

REVIEW OF A POLY HERBAL SIDDHA FORMULATION VEEZHI ENNEI IN THE TREATMENT OF GARPA VAAYU (POLYCYSTIC OVARIAN SYNDROME)

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ABSTRACT

Veezhi ennei is a traditional Siddha poly herbal formulation being prescribed for Garpa vaayu (Polycystic ovarian Syndrome). This formulation composed of 11 herbal ingredients. According to the scientific review each ingredients of Veezhi ennei possesses antidiabetic, antioxidant and hypolipidemic activity which could have potent therapeutic role in the management of Garpa vaayu (Polycystic ovarian Syndrome)

KEYWORDS: Veezhi ennei, Siddha medicine, polycystic ovarian Syndrome.

INTRODUCTION

Siddha system of medicine is the traditional medicine of our ancestors which has its foundations from superior wisdom of siddhars. Siddhars are those who lived and maintained the body as they desired best. They are responsible for the tamil medicine of the present day and also for many other sciences of public utility. Siddha system spread worldwide because of its significant beneficial effect with insignificant side effect. The disease which were challenging to the medical world were often treated well by our system. One of such disease is Garpavaayu. As per the text, Pararasasekeram, Garparogam is classified into 9 types. Garpavaayu is one among them. The symptoms of garpavaayu are abdominal discomfort, dysmenorrhoea, low back ache, constipation, amenorrhoea, and heaviness of thigh. It may be

correlated with Polycystic Ovarian Syndrome of modern science of medicine. The classical Siddha literature Pararasasekaram cites that any imbalance in three humours may inhibit the release of ovum from the ovaries. This may be related to the subfertility due to ovulatory factors ^[1].

Polycystic ovarian syndrome (PCOS) is one of the most common reproductive health problems of women. It was considered as a problem of anovulation and infertility, which is characterised by irregular menstruation, obesity, insulin resistance, hirsutism, acne, alopecia and recurrent miscarriage ^[2]. The incidence appears to increase due to change in life style and stress. Its prevalence in India ranges from 2.2 to 26% with the age 18 – 45 years ^[3]. It is one of the most poorly defined endocrinological conditions with a complex pathophysiology that has produced considerable scientific debate.

Women with PCOS are at increased risk of reproductive problems including infertility, endometrial CA, late menopause, and also metabolic disturbances including insulin resistance, type II diabetes mellitus, cardiovascular disease, dyslipidemia ^[4]. Despite this, its effective treatment remains a significant challenge to medical profession.

Treatment of PCOS may be enhanced in all aspect of syndromes including short term problems like acne and infertility, long term problems such as obesity, DM, atherosclerosis and even possibly breast CA. Now a day's treatment like clomiphene induces ovulation in case of infertility, metformin treat root cause of PCOS, rectifies endocrine and metabolic functions and improve fertility, surgery comprises laparoscopic multiple punctures of the cyst restore endocrine milieu and improves fertility ^[2].

Many single herbal medicines, poly herbal and herbo mineral formulations are indicated for the above disease in the ancient siddha text. One of such poly herbal formulation is Veezhi ennai mentioned in the text Vaithya saara sangiragam ^[5]. for Garpavaayu. In this each ingredients have been studied for several activities in various animal models such as anti oxidant, anti diabetic, anti hyperlipidaemic, which provides the strong evidence of this formulation in the treatment of PCOS. The present study was carried out to create a scientific data about the Siddha formulation Veezhi ennei by means of analysing the phytochemical constituents, pharmacological actions supporting in the management of PCOS and traditional uses of each ingredients of this formulation.

Ingredients of Veezhi Ennei ^[5]




Aamanakku ennai (*Ricinus communis*.Linn), Aavin nei (Cow's ghee), Veezhi elai saru(*cadaba trifoliata*.Roxb), Venkayam (*Allium cepa*.Linn), Poondu (*Allium sativum*.Linn), Vasambu (*Acorus calamus*.Linn), Lavangam (*Syzygium aromaticum*.Linn), Kottam (*costus speciosus*.sm), Sukku (*Zingiber officinale*.Rosc), Milagu (*Piper nigrum*.Linn) Thippili (*Piper longum*.Linn) and Cow's milk.

Therapeutic dosage: ¼ saer i.e., 70ml once a day for three days.




Studies on the Ingredients of Veezhi Ennei

Morphological characters ^[7], chemical constituents, traditional use ^[8]. and pharmacological studies of each ingredient are discussed.

Table: 1 Plant Description

Tamil name	Botanical name/ Family name	Phytochemicals	Traditional uses ^(10,12)	Action ⁽⁶⁾
Veezhi 	Cadaba indica.Lamk Capparidaceae	Cadabicine, Cadabicine methyl ether, Cadabicine diacetate, α, β-Dihydroferulic acid, capparisine, cadibicilone, aromatic acid and kamphefrol	Gout, Ezema, leucorrhoea, boils, indigestion, constipation, worms in stomach, uterine obstruction, skin diseases, anthelmintic.	Purgative, antivatha, emmenagogue, deobstruent, anthelmintic, stimulant
Sukku 	Zingiber officinalis.Linn Ziniberaceae	Volatile oil, gingerol, alkaloids, flavonoids carbohydrates, proteins, glycosides, saponins, steroids, terpenoids ⁽²⁷⁾ . Aldose reductase inhibitors, curcumene, calamine	Relieve labour pain and to facilitate child birth, migraine, dyspepsia, anorexia, cough, eye diseases, diarrhoea, bone fracture	Carminative, stomachic, stimulant, antioxidant, antidiabetes, expectorant
Milagu 	Piper nigrum.Linn Piperaceae	volatile oil, chief components are sabinene, limonene, chavicine, caryophyllene, α and β-pinene, acid amides, piperine. piperetine, alkaloids, tannins, phenols, coumarins, essential oil, carbohydrates,	Indigestion, dysentery, cough, asthma, peptic ulcer, head ache, anemia, suram, gum ache, cold, larvicidal, taenicidal.	Acrid, carminative, antiperiodic, rubefacient, stimulant, antibacterial, antifungal, resolvent, antivatha, antidote

		proteins, amino acids ⁽⁴⁶⁾ .		
Thippili 	Piper longum.Linn Piperaceae	Piperine and piperatine, alkaloids, tannins, phenols, coumarins, essential oil, piperlongumine, piper longuminine.	Cough, asthma, ulcer, anemia, headache, ear disease, eye diseases, worm infestations, fever, hair loss, rheumatism,	Carminative, stomachic, stimulant, appetizer, antibacterial, antimicrobial, anti inflammatory, antifertility, hypoglycaemic ,
Vasambu 	Acorus calamus.Linn Araceae	α & β asarons, glucoside acorin , calamine, calammenol, eugenol, calamol ⁽¹³⁾ calamine, calamine.	Snake bite, ulcers, epilepsy, halitosis, cough, liver diseases, elephantiasis, head ache, giddiness, painful menstruation, improves speaking ability in children, conjunctivitis	Carminative, stomachic, stimulant, antiperiodic, nauseant, emetic, disinfectant, germicide
Vengayam 	Allium cepa.linn Liliaceae	Acrid volatile oil which contain sulphur, essential oil and organic sulphides, allinins in particular allylalliin, flavonoids.	Body heat, piles, hypertension, aphthous ulcer, thirst, cough, abdominal discomfort, malarial fever, arthralgia, skin diseases	Stimulant, diuretic, expectorant, emmenagogue, rubefacient, demulcent, aphrodisiac. Carminative, antiperiodic, anodyne
Kostam 	Costus speciosus.Retz Asteraceae	Flavonoids, alkaloids, tannin, saponin, sterols ⁽⁹⁾ Diosgenin, tigogenin	Diseases of eye, stomach, neck, head, tongue and mouth, snake bite, piles, ulcers, female sterility, fever, wound, chicken pox, abortion	Stomachic, expectorant, tonic, stimulant, diaphoretic, tigogenin, diosgenin, antifertility, anti inflammatory

Lavangam 	Syzygium aromaticum.Linn Myrtaceae	Alkaloids, saponins, flavonoids terpenoids, tannin, eugenol, caryophyllene, eugenol acetate.	Giddiness, vomiting, diarrhoea, ear disease, cataract, perfumes and soaps	Antispasmodic, carminative, stomachic
Poondum 	Allium sativum.Linn Liliaceae	Alliins especially allylalliin, propenylalliin and methylalliin.	Boils, hearing problem, cough, asthma, worm infestation, vatha diseases, head ache, piles, diarrhoea, night blindness	Carminative, stomachic, tonic, alterative, anti inflammatory, stimulant, antitumour expectorant, antidiabetic diuretic, anthelmintic
Aamanakku 	Ricinus communis.Linn Euphorbiaceae	ricinone, toxalbumin richer, steroids and alkaloids, Methyl ricinoleate, Ricinoleic acid, 12 octadecadienoic acid and methyl ester	Ulcer, burning sensations in eye, nose, ear and mouth, irregular menstruation, Abortifacient, tooth ache.	laxative, diuretic, anticancer, antiprotozoal, abortifacient

1. Costus Speciosus

Morphological Character: A perennial herbs with creeping tuberous rhizome, leaves oblong-lanceolate, flowers white with yellow tinge at throat in terminal globose spike, fruit globose capsule, seed crillate.

Pharmacological Studies

Antidiabetic and Hypolipidemic Activity: J. Eliza *et.al*, isolated Eremanthin from *C. speciosus* and was administered to streptozotocin (STZ) (50 mg/kg bw) induced diabetic male Wistar rats at different doses (5, 10, 20 mg/kg bw) for 60 days. Results of this experimental study indicated that eremanthin possessed hypoglycemic and hypolipidemic activities^[14]

Estrogenic Activity: Choudhury Najma *et al.* investigated the effect of methanolic rhizome extract on ovary and uterus of Gonado-intact female adult mice. The extract showed significant decrease in ovarian weight and increase in uterine weight in comparison with normal control. This might be due to inhibition of release of tropic pituitary gonadotropins

due to negative feedback mechanism and also indicated that the plant had endocrine active estrogenic activity which leads to increase in uterine weight ^[15].

Antioxidant Activity: Nehete et al., 2010 evaluated in vitro antioxidant activity of different extracts of this plant by DPPH radical scavenging activity, total antioxidant capacity, nitric oxide scavenging activity, ion chelating activity, hydroxyl radical scavenging activity and its correlation with total phenolic content. Among all the extracts analyzed, a significant phenolic content and antioxidant activity were found for benzene extract which predicted that the antioxidant activity may be due to the total phenolic content in the plant. Scientific evidences suggest that antioxidants reduce risk for chronic diseases including cancer and heart disease ^[16]

2. *Allium Cepa*

Morphological Character: Perennial or biennial with globose bulb, leaves tubular, blue green inflorescence, stalk hollow, flower greenish white in umbels, fruit thin skinned capsule, seed black and angular.

Pharmacological Studies: Antidiabetic and Antihyperlipidemic effect

Kumari K et.al, evaluated , S-methyl cysteine sulfoxide (SMCS), a sulphur containing amino acid isolated from onion (*Allium cepa* Linn) showed antidiabetic and antihyperlipidemic effects in alloxan diabetic rats, controlled significantly their blood glucose and lipids in serum and tissues and altered the activities of liver hexokinase, glucose 6-phosphatase and HMG CoA reductase towards normal. ^[17]

3. *Acorus calamus*

Morphological Character: Semi aquatic herb with a creeping and branched aromatic rhizome leaves grass like or sword shaped arranged alternately in two vertical rows on the rhizome. Flowers light brown in sessile cylindrical spadix, fruit oblong berry. ^[13]

Pharmacological Studies

Anti-Oxidant Activity: S. Asha devi et.al, isolated Phenolic compounds present in the plants is well known for their ability of scavenging free radical which shows antioxidant

activity^[18]. It has been found to render the protection against γ -radiation induced oxidative stress^[19].

Antidiabetic Activity: David Hansi Prisilla et.al, studied the methanol extract of AC rhizome possesses potent antihyperglycemic activity in STZ induced diabetic rats.⁽²⁰⁾ The ethyl acetate fraction of *Acorus calamus* L. has been found to possess hypoglycemic, hypolipidemia and other beneficial effects through the mechanism of insulin sensitizing and hence possess the great potential for the treatment of diabetes and other cardiovascular complications without any gain in body weight^[20].

Hypolipidemic Activity: Administration of the 50% ethanolic extracts (100 and 200 mg/kg) as well as saponins (10 mg/kg) isolated from the extract demonstrated significant hypolipidemic activity^[21].

4. *Cadaba Indica*

Morphological Character: Unarmed straggling much branched shrub leaves elliptic-oblong, flowers greenish white in few flowered terminal corymbs, fruit berry, and cylindrical torulose.

Pharmacological Studies

Anti -Diabetic Activity: Arokiyaraj S et.al, evaluated the alcohol and aqueous extract of *Cadaba farinosa* (leaves) were subjected for hypoglycemic activity in wistar rats (160- 200 g). The oral administration of leaf extracts at dose 1000 mg/kg led to a significant blood glucose reduction^[22].

Antioxidant activity

Umesh BT et.al determined 250 and 500 mg/kg of ethyl acetate and aqueous fraction of *Cadaba farinosa*, Forsk shows significant antioxidant activity (DPPH scavenging method, Nitric oxide scavenging method, Super oxide anion radical scavenging method, Hydroxyl scavenging activity⁽²³⁾

5. *Ricinus Communis*

Morphological Character: A tall glabrous annual or perennial shrub, stem hollow or pithy often brittle, leaves palmately 7-11 lobed long petioled. Flower greenish in terminal panicles, unisexual, fruit capsule or schizocarp, 2-3 valved pericarp warty, seeds mottled.

Pharmacological Studies

Antioxidant Activity: *R. communis* shows antioxidant activity by using lipid method and free radical scavenging effect on 2, 2 picrylhydrazyl radical (DPPH) and hydroxyl hydrogen peroxide ^[25].

Anti -Diabetic Activity

Shoken P et.al, Ethanolic extract of root of plant significantly decreased the fasting blood glucose of the diabetic rats from an initial level of 386 ± 41 mg/dl to 358 ± 3 , 293 ± 28 , 191 ± 25 , 13 ± 29 , 96 ± 20 and 79 ± 16 mg/dl on 2nd, 5th, 7th, 10th, 15th and 20th day, respectively^[26].

6. *Allium Sativum*

Morphological Character: Perennial herb, stem erect, leafy in the middle, leaves flat, garlic bulb is usually a compound bulb oval in shape, the skin colour of the bulb is silky white, flowers reddish or greenish white in cluster.

Pharmacological Studies

Lipid Lowering Effect: Adesh K. Jain et.al, evaluate the lipid lowering effect of standardized garlic 900 mg/d produced a significantly greater reduction in serum TC and LDL-C in controlled clinical study. The baseline serum TC level of 262 ± 34 mg / dL was reduced to 247 ± 40 mg/dL ($p < 0.01$) after 12 weeks of standard garlic treatment ^[27].

Antidiabetic Activity: Martha Thomson et.al, determined raw garlic has significant hypoglycaemic, hypocholesterolaemic and hypolipidaemic effects STZ-induced diabetic rats. The hypoglycaemic action of garlic could possibly be due to an increase in pancreatic secretion of insulin from β -cells, release of bound insulin or enhancement of insulin sensitivity^[28].

Antioxidant Activity

Muhammed et.al, found S-Allylcysteine, a key component of aged garlic, is a potent antioxidant and can inhibit advanced glycation end products (AGEP) formation⁽²⁹⁾.

7. *Zingiber Officinale*

Morphological Character: Rhizomatous perennial herb, aerial shoot leafy, leaves sheathing, alternate, linear, lanceolate, flowers yellow with dark purplish spots in condensed spikes, fruit oblong capsule.

Pharmacological Studies

Anti-Oxidant Actions: The anti-oxidant action of ginger has been proposed as one of the major possible mechanisms for the protective actions of the plant against toxicity and lethality of radiation ^[30, 31] and a number of toxic agents such as carbon tetrachloride and cisplatin ^[32, 33] gingerol is endowed with strong anti-oxidant action both in vivo and in vitro, in addition to strong anti-inflammatory and anti-apoptotic actions ^[34]. This makes it a very effective agent for prevention of ultra violet B (UVB)-induced reactive oxygen species production and COX-2 expression, and a possible therapeutic agent against UVB-induced skin disorders. ^[35]

Effect On Lipid And Glucose Concentrations In Blood: It has been reported that treatment with a methanolic extract of dried rhizomes of ginger produced a significant reduction in fructose-induced elevation of lipid levels, bodyweight, hyperglycemia and hyperinsulinemia. Treatment with an ethyl acetate extract of ginger did not produce any significant change in either of the last two parameters. However, it produced a significant reduction in elevated lipid levels and body weight. The extent of activity appears to be dependent on the concentration of gingerol present in the extracts ^[36].

Hypoglycemic

Potentials of aqueous extract of raw ginger given in streptozotocin (STZ)-induced diabetic rats for a period of 7 weeks. These results confirmed the earlier reports that suggested that raw ginger possesses hypoglycemic, hypocholesterolemic and hypolipidemic potential ^[37].

8. Piper Longum

Morphological Character: Slender, aromatic, dioecious root climber, leave simple, alternate, ovate to oblong, deeply cordate, flowers minute on axillary spikes, green at first turning yellow later, unisexual, fruit berry, red when ripe and partially sunk in the fleshy axis of the spike.

Pharmacological Studies

Antidiabetic Activity: Oral administration of dried fruits has shown significant anti-hyperglycemic, anti-lipidperoxidative and antioxidant effects in diabetic rats comparable to that of the standard reference drug glibenclamide ^[38].

Hypochoesterolaemic Activity: Methyl piperine significantly inhibited the elevation of total serum cholesterol, and the total cholesterol to HDL-cholesterol ratio, in rats fed with a high cholesterol diet ^[39]. The unsaponifiable fraction of the oil of *P. longum* also significantly decreased total serum cholesterol and hepatic cholesterol in hypercholesterolaemic mice ^[40].

Antioxidant Activity: The analysis of combination of species (*Piper nigrum*, *Piper longum* and *Zingiber officinale*), herbs (*Cyperus rotundus* and *Plumbago zeylanica*) revealed the antioxidant potential of the ingredients in the following order: *Piper nigrum* > *Piper longum* > *Cyperus rotundus* > *Plumbago zeylanica* > *Zingiber officinale* ^[41].

9. *Syzygium Aromaticum*

Morphological Character: Pyramid shaped evergreen tree, leaves elliptic to lanceolate, coriaceous. Flower buds borne in small clusters at the ends of branches, greenish turning pink at maturity, aromatic, fruit drupe, fleshy dark pink one seeded.

Pharmacological Studies

Antioxidant Activity: The antioxidant activity of clove bud extract and its major aroma components were comparable to that of the natural antioxidant, α -tocopherol (vitamin-E) ^[42]. Antioxidant activity of *S. aromaticum* flower clove is higher (68.65%) than natural antioxidant to copherol (65.21%) ^[43]. The ethanol extract of the clove buds showed remarkable scavenging activity (93%), as compared with synthetic antioxidants ^[44]. Scott *et al.*, ^[45] has observed that *S. aromaticum* possesses both anti-inflammatory and antioxidant properties.

Hypolipidemic Activity: According to Shyanala *et al.*, Hypolipidemic effect of *S. aromaticum* is due to its ability to combat oxidative stress by quenching free radicals generated in the body as a result of high fat diet. They suggested that use of moderate quantity of cloves in diet as an antioxidant is offering protection against hyperlipidemia ^[46].

10. *Piper Nigrum*

Morphological Character: A stout glabrous climber stem terete, leaves broadly ovate. Flower bisexual in axillary spikes. Fruit black when matured.

Pharmacological Activity

Antioxidant Activity: İlhami Gülçin et.al, determined water extract (WEBP) and ethanol extract (EEBP) of black pepper exhibited strong total antioxidant activity. The 75 µg/ml concentration of WEBP and EEBP showed 95.5% and 93.3% inhibition on peroxidation of linoleic acid emulsion, respectively. On the other hand, at the same concentration, standard antioxidants such as butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT) and α -tocopherol exhibited 92.1%, 95.0%, and 70.4% inhibition on peroxidation of linoleic acid emulsion, respectively.

CONCLUSION

The literature evidence thus revealed many relative therapeutic properties like hypoglycaemic, hypolipidemic and antioxidant in each ingredient of Veezhi ennei. The above said effects of these plants are due to the presence of polyphenols, terpenoids, alkaloids, flavanoids, glycosides and other active constituents. In this hypoglycemic effect of the plants correct insulin resistance, antifertility activity regularise the menstruation, hypolipidaemic effect reduces obesity thus the complications of PCOS like metabolic disturbances including insulin resistance, type II diabetes mellitus, cardiovascular disease, dyslipidemia are reduced. Therefore this review concludes that the poly herbal formulation Veezhi ennei may be effective in the treatment of PCOD. Result of the present study suggested that Veezhi ennei may have potential role in treatment of PCOD either by its hypoglycemic or hypolipidemic or anti oxidant action or by the combined effect of all.

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