



## Therapeutic Potential of Siddha Herbomineral Formulation “Kukkilathy Chooranam” in Parkinsonism - A Review

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### ABSTRACT

Siddha System of medicine is widely practised in southern parts of India. The basis of the Siddha system is "anda pinda thathuvam," or the relationship between the universe and the human body, and 96 thathuvams (fundamental principles), which consist of three vital humours, five elements, and seven physical constituents. Based on the three humoral pathologies vaadham (air), pittham (fire) and kapam (water), Siddhars have categorized 4448 diseases. Siddha medications are divided into two groups based on how they are applied: 1. Internal medicine (32 types), 2. External medicine (32 types). One of the 32 types of internal medicine is chooranam. *Kukkilathy Chooranam*, a Siddha herbomineral formulation mentioned in the text of *Anuboga vaithya navaneedham*, has been indicated for Nadukkuvaatham (Parkinsonism). Parkinson's disease is considered to be the second most common age-related degenerative brain condition in India. Nadukkuvaatham is related with Parkinsonism based on the symptoms. This review will explore the potentials of the drug *Kukkilathy chooranam* in treating Parkinsonism.

**Keywords:** *Kukkilathy chooranam*, Siddha medicine, Nadukkuvaatham, Parkinsonism, Neuroprotective.

### INTRODUCTION

The Siddha medical system is one of the native Indian medicinal systems that originated in the Dravidian culture. According to Sangam Era literary evidence, this system goes back to approximately 10,000 BC. The word "siddha" comes from the root word "siddhi," which means attaining perfection. The system emphasizes health as the ideal state of mental, emotional, and physical well-being and spiritual components of a human being<sup>1</sup>.

Siddha views disease as a condition caused when the normal equilibrium of the three humors (collectively called mukkuttram) – vaadham (air), pittham (fire) and kapam (water) is disturbed<sup>2</sup>. The ancient Siddha system of medicine describes the Parkinsonism as Nadukkuvaatham. Nadukkuvaatham is one of the 80 varieties of Vatha noigal that are produced when the Vata dosha becomes unbalanced. Nadukkuvaatham, a persistent tremor resembling that of paralysis agitans marked by pain all over the body, tremor of the nape and the head, hands and legs, incoherent utterance, reddening of the face and the eyes, whirling of the eyes, frequent winking etc,<sup>3</sup>

Parkinson's disease is considered to be the second most common age-related degenerative brain condition in India, after Alzheimer's disease. Additionally, it is the most prevalent motor (movement-related) brain illness. Over 8.5 million people worldwide were estimated to have Parkinson disease (PD) in 2019. The disease has doubled in prevalence over the last 25 years<sup>4</sup>. The prevalence of Parkinson disease is typically 1 to 2 per 1000 people. It typically manifests in middle and advanced age and it affects males more frequently than women. Muscle

rigidity, or stiffness in the muscles, can cause discomfort and difficulty moving, as well as contribute to a stooped posture. Clinical characteristics of Parkinsonism that are commonly observed are akinesia, rigidity, tremors, masked and expressionless faces, and Cesar gait<sup>5</sup>.

*Kukkilathy Chooranam*, a Siddha herbomineral formulation mentioned in the text of *Anuboga vaithya navaneedham*, has been indicated for Vipparuthi, pakkasoolai, alkul putru, powthiram, kandamaalai, moolam, pilavai, kabala soolai, pun, kiranthi, 21 types of meganoigal, megasoolai, megaranam, naabipun, araiyappu, megavayu, thimirvadham, nadukuvatham. The ingredient of *Kukkilathy Chooranam* is *Kukkil* (*Shorea robusta*), *Parangipattai* (*Smilax china*), *Gandhagam* (Sulfur), *Arisithippili* (Fruit of *Piper longum*), *Kandanthippili* (Root of *Piper longum*), *Vetpalaiarisi* (*Wrightia tinctoria*), *Vaividangam* (*Embelia ribes*)<sup>6</sup>. This review will explore the potentials of the drug *Kukkilathy chooranam* in treating Parkinsonism.

### SIDDHA ASPECTS OF PARKINSONISM IN VARIOUS BOOKS:

#### Nadukku vaatham:

Thidukkamurave udal nadukkamurum vaadhamithu seiyumathu thanmaikkelu

Kenidhamurave perum narambadhukal vetiye udal kidukkum nadukkum

Vedukkuriya kaikaalu thimiraagiye varum viraikkum belam kundriye

Vidhamana naaku asaiyathu vaipesidathu viraitudhan thegam vettum



Nadukkamudiyathudal kulirathimamagume vayiru porumiye veekam

Nalinamodu thalai kuninthudal thalai verkum nayanamathu oli kuraiyume

Thidikkidumudal ayarum angamathu meliyume thidamagalu udalumeliyum

Thegamathile pinamaga nadaiyaagume thelivagum idhu paaru nee.

- Vaatha Nithanam-800 <sup>7</sup>

Vitiation of vaatham produces startling with tremors. Shivering of the body with tremors due to defect in the nerves. Loss of strength and numbness over the hands and legs with rigidity. Difficulty in speaking with abnormal movements of the body. Difficulty in walking, flatulence and chilliness of the body. Bowing down of head and reduced vision. Tiredness, loss of weight and depression. Slow walking.

#### Patharu Vaatham:

Udhariye sariramutru mukkave nadukka mundaai

Kadharave ulaindu kutthik kaalkaiyundh thimirundaagum

Sidharave uraindu mindith thiyangave yuvaathi seiyyum

Patharave udharuvaadhandh seigunam pagarungkaale

Nadukkidum padharu meni nalangida udhariththallith

Thidukkida nadukka mindith thiyangida kaikkal sodum

Viduththida kaduthu nondhu visaikkodu thalli viilthum

Madakidap padharuvaatha gunamidhu maaraathendrar

-Pararasa Sekaram <sup>8</sup>

Tremors with shivering occur in the body. Numbness in the hands and legs with pain. Lack of expression and difficulty in initiating activities. Difficulty in performing activities due to tiredness.

#### Nadukkuvaatham:

Nadukkumpidarithalaithaanum nallakaramumviduviduku

Madukkungkadukumpalanaalu madavaaivasanthadumarung

Kadukkumugamumavizhithaanung kannunjchuzhiyanimaikotyum

Madukkungunameyidhukandaa isaindhanadukuvaathamithe.

-Yugimuni vaithiya kaviyam<sup>9</sup>

Pain in occipital area, head, hands. Lack of appetite, Pain in eyes and in face. Eyes are blinking continuously are the symptoms of Nadukkuvatham.

#### Udharuvaatham:

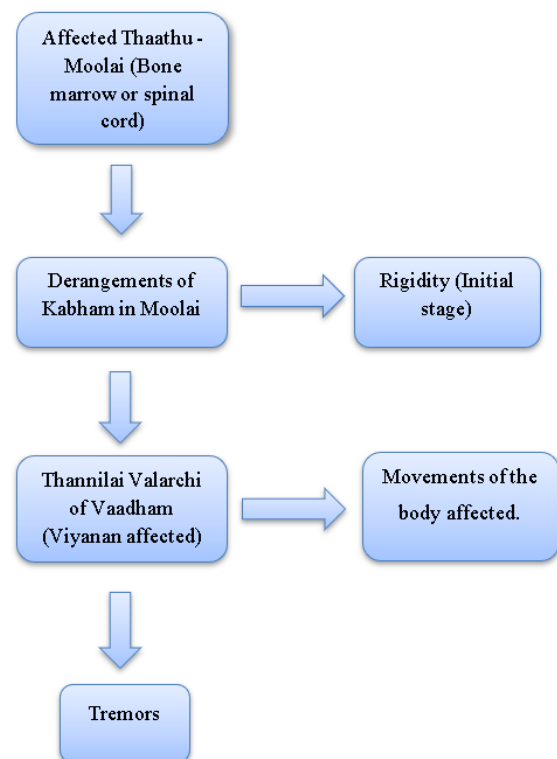
A nervous disease late in life, marked by a peculiar gait in which one foot is passed in front of the other producing a cross legged progression like the movements of a pair of scissors and a muscular contraction causing peculiar characteristic positions of the limbs. The disease is attended with extreme pain in the thighs and giddiness. In advanced stages, it affects the whole body, causing tremor. It is due to the deranged condition of vaayu arising from errors in diet (especially taking cold foods commonly) and finding its lodgements in the extremities of the body<sup>10</sup>.

#### Angasalanavaatham:

Angam + Salanam + Vaatham - Body + Movements + Vaadha disease - a kind of paralysis, progressive in its course by the aggravated condition of Vaayu arising from consumption of food containing excess of starchy substances. It affects the whole nervous system and is marked by a characteristic tremor of the limbs and the head. It is also known as Paralysis agitans, Shaking palsy or Parkinson's disease. It is most common in males over 40 years of age<sup>11</sup>.

#### PATHOPHYSIOLOGY OF NADUKKUVATHAM:

Based on Udal thaathus: <sup>12</sup>



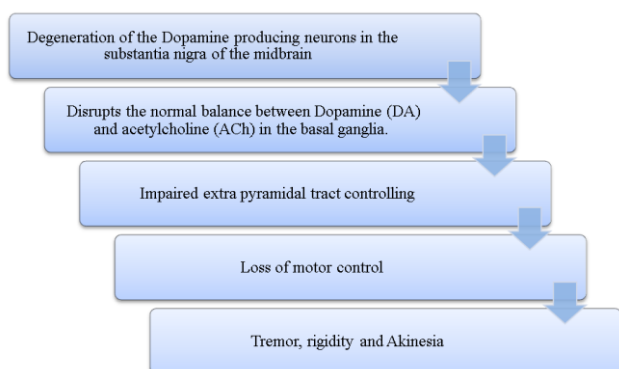
#### CLINICAL FEATURES OF PARKINSONISM:

Modern science predicts that dopamine, an adrenergic neurotransmitter, will be depleted in presynaptic neuronal endings in the limbic system, thalamus, substantia nigra, and reticular activating system.

One of the first signs of Parkinson's disease (PD) is frequently bradykinesia, or slowness of movement (difficulty to begin a movement), which can impair daily

activities like walking and writing. A hallmark of Parkinson's disease (PD) is resting tremor, which usually affects the hands, however not everyone with the disease has tremors. Advanced Parkinson's disease is often characterized by postural instability, which can result in falls and other accidents. Oxidative deamination, which is mediated by mitochondrial monoamine oxidase (MAO) and produces H<sub>2</sub>O<sub>2</sub> and ammonia, is the first step in the catabolism of dopamine. According to neuropathological research on Parkinson's disease, the DAergic neurons loss in the SNpc occurs before the loss of nerve terminals in the striatum.<sup>13</sup>

#### Pathophysiology of parkinsonism: <sup>14</sup>



#### Pathological changes in Parkinsonism:

Loss of substantia nigra neurons → reduced activity of dopamine-producing neurons.

Presence of Lewy bodies in neurons, a cytoplasmic filamentous aggregates, which consist of a protein "alpha-synuclein". It may appear as "halos" when examined in brain tests.

#### DRUG PREPARATION:

##### Ingredients:

Purified *Kukkil (Shorea robusta)* : 32 Varagan (134.4 gm)

Purified Parangipattai (*Smilax china*) : 16 Varagan (67.2 gm)

Purified Gandhagam (Sulfur) : 8 Varagan (33.6gm)

Arisithpilli (Fruit of *Piper longum*) : 2 Varagan (8.4 gm)

Kandathippili (Root of *Piper longum*) : 2 Varagan (8.4 gm)

Vetpalaiarisi (*Wrightia tinctoria*) : 2 Varagan (8.4 gm)

Vaividangam (*Embelia ribes*) : 2 Varagan (8.4 gm)

##### Mode of preparation:

Mix all the ingredients together, grind and sieve them with a cloth. Grind the Nellikai Gandhagam separately into a powder and sieve it. Combine it with other ingredients.

**Dosage:** 1-1.5 Varagan (4.2-6.3 gm)

**Adjuvant:** Honey, Ghee, Sugar, Hot water

**Indication:** Vippuruthi, pakkasoolai, alkul putru, powthiram, kandamaalai, moolam, pilavai, kabala soolai, pun, kiranthi, 21 types of meganoigal. megasoolai, megaranam, naabipun, araiyappu, megavayu, thimirvadham, nadukuvatham.

**Reference:** Anuboga vaithya navaneedham (Part 8)

#### LITERATURE REVIEW:

##### *KUKKIL (Shorea robusta)*



Figure 1: *Shorea robusta*

##### Synonym:

Tamil : Kungiliyam, Sarauvarasam, Gugglu

Sanskrit : Sala, Sarja, Guggilam

Hindi : Damar, Dhuna

Parts Used: Resin

##### Organoleptic Characters:

Taste : Bitter

Potency: Heat

Division : Acrid

##### Action:

Stimulant, Expectorant, Diuretic, Anti-Vatha, Styptic, astringent, carminative, stomachic, aphrodisiac.<sup>15</sup>

##### General Characteristics of Kukkil:

Perumbaadu megampom pera thudalil

Arumbiya pun naarumivai yallal- kurumbaam

Elumburukki pun seezhum eazhum ulagil

Salamperugun kungiliyatha thaal.

-Agathiyar Gunavagadam<sup>16</sup>

Diseases such as leucorrhoea, menorrhagia, ulcers, pustules, and deep wounds can all be treated using this resin.

##### Vellai Kungiliyum:

Vellai yalitha virananaa bikkamalath

Thollaivira nammegath thotruginum – ulle

Varuvarasa merppun varinunsu vedhach

Saruvarasa merpahiyaich chaatru.

-Pathartha Guna Vilakam (Moola Varkam)<sup>17</sup>

Vellai kungiliyam treats Megathar pirandha naalapun,  
Unthikkamala viranam, seelmegam, ulmoolaviranam.

Gugglu thuvark kaip pagum

Viyar tharung kirumi kollung

Kuku rogang kanamegam

Kunma sobai galaitheerkum

Meikiranthi vilaipushna

Vegaththai pokkum mepa

Lakkira kanga lotum

Pidarvali matru daathe

-Mooligai Vilakam<sup>18</sup>

Kukkil has sour and astringent taste. It eliminates  
Kirumigal, kunmam, sobai. It cures Kiranthe, ushnavagam.  
It eliminates the balakirangal.

#### Medicinal Uses:

The powdered resin is combined with sugar and administered to children who have diarrhoea. It is employed to fumigate sick people's rooms. It is applied as a wound ointment.

It is useful in hyperhidrosis, vitiated conditions of pitta, wounds, ulcers.<sup>15</sup>

#### Phytoconstituents:

Mono, sesqui triterpenoids, includes uvaol, ursolic acid, shorbic acid, asiatic acid, corilagin, ellagic, gallic acid, tri and tetrahydroxy ursenoic acid,  $\alpha$  and  $\beta$ -amyrin, and  $\alpha$  – amyrenone.<sup>19</sup>

#### Pharmacological activities:

##### Neuroprotective activity:

Patel et al., state that the neuroprotective effect of *Shorea robusta* resin extract on rats with 3-nitropropionic acid-induced Huntington's disease was mediated by a reduction in oxidative stress, indicating the potential use of *Shorea robusta* in the treatment of Huntington's disease.<sup>20</sup>

##### Antioxidant activity:

According to Khaga Raj Sharma et al., *Acacia catechu*, *Bauhinia variegata*, *Shorea robusta*, and *Phyllanthus emblica* are powerful antioxidant sources with the strongest DPPH radical scavenging activity. The plant's methanolic extract eliminated the DPPH radical, which demonstrated free radical scavenging action. It results from having the greatest levels of flavonoids and phenolics.<sup>21</sup>

#### PARANGIPATTAI (*Smilax china*)



Figure 2: *Smilax china*

#### Synonym:

Tamil: Mathusmigam, Mathusmigi, Seenapattai, Parangichakkai

Sanskrit : Madhusnuhi

Hindi : Chobchini

Parts Used: Root tuber.

#### Organoleptic Characters:

Taste : Sweet

Potency: Coolant

Division : sweet

#### Action:

Alterative, Antisyphilitic, Aphrodisiac, Depurative

#### General characteristics of Parangi Pattai:

Dhaagam palavaadhandh thaathunattam punpilavai

Megam kadikiranthe veezhmoolandh thegamudan

Sootai paganthamer kolvamanam pomparangip

Pattaiyinai ucharithup paar

-Theraiyar Gunavagam<sup>22</sup>

The powder decoction is used to treat leprosy, scabies, ulcers, diabetes, carbuncles, haemorrhoids, and thirst.

#### Medicinal Uses:

The root powder is used for ulcer, eczema, leucorrhoea, indigestion, diarrhoea, and belching.

#### Phytochemical constituents:

The root contains well-known steroidal saponins. Me-protodioscin and its 22-hydroxy counterpart, me-protogracillin, are pro-sapogenin-A of dioscin, also known as gracillin.

#### Pharmacological activities:

##### Neuroprotective activity:

*Smilax china* extract significantly reduced motor defects as measured by catalepsy score using a bar test compared to a group that was given rotenone, according to Sayyad, A. et al. Additionally, via up regulating superoxide dismutase,



it shielded the brain from oxidative damage offers a potentially neuroprotective with antioxidant properties that is effective in treating male Wistar rats with Parkinson's disease.<sup>23</sup>

*Ju Yeon Ban et al.*, showed that rats given *Smilax china* rhizome (SCR) (30 and 50 mg/kg, orally) had a considerably smaller ischemic infarct and improved neurological function. It has been suggested that the neuroprotective benefits of SCR against ischemia-induced brain damage *in vivo* and NMDA-induced neurotoxicity *in vitro* are due to the active components of SCR, resveratrol and oxyresveratrol. It could be a helpful therapy for illnesses caused by neurodegeneration.<sup>24</sup>

*Sabari Senthil et al.*, discovered that in all four behavioral tests- locomotor activity, EPM, Y-maze, and Morris water maze, the ethanolic extract of *S. china* (EESC) at both doses (150 mg/ kg and 300 mg/ kg of body weight) prevented AlCl<sub>3</sub>-induced Alzhiemers Disease in the rats, suggesting enhanced learning and memory. A notable reduction in AChE activity in rat brain areas including the cortex and hippocampal regions was also linked to the AD impact of EESC.<sup>25</sup>

*Chang Ho Jeong et al.*, discovered that the *Smilax china* ethyl acetate fraction exhibited the greatest antioxidant effects associated with its high phenolic content, namely epicatechin and catechin. The body's antioxidant defense mechanism against oxidative damage may benefit from the strong antioxidant qualities of *S.china* root.<sup>26</sup>

In cultured rat cerebral cortical neurons, *Ju Yeon Ban et al.*,found that the methanolic extract of *Smilacis china* rhizome (SCR) showed protection against the neurotoxicity generated by amyloid  $\beta$  protein (A $\beta$ ). SCR (10–50  $\mu$ g/ml) inhibited the production of reactive oxygen species, activation of caspase-3, elevation of cytosolic calcium concentration, and glutamate release into medium as measured by HPLC. It also inhibited the neuronal cell death induced by 10  $\mu$ M A $\beta$  (25–35).<sup>27</sup>

#### THIPPILI (*Piper longum*)



Figure 3: Fruit of *Piper longum*

#### Synonyms:

Tamil: Aargathi, Unrasam, Ulavainesi, Kaman, Kudori, Kolagam, Koli, Saram, Kanai, Aathi marunthu. Thippilikodi,

Sowsandi, Thanduli, Ganam,surutti.

Sanskrit: Krishnapippali

Hindi : Pippal

Parts used:Fruit

#### Organoleptic characters:

Taste : Acrid

Potency: Heat

Division : Sweet

#### Action:

Thermogenic, tonic, diuretic, purgative, expectorant, anthelmintic, stomachic, digestive and emmenagogue.<sup>28</sup>

#### General characteristics of Thippili:

Thippiliyin rendulanj silethumathaip pokividum

Uppisathai mgathai otungan – thappamal

Vaadha suranthanikum maakaparo gantholaikum

Thaadhuvai valarpikunj saatru.

- Agathiyar Gunavagadam.<sup>29</sup>

It treats cough, ulcers, bronchial asthma, kapha illnesses, headaches, delirium, sinusitis, and sore throats.

#### Medicinal uses:

- For fever and cough, this fruit powder combined with honey and bettle leaf juice is administered.
- For delirium, a fruit powder and milk mixture is used.
- The teania infection can be cured by combining fruit powder and honey.

#### KANDAN THIPPILI (*Piper longum*)



Figure 4: Root of *Piper longum*

#### Synonyms:

Tamil: Kiranthigam, Thanmoolam, Thippili Kattai, Nathikaranthai, Narukkuver, Narukku Thippili, Modiver, Thipilli moolam, Narukku moolam, Thandu moolam, Desavaram.

Parts Used:Root

### Organoleptic charaters:

Taste : Acrid

Potency: Heat

Division : Acrid

### Action:

Thermogenic, Acrid, stomachic, carminative, aphrodisiac, expectorant, digestive, emollient,

antiseptic.<sup>28</sup>

### General characteristics of Kandan thippili:

Dhaagappithanj sogandh thaniyaa suramirumal

Megang kurarkammal meikaduppum – yegungaan

Thippilimoo langkandath thippiliya dhaamnarukkuth

Tippiliyen reyorkkaar seppu.

-Agathiyar Gunavagadam<sup>29</sup>

It treats thirst, pitha illness, cough, diabetes, fever, delirium, cough, diarrhoea, and body aches.

### Thippili Moolam:

Thippili moola mushna

Madhigandh thuvarppin vashththa

Moppil setruma vigatha

Mozhithidum vaadhandh theerkum

Meipadu krumi pokku

Marusiyi vilakkung kolach

Seppural moolaiyaa kenmo

deepanak kiniyai mootum.

-Mooligai vilakam.<sup>30</sup>

It has hot potency and astringent action. It treats aggravated kabam, vaadham. It also eliminates the germs and reduces the ageusia.

### Medicinal uses:

#### Root:

- Used to treat respiratory tract conditions such as asthma, bronchitis, and hiccough.
- A sedative for sleeplessness. Hematinic and general tonic.
- Anorexia, dyspepsia, flatulent colic, hiccups, gastropathy, epilepsy, fevers, gonorrhoea, haemorrhoids, vitiated vata diseases, gout, and lumbago can all benefit from them.<sup>28</sup>

#### Fruit:

- Fruit is used to treat lumbago, gout, and palsy. It is also a useful substitute tonic for paraplegia, chronic cough,

and spleen enlargement.

- Infections of the respiratory tract, sleep disorders.<sup>28</sup>

### Phytochemical constituents:

Piperine, pipartine, piperlongumine, piperlonguminine, triazontane, dihydro stigmasterol, reducing sugars, and glycosides are all found in *Piper longum* roots.

The fruit includes pipartine and piperine (4-5%), piperlongumine, Rosin and Piperchabaoside, Sesamin, pulvuatilol, fargesin

- Amygdalins, starch, protein, carbs, saponins, and volatile oils.

### Pharmacological activities:

#### Neuroprotective Activity:

*Ying Bi et al.* discovered that PLA (Alkaloids of *Piper longum* L.) protected dopaminergic cells from MPTP neurotoxicity in an MPTP-induced chronic mouse model of Parkinson's disease (PD). This resulted by reducing MDA levels (a byproduct of lipid peroxidation), improving antioxidative defense by raising GSH levels and SOD activity, and ameliorating behavioral abnormalities.<sup>31</sup>

According to research by *Hao Wang et al.*, rats given *Piper longum* L (PLL) derived alkaloids had improvements in rotenone-induced motor impairments, reduced formation of reactive oxygen species (ROS), and stabilized mitochondrial membrane potential, prevented rotenone-induced apoptosis, and a pretreatment triggered autophagy, which probably reduced neuronal damage. In a rat model with Parkinson's disease, the results might indicate that PLL alkaloid extracts offer neuroprotective effects by impacting mitochondrial activity.<sup>32</sup>

The results of *Shiyao Hua et al.*'s study demonstrate that oral piperine therapy may effectively mitigate the extent of brain damage, enhance behavioral impairment, and lessen the degree of cellular damage following pMCAO injury. In permanent cerebral ischemia injury, piperine (10 and 20 mg/kg) was able to maintain low levels of Cyt-c, Caspase-3, and 9. This suggests that piperine may have a neuroprotective impact by controlling the proteins Cyt-c, Caspase-9, and Caspase-3.<sup>33</sup>

A combination of piperlonguminine and dihydro piperlonguminine can significantly control the expression of APP (Amyloid Precursor Protein), according to research by *Hong-Shun Qi et al.*, Patients with Alzheimer's disease benefit from this protein when its synthesis is controlled.<sup>34</sup>

#### Antioxidant activity:

As reported by *Suresh Kumar et al.*, lipid peroxide levels are decreased and glutathione levels are maintained when piperine and root petroleum ether extract from *P. longum* Linn. are used to demonstrate antioxidant function.<sup>35</sup>



**Anti-depressant activity:**

Song Li *et al.*, found that CMS (chronic mild stress) induced elevation of plasma corticosterone level was reversed by chronic piperine administration, significantly ameliorated the reduced proliferation of hippocampal progenitor cells. Antidepressant effects of piperine might be partly related to its modulating in hypothalamo-pituitary- adrenal activity and thereby the resulting neurogenesis.<sup>36</sup>

Seon A Lee *et al.*, discovered that regulation of MAO-A (IC<sub>50</sub> value: 20.9 micro M) activity has been thought to be an effective approach for the treatment of depression and anxiety, while controlling MAO seems to be beneficial in both preventing and treating Parkinson's disease. In a dose-dependent way, piperine shortened the immobility period. It is suggested that MAO-A acts preferentially on serotonin and norepinephrine, while MAO-B (IC<sub>50</sub> value: 7.0 microM) acts preferentially on dopamine. Dopamine is a substrate for MAO-B and is known to play a significant antidepressant role.<sup>37</sup>

**Anticonvulsant action:**

Juvekar *et al.*, proved that the *Piper longum* extract was tested against seizures produced in mice by strychnine, 4-aminopyridine, and pentylenetetrazole (PTZ). Furthermore, giving the groups both doses protected them from PTZ-induced convulsions but not from mice-induced convulsions caused by strychnine or 4-aminopyridine. Reduced GABA levels in the brains of mice given extract compared to animals given vehicle treatment clearly suggested that GABAergic pathways were involved in the anticonvulsant action.<sup>38</sup>

**VAIVIDANGAM (*Embelia ribes*)**

Figure 5: *Embelia ribes*

**Synonym:**

Tamil: Vaivilangam, Varnanai, Keralam

Sanskrit : Jantughna, Krmighna, Vella, Krmihara, Krmiripu

Hindi : Vayavidanga, Bhabhiranga, Baberang

Parts used:Seed

**Organoleptic charaters:**

Taste : Bitter

Potency: Heat

Division : Acrid

**Action:**

Anthelmintic, Carminative, Stomachic, Stimulant<sup>39</sup>

**General characteristics of *Vaividangam*:**

Paandukuttam kunmam parunthoola noivaadhandh

Neendu thirividanj siranthudam poondamadi

Noivilangak kaatadha nunkirumi yaasanappun

Vaivilangankata virumar.

- Agathiyar Gunavagadam<sup>40</sup>

Anaemia, peptic ulcers, obesity, snake bites, and anorectal ulcers are all healed by

*vaividangam*

Vaaivilanga mushnaathikang kaippuru vastthu

Vaayu vaiyaththai manthathoshathth thinaimatrundh thiyavev

Vidangirumi manthakkini theerkum paayuver

Kuraiyenamai yezhudhu mampagathai

- Mooligai Vilakam.<sup>41</sup>

It increases heat and possess sour taste. It controls Vaayu, mandhadhosa kudarkirumigal, manthakkini.

**Uses:**

- It is administered with honey to have an anthelmintic effect.
- Children with bloating, abdominal discomfort, and indigestion are treated with a powdered seed mixed with milk.
- The seeds are ground with butter and administered externally for scorpion bites. It is used topically for headaches.
- Utilised in decoction to treat skin and chest ailments as well as fevers.
- Fruit aqueous extract exhibits antibacterial action against *E. coli* and *Staph aureus*.
- The herb has blood-purifying qualities and is also beneficial.<sup>39</sup>

**Phytochemical constituents:**

- The berries of the *Embelia ribes* plant are rich in chemical components, including tannin, volatile and fixed oils, embelic acid, resin, christembine.
- Phenolic acids such as vanillic acid, chlorogenic acid, cinnamic acid, and ovalbaceous acid [4.33% of the embelin



content] are found in the berries of the *Embelia ribes* plant. Embelin, quercitol, tannin.<sup>42</sup>

#### Pharmacological activities:

##### Anti-Parkinsonism activity:

Koppal A *et al.*, observed that in PD mice, treatment with embelin alone (40 mg/kg) or embelin plus levodopa (7.5 mg/kg) improved brain and liver tissue damage, thyroid hormone changes, peripheral oxidative stress, and brain alpha synuclein expression. These findings suggest that embelin and embelin plus levodopa therapy are therapeutically effective.<sup>43</sup>

##### Neuroprotective activity:

M. Nazam Ansari, *et al.*, observed that in the hippocampus and frontal cerebral cortex, the ethanolic extracts of *E. ribes* dramatically increased the levels of GSH, GPx, GR, and GST as well as the grip strength activity. And decrease in the levels of LDH in the serum and TBARS in the hippocampus and frontal cortex. From the study's findings, therapy over an extended period of time strengthens rats' antioxidant defenses against MCAO-induced localized cerebral ischemia and has neuroprotective effects.<sup>44</sup>

Thippeswamy *et al.*, found that pretreatment of embelin (25 and 50 mg/kg, p.o.) enhanced locomotor activity and hanging latency time and lowered beam walking delay on global ischemia/reperfusion-induced brain damage in rats. Additionally, it enhanced glutathione-S-transferase activity, total thiol content, and decreased lipid peroxidation by a substantial amount in brain homogenates. The reduced cerebral infarction area in groups treated with embelin and histopathological observations<sup>45</sup>

##### Anti-Alzheimer's activity:

The raised plus maze and Morris water maze models were used to assess the anti-Alzheimer's activity of karanjin and embelin in Swiss albino mice, according to Saini *et al.* Improvements in memory and learning have been observed. Alzheimer's disease and other neurological diseases can be treated with both the isolated compounds and the plant that produced them.<sup>46</sup>

##### Antioxidant activity:

According to Bhandari *et al.*, giving hyperhomocysteinemic rats an aqueous extract of *Embelia ribes* (100 and 200 mg/kg, p.o.) for 30 days dramatically reduced the levels of homocysteine, LDH, total cholesterol, triglycerides, LDL-C, and VLDL-C in their serum while raising HDL-C levels. Additionally, a substantial decrease in LPO levels was noted as the GSH content increased. The outcomes were similar to those of folic acid, a commonly used antihyperhomocysteinemic medication.<sup>47</sup>

#### VETPALAI ARISI (*Wrightia tinctoria*)



Figure 6: *Wrightia tinctoria*

#### Synonym:

Tamil: Girimalligai, Kudasam, Varsam

Sanskrit: Hyamaraka

Hindi: Mitha Indrajava

Parts Used: Leaves bark and seed.

#### Oranoleptic charaters:

Taste : sweet

Potency: Coolant

Division : Sweet

Action:

Leaves, bark: Aphrodisiac, Astringent

Seed: Tonic

#### Actions:

Anthelmintic, Stomachic, Aphrodisiac, Astringent, Carminative, Alterative, Stimulant.<sup>48</sup>

#### General Characteristics of Vetpalai arisi:

Vetpaalai thannarisi veeruppitha vaadhamodu

Kotpaar karappan kudalvaadha – uppisathaik

Kaanama lenaalung kandikkung kaasiniyir

Poonar mulaya pugal.

-Agathiyar Gunavagadam.<sup>49</sup>

It treats diarrhoea, bloating, skin conditions and vatha ,pitha disease

#### Medicinal Uses:

- The leaf has the ability to relieve dental pain.
- A bark infusion is administered for fever.
- Bark and seeds are used to treat bilious diseases.
- They are useful in vitiated conditions of pitta and kapha, dyspepsia, flatulence, colic, diarrhoea, Non-specific dermatitis and psoriasis were treated by the bark and seeds.<sup>48</sup>



**Phytochemical constituents:**

Tannins, phenols, steroids, and flavonoids, 9-Hydroxy-cis-12-octadecenoic acid (isoricinoleic acid), 9-hydroxystearic acid, triisoricinoleoyl glycerol, di- and tri-isoricinoleoyl glycerols, arachidic, linoleic, oleic, myristic, palmitic and stearic acids (seeds); B-sitosterol; a-amyrin and its acetate (also in bark); oleanolic and ursolic acids (pods).<sup>50</sup>

**Pharmacological activities:****CNS Activity:**

According to studies conducted by *Ganga Rao et al.*, the brain's expression levels of dopamine, serotonin, and norepinephrine were modulated by the methanol extract of *W. tinctoria* leaves. This implies that the extract could be particularly beneficial in the treatment of depression and anxiety.<sup>51</sup>

**Antioxidant activity:**

In DPPH, H<sub>2</sub>O<sub>2</sub>, and nitric oxide scavenging experiments, *Wrightia tinctoria* extract showed extremely strong antioxidant activity, according to *Dhanabal SP et al.* The IC<sub>50</sub> values were 14.12 ± 0.71 µg/ml, 34.48 ± 5.84 µg/ml, and 71.47 ± 5.95 µg/ml, respectively. These tests included rutin and ascorbic acid as standards to confirm the extract's antioxidant capacity.<sup>52</sup>

**Anticonvulsant activity:**

*Anupama Koneru et al.*, have established that the Cl channel of the GABA/benzodiazepine receptor complex mediates the anticonvulsant activity of the formulation Hab ejund (HJ), which has *Wrightia tinctoria* as one of the ingredients. This study indicates the beneficial role of HJ in generalized tonic, clonic, and absence seizures since inhibition of MES-induced convulsions predicts activity against generalized tonic-clonic seizures (Grandmal epilepsy) and cortical-focal seizures, as well as inhibition of PTZ-induced convulsions against partial or absence seizures.<sup>53</sup>

**GANDHAGAM (SULPHUR)**

**Figure 7:** Sulphur

Sulphur has an astringent and bitter flavour and is one of the natural Paashaanas.

**Synonyms:**

Tamil: Naatham, Paraiveeriyam, Athitha Prakasam, Beejam, Shakthi, Chendurathathi, Deviuram, Ponvarni

Sanskrit: Gandhak

Hindi: Gandhak

English: Brimstone, Sublimed Sulphur

Telugu, Malayalam: Gandakam

**Organoleptic Characters:**

Taste: Astringent, Sweet, Pungent, Bitter.

Potency: Heat

Division: Pungent

Action: Laxative, Tonic, Cholagogue, Antiseptic, alterative, diuretic.<sup>54</sup>

**General characters of Gandhagam:**

Nellikai gandhikku neelpathinen kuttamandham

Vallai kavisaikunma vaayukannoi- polla

Vidakkadivan meganoi veerusuram bedhi

Thidakiraga nikabamondh ther.

- Gunapadam thadhu seeva vaguppu<sup>55</sup>

This is considered to useful in the treatment of 18 types of skin disease. Liver Enlargement, Abdominal distension, Eye diseases, Chronic venereal diseases, Vadha diseases, Chronicdiarrhoea, Gastric ulcer, Poisonous bites, Fever, Chronic dysentery, Kabham.

Katti sorisirangu kaanum kiranthivagai

Kuttal kurainoi kuzhiranam vattamitte

Vandha puraipungal vaikathari yottamidum

Gandhagathin panbithu vekel

-Pathartha guna vilakkam (Thaadhu jeeva vargam)<sup>56</sup>

Generally, sulfur is used to treat boils, itching, scabies, eczema, leprosy, deep wounds and other skin conditions, as well as ringworm, redness, and blackness, which will be cured.

**Medicinal Uses:**

Sulphur is used medicinally to treat scabies. It is thought that sulphur fumes can treat rheumatic diseases and gout. It is also used as the following purposes in medical uses such as, Ring worm, Indigestion, Diarrhoea, Hemorrhoids and anal fissures, Insomnia, Pre-menstrual syndrome, Headache, Dizziness, Mental tension, Lack of memory, Bronchitis, Migraine, Fever and Conjunctivitis.

**Pharmacological activities:**

According to research by *Yuri Yoshioka et al.*, various sulfur compounds in garlic essential oil (GEO) strongly suppressed enzymes linked to Alzheimer's disease. Allyl

mercaptan or allyl methyl sulfide was produced by the body from the organosulfur compounds. After 6 hours of

treatment, sulfur compounds were found in the brain and serum.<sup>57</sup>

**Table 1:** Inferences

S.No	Drugs	Siddha Aspects	Modern Aspects
1.	<i>Kukkil (Shorea robusta)</i>	Taste : Bitter Potency: Heat Division : Acrid Action: Stimulant Expectorant Diuretic <b>Anti-Vatha</b> Styptic. Since it has bitter taste and heat potency, it may help in treating the disease by correcting the deranged <b>kabam</b> .	<b>Neuroprotective activity:</b> <i>Patel et al.,<sup>20</sup></i> <b>Restored motor coordination</b> , Mitochondrial complex function. Possess antioxidant enzyme activity in brain tissue. <b>Free radical scavenging activity:</b> <i>Khaga raj sharma et al.,<sup>21</sup></i> Highest phenolic content and flavonoid content, indicated that the plants are the <b>potent antioxidant source</b> .
2.	<i>Parangipattai (Smilax china)</i>	Taste : Sweet Potency: Coolant Division : sweet Action: Alterative Antisyphilitic Aphrodisiac Depurative It has sweet taste which is able to reduce vaadham as per the song “ <b>Vaatham meliittal mathuram puli uppu</b> ”( mathuram – Sweet)	<b>Neuroprotective activity:</b> <i>a.Sayyed A et al.,<sup>23</sup></i> <b>Improved mobility, coordination</b> and lower incidence of catalepsy recorded. Histology of treated rats reveals that Substantia nigra and basal ganglia in brain of rats reveals mild neuronal degeneration. Alpha synuclein aggregation. Reversal of neuronal damage. Increased SOD, CAT, GSH indicates <b>antioxidant effect</b> . <i>b.Ju Yeon Ban et al.,<sup>24</sup></i> Reserveratrol <b>attenuate neuronal cell damage</b> . <i>c. Sabari senthil et al.,<sup>25</sup></i> Reduced AchE activity in brain. <b>Reversed cognitive impairment</b> . <i>d.Chang-ho jeong et al.,<sup>26</sup></i> High level of phenolics, particularly catechin and epicatechin suggest that S.china root possess excellent antioxidant activities thereby <b>protects against oxidative damage</b> . <i>e.Ju Yeon Ban et al.,<sup>27</sup></i> <b>Inhibited neuronal cell death</b> Increased superoxide dismutase (SOD), catalase and glutathione peroxidase (GPX) enzymes.
3.	<i>Arisi thippili &amp;Kandanthippili (Fruits and Roots of Piper longum)</i>	Arisi thippili: Taste : Acrid Potency: Heat Division : Sweet Action: Thermogenic, tonic, stomachic, digestive, anthelmintic, expectorant, anthelmintic, stomachic, digestive and emmenagogue.  Kandanthippili : Taste : Acrid Potency: Heat Division : Acrid	<b>Neuroprotective activity:</b> <i>a.Ying Bi et al.<sup>31</sup></i> <b>Increase total movement time and distance to walk</b> . Increase levels of <b>Dopaminergic neurons and DOPAC and alleviate bradykinesia</b> . Increase glutathione (GSH) level and superoxide dismutase (SOD) activity and decrease the lipid peroxidation of malondiadehyde. Attenuate the reduction in TH levels, suggesting that PLA might <b>inhibit the injury to dopaminergic neurons</b> . <i>b.Hao Wang et al.,<sup>32</sup></i>

		<p>Action: Acrid, stomachic, carminative, aphrodisiac, expectorant, digestive, emollient, antiseptic.</p> <p>As it has heat potency, it may help in treating the disease by <b>correcting kabam</b>.</p>	<p>Effectively reverse the TH level in midbrain compared to rotenone injury.</p> <p><b>PLL alkaloids protects against the loss of dopaminergic neurons</b> resulting from rotenone exposure.</p> <p>PLL alkaloids acts on mitochondria, <b>suppressing rotenone induced cell death</b>.</p> <p><i>c. Shiyao Hua Ms et al.,<sup>33</sup></i></p> <p><b>Piperine improves grip strength, beam balancing, body sway, and postural reflex test</b> Piperine (10 and 20 mg/kg) was able to maintain low levels of Cyt-c, Caspase-3, and Caspase-9.</p> <p><i>d. Hong-Shun Qi et al.,<sup>34</sup></i></p> <p><b>Decreased the APP protein level</b> and ultimately the production of Aβ.</p> <p><b>Antioxidant activity:</b> <i>e. Sureshkumar et al.,<sup>35</sup></i></p> <p>Decreased lipid peroxide levels and maintain glutathione content, demonstrating <b>antioxidant activity</b>.</p> <p><b>Anti-Depressant activity:</b> <i>f. Song Li et al.,<sup>36</sup></i></p> <p>Elevation of plasma corticosterone level was reversed by chronic piperine administration, significantly <b>ameliorated the reduced proliferation of hippocampal progenitor cells</b>.</p> <p>Antidepressant effects of piperine resulting <b>neurogenesis</b>.</p> <p><i>g. Seon et al.,<sup>37</sup></i></p> <p>Piperine decreased <b>the immobility time</b>. Anti depressant-like effect of piperine enhancement of serotonergic and norepinephrinegic neurotransmission, as well as by <b>dopaminergic neurotransmission</b>.</p> <p><b>Anti-Convulsant activity:</b> <i>h. Juvekaret al.,<sup>38</sup></i></p> <p>Reduced <b>GABA levels</b> in the brains</p>
<p>4.</p>	<p><i>Vaivilangam (Embelia ribes)</i></p>	<p>Taste : Bitter Potency: Heat Division : Acrid Action: ☑ Anthelmintic ☑ Carminative ☑ Stomachic ☑ Stimulant</p> <p>Because of it's bitter taste and also due to its heat potency, it helps in <b>reducing the kabam</b>. Which may be helpful in correcting the disease.</p>	<p><b>Anti Parkinsonism activity:</b> <i>a. Koppal et al.,<sup>43</sup></i></p> <p>Embelin (10 mg/kg) could <b>mitigate</b> MPTP-induced loss of TH staining and <b>altered striatal dopamine levels</b>.</p> <p>Embelin or levodopa or a combination of embelin and levodopa <b>increased the levels of TAC and SOD</b>, which is decreased in SNpc neurons of PD patients that indicates oxidative damage.</p> <p><b>Neuroprotective activity:</b> <i>b. Nazam Ansari M, et al.,<sup>44</sup></i></p> <p><b>Improved grip strength activity</b>, and levels of GSH, GPx, GR, and GST levels and decrease in the levels of LDH.</p> <p><i>c. Thippeswamy et al.,<sup>45</sup></i></p> <p><b>Enhanced locomotor activity</b> and hanging latency time and lowered beam walking delay. Enhanced glutathione-S-transferase activity, <b>glutathione</b></p>

			<p>content, and decreased <b>lipid peroxidation</b> by a substantial amount in brain homogenates.</p> <p><b>Anti Alzheimer's activity:</b> d.Saini <i>et al.</i>,<sup>46</sup></p> <p>Both isolated compounds (karanjin and embelin) decreased the escaped latency in dose dependent manner on day 8 and day 9; this indicates <b>learning behavior</b> and retention of memory.</p> <p><b>Anti oxidant activity:</b> e.Bhandari <i>et al.</i>,<sup>47</sup></p> <p>Increased HDL-Clevels in serum and GSH in brain homogenates, enhancing the endogenous <b>antioxidant levels</b>. Histopathology shows <b>absence of degenerative changes or necrosis</b>.</p>
5.	Vetpaalai arisi (Seeds of <i>Wrightia tinctoria</i> )	<p>Taste : sweet Potency: Coolant Division : Sweet Action: Leaves, bark: Aphrodisiac, Astringent Seed: Tonic Actions: Anthelmintic Astringent Carminative Alterative Stimulant. Because of it's sweet taste it is able to reduce or correct <b>vaadham</b>, which is affected in this disease.</p>	<p><b>CNS Activity:</b><sup>51</sup> a. Ganga Rao <i>et al.</i>, Exhibited a modulatory role in the brain's expression levels of <b>dopamine</b>, serotonin, and nor-epinephrine treating anxiety and depression.</p> <p><b>Anti Oxidant activity:</b><sup>52</sup> b.Dhanabal SP <i>et al.</i> <i>Wrightia tinctoria</i> extract shown extremely <b>strong antioxidant</b> activity.</p> <p><b>Anti convulsant activity :</b><sup>53</sup> c. Anupama Koneru <i>et al.</i> Doses 100 and 300mg/kg significantly reduced the severity of seizures. Myoclonic spasm and clonic convulsions inhibited by Hab ejund (HJ)</p>
6.	Gandagam (Sulphur)	<p>Taste: Astringent, Sweet, Pungent, Bitter. Potency: Heat Division : Pungent Action: Laxative, Tonic, Antiseptic, alterative, diuretic. It has bitter taste and heat potency. So it may help in <b>reducing the kabam</b>. It has sweet taste which is able to <b>reduce vaadham</b>. These properties may help in treating the disease.</p>	<p><b>Anti-Alzheimer's activity</b><sup>57</sup> Yuri Yoshioka <i>et al.</i>, Sulfur compounds in garlic essential oil (GEO) strongly <b>suppressed enzymes</b> linked to Alzheimer's disease</p>

## CONCLUSION

From the scientific evidences and literature reviews, it is clear that the Siddha herbomineral drug *Kukkilathy Chooranam* is effective in the management of Parkinsonism both by thodam theory and also by scientific validation of its ingredients. We suggest that future research should focus on *In vitro*, *In vivo* and Clinical trials of Siddha herbomineral drug *Kukkilathy Chooranam* to prove its effectiveness for Parkinsonism (Nadukkuvatham).

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