



Review Article

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A SIDDHA CLASSICAL PREPARATION THE TRANVITHAI KUDINEER FOR MATHUMEGAM (TYPE 2 DIABETES MELLITUS): AN OVERVIEW

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ABSTRACT

In present era, Diabetes mellitus has emerged as a major health hazard in both the developed countries and developing countries. There were 69.12 million cases of diabetes in India as per the data 2015. Out of these 36 million people remained undiagnosed. Diabetes mellitus is a disorder characterized by the presence of chronic hyperglycemia either immune mediated (Type 1 diabetes), Insulin resistance (Type 2 Diabetes), Gestational or other. Diabetes Mellitus is referred as Mathumegam, neerizhivu, in Siddha Classical texts. Thetranvithai kudineer is a classical siddha formulation which has renowned medicinal values. This article provides comprehensive information of individual ingredients of Thetranvithai Kudineer with special reference to Diabetes mellitus.

Keywords: Siddha Medicine, Thetranvithai, Kudineer, Diabetes mellitus, Antidiabetics, Hypoglycemic drugs.

INTRODUCTION

Diabetes mellitus is a disorder that affects the body's ability to make or use insulin. Insulin is a hormone produced in the pancreas that helps transport glucose (blood sugar) from the bloodstream into the cells so they can break it down and use it for fuel. People cannot live without insulin (ADA, 2007).¹ Human bodies possess enzymatic and non-enzymatic and oxidative mechanisms which minimize the generation of reactive oxygen species, responsible for many degenerative diseases including diabetes.² Diabetes mellitus is recognized by chronic elevation of blood glucose level. This is sometimes accompanied by symptoms such profuse urination, severe thirst, weight loss, stupor, culminating in coma, and death in the absence of effective treatment.³ Type 2 diabetes or non-insulin-dependent diabetes mellitus, is the most common form of the disease, accounting for 90%–95% of cases in which the body does not produce enough insulin or properly use it.⁴ It has already been established that chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and eventually the failure of organs, especially the eyes, kidneys, nerves, heart and blood vessels.¹

In Siddha system of medicine, Diabetes Mellitus is referred by various terminologies such as Mathumegam, Neerizhivu, Innippu megam, Miguneer, Meganeer etc. Taking excess of sweet, oily foods, sedentary life style, stress, indulging in excess sexual activities are mentioned as etiological factors of Mathumegam in Siddha classical texts. Excessive hunger, excessive thirst, excessive urination, loss of general vitality, emaciation, anxiety, dyspnoea are said to be the clinical symptoms of mathumegam.⁵

Due to the above referred etiological factors and other environmental factors kapha humor gets altered, resulting in the step by step deterioration of seven udal thathus. As a result of this general debility and emaciation occurs. If left untreated results in other diseases such as karapatha soolai, pilavai, siruneeraga kollaru etc.⁵

The drug Thetranvithai kudineer mentioned in Theraiyar kudineer for Neerizhivu is a classical polyherbal formulation containing Thetran Vidhai (*Strychnos potatorum seed*), Kadukkai (*Terminalia chebula fruit rind*), Aavaarai seed (*Cassia auriculata seed*), Vilam pisin (*Limonia acidissima gum*). For preparing the kudineer, the ingredients are made into coarse powder and 2 grams of powder is added to 240 ml of water, boiled and reduced to 60 ml. Dose of kudineer is 60 ml twice daily.⁶

The ingredients of the Thetranvithai kudineer have usna veeryam⁷ and so they are capable of pacifying vitiated Kapha humor in Madhumegam. The drugs being alterative, tonic, and demulcent⁷ generally have Anti diabetic effect. Though there are different types of Oral hypoglycemic agents available in modern medicine, there is increasing demand for polyherbal formulations because of their safety. The individual ingredients of the drug Thetranvithai kudineer itself have anti diabetic activity⁷ and so they enhance the activity of one another. The other complications like diabetic ulcers, eye diseases, renal dysfunction can also be prevented by the use of above polyherbal formulation.

THETTRAN VITHAI (*STRYCHNOS POTATORUM SEEDS*)

Morphology

Macroscopically, the seed of *Strychnos potatorum* is spherical in outside. No definite odor or taste is marked. The seeds are tough and sturdy, become soft on extended boiling. The seeds are yellowish white in colour and measure 6-7 mm in diameter, and 4-5 mm in thickness. The surface of the dry seed exhibited fine reticulate marking.⁸

Phytochemicals

Preliminary phytochemical screening revealed the presence of carbohydrate, fixed oil, saponins, phenolic compounds, phytosterols, alkaloids, flavonoids in 50% ethanolic extract of seeds⁸ (Table 1)

Table 1: Preliminary phytochemical screening of the 50 % ethanolic extract of *S. potatorum*

S. No	Constituents	Tests	50% Ethanolic extract
1.	Carbohydrate	Mohlich test Fehlings test	Positive Negative
2.	Fixed Oils & Fats	Spot test Saponification test	Positive Positive
3.	Proteins & amino acids	Ninhydrin test Millon's test Biuret test	Negative Negative Negative
4.	Saponins	Foam test	Positive
5.	Phenolic compounds	FeCl ₃ test Pot. permanganate test Lead acetate test	Positive Negative Positive
6.	Phytosterol	Salkowski test Liebermann burchard test	Positive Positive
7.	Alkaloids	Dragendroff's test Mayer's test Wagner's test Hager's test	Positive Negative Positive Negative
8.	Gum & mucilage	Swelling test	Negative
9.	Flavonoids	Aqueous NaOH test Con. H ₂ SO ₄ test Shinoda's test	Positive Positive Negative

PHARMACOLOGICAL ACTIVITIES

Anti Diabetic Activity⁹

The antidiabetic effect of *Strychnos Potatorum Linn* (S.P. Linn) was studied on streptozotocin induced male diabetic rats. In normal animals, the fasting blood sugar level at day 0 was 71.2 ± 11.0 mg/dl and remained unchanged till day 90 (Table 1). In S. P. Linn treated normal rats, the mean fasting blood sugar level at day 0 was 70.0 ± 8.7 mg/dl and significantly decreased to 60 ± 8.7 mg/dl at day 90 (P<0.05). In Glipizide treated normal rats (Group

C), the mean fasting blood sugar level at day 0 was 72.0 ± 5.7 mg/dl and was significantly decreased to 62.0 ± 5.8 mg/dl (p < 0.05) at day 90. In streptozotocin-treated diabetic rats (group D), the mean FBS at day 0 was 175.0 ± 5.5 mg/dl which was significantly higher than normal controls (p<0.01) (Table 1) and remained unchanged at day 90 (Table 1). On day 0, in the STZ + S.P. Linn treated group, the mean FBS was significantly increased to 182.5 ± 12.0 mg/dl as compared to Group A (p<0.01) and decreased at day 90 to 71.3 ± 5.0 mg/dl (p<0.01). In STZ+Glipizide group, the mean FBS significantly decreased from 184.3 ± 11.2 mg/dl at day 0 to 74.8 ± 6.2 mg/dl at day 90 (p<0.01).

Table 2: Effects of S. P. Linn. And Glipizide on Fasting Blood Sugar

Groups	Day 0	Day 90
Normal control (Group A)	71.2 ± 11.0	70.6 ± 13.0
Normal control +S.P. Linn (Group B)	70.0 ± 8.7	60.0 ± 8.7*
Normal control +Glipizide (Group C)	72.0 ± 5.8	62.0 ± 5.8*
STZ-diabetic (Group D)	175.5 ± 5.5**	169.5 ± 21.5**
STZ+ S.P. Linn (Group E)	182.5 ± 12.0**	71.3 ± 2.0†
STZ+ Glipizide (Group F)	184.3 ± 11.2**	74.8 ± 6.2†

**p<0.01(as compared to gr-A); *p<0.05(as compared to gr - B)†p<0.01(as compared to gr - D)
S.D=Standard Deviation

KADUKKAI (*TERMINALIA CHEBULA* FRUIT RIND)

Morphology

The fruit or drupe is about 1-2 inches in size. It has five lines or five ribs on the outer skin. Fruit is green when unripe and yellowish grey when ripe. Fruits were collected from January to April, fruit formation started from November to January¹⁰.

Phytochemicals

Terminalia. chebula, though, contains several phytoconstituents like tannins, flavonoids, sterols, amino acids, fructose, resin, fixed oils etc., however, it is fairly rich in different tannins (approximately 32% tannin content). Further, tannin content of *T. chebula* largely depends on its geographic location. *T. chebula* are of pyrogallol (hydrolysable) type, they contain 14 components of hydrolysable tannins (gallic acid, chebulic acid, punicalagin, chebularin, corilagin, neochebulinic, ellagic acid, chebulegic acid, chebulinic acid, 1,2,3,4,6- penta-Ogalloyl-β-D-glucose, 1,6,-di-O-galloyl-D-glucose, casuarinin, 3,4,6-tri-O-galloyl-D-

glucose and terchebulin)¹¹. Flavonol glycosides, triterpenoids, coumarin conjugated with gallic acid called chebulin, as well as phenolic compounds were also isolated¹². In addition, ethyl gallate and luteolin were isolated from the fruit of *T. chebula*¹³. It also consists of nutrients such as vitamin C, protein, amino acids and minerals¹⁴.

Pharmacological activities

Anti Diabetic Activity¹⁵

Anti diabetic activity potential of *Terminalia chebula* fruit was evaluated on streptozotocin(STZ) – induced experimental diabetes in rats. The animals were divided into two sets, one for the evaluation of a glucose tolerance test and a second one for the analysis of biochemical parameters. Each set was further divided into four groups; each comprising a minimum of six animals in each group as detailed below: Group I: Normal control rats. Group II: Diabetic control rats. Group III: Diabetic rats given *T. chebula* fruit extract (200 mg/kg body weight/day/rat) in aqueous solution orally for 30 days. Group IV: Diabetic rats administered with

glibenclamide (600 µg/kg body weight/day/rat) in aqueous solution orally for 30 days. It significantly reduced the blood glucose levels and glycosylated haemoglobin in diabetic rats. The

fasting blood glucose levels of all the rats were recorded at regular intervals during the experimental period.

Table 3. Changes in the Level of Blood Glucose, Plasma Insulin, Hemoglobin, Glycosylated Hemoglobin and Urine Sugar in Control and Experimental Groups of Rats

Groups	Blood glucose milligram/deciliter (mg/dl)	Plasma insulin microunit/milliliter (U/ml)	Hemoglobin (g/dl)	Glycosylated Hemoglobin (% HbA1c)	Urine sugar
Control	85.43 5.72	16.54 1.07	13.52 0.81	6.24 0.38	Nil
Diabetic control	265.08 20.14*	5.27 0.76*	9.25 0.67*	12.36 0.91*	+++
Diabetic + <i>T. chebula</i>	92.30 6.09*	15.26 0.71*	12.93 0.82*	6.72 0.42*	Nil
Diabetic + Glibenclamide	102.40 6.45*	13.86 0.62*	12.46 0.77*	6.95 0.42*	+

Values are given as mean S.D. for groups of six animals in each group. Values are statistically significant at **p* < 0.05. Diabetic control rats were compared with control rats. Diabetic + *T. chebula* and diabetic + glibenclamide treated rats were compared with diabetic control rats. (+) indicate 0.25% sugar and (+++) indicates more than 2% sugar.

AVARAM VITHAI (CASSIA AURICULATA SEEDS)

Morphology

Seeds 6 or more, ovoid, longitudinal (Pocket flora of Sirumalai Hills, South India), Seeds aerolate, Seeds' apices abruptly narrowed towards hilum ends¹⁶.

Phytochemicals

GC-MS chromatogram of the ethanolic seed extract of *Cassia auriculata* showed 18 peaks indicating the presence of eighteen compounds. The chemical compounds identified in the ethanolic

extract of the seed of *Cassia auriculata* are presented in Table 1. GC-MS analysis revealed that the presence of benzoic acid, 2-hydroxy-, methyl ester(0.07%), Glycine, N-(trifluoroacetyl)-, 1-methylbutyl ester(0.10%), 2,3-dihydro-3,5-dihydroxy-6-methyl-4Hpyran-4-one(0.12%), Capric acid ethyl ester(0.16%), Resorcinol(0.21%) are showed as minimum percent. The fatty acid and fatty acid ester derivatives are recorded predominantly. Grape seed oil(Linoleic acid-21%, Oleic acid-7%, Palmitic acid-2.95%,) n-Hexadecanoic acid(21.31%), 9-Octadecenoic acid, (E)-(12.60%), Stearic acid(9.39%) and also the contribution of long chained unsaturated hydrocarbon presents E,Z-1,3,12-Nonadecatriene(12.27%), dl- α - Tocopherol(1.22%), stigmasta-5,23-dien-3-ol, (3 β)-(1.21%)¹⁷.

Table 4: Qualitative chemical examination of alcoholic, petroleum ether and water extracts of *Cassia auriculata*¹⁸

Plant constituents test / Reagent used	Extracts		
	Alcoholic	Petroleum Ether	Water
Flavonoids			
Ferric chloride test	+	-	-
Shinoda test	-	-	-
Zinc hydrochloric acid reduction test	+	-	-
Alkaline reagent test	-	-	-
Lead acetate test	-	-	-
Lipids tests	+	+	-
Saponins			
Foam test	-	-	+
Haemolysis test	-	-	+
Sterols			
Salkowski test	+	+	-
Liebermann-Burchard test	+	+	-
Sulphur test	+	+	-
Tannins			
Ferric chloride test	+	-	+
Gelatin test	+	-	+
Triterpenoids			
Salkowski test	-	-	+
Liebermann-Burchard test	-	-	+

PHARMACOLOGICAL ACTIVITIES

Anti Diabetic Activity¹⁹

In the experiment rats were divided into the following groups with six animals in each • Group I: Normal control received 1% w/v gum acacia 1ml/kg • Group II: Diabetic control received with alloxan at a dose of 150 mg/kg b.w • Group III: Diabetic rats

treated with petroleum ether extract at 200mg/kg b.w • Group IV: Diabetic rats treated with chloroform extract at 300mg/kg b.w • Group V: Diabetic rats treated with ethyl acetate extract at 200mg/kg b.w • Group VI: Diabetic rats treated with ethanol extract at 200mg/kg • Group VII: Diabetic rats treated with aqueous extract at 100mg/kg • Group VIII: : Diabetic rats treated with tolbutamide 250mg/kg b.w.

Table 5: Effect of Petroleum ether and ethyl acetate extract of *Cassia auriculata* Linn seed on Blood glucose levels on prolonged treatment of 7 days. Groups Treatment Initial after 7 days

Group	Treatment	Blood glucose levels(mg/100ml)	
		Initial	After 7 Days
I	Control(Saline)	86.00±0.98	85.86±0.45
II	Diabetic control	216.60± 2.25	315.80± 2.81
III	Diabetic+ PE Extract	213.00± 2.15	85.12±0.20*
IV	Diabetic+EA Extract	207.98± 1.70	89.16±2.15*
V	Diabetic+tolbutamide (250mg/kg)	212.30± 2.70	81.30±1.98*

PE: Petroleum ether extract, EA: Ethyl acetate extract. One way ANOVA followed by Dunnett's Test. Values were expressed as Mean ± SEM. * P< 0.05 as compared to Control group

Ingredients of *Thetranvidhai kudineer*



VILAM PISIN (*LIMONIA ACIDISSIMA* GUM)

Morphology²⁰

The tree exudes a gum from trunk and branches. This gum resembles gum Arabic in properties. The exudation is profuse after the rainy season. This gum is considered to be good substitute for gum Arabic. Ferronia gum occurs in irregular semi transparent tears varying in colour from reddish brown to pale yellow or colourless. The gum dissolves in water forming tasteless mucilage, more viscous than the gum Arabic.

Therapeutic uses

The gum is demulcent and constipating, and is useful in diarrhea, dysentery, gastropathy, hemorrhoids and diabetes²¹. The 'Ferronia gum', in the trunk and branches of the wood apple tree, counteracts diabetes by reducing the severity of the condition. It also helps in managing the flow, secretion, and balance of sugars in the bloodstream. By managing the insulin and glucose levels, it prevents the spikes and plunges that can be dangerous to diabetics²²

Nutritional value of *Limonia*

Limonia fruit is a good source of protein, carbohydrates and dietary fiber. It is rich in vitamins like vitamin C, B vitamins like thiamin, niacin and riboflavin and beta- carotene, which a precursor to vitamin A. Essential minerals like calcium, phosphorus and iron can be found in good amounts in this fruit. Various phytochemicals have been isolated from the plant

including flavanoids, glycosides, saponins, tannins, coumarins and tyramine derivatives. Acidissimin is tyramine derivative present in the fruit which gives its species name²³

Pharmacological activity

Though the Anti diabetic activity of Ferronia gum was not studied other parts of the *Limonia acidissima* is known to have potential anti diabetic activity. According to a study the extracts obtained from *Limonia* have the ability to lower glucose, which is extremely useful in the treatment of diabetes. This particular study which was carried out on diabetic male albino rats, found that the extract helped in lowering the levels of glucose in the rats by a significant amount. Ferronia gum obtained from the branches and trunks of the wood apple tree have been found to help in balancing the amount of sugar in the blood stream and managing the insulin levels, thereby preventing huge spikes in the blood sugar levels²³. The leaf²⁴, stem bark²⁵, fruit pulp²⁶ has anti diabetic activity and so gum obtained from the stem bark may also have anti diabetic activity.

CONCLUSION

According to Siddha system of medicine the main causative factor of diabetes is the predominance of kapha Dhosam. The ingredients of Thetranvidhai kudineer are mostly bitter in taste. So it is a good drug of choice for type 2 Diabetes Mellitus. Moreover from the above review it is very clear that the individual ingredients of Thetranvidhai kudineer have potent anti diabetic activity. Pharmacological studies and Clinical Studies on Thetranvidhai kudineer have to be carried out to prove the

therapeutic efficacy of the drug on Type 2 Diabetes mellitus. When proven Pre Clinically and Clinically it would be a cost effective, potent anti diabetic drug. A Multi centric study with large sample size has to be carried out to establish its efficacy.

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