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THERAPEUTIC EFFECTIVENESS OF A SIDDHA FORMULATION *"THIRUTHARATCHATHA CHOORANAM"* - A REVIEW

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ABSTRACT

Depression is a mood disorder that causes a persistent feeling of sadness and loss of interest. It is a disorder of major public health importance, in terms of its prevalence and suffering, dysfunction, morbidity and economic burden. Depression is more common in women than men. *Siddha* system of medicine is an ancient system of medicine, which focus on physical, mental, social and spiritual wellbeing of an individual. In *Siddha* system of medicine, *Siddhars* who are spiritual scientists have briefly explained about Depression and specific medicines to cure the disease. *Thiutharatchatha chooranam* is a poly herbal preparation with 14 herbal ingredients which treats psychiatric diseases particularly *unmatham* (Depression). This review is aimed to bring out the scientific evidence for the therapeutic usage and pharmacological activities of *Thirutharatchatha chooranam* and focus its its curative nature of the drug. Most of the *siddha* drugs have anti-depressant, antioxidant, anti-inflammatory, sedative and aphrodisiac activity hence justifying its usage in above mentioned disease.

KEYWORDS: *Siddha* medicine, *Thirutharatchatha chooranam*, *unmatham*, pharmacological activity.

INTRODUCTION

Siddha system of medicine is a unique traditional system of medicine in the world. It is also referred to as *Tamil Maruthuvam* and commonly followed by Tamil people since time immemorial. Herbs, minerals and products of animal origin are basic raw materials of *Siddha* system. According to *Siddha* system of medicine, perfect health is maintained by *Uyir*

thathukkal (*Vaatham, Pitham* and *Kabam*) literally means 'life force' and seven basic tissues (*Udal Thathukkal*). Their proportions in the body govern a person's physical and mental disposition. Whenever there is a derangement in these three *uyirthathukkal (*humors), the resultant will be a disease. The factors that affects this equilibrium are environment, climatic conditions, diet, physical activities and stress. The treatment in *Siddha* medicine is aimed at keeping these three humors in equilibrium and maintenance of seven elements. So proper diet, medicine and a disciplined regimen of life are advised for a healthy living and to restore equilibrium of humors in diseased condition.

Siddha system has a wonderful principle which is *Panchapootham* theory. According to *Panchapootham* theory, the universe and the human body are formed by five elements i.e. Space, Air, Fire, Water and Earth. Likewise, the diseases and the medicines are also based on *Panchapootham* theory. The ultimate aim of *Siddhars* is salvation. They believed in the concept that a healthy soul can be developed only from a healthy body. To achieve this state, they developed methods and medications to strengthen their physical body and thereby their souls.

Siddhars have listed the diseases of mankind as 4448, based on the *Mukkutram* i.e., *Vali, Azhal, Iyyam*. Among the 4448 diseases, Psychological related diseases are classified into 18 varieties by *Siddhar Agasthiyar*. The other imperative *Siddhars Yugi Munivar* and *Theraiyar* have also described about psychiatric diseases in their text.

Depression is a common mental disorder, characterised by sadness, loss of interest or pleasure, feeling guilt or low self-esteem, disturbed sleep, appetite, lethargy and poor concentration. It is a syndrome that reflects a sad and irritable mood exceeding normal sadness or grief. More specifically, the sadness mentality is characterized by a greater intensity, duration with severe symptoms and functional disabilities than normal. In this condition, anxiety and depression are due to lack of courage, sorrow, grief, paleness, loss of wealth and crying with tears are the symptoms of the diseases.

Thirutharatchatha chooranam is a classical *siddha* compound drug mentioned in *siddha* book *Agathiyar vaithiya rathina surukkam.* This medicine is used to treat *unmatham* (depression). This review focuses on the pharmacological activities of each ingredients that supports the traditional claim and the literature search is confined to that area. The search was made from the textbooks in the library of National Institute of Siddha, journals, internet, databases etc.

MATERIALS AND METHODS

1. Collection and authentification of raw drugs

The raw drugs were procured from raw drug store in Chennai and authenticated by competent authority of Department of *Gunapadam*.

2. Purification of raw drugs

All the raw drugs were purified as per the methods mentioned in *siddha* literature.

3. Preparation of the drug '*Thirutharatchatha chooranam'*

The ingredients mentioned in table-1 were powdered separately, mixed well together and equal amount of sugar was added and preserved in an air tight container.

Table 1: Ingredients of '*Thirutharatchatha chooranam*'.

S,no	Tamil name	Botanical name	Part used	Quantity
1.	*Mundhiri*	*Anacardium occidentale*	Nut	35 grams
2.	*Pericham*	*Phonenix dactilifera*	Dry Fruit	35 grams
3.	*Adhimadhuram*	*Glycyrrhiza glabra*	Root	35 grams
4.	*Elam*	*Elettaria cardamoum*	Seed	35 grams
5.	*Thippili*	*Piper longam*	Fruit	35 grams
6.	*Nerpori*	*Oryza sativa*	Fried seed	35 grams
7.	*Kirambu*	*Syzigium aromaticum*	Dried bud	35 grams
8.	*Ilavangapathiri*	*Cinnamomum tammla*	Dried leaf	35 grams
9.	*Kodiveli*	*Plumbago zeylanica*	Root	35 grams
10.	*Koogaineer*	*Maran arundinacea*	Root	35 grams
11.	*Muthakasu*	*Cyprus rotundus*	Root	35 grams
12.	*Nalvelai*	*Gynandropis gynandra*	Root	35 grams
13.	*Milagu*	*Piper nigram*	Seed	35 grams
14.	*Kothumalli*	*Coriandrum sativam*	Seed	35 grams

Table 2: Information about the ingredients of '*Thirutharatchatha chooranam*' as per the *Siddha* text *Gunapadam mooligai vaguppu.*

S. no	Botanical name	Vernacular name				Part used
		Tamil	English	Hindi	Sanskrit	
1.	*Anacardium occidentale*	*Mundhiri*	Cashew nut	Kaju	Shophakara	Nut
2.	*Phonenix dactilifera*	*Pericham*	Date palm	Kajur	Kharjjuram	Fruit
3.	*Glycyrrhiza glabra*	*Adhimadhuram*	Jequitity	Mulath	Yashti-madukam	Root
4.	*Elettaria cardamoum*	*Elam*	Cardamom	Elachi	Ela	Seed
5.	*Piper longam*	*Thippili*	Long pepper	-	Pippali	Fruit
6.	*Oryza sativa*	*Nerpori*	Paddy	Chaval	Vrihi	Fried seed
7.	*Syzigium aromaticum*	*Kirambu*	Clove	Long	Lavangam	Dried bud
8.	*Cinnamomum tammla*	*Ilavangapathiri*	Cassia cinnamom	Tejpatt	Tamalapatram	Dried leaf
9.	*Plumbago zeylanica*	*Kodiveli*	Lead-wort	Chitra	Chidraka	Root
10.	*Maran arundinacea*	*Koogaineer*	Arrow root	Tikhar	-	Root
11.	*Cyprus rotundus*	*Muthakasu*	Nut grass	Mutha	Mutha	Root
12.	*Gynandropis gynandra*	*Nalvelai*	Dog mustard	Hurhur	Ajaganda	Root
13.	*Piper nigram*	*Milagu*	Pepper	Kali-mirch	Maricha	Seed
14.	*Coriandrum sativam*	*Kothumalli*	Coriander seed	Dhanya	Kustumbaridhanyaka	Seed

Pharmacological activities of the ingredients of *Thirutharatchatha chooranam*

1. *Mundhiri* (*Anacardium occidentle)*

The main constituent of *A.occidentale* are flavonoids, quercetin, apigenin, tannins and alkaloids. The flavonoids apigen and quercetin act as a reversible monoamine oxidase inhibitors and selectively binds with high affinity to the central benzodiazepine receptors possesses important antidepressant activity. Administration of ethanolic extract of *Anacardium occidentle* at 200mg/kg and 400mg/kg produced a significant antidepressant like effect in both TST (Tail Suspension Test) and FST (Forced Swimmming Test) and their efficacies were found to be comparable to imipramine (15mg/kg) and Fluoxetne (20mg/kg). The extract of *Anacardium occidentle* exerted the antidepressant activity through interaction with adrenergic, dopaminergic, serotonergic and GABAnergic system.[6]

2. *Pericham* (*Phoenix dactylifera*)

The extract of *P.dactylifera (*100 and 300 mg/kg) provides significant neuroprotection against cerebral ischemia induced by bilateral common carotid artery occlusion and post ischemic reperfusion by reversing the changes in biochemical parameters of the brain produced due to oxidative stress and histopathological alterations associated with ischemic reperfusion validates its claim as neuroprotective agent. The neuroprotective effect of the drug may also be contributed to the polyphenolic compounds such as flavonoids, plant sterols, ascorbic acid present in the drug. *Phoenix dactylifera* may have the potential to be used as a protective agent against a variety of conditions where cellular damage are due to consequence of oxidative stress.[8]

3. *Athimaduram* (*Glycyrrhiza glabra)*

Glycyrrhizn is a triterpenoid saponin present in *Glycyrrhiza glabra*. Other important constituents are flavonoids, sterols, polysaccharides, coumarins, glabrol, glucose, sucrose, resin and volatile oil.

Glycyrrhizn (3.0mg/kg) produced significant anti-depressant effect in mice in both FST and TST. Both these models of depression are widely used to screen new antidepressant drugs. The glycyrrhizin might produce antidepressant-like effect by interaction with α_1- adrenoceptors and dopamine D_2- receptors, thereby increasing the levels of norepinephrine and dopamine in brain of mice. Glycyrrhizin has MAO inhibiting activity. Therefore antidepressant-like effect of glycyrrhizin in mice might be through increase in the brain levels of monoamines like epinephrine and dopamine by inhibiting monoamine oxidase.[12]

4. *Elam* (*Elettaria cardamomum*)

The *E.cardamomum* properties were assessed by TST (Tail Suspension Test) and FST (Forced Swimmming Test), prescient models of an anti-depressive activity. The results were compared with the standard reference drugs to evaluate the efficacy of crude extract of *E. cardamomum*. The biochemical analysis of tissues of mice treated with *E. cardamomum* revealed that *E. cardamomum* reduced the lipid peroxidation at doses of 200 and 400 mg/kg. The role of oxidative stress was reported to be one of the important factors in the development of brain cell injury. In the brain structures, *E. cardamomum* was effective in reducing lipid peroxidation in the cortex of the brain at doses 200 mg/kg. However, *E. cardamomum* enhanced the levels of MDA in hippocampus of mice.[13]

5. *Thippili* (*Piper longum*)

A bioassay guided isolation of the ethanolic extract from the fruit yielded a piperine alkaloid and it has a potent antidepressant like activity, which are mediated in part through the inhibition of MAO activity. Treatment with piperine (6.25-25mM) for 72h reversed the corticosterone induced reduction of BDNF mRNA expression in cultured hippocampal neurons. Therefore, the fruits of *Piper longum* represent a promoting pharmacotherapeutic agent against depression.

The aqueous extract of *Piper longum* was evaluated for anti-stress activity in stress rat models. The extract of *Piper longum* decreased the latent period indication extract-produced nootropic activity.[15]

6. *Nerpori* (*Oryza sativa*)

The total antioxidant assay was performed with petroleum ether and methanol extracts to analyse them qualitatively. The antioxidant activity of BHT (beta hydroxyl toluene) (0.5mg/ml) was also assayed for comparison. The total antioxidant assay and DPPH assay performed in methanol extract of all the plant parts showed very much comparable results with the available standards BHT and alpha tocopherol. The results for antioxidant activity revealed that rice grain possessed good anti-oxidant potential. The absorption value at 695nm and 517nm of all the extracts were recorded and later on compared with the standard anti-oxidant chemical, BHT (butyl hydroxy touline) and α-tocopherol. Thus, it can be concluded that these varieties of *Oryza sativa* reservoir of potentially useful chemical compounds and good source of antioxidants as well.[17]

7. *Kirambu* (*Syzygium aromaticum*)

Clove oil has the highest antioxidant capability and perhaps one of the best oil for food or supplement. For this reason, it has been included in some longevity formulae. Clove and eugenol possess strong antioxidant activity, when compared to other synthetic antioxidants, such as BHA and pyrogallol. Clove oil inhibited 97.3% lipid peroxidation of linoleic acid emulsion at 15µg/ml concentration. However, the standard antioxidant compounds such as butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), α-tocopherol and trolox demonstrated inhibition of 95.4, 99.7, 84.6 and 95.6% on peroxidation of linoleic acid emulsion at 45 µg/mL concentration respectively. From the results, clove oil was found to be an effective antioxidant in different in vitro assays including reducing power, DPPH radical ABTS radical and superoxide anion radical scavenging, hydrogen peroxide scavenging and metal chelating activities when it is compared to standard antioxidant compounds such as α-BHA, BHT, tocopherol, a natural antioxidant, and trolox which is a water-soluble analogue of tocopherol.[18]

8. *Ilavanga pathiri* (*Cinnamomum tamala*)

The methanolic extract of *Cinnamomum tamala* showed antioxidant activity in vitro assays. A significant increase in the levels of lipids and lipid peroxidation products and a decline in antioxidant potential were observed in diabetic rat brain synaptosomes. The extract of *Cinnamomum tamala* displayed scavenging activity against superoxide and hydroxyl radicals in a concentration-dependent manner. Maximum inhibition of lipid peroxidation, radical scavenging action and reducing power of extract were observed at a concentration of 220 microgram. These effects of extract in vitro were compared with butylated hydroxyl toluene (BHT), a synthetic antioxidant.[22]

Quantification of antioxidants of the leaves-phenols, ascorbate and carotenoids revealed that *C.tamala* leaves have high antioxidant. The scavenging effect of the essential oils and acetone extracts on DPPH radical linearly increased with increasing concentration. This could be due to the presence of phenolic compounds such as eugenol, spathulenol in essential oil. The sample with volatile oil and oleoresins were found to be significantly ($p<0.05$) more effective than control.[20]

9. *Kodiveli* (*Plumbago zeylanica*)

The root bark of *P.zeylanica* contains plumbagin which is a naphthoquinone and a major component is considered to be the active ingredient responsible for the therapeutic effects.

Scopolamine induced amnesia is employed to evaluate the effect of *Plumbago zeylanica* roots on learning and memory of mice. The chloroform extract of plant at dose 200 mg/kg has shown promising memory enhancing effect in mice. This extract significantly reversed the amnesia induced by scopolamine (0.4 mg/kg).[24]

The aqueous/alcoholic extracts of the root has antioxidant effect. The anti-oxidant activity was studied by free radical scavenging and superoxide radical scavenging methods. The IC50 value (the concentration required to inhibit radical formation by 50%) of *Plumbago zeylanica* root extract by DPPH assay is 96 µg/ml and by superoxide radical scavenging activity assays (NBT Assay) value is 4.6 µg/ml which is greater than the IC50 value of standard quercetin 45 µg/ml by DPPH assay and 10µg/ml by NBT assay. Thus the plant root extract revealed significant antioxidant activity as compared to standard flavonoid (quercetin).[25]

10. *Koogai kizhangu* (*Maran arundinacea*)

The edible tuberous rhizome is rich in starch. The ethanolic extract of *M. arundinacea* exhibited high antiradical activity against DPPH, ABTS, hydrogen peroxide and nitric oxide radicals with IC50 value of 293.4, 297.4, 336.1 and 258.7 µg/ml respectively. The Reducing power and Ferric Reducing Antioxidant Power (FRAP) are increased with increasing concentration of ethanolic extracts of *M. arundinacea*. Thus the results indicate that *M. arundinacea* extract attenuated oxidative stress via its antioxidant properties and was found to be an effective scavenger of ABTS, H_2O_2 & NO and also possess good reducing power and frap activity. The consumption of this arrowroot may play a role by its anti-oxidant activity in preventing human diseases such as cancer, cardiovascular diseases and aging.[26]

11. *Korai kizhangu (Cyperus rotundus)*

Extract of *C.rotundus* showed high potent inhibitory activity on crude enzyme Na +/K+-ATP -ase from rat brain. The pre-treatment with ethanolic extract of *C.rotundus* caused significant protection against strychnine and leptazol-induced convulsions in mice. In MES (Maximal electroshock) induced seizures the ethanol extract of rhizomes (100 mg/kg) exhibited significant decrease in the duration of hind limb extension and in PTZ (Pentylenetetrazole) induced seizures the ethanol extract showed significant reduction in the duration of convulsion which was comparable to standard drug phenytoin (25 mg/kg i.p) and diazepam (4mg/kg I.p) respectively. These results suggest that the ethanol extract of *Cyperus rotundus* rhizome is worthwhile to develop potent phytoconstituent for the treatment of epilepsy and the flavonoids present in ethanol extract could attribute for anticonvulsant activity.[30]

12. *Nal velai* (*Gynandropsis gynandra*)

The phytochemical analysis of the plant revealed that the seeds contain cleomin, hexacosanol, free β-sitosterol and kaempferol. The flavonoids such as quercetin and kaempferol are recognized as antioxidants and inhibitors of carcinogenesis. Glucosinolates and isothocyanates are also found to be strong chemopreventing agents, which are essentially involved in detoxification process. Wistar albino male rats received 250mg/kg extract of *Gynandropsis gynandra* for 7 days followed by a single dose of AFB_1 (Aflatoxin B_1) after 7 days. The results showed significant scavenging role against AFB_1 (Aflatoxin B_1) induced oxidative stress. Further the maintained antioxidant defense and MDA (Malondialdehyde, a major end product of lipid peroxidation which promotes carcinogenesis) production may prove the anticarcinogenic action of the drug. Thus, *Gynandropsis gynandra* may be a beneficial chemopreventive agent.[31]

13. *Milagu (Piper nigrum)*

The chemical constituents in *Piper nigrum* includes approximately 5-9% alkaloids structurally related to piperine, piperidine, piperettine, piperlongumminine, guineensine and pipericide as well as 2-4% volatile oil containing safrole. Piperine is the principle constituent, possessing anti-depressive activity. Anti-depressive activity of *Piper nigrum* fruit extract was evaluated by Forced Swimming test (FST) and Tail Suspension Test (TST) compared with standard antidepressant imipramine. The Locomotor activity was monitored by using Actophotometer. These test are based on the observations that rodents mostly mice and rats are used after initial escape behaviour, develop an immobile position when subjected to inescapable stress full situation. Treatment with antidepressant drugs will reduce the immobility time. In this study both high dose (500 mg/kg) and low dose (250 mg/kg) of aqueous extract and standard drug imipramine (10 mg/kg) treated for 14 days showed reduced immobility time in mice of which high dose was more effective when compared to low dose extract. Thus the present study confirms the aqueous extract of *Piper nigrum* fruit has anti depressant activity.[32]

14. *Kothamalli* (*Coriandrum sativum*)

Coriandrum sativum has been recommended for relief of anxiety and insomnia in Iranian folk medicine. 300mg/kg and 600mg/kg of aqueous extract and 6ml/kg and 8ml/kg of diethyl ether extract *of the seeds of Coriandrum sativum* was administered to male albino mice for 14 days. The diethyl ether extract from the *Coriandrum sativum* seed showed more significant

antidepressant effect than that of aqueous extract. This suggests that both these extracts produce anti depressant effect by interacting with dopamine D_2 and α1 adrenoceptors receptor. Thereby aqueous extract and diethyl ether extract of coriander seeds increase the level of noradrenaline, dopamine and decrease the level of GABA.[33]

DISCUSSION

Depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy and poor concentration. These problems can become chronic or recurrent and lead to substantial impairments in an individual's ability to take care of his or her everyday responsibilities. Many people with a depressive illness never seek treatment. But the majority, even those with the most severe depression can get better with treatment. Medications, psychotherapies and other methods were effective in the treatment of people with depression.

From this literature review it is evident that most of the ingredients of *thirutharatchatha chooranam* has pharmacological activities like anti-depressive, anti-oxidant, immunomodulatory which are responsible for its therapeutic activity claimed in *Siddha* text *Agathiyar vaithiya rathina surukkam.*

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