



Anti-Diabetic Polyherbal Siddha Formulation Atthippattaiyathi Kasayam: A Review

Nalini Sofia.H^{1*}, Vetha Merlin Kumari.H¹, Thomas M. Walter², Senthil Kumar SG³

¹Department of Maruthuvam, National Institute of Siddha, Chennai, India.

²Department of Pharmacology, Govt. Siddha Medical College, Palayamkottai, India.

³Siddha Physician, Herbal Medical Centre, Thanjavur, Tamil Nadu, India.

*Corresponding author's E-mail: dr.nalinisofiah@gmail.com

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ABSTRACT

In South India, indigenous remedies have been used in the treatment of Madhumegam (Type-2 Diabetes mellitus) since the time of Agathiyar and Thirumoolar. Plants have always been an exemplary source of drugs and many of the currently available drugs have been derived directly or indirectly from them. The ethno botanical information reports that about 800 plants may possess anti-diabetic potential. *Atthippattaiyathi kasayam*, a polyherbal anti-diabetic Siddha formulation containing 22 ingredients of plants origin. They are *Ficus recemosa*, *Cassia fistula*, *Cassia auriculata*, *Salacia reticulata*, *Madhuca longifolia*, *Tamarindus indica*, *Terminalia arjuna*, *Hemidesmus indicus*, *Amaranthus tricolor*, *Phyllanthus reticulatus*, *Aloe barbadensis*, *Cyperus rotundus*, *Tinospora cordifolia*, *Zingiber officinale*, *Piper nigrum*, *Piper longum*, *Myristica fragrans*, *Syzygium aromaticum*, *Spermacoce hispida* and *Ferula asafetida*. Overall, this review presents the profiles of ingredients of *Atthippattaiyathi kasayam* with anti diabetic properties reported in the literature and in various research studies.

Keywords: Antidiabetic plants, Atthippattaiyathi kasayam, Diabetes Mellitus, Siddha medicine.

INTRODUCTION

Siddha System of Medicine is an integrated part of Indian System, which is very potent and unique system when compared with other traditional systems in existence. Siddha Medicine is contributing much to the health care of human beings and Siddha Vaidya could be considered as the crown of all the traditional arts of the ancient world owing to its richness and simplicity. Siddha medicine, one of the medical systems legally recognized and supported by the Government of India, is, however, little known outside Tamil Nadu and its practice limited mainly to the Tamil populations of India and overseas. Moreover, it has received scant attention from the social sciences to date. The WHO has documented that the vast majority of people (75-80%) mostly living in the "developing countries", and significant number in the "developed industrialized nations, prefer and resort to Alternate (Traditional) Medicine for treating common ailments and chronic diseases.

Diabetes Mellitus is a chronic endocrine disorder caused by an absolute or relative lack of insulin and/or reduced insulin activity that results in hyperglycemia and abnormalities in carbohydrate, fat and protein metabolism. Diabetes has emerged as a major healthcare problem in India. A national urban survey in 2005 observed that the prevalence of diabetes in urban India in adults was 15.1%. Recent data have illustrated the impact of socio-economic transition occurring in rural India. The transition has occurred in the last 15 years and the prevalence has risen from 2.4% to 6.4%.¹ Type 2 Diabetes is one of the major health problems all over the world.

The management of diabetes is considered a global problem. The modern drugs including insulin and oral hypoglycemic agents control the blood sugar level as long as they are regularly administered, and also produce a number of undesirable side effects. The treatment of diabetes has been attempted with different indigenous plants and polyherbal formulations. Pre-clinical toxicity studies are essential for determining a safe dose for human trials.²

Many studies have confirmed the benefits of medicinal plants with hypoglycemic effects in the management of diabetes mellitus. The effects of these plants may delay the development of diabetic complications and even assist in correcting the metabolic abnormalities. Moreover, during the past decade and especially in last few years some of the new bioactive drugs isolated from hypoglycemic plants showed anti-diabetic activity with more efficacy than synthetic oral hypoglycemic agents. Therefore, plants, as folk remedies, are widely used to treat diabetes mellitus.

In modern science of medicine, however, their role is limited to the use of natural polymers like guar gum, gum acacia, gum arabic, etc. The therapeutic benefit of gums derived from natural origin resides in their ability to reduce the calorific value of consumed diet by reducing absorption of carbohydrates from the gastrointestinal tract. Therefore, search for a novel anti-diabetic drug from plants, plant parts and their aqueous or alcoholic extracts should be advocated, since they have well been recognized as an important source of providing new drugs.³



Ingredients of *Atthippattaiyathi kasayam*

Atthippattaiyathi kasayam, a polyherbal anti diabetic Siddha formulation containing 22 ingredients of plants

origin,^{33, 34} their specific and individual locality names and siddha medicinal uses are tabulated below in Table 1.

Table 1: Information about the Ingredients³⁵

Common name Tamil/English	Botanical name/ Family	Phytochemistry	Actions	Uses in Siddha
Aththi/Fig	Ficus recemosa/ Moraceae	Sterols, Lanosterol, tannins, flavonoids. gluanol acetate, β -sitosterol	Astringent Laxative	Improves cordial blood, Laxative, Anti-vatha
Sarak konrai/ Golden shower tree	Cassia fistula/ Fabaceae	lupeol, β -sitosterol and hexacosanol	Laxative Vermifuge	Increases body weight, Piles, Leucorrhoea, anemia
Avarai/Senna	cassia auriculata/ Cesalpiniaceae	α - Tocopherol- β -D- mannoside, Resorcinol, n- Hexadecanoic acid, 13-Octadecenal,	Astringent Tonic	UTI, cures eye diseases, Constipation, Leucorrhoea
Kadalazhinjil/ Salacia, Salaretin	Salacia reticulata/ Celastraceae	mangiferin, epicatechin, epigallocatechin, Polyphenols	Astringent	Diabetes, Rheumatoid arthritis, Bronchial asthma
Ilupai/Mahua	Madhuca longifolia/ Sapotaceae	Saponins, β -amyirin acetate, 21-Hydroxy-3-oleanyl myricitate, Ursolic Acid.	Astringent, Stimulant, Tonic	Cough, Thirst, Wheezing, Orchitis
Pulli/Indian date	Tamarindus indica/ Fabaceae	Heptadecanoate, Hexadecanoic acid, n- Nonadecanoate, n- Octadecanoic	Refrigerant Astringent Antibilious	Anaemia, Eye diseases, Vomiting, improves digestion
Marutham/Arjuna	Terminalia arjuna/ Combretaceae	Tannins, flavonoids, sterols, Amino acids	Tonic Astringent	Cardiac diseases, Giddiness, Leucorrhoea
Nannari/Sarasaparilla	Hemidesmus indicus/ Apocynaceae	glycosides, flavonoids, tannins, sterols, volatile oils	Tonic Demulcent Diaphoretic	Fever, Thirst, Head ache
Siru keerai/ Joseph's Coat	Amaranthus tricolor/ Amaranthaceae	phenols, coumarins, lignans	Tonic, Anti oxidant, anti inflammatory	Eye diseases, UTI, Vatha diseases
Neerpoola/ sour grapes	Phyllanthus reticulatus /Euphorbiaceae	lupeol acetate, stigmasterol, lupeol	Diuretic, anti diabetic, anti oxidant.	Malaria, dysentery.
Katralai/ Aloes	Aloe barbadensis/ Xanthorrhoeaceae	aloeemodin, aloin A, elgonica dimer A	Tonic Alterative	Laxative, Stomach ulcer(APD), eye diseases
Korai kilangu/ Nut grass	Cyperus rotundus/ Cyperaceae	terpenoids, cyprotene, cyperene, rotundene, valencene, cyperol	Astringent, Stimulant, Tonic	Worm infestation, Tri-dosa, Laxative, Blood pressure.
Seenthil/ Guduchi	Tinospora cordifolia/ Menispermaceae	Giloin, tinosporone, tinosporic acid, cordifolisides A to E	Alterative Demulcent Tonic	Anti-vatha, Improves immunity, Cough, vomiting, Splenomegaly.
Inji / Ginger	Zingiber officinale/ Zingiberaceae	Amaldehyde, Gingerol, Shogaol, Paradol	Carminative, Stomachic, Sialogogue, Digestive, Stimulant, Rubefacient	Pitha Diseases, Tridosha diseases, Cough, Cold, Nausea, Diarrhoea,
Milagu / Black Pepper	Piper nigrum / Piperaceae	alpha-tocopherol, amide, feruperine	Carminative, Antiperiodic, Rubefacient, Stimulant, Antidote	Vatha, Pitha, Kapha Diseases, Cold, Fever, Anemia, Jaundice, Diarrhoea, Ulcer, Indigestion.

Table 1: Information about the Ingredients³⁵ (Continued.....)

Common name Tamil/English	Botanical name/ Family	Phytochemistry	Actions	Uses in Siddha
Thippili/Long pepper	Piper longum/ Piperaceae	Coumaperine, piperidine, piperolactam A	Stimulant Carminative	Anti-pitha, Head ache, APD, cough, Tastelessness
Sathikkai/Nut mug	Myristica fragrans	terpinene, alpha-terpineol, camphene, b-pinene	Stimulant Carminative Tonic	Dysentery, Head ache, Improves sperm count, Stomach pain
Krambu/ Clove	Syzygium aromaticum/ Myrtaceae	Essential oil- Eugenol, Tannins-Bicomin, Methyl salicylate (Pain killer), Kampferol & Triterpenoids	Antispasmodic, Carminative, Stomachic.	Relieves Pain, Vomiting, Diarrhea, Dysentery, Dental Problems.
Naththai churi/ Shaggy Button weed	Spermacoce hispidia/ Rubiaceae	ursolic acid, stigmasterol,	Alterative Tonic Demulcent	Dysentery, Fever, Tri-dosa.
Perungayam/Asa feetida	Ferula asafetida/ Apiaceae	Assa foetidol A and assa foetidol B, Terpenoids.	Stimulant Carminative	Laxative, Anti-vatha, Ulcer (APD), Head ache.
Kadanarathai/Citron	Citrus medica / Rutaceae	limonene, geranial, limettin, stigmasterol	Anthelmintic	Vomiting, Urinary calculus, constipation
Thalisa phathiri/Flaurtia calaphracta	Abies spectabilis/ Pinaceae	abieta-7,13-diene-12 α - methoxy-18-oic acid , 7 α - methoxy-dehydroabietic acid	Stomachic Carminative Expectorant	Gum bleeding, Asthma, Cough, aphthous ulcer

Anti diabetic activity of herbs in *Atthippattaiyathi kasayam*

The efficacy of *all the ingredients of Atthippattaiyathi kasayam* was proved through the following In-vivo studies.

Ficus racemosa

In a study oral administration of *Ficus racemosa* ethanolic extract 400 mg/kg, showed the significant decrease in the blood glucose level in alloxan induced diabetic rats.⁴ In another study oral administration of 300 mg/kg ethanolic extract of *Ficus racemosa* bark to alloxan induced diabetic rats restored the status of blood glucose, lipids and lipoproteins to near normal range. These effects were much comparable to that of the standard reference drug, glibenclamide.⁵

Terminalia arjuna

The *Terminalia arjuna* bark ethanolic extract containing 250 and 500 mg/kg, showed the significant decrease in the blood glucose level and a decrease in the activities of glucose-6-phosphatase, fructose-1, 6-diphosphatase, aldolase and an increase in the activity of phospho gluco isomerase and hexokinase in tissues of alloxan induced diabetic rats.⁶

Tinospora cordifolia

In a study oral administration of 250 mg/kg of the methanol extract of *Tinospora cordifolia* stem significantly reduces the fasting blood glucose level and significantly decreases the glycosylated hemoglobin level, reduced glucokinase and increased glucose-6-phosphatase activity

were reversed significantly and the insulin and C-peptide levels were improved in streptozotocin induced diabetic rats.⁷

Madhuca longifolia

Oral administration of 100 and 200 mg/kg of the methanolic extract of *Madhuca longifolia* bark, a significant reduction was observed in the blood glucose level of streptozotocin induced diabetic rats. The extract was highly effective in managing the complications associated with diabetes mellitus, such as hypercholesterolemia and impaired renal function.⁸ Srirangam Prashanth et al study indicated that, the ethanolic bark extract of *Madhuca longifolia* at a dose of 100 and 200 mg/kg to be a potential antidiabetic and antioxidant properties and the extract also exhibited significant free radical scavenging activity and superoxide scavenging activity.⁹

Salacia reticulata

Chandrashekar CN, et al reported that *salacia reticulata* extract of bark or core root alone are more effective in decreasing blood glucose level in alloxan induced diabetic rats. *In vitro* studies confirmed scavenging activity of free radicals, superoxide and hydrogen peroxide.¹⁰

Cassia auriculata

In a study oral administration of methanolic extract of *cassia auriculata* bark of 250 mg/kg showed a significant reduction was observed in the blood glucose level of streptozotocin induced diabetic rats.¹¹ Mahendra Shiradkar et al reported that, the methanolic extract of



Cassia auriculata bark were found to possess promising anti-diabetic, antimutagenic and anti-fertility activities in streptozotocin induced diabetic rats.¹²

Cassia fistula

Ethyl acetate fraction of total alcoholic extract of the bark of *Cassia fistula* at the dose of 200 mg/kg body weight possesses significant antidiabetic activity in alloxan induced diabetic rats. It was also found effective in normalizing blood lipids like total cholesterol and total triglyceride.¹³ M. Ashraf Ali et al experimental animal study indicate that, *Cassia fistula* stem bark ethanolic extract have analgesic activity in mice by acetic acid induced writhing test method and antihyperglycemic activity in alloxan induced diabetic rats. Diclofenac and Metformin were used as reference drugs for comparison.¹⁴

Cyperus rotundus

Oral daily administration of 500 mg/kg of the *Cyperus rotundus* extract significantly lowered the blood glucose level in alloxan induced diabetic rats. This antihyperglycemic activity can be attributed to its antioxidant activity as it showed the strong DPPH radical scavenging action *in vitro*.¹⁵

Phyllanthus reticulatus

The petroleum ether and ethanolic extracts of roots of the *Phyllanthus reticulatus* orally tested at 500 and 1000 mg/kg for hypoglycemic effect in alloxan induced diabetic mice. It shows very good hypoglycemic activity at the dose of 1000 mg/kg.¹⁶

Hemidesmus indicus

2-Hydroxy 4-methoxy benzoic acid (HMBA) isolated from the root of *Hemidesmus indicus* was administered 500 µg/kg orally to STZ-induced diabetic rats. After administration of HMBA, the levels of Glycosylated hemoglobin, total cholesterol, triglycerides, LDL-cholesterol were normalized. It also reversed the elevated levels of AST, ALT, ALP, γ-GT and CK to near normal level.¹⁷

Tamarindus indica

The alloxan induced diabetic rats treated with ethanolic extract of bark of *Tamarindus indica* at a dose of 200 mg/kg caused reduction in blood glucose level and produced a significant decrease in peroxidation products, viz., thiobarbituric acid reactive substances. The effect of ethanolic extract at 200 mg/kg was more effective than glibenclamide.¹⁸

Piper longum

Oral administration of ethanolic extract of *Piper longum* dried fruits has shown significant anti-hyperglycemic, anti-lipid peroxidative and antioxidant effects in alloxan induced diabetic rats. It also corrected the metabolic alteration observed by the activities of several carbohydrates metabolizing enzymes.¹⁹

Syzygium aromaticum

Clove (*Syzygium aromaticum* flower buds) EtOH extract significantly suppressed an increase in blood glucose level in type 2 diabetic KK-A(y) mice. In-vitro evaluation showed the extract had human peroxisome proliferator-activated receptor (PPAR)-γ ligand-binding activity in a GAL4-PPAR-γ chimera assay.²⁰

Ferula asafetida

The aqueous extract of *Ferula asafetida*, administration at dose of 50 mg/kg has shown the hypoglycemic activity in streptozotocin-diabetic rats. This effect can be explained at least in part by the presence of the phenolic acid (ferulic acid) and tannins in the extract.²¹ The Asafetida extract stimulate the changes of the functional state of pancreatic β-cells. At the same time the capacity of the organism to produce and secrete insulin is increasing, the glucose level in blood is decreasing.²² *Ferula asafetida* treatment led to a significant improve in hyperglycemia, hypo insulinemia, decreased liver glycogen and increased percentage of body weight change caused by alloxan.²³

Aloe barbedensis

The ethanolic extracts of *Aloe vera* were caused significant reduction in the fasting serum glucose levels of the rats. These extracts exhibited high DPPH scavenging activities and FRAP values, indicating the potential of this plant to be used as an antioxidant.²⁴

Amaranthus tricolor

In a study oral administration of 400 mg/kg of the *Amaranthus tricolor* aqueous extract significantly reduced serum glucose, serum triglyceride, total cholesterol, low density lipoprotein and very low density lipoprotein, but elevated high density lipoprotein in alloxan induced diabetic rats.²⁵

Zingiber officinale

Treatment with juice of *Zingiber officinale* produced a significant increase in insulin levels and a decrease in fasting glucose levels.²⁶ In an oral glucose tolerance test, treatment with *Z. officinale* was found to decrease significantly the area under the curve of glucose and to increase the area under the curve of insulin in STZ-diabetic rats. Treatment with *Z. officinale* also caused a decrease in serum cholesterol, serum triglyceride and blood pressure in diabetic rats.²⁷ Fresh juice of *Z. officinale* produced a time dependent decrease in blood glucose level significantly compared to both Glibenclamide and metformin.²⁸

Piper nigrum

Shubham et al, et al suggest that sub acute (14 days) oral administration of Piperine, the chief alkaloid present in *Piper nigrum* at dose of 20 mg/kg has significant blood glucose lowering effect in alloxan induced diabetic rats.²⁹



Myristica fragrans

Macelignan, a natural compound isolated from *Myristica fragrans*, as a dual agonist for PPAR α/γ . Macelignan enhanced insulin sensitivity and improved lipid metabolic disorders by activating PPAR α/γ and attenuating ER stress, suggesting it has potential as an anti diabetic agent for the treatment of type -2diabetes.³⁰

Spermacoce hispida

Spermacoce hispida was investigated and reported to have hypoglycemic activity in an animal model of diabetes upon subcutaneous administration. The oral administration of *Spermacoce hispida* in alloxan induced diabetic rats showed significant hypoglycemic effect. Recently, it was observed that chronic BQ use is associated with a higher risk of type 2 diabetes mellitus and metabolic syndrome.³¹

CONCLUSION

Herbal treatments are the most popular form of Traditional medicine, and are highly lucrative in the International marketplace. In ancient literature, it is said that the ingredients present in this formulation '*Atthippattaiyathi kasayam*' has effectiveness in the treatment of Diabetes etc. Based on the evidence of Siddha literature, the modern scientific research studies also provide supporting results of anti diabetic, anti oxidant, anti-lipid of each ingredient. Thus, *Atthippattaiyathi kasayam* provides solid benefits in the treatment and management of life style disorders like Diabetes and Obesity.

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