garudan kizhangu is the main ingredient of garudan kizhangu ennai. This is also named as “kollan kovai kizhangu”, “garudan”, “aagaya garudan”, “Peicheenthil” etc. The therapeutic uses of aagasa garudan kizhangu are indicated for virulent poison (Kodiya nanju), Anemia (Paandu), Pruritus (Namaichal), Thyroidism (Kazhuththu kazhalai), Leprosy (Perunoi), Herpes zoster (Akkipun)[3].

Non-scarring hair loss is caused by the complex autoimmune disorder known as alopecia areata (AA). It often manifests as circular, strongly defined patches of hair loss and can happen at any age[4]. The prevalence of AA varies by country, from 2.1% in the USA to 2.3% in Saudi Arabia to 0.7% in India[5]. Nearly 20% of all occurrences of pediatric alopecia areata (age ≤16 years) can be attributed to this condition. The overall incidence is about 20.2 per 100,000 person-years[6]. It seems that alopecia areata is inherited. There is a 55% concordance rate between identical twins. A recent meta-analysis of genome-wide association studies (GWAS) has focused on the HLA-DRB1 to identify the HLA signal of AA[7]. Conventional therapies include corticosteroids, immunotherapy, and light therapy for managing alopecia areata[8]. Dissatisfaction with conventional medicine and the use of traditional medicines and supplements has increased tremendously worldwide, especially in South India. The tremendous ancient sages mentioned various herbal formulations to manage chronic ailments in the literature. According to the Siddha system of medicine, alopecia is termed “puzhuvettu”. Hence, this review aims to emphasise the potential role of Garudan kizhangu ennai in managing alopecia areata.

Review of Garudan Kizhangu Ennai

The ingredients of Garudan kizhangu ennai are mentioned in Table 1 [2,3], the taste of each drug, parts used, and actions of the drug are mentioned in Table 2 [3] and also the pharmacognostic aspect, chemical constituents are mentioned in Table 3.

Method of preparation: 420 gm of *Corallocarpus epigaeus* and 35 gm of *Embelia ribes, Celastrus paniculatus, Zingiber officinale, Piper nigrum, Piper longum, Nigella sativa* are powdered and taken in a suitable vessel. Add 650ml of castor oil and 420 gm of smashed onion and heat until it reaches the waxy consistency.

Indications: Puzhuvettu (alopecia areata), malachikkal (constipation), kiranthi (venereal disorders), kuttam (leprosy), megaranam (syphilitic ulcer), karumegam (eczema), ulranam (internal ulcers) megaooral (skin itching), vellai (leucorrhoea).

Pharmacological Aspect

Garudan kizhangu (*Corallocarpus epigaeus*): Garudan kizhangu is one of the ingredients in drug G7 due to its antiallergic activity[31]. Gnananath documented that ethanolic extract of *Corallocarpus epigaeus* rhizomes possesses antidiabetic activity comparable with that of the standard Glibenclamide[32]. Venkata nagaanantha and Bhavani *et al*. revealed that root extract of *Corallocarpus epigaeus* showed cytotoxic activity against HT-29, K562 and MCF-7 cell lines with the percentage mortality increased with an increase in concentration[33,34]. Saranya *et al.* documented that *Corallocarpus epigaeus* has the capability of antifungal and antibacterial activity[35]. Jayaseelan studied the different extracts of *Corallocarpus epigaeus* rhizomes and found valuable levels of total free phenol, tannins and flavonoids, which have promising antioxidant activity and exhibit potential anti-inflammatory effects. The extract is almost compared with the standard indomethacin[36]. Vijaya Ponna *et al.* and Hemalatha *et al*. reported that extracts of *Corallocarpus epigaeus* exhibit antidote and anti-snake venom activity[37,38]. Shree Vijaya Kiruba *et al.* and Vasantha *et al*. revealed the anthelmintic and antifungal activity[39,40]. Uthrapathi *et al.* reported the anti-inflammatory activity of *Corallocarpus* by carrageenan-induced paw oedema and the antiarthritic effect by completing Freund's adjuvant-induced arthritic model[41].

Vaividangam (*Embelia ribes*): The methanolic and aqueous extracts of E. ribes showed antibacterial activity against *Salmonella typhi, Staphylococcus aureus, Streptococcus pyogenes, Shigella flexneri, S. sonnei, pseudomonas aeruginosa, E. coli* and *klebsiella*[42-44]. Jalalpure *et al*. reported that *E. ribes* showed the best anthelmintic properties when compared to other plants like *Gynandropsis gynandra, Impatiens balsamina, Celastrus paniculata* and *Mucuna pruriens*[45]. Gupta *et al*. studied the embelin component, and its salts showed significant analgesic property[46]. Ravi Joshi *et al*. demonstrated the antioxidant activity of *Embelia ribes* through DPPH radical scavenge and hydroxyl radical-induced deoxyribose degradation. It has also been found to inhibit lipid peroxidation and restore impaired Mn-superoxide dismutase in rat liver mitochondria[47]. The other pharmacological activities include antidiabetic, hepatoprotective, wound healing activity, antitumor and anti-fertility activity[48-52].

Valuluvai (*Celastrus paniculatus*): Patil *et al.* revealed that methanolic seed extract (50%) of *Celastrus paniculatus* at the optimal dose of 65 mg/kg body weight significantly lowered cholesterol level showed hypolipidemic activity[53]. Bidwai evaluated the seed oil had antispermatogenic effects in adult albino rats when given at a dose of 0.2 ml/48 hours (i.p.) for 30 days[54]. Bhanumathy *et al*. studied the aqueous extract of *Celastrus paniculatus* seed, which showed 50% angiotensin-converting enzyme (ACE) inhibition; ethanol extract showed mild activity, while the acetone extract was devoid of it[17]. Hot water tail immersion test in mice and carrageenan-induced paw oedema in rats revealed the analgesic and anti-inflammatory activities of *C.paniculatus*[55]. Katekhaye *et al*. documented that the antimalarial activity of chloroform extract of the root bark of *Celastrus paniculatus* was the strongest[56]. The other pharmacological activities, such as wound healing, antioxidant activity, and antiarthritic and antiulcer activity, are exhibited through some studies[57-59].

Chukku (*Zingiber officinale*): Mesomo *et al.* studied the antimicrobial activity of ginger against *Staphylococcus aureus* and *Listeria monocytogenes*, followed by *Pseudomonas aeruginosa. Salmonella typhimurium, Shigella flexneri* and *Escherichia coli*[60]. Mangprayool *et al.* revealed that ginger essential oil with citral, eucalyptol and camphor had a relaxing effect on rat's airway and inhibited the carbachol-induced rat tracheal contraction and reported that the bronchodilator activity[61]. Funk *et al.* demonstrated ginger essential oil's anti-inflammatory and analgesic effects in the streptococcal cell wall-induced rheumatoid arthritis model in female Lewis rats. This can inhibit chronic joint inflammation without any effects in the initial acute phase of joint inflammation or granuloma formation at the site of streptococcal cell wall deposition in the liver[62]. Lee studied the gingiberene as the main component for anticancer activity in HeLa, SiHa, MCF-7 and HL-60 cell lines[63]. Khushtar *et al.* revealed the good potency of antiulcer activity of ginger through the aspirin-pylorus ligation-induced ulcer model in Wistar rats[64].

Milagu (*Piper nigrum*): According to Rani *et al*., piperine had potential antimicrobial as well as antifungal effects against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Aspergillus niger, A. flavus, Alternaria alternata* and *Fusarium oxysporum*[65]. Samykutty *et al*. evaluated that piperine significantly suppressed the tumour growth of both androgen-dependent and androgen-independent prostate cancer cells[66]. De Souza and Mona *et al*. revealed that piperine possesses anticancer activity against lung cancer[67] and osteosarcoma[68]. Greenshields *et al*. reported that a combination of piperine and γ-radiation had higher cytotoxicity and effectiveness in stopping the growth of tripe-negative cancer cells than radiation alone in immune-deficient mice[69]. Jeena *et al*. recorded that the essential oil of black pepper exhibited antioxidant activity through scavenged superoxide and inhibited tissue lipid peroxidation[70]. Piperine exhibits many more Pharmacological activities like antihypertensive[71], antioxidant, analgesic, antidepressant and anti-diarrheal activities[72] etc.

Thippili (*Piper longum*): Lokhande *et al.* and Singh *et al.* revealed the potent antimicrobial, antiparasitic, and anthelminthic activity of *Piper longum*[73,74]. Mamun *et al.* studied the anti-inflammatory, analgesic and antiarthritic activity[75]. The essential oils from the roots and fruit of *Piper longum* possess antioxidant, anticancer, neuro-pharmacological, antihyperglycaemic, hepato-protective, antihyperlipidaemic, antiangiogenic, immunomodulatory, antiulcer, antiasthmatic, cardioprotective, and anti-snake-venom agents. Many of its pharmacological properties were attributed to its antioxidative and anti-inflammatory effects and its ability to modulate several signalling pathways and enzymes[76-80].

Karunjeeragam (*Nigella sativa*): Umar *et al*. examined the anti-inflammatory and analgesic activity of *Nigella sativa*[81]. Salama *et al*. evaluated the antidiabetic activity of *Nigella sativa*[82]. Bakathir and Salem *et al*. documented the anticancer and antimicrobial activity of *Nigella sativa*[83,84]. Alemi *et al*. studied the antioxidant, antispasmodic, and bronchodilator activity[85]. Kapoor and Saleem *et al*. revealed hepato-protective, renal-protective and gastro-protective properties[86,87].

Vengayam (*Allium cepa*): Abouzed *et al*. reported that the anti-diabetic activity of the onion significantly reduced the blood glucose levels in streptozocin-induced rats[88]. Moriarty *et al.* revealed that organosulfur compounds and high selenium content are responsible for anticancer activity[89]. Muhlbaueret *et al*. said that onion can inhibit bone resorption and increase total mineral content[90]. The other activities include antispasmodic, anti-diarrheal[91], anti-hypertensive, neuro-protective, antiasthmatic and diuretic effects[92-94].

Amanakkuennai (Castor oil): Rajeshkumar *et al*. reported that analgesic activity is exhibited due to saponin, steroids and

alkaloids in castor oil[95]. Jena *et al*. studied the antinociceptive, antiasthmatic, antioxidant, and anti-fertility activity of castor oil[96]. Flavonoids, alkaloids and tannins are responsible for the anti-inflammatory activity of castor seeds. Upasani *et al.* examined the insecticidal ovicidal activity of castor[97]. Visen *et al.* documented that the extract of castor leaf has hepatoprotective, choleretic and anticholestatic effects[98].

Table 1: Ingredients of Garudan kizhangu ennai

Tamil name	Botanical name	Quantity
GarudanKizhangu	*Corallocarpus epigaeus* Rottl. Willd.	12 palam (420 grams)
Vaivilangam	*Embelia ribes* Burm.f.	1 palam (35 grams)
Valuluvai	*Celastrus paniculatus* Willd.	1 palam (35 grams)
Chukku	*Zingiber officinale* Roscoe	1 palam (35 grams)
Milagu	*Piper nigrum* Linn.	1 palam (35 grams)
Thippili	*Piper longum* Linn.	1 palam (35 grams)
Karunjeeragam	*Nigella sativa* Linn.	1 palam (35 grams)
Vengayam	*Allium cepa* Linn.	12 palam (420 grams)
Amanakkuennai	Castor oil	½ padi (650 ml)

Table 2: Parts used, taste and action of the ingredients

Tamil name	Parts used	Taste	Actions
Garudan Kizhangu	Rhizome	Bitter	Tonic, alterative
Vaivilangam	Seeds	Bitter	Stomachic, carminative, anthelmintic, stimulant.
Valuluvai	Seeds	Bitter	Stimulant, alterative, aphrodisiac, diaphoretic, nervine tonic.
Chukku	Rhizome	Pungent	Stomachic, carminative, sialogogue, digestive, stimulant, rubefacient
Milagu	Seeds	Bitter, pungent	Stimulant, rubefacient, carminative, Antivata, resolvent, antiperiodic.
Thippili	Fruit	Pungent	Carminative, Stimulant.
Karunjeeragam	Seeds	Bitter	Carminative, emmenagogue. Diuretic, galactagogue, anthelmintic, stomachic, parasiticide, emollient.
Vengayam	Bulb	Bitter	Stimulant, rubefacient, emmenagogue, expectorant, demulcent, diuretic, aphrodisiac.
Amanakkuennai	Seeds	Bitter	Antivata, lactagogue.

Table 3: Pharmacognostic aspect and chemical constituents

Plant name	Family	Botanical description	Chemical constituents
Garudankizhangu	Cucurbitaceae	A perennial climber found in dry, arid areas throughout India. Roots conical or napiform, yellowish white, marked externally with circular rings[9].	p-hydroxybenzoylester, named epigaeusyl ester, a sestertepene lactone, viz. corallocarpscalarolide, a pyridine carboxylic ester, designated as corallocarpeonyl ester and an aliphatic C-32 keto-diol[10,11].
Vaividangam	Myrsinaceae	A large, wood-flexible, long shrub also called as the climber. The seeds are horny, reddish, covered and enclosed in a brittle pericarp covered by a thin membrane depressed at the base with ruminate endosperm[12,13].	Vilangin, embelin, christembine (alkaloid), phenolic acids such as caffeic acid, vanillic acid, chlorogenic acid, cinnamic acid, and o-coumaric acid[14].embelinol, embeliaribyl ester and embeliol are also present[15].
Valuluvai	Celastraceae	This is a scrambling shrub with pendulous branches, especially young shoots. Fruits are yellow, capsule-like globules containing 3 valves and 3 cells containing 3-6 seeded. Seeds showing reddish coloured/reddish brown with enclosed aril and having orange yellowish stain[16].	Malkanguniol, malkangunin, celapanine, callappengine, celapagin, celastrine, paniculatine, celastrol, pristimerin, zeylasteral, acetic acid,benzoic acid, oleic, linoleic, palmitic, stearic, crude lignoceric acid, tetracasanoi, tetra sterol, beta amyrin, beta sitosterol, phytol, erucic acid, trans beta copaene, linalool, murrolene, cubenol, valeric acid, pentadecylester, phytone[17, 18].
Chukku	Zingiberaceae	It is a perennial rhizomatous herb with irregularly branched rhizomes, which are white to yellowish brown. Rhizome has a smooth surface and fibrous elements; longitudinal striations are present in the cut if broken[19].	Gingerols (6-gingerol, 8-gingeroland 10-gingerol), shogaols, paradols. quercetin, zingerone, gingerenone-A, and 6-dehydrogingerdione are the main phenolic and terpene compounds such as Curcumene, zingiberene, farnesene, bisabolene, sesquiphellandrene[20].
Milagu	Piperaceae	The pepper plant is a perennial that climbs and spreads. The stem is broad and has knuckles—a plant height of up to 10 metres and a crown diameter of up to 1.5 meters. Pepper seeds have a white, brown seed coat and smooth surface of 3-4 mm diameter[21].	Piperine and other phytochemicals are amides, piperidine, pyrrolidines, and trace amounts of safrole[22].
Thippili	Piperaceae	It has slender, aromatic, perennial climber, woody roots and numerous broad ovate, cordate leaves. The inflorescence is a cylindrical, pedunculate spike; the female flower is up to 2.5 cm long and 4-5 mm in diameter, but the male flower is larger and slender. The fruits are small, ovoid berries,	Piperine along with methyl piperine, iperonaline, asarinine, pellitorine, piperlongumine, piperlonguminine, Brachystamide-A, pipercide and piperidine. Lignans present in P.longum are Sesamin, Fergesin[24].

		shiny blackish green, embedded in fleshy spikes[23].	
Karunjeeragam	Ranunculaceae	This is a small annual flowering plant; the inflated capsule contains numerous oval-shaped black tiny seeds, about 1mm in diameter[25].	Thymoquinone,thymohydroquinone, dithymoquinone, thymol, carvacrol, nigellimine- N-oxide, nigellicine, nigellidine and alpha-hederin[26].
Vengayam	Liliaceae	A biennial plant, the bulb is made of concentric, enlarged, fleshy leaf bases. The outer leaf base dries and becomes thin and variously coloured[27].	Kaempferol, ferulic acid, quercetin, gallic acid, and protocatechuic acid are identified in the onion[28].
Amanakkuennai	Euphorbiaceae	Castor oil is extracted from the Castor beans. Castor seed is characterised by its elongated, ovoid, oval, or square shape; size variable, 0.5 to 1.5cm long. Its Seed colour comprises a base colour that varies from brown or red to black[29],	Glyceride of ricinoleic acid, iso ricinoleic, stearic, linoleic, oleic and dihydroxy stearic acids[30].

CONCLUSION

The scientific studies explored the ingredients of Garudan kizhangu ennai, predominantly possessing antihistamine, anti-snake venom, hepatoprotective, antipyretic, anti-inflammatory, analgesic, antimicrobial, immunomodulatory, anticancer and antioxidant activities etc. This review may initiate various preclinical and clinical studies on this drug to validate its clinical efficacy. As there is a lack of effective treatment for the alopecia areata, Garudan kizhangu ennai would be a cost-effective, potent drug that must be explored.

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