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"*AGATHIYAR KUZHAMBU*"- NOT ONLY A PURGATIVE- AN OVERVIEW

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Keywords:

Siddha medicine, Internal medicine, *Agathiyar Kuzhambu*, Purgative medicine, Adjuvant

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ABSTRACT: The Siddha System of Medicine is one of the most ancient traditional medical systems was popular in the ancient Southern part of India. In this system, the herbals, metals, minerals and animal products have been used to prepare the medicines for treating diverse illness. Siddha medicines are divided into inner drug treatments and external drug treatments. *Agathiyar Kuzhambu* is one among the 32 internal medicines contains 11 ingredients which has a vast area of indications. *Agathiyar kuzhambu* is mainly used as purgative medicine. But its action changes widely based on the adjuvant or vehicles used along with it. Being an internal medicine, it not only shows its action internally but also externally. Its external applications sometimes act surprisingly and effectively which gives evidence for its therapeutic action mentioned in the literature. This review describes the phytochemicals and medicinal uses of the part of each ingredient used in this formulation. Ingredients of the formulation and their pharmacological action in various research studies are discussed in this review.

INTRODUCTION: The Siddha System of Medicine originated from the Southern part of India is one the major traditional medical system. It mainly dealt with spiritual and psychosocial well-being of every human. This system mainly helps to attain eternal bliss to prevent mortality. The heritage of medical knowledge was further developed by Siddhars, a group of saints with the goal of immortal human body and soul [1]. The Siddha system of medicine is 32 forms of Internal medicine were described in Gunapadam Siddha text literature. *Kuzhambu* is the one form of internal medicine in which mercurial compounds are ground individually or with other raw drugs into a semisolid form or prepared in a specific process if mentioned [2].

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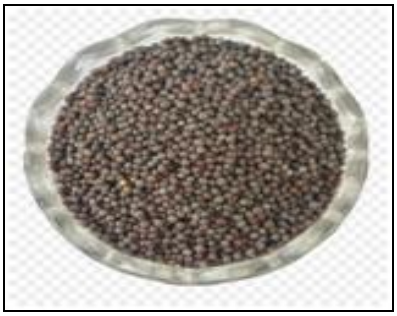
Agathiyar Kuzhambu is one among the Herbo-Mineral formulation contains 11 ingredients which is mentioned in the Siddha formulary of India - part -1. This drug with proper adjuvant and correct dosage, it can cure many diseases [3]. The drug review of '*Agathiyar Kuzhambu'* is a Herbo - Mineral formulation gives evidence for its therapeutic action mentioned in literature. The major ingredients of this drug are *Perungayam, Kadugu, Induppu, Rasam, Vengaram, Naabi, Manosilai, Omam, Aritharam, Karunjeerakam, Nervalam*. The images of the ingredients of *Agathiyar kuzhambu* are shown in **Fig. 1**. This review describes the phytochemicals, action and medicinal uses of the part of each ingredient used in this formulation. Ingredients of the formulation and their pharmacological action in various research studies are discussed in this review.

Agathiyar Kuzhambu is a Herbo-mineral Siddha formulation containing 11 ingredients of herbal and mineral origin their specific and individual locality names, action, phytochemistry, and Siddha medicinal uses are tabulated below in **Table 1**.

Ferulaassa-foetida



Brassica nigra

Aconitum ferox

Trachyspermum ammi

Nigella sativa

Croton tiglium

Sodium chloride impura

Hydrar gyrum

Sodium biborate

Arsenicum rubrum

Arsenii trisulphidum

FIG. 1: INGREDIENTS OF *AGATHIYAR KUZHAMBU*

TABLE 1: INFORMATION ABOUT INGREDIENTS OF *AGATHIYAR KUZHAMBU* [3, 4, 5, 6, 7]

S. no.	Botanical name	Tamil name/ English name	Parts used	Phytochemistry	Action	Medicinal uses in Siddha
1	*Ferulaassa-foetida* L.	*Perungaayam* / Asafoetida	Aromatic Gum-resin obtained by incision from the roots	Organic sulphur compound, Essential oil of garlic-allyl, allyl persulphide, Ferulic acid, Malic acid, Acetic acid, Formic acid, Valerenic acid	Stimulant, Carminative, Antispasmodic, Expectorant, Laxative, Anthelmintic, Diuretic, Aphrodisiac, Emmenagogue	Diseases of the gum and teeth, Snake and scorpion poison, Belching, Indigestion, Vatha diseases, Gastric ulcer, Ascites, Dysmenorrhea, and other menstrual disorders, Body pain due to Iyam

2	*Brassica nigra* (L.) Koch.	*Kadugu* / Black mustard	Seed, oil, and leaves	Myrosin, Sinigrin, Sinapine Sulpha-cyanide, Lecithin, Mucilage, Proteids Glycerides of oleic, stearic, erucic or brassic acids	Emetic, Stimulant, Mild counter-irritant, Rubefacient, Vesicant, Digestive, Diuretic, Pungent stomachic	Cough which causes headache, Running nose, Phlem, Mental disorder, Urticarial poison, Pain, Indigestion, Diarrhoea, Abdominal pain, Delirium, Dysentery, Arthritis, Giddiness Hiccough
3	*Aconitum ferox* Wall. Ex Seringe	*Naabi* / Indian aconite, Monk's hood	Dried root tuber	Pseudo-aconitine, Aconitine, Picro-aconine, Aconine, Benzyl-aconine, Homo-napelline	Diaphoretic, Diuretic, Anti-periodic, Anodyne, Antidiabetic, Antiphlogistic, Antipyretic, Narcotic sedative	Indigestion, Leprosy, gastric ulcer, Scorpion poison, Tenesmus, Diseases of Iyam
4	*Trachysper mumammi* (L.) Sprague	*Omam* / Bishops seed	Seed	Essential oil Thymol	Stomachic, Antispasmodic, Carminative, Antiseptic, Tonic, Sialogogue	Cough, Diarrhoea, Cholera, Bronchial asthma, Dental diseases, Anal diseases, Indigestion, Fever due to Iyam
5	*Nigella sativa* L.	*Karunjeeragam* / Black cumin, Small fennel	Dried fruit and seeds	Essential oil, Albumin, Sugar, Mucilage, Organic acids, Metarbin, Toxic glucoside, Melanthin resembling helleborin, Arabic acid, Carvone, Carvene, Cymene	Carminative, Diuretic, Emmenagogue, Galactogogue, Anthelmintic, Stomachic, Parasiticide, Emollient	Ulcer, Internal body heat, Diseases of eye and head, Scabies, Scalp dermatitis, Cough, Nausea and vomiting, Swelling, Jaundice Chest pain, Abdominal flatulence, Gastric ulcer
6	*Croton tiglium* L.	*Nervaalam* / Purging croton, Croton-oil seed	Seed and fixed oil from the seed	Tiglinic acid, Crotonic or quartenylic acid, Croton oil, Glycerides of stearic, palmitic, myristic and lauric acids, Crotonoleic acid, Crotonol	Purgative, Vermifuge rubefacient	Diseases of rectum and anus, Vatha diseases
7	*Hydrar gyrum*	*Rasam* / Mercury, Quicksilver			Alterative Nutrient, Laxative, Antibilious, Deobstruent, Sialagogue, Diuretic, Antisyphilitic	Diseases of the eye, Syphilis, Eight types of gastric ulcer, Pricking pain, Chronic ulcer, Leprosy, Skin diseases
8	*Arsenii disulphidum*, Bisulphuret of Arsenic, *Arsenicum rubrum*	*Manosilai* / Realgar, Red orpiment			Alterative, Febrifuge, Tonic	Skin diseases, Fever with rigor, Bronchial asthma, Spider poison, Boils
9	*Arsenii trisulphidum* (AS_2, S_3) Trisulphuret of Arsenic	*Arithaaram*, T*haalagam* / Orpiment, Yellow sulphured of arsenic, Yellow Arsenic trisulphide			Expectorant, Anti-pyretic, Emetic, Antidote, Alterative, Nutrient	Diseases of tongue and cranium, Skin diseases, Fiver with rigor, Disease of the eye and head, Syphilitic ulcer of the urethra, Vatha diseases, Itching, Pain, Poisons, cough and cold, Phlem, Tuberculosis, Eczema, Unhealed ulcer, Eight types of gastric ulcer, Fever, Bronchial asthma

10	*Sodii chloridum* impura, Sodium Chloride Impura	*Indhuppu* / Rock-salt, Sea salt, Bay salt, Sodium chlorate		Laxative, Carminative, Diuretic, Stomachic, Digestive, Emetic, Cathartic	Eight types of gastric ulcer, Indigestion, Diseases of the eye, head, tongue, gum, cheek, neck, vagina and sperm, Delirium, Thirst, Breathing diseases, Bleeding piles, Pricking pain, Vatha diseases, Spider, scorpion, and rat poison
11	*Sodii biboras, Sodii boras, Sodium biborate*	*Vengaaram*/ Borax, Sodium Biborale, Sodium Borate, Biborate of Soda, Borax tynkal, Biborate of Sodium, Pyroborate or Tetraborate Sodium, Sodium Pyroborate		Refrigerant, Diuretic, Emmenagogue, Parturifacient, Lithotriptic, Alterative, Antiseptic, Neutralizer, Astringent, Antacid, Local sedative	Itching, Toad skin, Eight types of gastric ulcer, Bleeding piles, Diarrhoea, Renal calculi, Delirium, Diseases of the teeth, Diseases of Iyam, UTI, worm and snake poison, Cough, Indigestion

The Pharmacological Activity of Individual Raw Drugs in *Agathiyar Kuzhambu*:

***Ferulaassa-foetida* L.:**

1. Antispasmodic Activity: The antispasmodic activity of the oleo gum resin by conducting the study of the aqueous extract of asafoetida on the isolated guinea pig ileum. The contractile responses on the isolated guinea pig ileum were induced by administering acetylcholine, histamine, and KCl and then the mean contractile response was noted. After induction of the contractile response on the ileum the aqueous extract was then administered, it was observed that after administration of 3 mg/ml of extract the average amplitude of spontaneous contractions on the isolated guinea pig ileum was decreased up to the extent of about 54 ± 7% [8].

2. Relaxant Effect: The relaxant effect of asafoetida was due to the potent inhibitory effect of the asafetida extract on the muscarinic receptor and also due to the partial inhibitory property of the herb on the histamine (H1) receptor [9].

3. Antifungal Activity: The 95% ethanolic extract of the dried gum was found active on the agar plate. Sitara *et al*., reported the antifungal effect of asafoetida oil against *Microsporum gypseum* and *Trichophyton interdigitale*.

It was observed that essential oil obtained from the rhizome was against the species above at a concentration of about 400 ppm on an agar plate, it also showed mild activity against *Trichophyton equinum* [10, 11].

4. Antioxidant Activity: The leaf aqueous-ethanolic extract showed better DPPH radical scavenging activity and also exhibited better H_2O_2 scavenging and Fe^{2+} chelating activity as compared to the other extracts whereas the stem extracts showed a better nitric acid scavenging activity as compared to the other two. It was observed that all the extracts exhibited good antioxidant activity in linoleic acid peroxidation test [12].

5. Anti-Diabetic Activity: The antidiabetic activity of aqueous extract of asafoetida against pancreatic *β*-cells damaged from alloxan-induced diabetes in rats. Asafoetida led to a significant reduction in blood glucose level and an increase in serum insulin level. It was observed that the level of glucose in animals subjected with alloxan was 10.28 ± 0.85 mmol/l whereas the level of glucose in the diabetic group treated with asafoetida extract was found out to be 6.75 ± 0.31.

There was also a significant rise in insulin secretion in diabetic animals which were subjected to asafoetida extract which was 0.48 ± 0.05 as compared to diabetic animals which were found out to be 0.33 ± 0.06. [13, 14]

6. Hepatoprotective Activity: The experimental data suggested that herbal suspension of the extracts showed promising activity against the carbon-tetrachloride induced hepatotoxicity [15].

7. Antihaemolytic Activity: The antihaemolytic activity of the aqueous-ethanolic extracts of flower,

stem and, leaf of *Ferula asafoetida* regel against H_2O_2 induced hemolysis in rat erythrocytes and it was observed that extracts yielded better results [12].

***Brassica nigra* (L.) Koch.:**

1. Antioxidant Effect: The total antioxidant capacity of the extract was found to be 97.08 mg/g of ascorbic acid. *Brassica nigra* showed an IC_{50} value of 63.09 µg/ml whereas the standard antioxidant showed IC_{50} value 14.45 µg/ml in the DPPH method. The standard antioxidants ascorbic acid, gallic acid, and quercetin showed the reducing power 485.75%, 736.30%, and 763.01%, respectively whereas *Brassica nigra* showed the value of 263.69%. The IC_{50} value in NO scavenging activity of the extract was found to be 118.21 µg/ml whereas ascorbic acid showed the value 5.47 µg/ml and quercetin had the value 15.24 µg/ml. [16]

2. Anti-Inflammatory Effect: The effect of *Brassica nigra* seed extracts on arthritic rats was assessed by the various models. In arthritic rats, inflammation reached maximum on day 3 and maintained till day 9. Paw maintained its inflammation till day 14. A significant reduction was recorded in the extracts treated group. Ankle diameter reached maximum on day 7 and maintained its inflammation till day 14. A non-significant reduction was observed in the extracts treated group [17].

3. Anti-Epileptic Effect: The anti-epileptic effect of the methanolic extract of *Brassica nigra* seeds (75, 150 and 300 mg/Kg; ip) was evaluated in pentylenetetrazole (PTZ) - induced kindling in mice. The methanolic extract of *Brassica nigra* seed reduced the intensity and duration of the seizure. Also, the *Brassica nigra* extract increased the SOD and NO levels and decreased the MDA level in the brain tissues [18].

4. Anti-Diabetic Activity: In streptozotocin-induced diabetic rats treated with aqueous, ethanol, acetone and chloroform extracts of the seeds of *Brassica nigra*, the increase in serum glucose value between 0 and 1 hr of glucose tolerance test (GTT) was the least (29 mg/dl) in aqueous extract treated animals, while it was 54, 44 and 44 mg/dl with chloroform, acetone and ethanol extracts respectively. Also, the effective dose of aqueous extract was found to be 200 mg/kg body weight in GTT. Administration of 200 mg/kg body weight of aqueous extract to diabetic animals once daily for one month brought down fasting serum glucose (FSG) levels. The glycosylated hemoglobin (HbA1c) and serum lipids in the treated group were much less than untreated diabetic controls [19].

***Aconitum ferox* Wall. Ex Seringe:**

1. Anti-Pyretic Activity: *Aconitum steps.* Possesses a wide range of alkaloids, flavonoids and other active constituents which is responsible for their medicinal properties. *Aconitum ferox* & *Aconitum chasmanthum* roots are potent antipyretic and analgesic & high therapeutic index [20].

Sodium Biborate

1. Anti-Inflammatory Activity: (Borax) has got potent anti-inflammatory and healing properties. Hence, it has been used as a treatment in chronic tonsillitis in the form of a gargle. To ensure the scientific validity of the efficacy, a comparative study was conducted between Aspirin tablet and Tankana bhasma which was statistically analyzed. In the study, Tankana bhasma showed significant relief of symptoms that were statistically significant [21].

2. Anti-Histaminic and Bronchodilator Activity: Antihistaminic activity of *Linga mathirai* (LM), where borax is an ingredient, was studied in guinea pigs using histamine-induced bronchospasm where pre-convulsive dyspnoea was used as an endpoint following exposure to histamine aerosol. It was evaluated for antihistamine and bronchodilator activities, and it administrated at the doses of 100, 200 and 400 mg/kg body weight. A dose-response curve for histamine + LM is lower when compared with histamine-induced contraction ($p<0.05$) at the moderate dose level. The LM at moderate dose level significantly prolonged the latent period of convulsions as compared to control following the exposure of histamine aerosol [22].

3. Ovulation-Inducing and Folliculogenesis Activity: This study has been undertaken to investigate the effect of *Uppu parpam* on folliculogenesis, relative ovary and uterus weight and the number of ovarian surface follicles in female Wistar albino rats. Significant increase in FSH, LH and estradiol levels, ovarian and uterine weight was noticed along with increased

folliculogenesis in the experimental groups treated with *Uppu parpam*. Thus, the results suggested the significant ovulatory response in female rats and can be used clinically in reproductive hormonal disorders and in infertility condition of female [23].

***Trachyspermum ammi* (L.) Sprague:**

1. Relaxant Effect on Intestinal Motility in the Ileum of Rats: It has been reported that *T. ammi* possesses bactericidal anticholinergic and anti-histaminic activities. Also, it also has β-adrenergic stimulatory effects. In a previous report, specific effects of *T. ammi* on the mechanical activity of ileum both qualitatively and quantitatively were determined. Anesthetized rats were used for mechanical recording through an isolated organ bath and oscillograph in the study. The effect obtained on intestinal motility was also tested for receptors identification and differentiation with cholinergic and adrenergic agents. The results demonstrate the effective concentrations of acetylcholine causing 50% of maximum response (EC_{50}) obtained in the presence of 0.01 extracts in all five sets of experiments, were significantly higher than those of saline ($P<0.000$) and also the maximum response to acetylcholine obtained in the presence of extracts were lower ($P<0.000$). The results of the study, therefore specified a competitive antagonism effect of *T. ammi* at acetylcholine receptors [24].

***Nigella sativa* L.:**

1. Antibacterial Activity: Antibacterial activity of *N. sativa* against and triple therapy in eradication of *Helicobacter pylori* in patients with non-ulcer dyspepsia were carried out. It was showed that *N. sativa* seeds possess clinically useful anti-*H. pylori* activity, comparable to triple therapy [25].

2. Antioxidant and Anti-Schistosomal Activity: The antioxidant and anti-schistosomal activities of the garlic extract (AGE) and NSO on normal and *Schistosoma mansoni* - infected mice was investigated. The Result showed that protection with AGE and NSO prevented most of the hematological and biochemical changes and markedly improved the antioxidant capacity of schistosomiasis mice compared to the infected-untreated ones. These results suggested that AGE and NSO may be promising agents to complement schistosomiasis specific treatment [26].

3. Anti-Diabetic Activity: The *in-vivo* antidiabetic activity of *N. sativa* seed ethanol extract (NSE) was evaluated in diabetic Merionesshawi. Plasma lipid profile, insulin, leptin, and adiponectin levels were assessed. ACC phosphorylation and Glut4 protein content were determined in liver and skeletal muscle. NSE animals showed a progressive normalization of glycemia. It was also demonstrated that *in-vivo* treatment with NSE exerts an insulin-sensitizing action by enhancing ACC phosphorylation, a major component of the insulin-independent AMPK signaling pathway, and by enhancing muscle Glut4 content [27].

4. Antitumor Activity: The effect of TPA (12-O-tetradecanoyl phorbol-13-acetate) in the patient with myelocytic leukemia and marked decrease in bone marrow myeloblasts, as well as temporary remission of disease symptoms, were observed when TPA was administered alone or in combination with vit. D3 and AraC [28].

***Croton tiglium* L.:**

1. Antinociceptive Effect: Seeds of *C. tiglium* are known to have the antinociceptive effect, and an *in-vitro* and *in-vivo* study was done to evaluate the antinociceptive effect using the seed oil of *C. tiglium* through writhing test in mice [29].

2. Gastrointestinal Activity: *C. tiglium* oil (CO) increase or decrease gastrointestinal motility by affecting contractile frequency and amplitude of intestinal smooth muscle depending on the dose of oil and also induce intestinal inflammation related to the immunological milieu and motor activity which may affect intestinal motility [30].

3. Haem Agglutinating and Haemolytic Activity: Banerjee and Sen (1981) described the purification of a lectin from *C. tiglium* seeds and physicochemical properties of the lectin. Lectin exhibits haemagglutinating activity towards erythrocytes of sheep, cow and a few other animals and haemagglutinating as well as hemolytic activity towards rabbit erythrocytes [31, 32].

4. Genotoxic Activity: The aqueous extract of *C. tiglium* have the potentiality to cause genotoxic activity and it was observed that the exposure of aqueous extract cause increase plasmid DNA strand breakage in a dose-dependent manner [33].

CONCLUSION: *Agathiyar Kuzhambu* is a most important medicine used among the Siddha physicians which contain 11 ingredients having effective in the treatment of all types of Delirium. Based on this evidence of Siddha literature and modern scientific research studies also provide keyhole which result are Anti-oxidant, Anti-Inflammatory, Antispasmodic, Anti-diabetic activities present in ingredients. As this medicine is purgative which can be administered in lower doses, it is an excellent remedial medicine for other therapeutic uses.

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