INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com
ISSN 2230 – 8407

Review Article

A COMPREHENSIVE REVIEW ON THETRAN VIDHAI KUDINEER: A SIDDHA POLYHERBAL FORMULATION

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Article Received on: 09/11/18 Approved for publication: 05/02/19

DOI: 10.7897/2230-8407.100376

ABSTRACT

In the present day, world's focus turns to the herbal medicine because of the safety, efficacy and easy accessibility of herbal plants and also mainly due to the side effects of modern drugs. Siddha system is practiced mainly in traditional tamil speaking people present in India and also throughout the world. It is a powerful system of medicine in Indian system and treats the diseases by using herbs, inorganic substances and animal products. Siddha system contains several types of formulations and Kudineer formulation is one of the types which include only dried and grinded herbs. 'Thetran vidhai kudineer', is a poly herbal siddha formulation comprising of four plants namely *Strychnos potatorum, Terminalia chebula, Cassia auriculata and Limonia acidissima.* This review describes various facets like morphological characters, active constituents and pharmacological properties of ingredients of Thetran vidhai kudineer.

Keywords: Thetran vidhai kudineer, *Strychnos potatorum, Terminalia chebula, Cassia auriculata and Limonia acidissima*, Siddha medicine.

INTRODUCTION

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 are requesting for alternate (traditional) medicine for treating common ailments and chronic diseases[1]. Siddha is one of the ancient traditional systems of medicine practiced in southern India. The word siddha means established truth and fundamental principles of siddha include theories of five elements (*Aim pootham*), and three forces/faults (Mukkuttram). The eight methods of examination (Envakai Thervukal) are used to determine diagnosis, etiology, treatment and prognosis[2]. Siddha formulations are presented in the books of GUNAVAGADAM (siddha pharmacology) quoted by siddhars. Siddha system has several types of formulations, in that Kudineer is one of the types and it is a decoction prepared by adding water to dry herbs, or fresh ones and boiling them so that the water content is greatly reduced to 1/16th or 1/8 of the water added. Sometimes, some substances are not directly added to the water but instead they are kept in a clean white cloth, tied and immersed in the water[3]. Examples of kudineer formulations are Atatotaik kudineer, Kapa curak kudineer, Manturati ataik kudineer, Nila vembu kudineer, Thetran vidhai kudineer etc[4].

The aim of this review is to describe various aspects like morphological characters, active constituents and pharmacological properties of ingredients parts used in Thetran vidhai kudineer.

Thetran vidhai kudineer (TVK)

The ingredients of Thetran vidai kudineer are effective and have broad spectrum activity. In ancient literature of siddha, it was said that the ingredients present in this formulation 'Thetran Vidhai Kudineer' has effectiveness in the treatment of Diabetes mellitus. (Table 1,2)

Composition of Thetran vidhai kudineer (TVK)

Thetran vidhai kudineer is a polyherbal siddha formulation containing four ingredients.
1. *Strychonus potatorum* (seed) - 1 part
2. *Terminalia chebula* (fruit) - 1 part
3. *Cassia auriculata* (seed) - 1 part
4. *Limonia acidissima* (Resin) - 6 parts
5. Water

Method of preparation

Powder the ingredients of Thetran vidhai kudineer separately and mix all the drugs thoroughly. Take 2 grams of powder and boil in 240 ml of water until it is reduced to 60ml.

Table 1: Taxonomical Description of ingredients of TVK

S.No	Name of the plant	Plant Part	Description
1	*S.potatorum*	Seeds	Globose in shape[5]
2	*T.chebula*	Fruit	Yellowish-green, five to six ribbed when dry[6]
3	*C.auriculata*	Seeds	12-20 seeds per fruit, ovoid and brown in color[7]
4	*L.acidissima*	Resin	Brown in color and collected from fruit[8]

Table 2: Morphological Description of ingredients of TVK

S.No	Name of the plant	Plant Part	Description
1	*S.potatorum*	Seeds	Globose in shape[5]
2	*T.chebula*	Fruit	Yellowish-green, five to six ribbed when dry[6]
3	*C.auriculata*	Seeds	12-20 seeds per fruit, ovoid and brown in color[7]
4	*L.acidissima*	Resin	Brown in color and collected from fruit[8]

Table 3: Phytoconstituents present in seeds of *Strychnos potatorum*

Seeds	Diaboline (alkaloid) and its acetate, brucine, loganin, strych-nine, mannose, sucrose, β-sitosterol, stigmasterol, oleanolic acid and saponin.

Table 4: Pharmacological activities of seeds of *Strychnos potatorum*

Plant Part Used	Type of Extract	Work done	Brief Result of the study
Seeds	Ethanolic Extract	Anti-diabetic activity in streptozotocin -nicotinamide-induced diabetes in rats	*S.potatoram* seed extract at doses of 200 mg/kg and 400 mg/kg body weight significantly reduced the blood glucose levels and also significantly increased the levels of Reduced Glutathione (GSH), Catalase (CAT), Superoxide dismutase (SOD), Glutathione-s-transferase (GST) and Glutathione peroxidase (GPx) in diabetic animals[9].
Seeds	Aqueous Extract	Acute and Chronic toxicity studies in rats	Animals did not show any toxic effects upto the dose 2000 mg/kg p.o[10].
Seeds	Chloroform Extract	Anti-microbial activity of alkaloid fractions of *S.potatoram* seeds by Agar-well diffusion method	Extraction of seeds with ethyl acetate followed by chloroform showed the presence of seven alkaloid fractions. These alkaloid fractions exhibited considerable anti-microbial activity against some pathogenic gram +ve, gram -ve and acid-fast bacteria[11].
Seeds	Ethanolic and Aqueous Extract	Analgesic and anti-inflammatory activity	For analgesic activity Eddy's hot plate in swiss mice and for anti-inflammatory activity Carrageenan induced edema techniques in albino rat model were used. Moderate to significant analgesic and anti-inflammatory activities were showed at 500 mg/kg body weight[12].
Seeds	Aqueous Extract	Anti-nociceptive and anti-pyretic effects in albino mice and rats	Administration of aqueous extract of seeds and seed powder extract at two dose levels 100 and 200 mg/kg p.o significantly decreased the abnormal contractions in acetic acid induced writhing model and significantly increased the reaction time in both hot plate and tail immersion techniques. The anti-pyretic activity was studied by injecting TAB vaccine (Typhoid-Paratyphoid A and B) at the dose 1ml/kg body weight. The aqueous extract exhibited dose dependent activity[13].
Seeds	Aqueous Extract	Anti-ulcerogenic activity by pyloric ligation-induced gastric ulcers in wistar albino rats	The results indicated *S.potatorum* seed powder and *S.potatorum* seeds aqueous extract at two doses 100 and 200 mg/kg body weight exhibited potential anti-ulcerogenic activity by both anti-secretory and mucoprotective action[14].
Seeds	Aqueous Extract	Anti-arthritic activity by Freund's complete adjuvant(FCA) induced arthritic rat paw edema	The extract treated groups showed significant reduction in paw volume and normal gain in body weight. The altered haemotological parameters and biochemical parameters in the arthritic rats were significantly brought back to near normal at a dose of 200 mg/kg p.o[15].
Seeds	Aqueous Extract	Hepatoprotective and anti-oxidant action in Carbon tetrachloride (CCl_4) induced acute hepatic injury	Both aqueous extract and whole seed powder at the doses 100 and 200 mg/kg p.o offered significant hepato-protective action by reducing the serum marker enzymes like Serum glutamic oxaloacetic transaminase (SGOT) and Serum glutamic pyruvic transaminase (SGPT) and also reduced the elevated levels of Alkaline phosphatase (ALP) & serum bilirubin. Reduced enzymic and nonenzymic

			antioxidant levels and elevated lipid peroxide levels were restored to normal[16].
Seeds	Methanolic Extract	Contraceptive efficacy in male rats	Methanolic extract of 100 mg/rat/day was administered orally to male rats of proven fertility for 60 days. The weights of testes, epididymides, seminal vesicle and ventral prostate were decreased significantly. Reduced sperm count and motility resulted in suppression of fertility by 91.81%. [17].
Seeds	Methanolic Extract	Anti-diarrhoeal activity in rats	The methanol extract of *S.potatorum* seeds, given by oral route to rats at doses of 100, 200 and 400 mg/kg, reduced significantly the frequency of defecation and wetness of fecal droppings in a dose dependent way. The fluid volume of the rat intestine was significantly increased by Prostaglandin E2 (PGE2). It was found that methanol extract in graded doses reduced diarrhoea by inhibiting intestinal peristalsis, gastrointestinal motility and PGE2 induced enteropooling[18].
Seeds	Methanolic Extract	Diuretic activity in wistar albino rats	Excretion of cations like sodium and potassium ions and anions like chloride ions also increased significantly with respect to the control group with the doses 200, 400 and 600 mg/kg body weight[19].

Table 5: Phytoconstituents present in fruits of *Terminalia chebula*

Fruits	Tannins like gallic acid, chebulic acid, punicalagin, chebulanin, corilagin, neochebulinic acid, ellagic acid, chebulinic acid

Table 6: Pharmacological activities of *Terminalia chebula*

Plant Part Used	Type of Extract	Work done	Brief Result of the study
Fruits	Ethyl alcohol extract	Anti-bacterial activity	Two anti-bacterial compounds, Gallic acid and ethyl ester against methicillin-Resistant *Staphylococcus*, have been isolated from ethyl alcohol extract of fruits of *T. chebula. T. chebula* is well effective against *Helicobacter pylori*, a bacterium responsible for gastritis, ulcer and stomach cancers[20].
Fruits	Petroleum ether, chloroform, and ethanol and water extracts	Anti-nociceptive activity	Petroleum ether, chloroform, and ethanol and water extracts of *T. chebula* fruits were evaluated for the analgesic activity by using the tail immersion method in mice. The ethanolic extract of the plant exhibited analgesic response at 200, 400 and 800mg/kg body weight day[21].
Fruits	Hydro alcoholic extract	Anti-ulcerogenic activity	200 and 500 mg/kg body weight with hydro alcoholic extract of *T. chebula* showed reduction in lesion index, total affected area and percentage of lesion in comparison with control groups in the aspirin, ethanol and cold restraint stress induced ulcer models[22].
Fruits	Hot water extract	Anti-viral activity	The fruit extracts of *T. chebula* showed inhibitory effects on human immunodeficiency virus-1 reverse transcriptase. Hot water extract of *T. chebula* in anti-herpes simplex virus (HSV) activity *in vivo*and anti-cytomegalovirus (CMV) activity. Both *in vitro* and *in vivo* inhibited HSV-1 entry at non-cytotoxic doses in A549 human lung cells by preventing binding, penetration, and cell to cell spread, as well as secondary infection[23].
Fruits	70% Methanolic extract	Anti-mutagenic and anti -carcinogenic activities	The effect of 70% methanolic fruit extract of *T. chebula* was studied on growth of several malignant cell lines. One of the fractionated compounds from ethanolic fruit extract of *T. Chebula*, chebulagic acid, showed potent dual inhibition against Cyclooxygenase (COX) and 5- Lipoxygenase (LOX). It also showed anti-proliferative activity against HCT-15, COLO-205, MDA-MB-231, DU-145 and K562 cell lines[24].
Fruits	Aqueous (Hot and Cold water) and Methanol Extract	Cyto-protective activity	The different concentrations of gallic acid and chebulagic acid, isolated from fruit extract of *T. chebula*, blocked cytotoxic T lymphocyte (CTL)- mediated cyto-toxicity. Granule exocytosis in response to anti-CD3 stimulation was also blocked by the above phyto-chemicals at the equivalent concentrations[25].
Fruits	Aqueous extract	Radio-protective activity	The aqueous extract of the fruit of *T. chebula* (50µg) was able to neutralize 1, 1-diphenyl-2 picrylhydrazyl (DPPH), a stable free radical by 92.9% and protected the plasmid DNA pBR322 from undergoing the radiation-induced strand breaks[26].

Fruits	Ethanolic extract	Cardio-protective activity in isoproterenol induced myocardial damage in rats	*T. chebula* extract had shown cardio-protective effect by stabilizing lysosomal membrane and preventing myocardial necrosis and inhibition of alterations in the heart mitochondrial and function[27].
Fruits	95% ethanolic extract	Hepato-protective activity	*T. chebula* fruit showed hepato-protective activity against anti- tubercular (anti-TB) drug induced toxicity which could be attributed to its prominent anti-oxidative and membrane stabilizing activities[28].
Fruits	Ethanolic extract	Anti-diabetic	Ethanolic extract of fruits of *T. chebula* (200 mg/kg body weight for 30 days) reduced the levels of blood glucose and glycosylated hemoglobin in streptozotocin (STZ)-induced experimental diabetic rats[29].
Dried Fruits	95% Ethanol, ethyl acetate and 5% $NaHCO_3$	Anti-oxidant activity by 1,1-diphenyl-2-picrylhydrazyl (DPPH) and 2',7'-dichlorodihydrofluorescin diacetate (DCFH(2)-DA)assay and lipid peroxidation, hydrogen peroxide (H_2O_2)-induced RBCs haemolysis and RBCs autoxidative haemolysis.	An triethylchebulate (TCL) aglycone isolated from the fruits of *T.chebula*, significantly inhibited ferrous sulfate(FeSO4) /Cysteine induced methylene dioxyamphetamine (MDA) formation as determined by thiobarbituric acid reactive substance assay (TBARS) and protected both H_2O_2- -induced RBCs haemolysis and RBCs auto-haemolysis in a dose dependent manner. [30].
Dried fruits	Water extract	Acute and chronic toxicity studies	*T. chebula* had showed no changes in body weight, internal organ weight, and general behaviors. Macroscopic or microscopic of internal organs or tissues in treated rats showed no changes. The water extract of *T. chebula* given orally to female and male rats did not produce both acute and chronic toxicities in rats[31].

Table 7: Phytoconstituents present in seeds of *Cassia auriculata*

Seeds	Grape seed oil, n- Hexadecanoic acid, 9-octadecenoic acid, (E)-E-Z-1,3,12-Nonadecatriene, stearic acid

Table 8: Pharmacological activities of *Cassia auriculata*

Plant Part Used	Type of Extract	Work done	Brief Result of the study
Seeds	Hydro-alcoholic extraction and technology-based supercritical fluid extraction	Cardiovascular variables and pharmacokinetic herb-drug interaction studies on rats	This study indicated that both Of these extracts are pharmacologically safe and did not show any significant adverse reactions at the tested doses. The traditional hydro-alcoholic extract did not show any significant effect on pharmacokinetics; however, the technology-based supercritical extract caused a significant reduction in absorption of metformin[32].
Seeds	Aqueous extract	Acute and Sub-acute toxicity studies	For acute study, aqueous extract of *C. auriculata* seeds was administered to rats in single dose of 0-5000 mg/kg and were determined for behavioural changes, adverse effects, body weight changes and mortality up to 14 days. In the sub-acute dose study the extract was administered orally at doses of 0, 1000 and 2000mg/kg daily for 28days to rats and biochemical, haematological parameters and histopathological study carried out after 28. In the acute and sub-acute toxicity study the aqueous extract of *Cassia auriculata* seeds did not show any behavioural changes sign of adverse effects or deaths[33].

Table 9: Phytoconstituents present in fruits of *Limonia acidissima*

Fruits	Stigmasterol, citric acid, alkaloids, coumarins, fatty acids, scoparone, xanthotoxin

Table 10: Pharmacological activities of *Limonia acidissima*

Plant Part Used	Type of Extract	Work done	Brief Result of the study
Fruit	Methanolic extract	Anticancer activity on Human Breast Cancer Cell Lines	Bioassay of the extract of *L. acidissima* showed that a fraction (fraction 3) of the ethanol extract had anticancer activity against SKBR3 and MDA-MB435 human breast cancer cells. The effective dose (ED50) of *L. acidissima* fraction 3 was 56.1 and 30.6 µg/ml for SKBR3 andMDA-MB435, respectively. After 48 h of exposure, this fraction (100µg/ml) significantly reduced cell proliferation in both cancer cell lines. In MDA-MB435 cells, cell cycle analysis showed that fraction 3 induced the

			accumulation of cells in G2/M phase, but no significant change in cell cycle was detected in SKBR3 cells[34].
Ripe Fruits	Methanolic extract	Anti-tumour activity in Mice model of Dalton's Ascitic Lymphoma (DAL)	In vitro cell cytotoxicity, Solid tumour and Liquid tumour models of DAL were used in this study to assess the anti-tumour activity. Post treatment changes in body weight, percentage increase in body weight, mean survival time (MST) and percentage increase in life span (%ILS) in group A; whereas tumour volume, tumour cell growth, haematological parameters, serological parameters and liver antioxidants in group B were observed. Tumour Bearing + extract groups showed significant ($P<0.05$) positive changes with respect to all parameters among all the groups in comparison to Tumour Bearing group[35].
Fruit Pulp	Methanol extract	Wound Healing and Anti-oxidant Activities in Rats	In incision wound model, wound breaking strength and epithelisation period were evaluated, while in excision wound model, wound contraction was studied. In dead-space wound model, granulation tissue dry weight, hydroxyproline levels in dry granulation tissue, as well as superoxide dismutase (SOD) and catalyse levels in wet granulation tissue were estimated. Granulation tissue was subjected to histopathological examination in order to determine whether there was healing by formation of collagen in the wound tissue in extract-treated animals. The methanol extract of *L. acidissima* possesses significant dose-dependent wound healing and anti-oxidant activities[36].
Fruit Pulp	Methanolic extract	Anti-diabetic activity was performed on the alloxan induced wistar rats	*L. acidissima* extract markedly improved the glucose tolerance and significant reduction in blood urea and creatinine in treated rats but significantly increased total protein level[37].
Fruit Pulp	Ethanolic extract	Hepatoprotective activity against carbon tetrachloride (CCl4) induced hepatic injury in rats.	Ethanolic extract exhibited significant dose dependent protective effect against CCl_4 induced liver damage which can be mainly attributed to the antioxidant property of the extract. This study rationalized the ethno-medicinal use of the plant for curing hepatic injuries[38].
Fruit Pulp	Ethanolic extract	Anti-spermatogenic activity	Administration of this extract to male rats brought about a significant weight loss of the reproductive organs of the rats, alterations in motility, viability and morphology of spermatozoa and had reversible anti-spermatogenic activity[39].

Strychnos potatorum

Strychnos potatorum Linn.F. a medicinally important endangered tree species which belongs to Loganiaceae and is also known as nirmali and clearing nut tree. The seeds of the plant possess important phytochemical constituents which may be responsible for many of the pharmacological activities such as diuretic activity, anti-diarrhoeal activity, contraceptive efficacy, hepatoprotective activity, anti-oxidant activity, anti-arthritic activity, anti-ulcerogenic activity, anti-nociceptive and anti-pyretic effect [5]. (Table 3,4)

Terminalia chebula

Terminalia chebula is a moderate tree used in traditional medicines. It is belongs to the family combretaceae and commonly called as Black myrobalan, Ink tree (or) Chebulic myrobalan and also known as "King of medicine" due to its wide spectrum of pharmacological activities associated with the biologically active chemicals present in this plant. It is used for the treatment of number of diseases like cancer, paralysis, cardio vascular diseases, ulcers, leprosy, arthritis, gout, epilepsy etc. It has beneficial effect on all the tissues[6]. (Table 5,6)

Cassia auriculata

Cassia auriculata commonly called Tanner's Cassia in English and in Tamil as "Avarai". C. auriculata (family: Caesalpinioideae) is an evergreen shrub that grows in many parts of India and in other parts of Asia. The flower, leaves, stem, root, and unripe fruit are profoundly used in Ayurvedic medicine as a remedy for diabetes, conjunctivitis, joint and muscle pain (rheumatism), ophthalmic, jaundice, liver disease, and urinary tract disorder[7]. (Table 7,8)

Limonia acidissima

The plant *L. acidissima* (Family- Rutaceae) is known as Kath bael in Bangla and is a common plant of Bangladesh. Its leaves, bark and then fruits have medicinal values and used as traditional medicines for centuries due to their anti-microbial, anti-fungal, astringent, anti-inflammatory and insulin secretogouges activities[8].(Table 9,10)

CONCLUSION

Herbal treatments are the most popular form of traditional medicine, and are highly lucrative in the International marketplace. This review distinctively exposes that ingredients of Thetran vidhai kudineer formulation have anti-diabetic, hepatoprotective, analgesic, diuretic, anti-spermatogenic, anti-oxidant, anti-microbial activities in common. The drugs of Thetran vidhai kudineer can hence be used in the treatment of Kapha and Vata doshas. As there is no scientific evidence of work done on the 'Thetran vidhai kudineer', to attain scientific stature, further studies on its safety and efficacy has to be carried out. Then this drug will surely become a blissful drug in the market.

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Cite this article as:

G. Dayanand Reddy *et al.* A comprehensive review on thetran vidhai kudineer: A Siddha polyherbal formulation. Int. Res. J. Pharm. 2019;10(1):42-48 http://dx.doi.org/10.7897/2230-8407.100376

Source of support: Nil, Conflict of interest: None Declared