RESEARCH ARTICLE PHARMACOLOGIA

DOI: 10.5567/pharmacologia.2013.77.81

Anti-obesity and Hypolipidemic Activity of Methanol Extract of Tecoma stans Flowers on Atherogenic Diet Induced Obesity in Rats

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ABSTRACT

Objective: *Tecoma stans* (Bignoniaceae) is conventionally used for a variety of treatments and also in the cases of arteriosclerosis and circulatory irregularities. Hence, the present exploration was intended to assess the potential effect of Methanol Extract of flowers of *Tecoma stans* (METS) on obesity and hyperlipidiemia on Atherogenic diet induced obese rats. **Methods:** METS at the doses of 100 and 200 mg kg^{-1} were administered along with atherogenic diet for a period of 42 days. Parameters such as body weight, body temperature, serum lipid profiles, SGOT and SGPT were evaluated. **Results:** METS at the dose of 200 mg kg^{-1} significantly ($p<0.001$) corrected the altered parameters, similar to that of standard drug sibutramine (2 mg kg^{-1}). **Conclusion:** From the observations of the study performed, it could be predicted that *Tecoma stans* flower extract exerted significant anti-obese and anti- hyperlipidemic effects in rats fed on Atherogenic diet.

Key words: obesity, hyperlipidemic, *Tecoma stans,* Atherogenic diet, lipid profile

Pharmacologia 4 (2): 77-81, 2013

INTRODUCTION

Obesity is a global health problem, resulting from an energy imbalance caused by an increased ratio of caloric intake to energy expenditure. Obesity is also known to be risk factor for the development of metabolic disorders, dyslipidemia, atherosclerosis and type 2 diabetes[1,2] pertension, hyperlipediemia, hypercholesteromia, insulin resistance and glucose tolerance are known as cardiac risk factors that cluster in obese individuals[3]. The persistence of hypercholesteromic state causes enhanced oxidative stress, leading to the development of atherosclerosis, coronary artery disease and other complications of obesity[4] Obesity is associated with many health problems including coronary heart disease, diabetes, kidney failure, osteoarthritis, back pain and psychological damage. Diseases such as hypothyroidism, insulin resistance, polycystic ovary syndrome and Cushing's syndrome are also contributors to obesity. The strong association between obesity and cancer has only recently come to light[5].

Tecoma stans (Common name: Yellow bell) is also known as yellow trumpet bush and belongs to the family Bignoniaceae. It is an erect ornamental plant and is a branched, slightly hairy or nearly smooth shrub 2 to 4 m in height. The leaves are opposite, odd-pinnate and up to 20 cm in length with 5 to 7 leaflets. The leaflets are lanceolate to oblong-lanceolate, 6 to 13 cm long, pointed at both ends and toothed on the margins. The trumpet-shaped flowers are yellow, faintly scented and occur in short, dense, terminal clusters. The calyx is green, 5 to 7 mm long and 5-toothed. Flowering can begin as early as April and continue into the fall (autumn)[6]. The leaves of *T. stans* contain the alkaloids tecomine and tecostamine, potent hypoglycaemic agents when given intravenously. Anthranilic acid is responsible for its antidiabetic activity and the roots exhibit a powerful diuretic and vermifuge activity[7]. Tecoma is not toxic and is used in Latin America as a remedy for diabetes and also for feeding cattleand goats in Mexico[8]. The present study was planned to investigate anti-obese and anti- hyperlipidemic activity of flower extract of *T. stans.*

MATERIALS AND METHODS

Collection of plants and preparation of extracts: The flowers of *T. stans* were collected in the month of May 2011 from Rasipuram (Namakkal District) Tamil Nadu. A herbarium specimen of the plant was deposited in the Department of Pharmacognosy. The plant was identified by Dr. G.V.S. Murthy, Joint Director of the Botanical Survey of India, Southern circle, TNAU Campus.

Coimbatore, who authenticated the plant from information available in the literature. The flower petals were dried in the shade and then powdered and 100 g of the dried powder was extracted with ethanol using a soxhlet apparatus. The solvent was removed under

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reduced pressure and controlled temperature using a rotary flash evaporator. Phytochemical screening of the extracts revealed the presence of tannin, flavonoids, phenols, alkaloids, steroids, triterpenes and saponins.

Animals: Wister rats (150-170 g) of both sexes were used in these experiments and they were housed under standard environmental conditions like, ambient temperature (25±1°C), relative humidity (55±5%) and a 12/12 h light dark cycle. Animals had free access to a standard pellet diet and water. All animal experiments were carried out in accordance with the guidelines of CPCSEA. The animal ethical committee of the institute gave its approval to conduct the animal experiments (approval No. 1158/ ac/07/CPCSEA).

PHARMACOLOGICAL STUDIES

Atherogenic diet induced obesity in experimental rats preparation of diet: Atherogenic Diet (AD) is a hyper caloric diet and was prepared by mixing the following constituents in fixed percentage. The mentioned percentage is for 100 g diet. The feed was prepared, dried and administered every day in morning to animals with water *ad libitum*[9].

Atherogenic diet formula:

- **Cholesterol:** 1%
- **Cholic acid:** 0.5%
- **Olive oil:** 5% To be provided in addition to the normal pellet chow everyday for 42 days

Experimental design: Female albino wistar rats (150-170 g) were divided into five groups of six rats each. The following schedule of dose and diet administration in experimental groups was followed:

Group 1: Animals fed with normal diet and served as normal control

Group 2: Animals received Atherogenic diet (1% cholesterol) and served as Obese contol

Group 3: Animals received Atherogenic diet+sibutramine (2 mg kg^{-1} b.wt.) suspended in 0.9% saline

Group 4: Animals received Atherogenic diet+METS (100 mg kg^{-1}) suspended in 0.9% saline

Group 5: Animals received Atherogenic diet+METS (200 mg kg^{-1}) suspended in 0.9% saline

The above mentioned treatment schedule was followed for the respective groups of animals for 42 days.

Pharmacological evaluations

Body weight: The body weight (g) was recorded on day one and then on every week for 42 days using digital weighing balance.

Body temperature: The body temperature was recorded on day 41 using rectal telethermometer before and after drug administration at 30, 60, 90, 120, 180 min with a contact time of 1 minute.

Biochemical estimations: On day 43, animals were sacrificed under anesthesia and blood was collected by direct cardiac puncture. Blood samples collected are to be centrifuged at 3500 rpm for 15 min at room temperature for separation of serum. The clear, non-haemolysed supernatant sera will be separated using clean dry disposable plastic syringes and parameters such as Total cholesterol, Triglycerides, HDL, LDL, VLDL[11], Atherogenic index (AI)[10], percentage protection, SGOT, SGPT, total protein, Blood glucose[12] and Urea were evaluated:

$$\text{Atherogenic index (AI)} = \frac{\text{Serum cholesterol}}{\text{Serum HDL} - \text{Cholesterol}}$$

$$\text{Protection (\%)} = \frac{\text{AI (Control)} - \text{AI (Treated)}}{\text{AI (control)}} \times 100$$

Estimation of internal organ weight: The animals were sacrificed and the organs like heart, liver and both the kidneys were separated out and blotted in a filter paper and immediately weighed in a digital balance.

Statistical analysis: All the results were expressed as mean±standard error of mean and were analyzed by Analysis of Variance (ANOVA) and groups were compared by Tukey-Kramer multiple comparison test. Differences between groups were considered significant at $p<0.05$ level.

RESULTS

Effect of METD on Body weight: Utilization of Atherogenic Diet (AD) for six weeks produced a significant ($p<0.001$) augment in body weight when compared with the consumption of normal control group (normal pellet chow). Treatment with METS at the dose of 200 mg kg^{-1} causes a significant reduction ($p<0.001$) initiated from the second week, whereas sibutramine also abridged the increased body weight. Changes in the body weight in the different group of animals, during the experiment is given in Table 1.

Effect of METD on body temperature: Animals fed with atherogenic diet exhibited decrease in body temperature. Sibutramine exhibited reverse effect by increasing the body temperature significantly ($p<0.001$) (Table 2). METS at both the doses (100 and 200 mg kg^{-1}) upturned the decrease in body significantly ($p<0.01$ and $p<0.001$), respectively at various time intervals.

Table 1: Effect of methanol extract of *Tabernaemontana divaricata* on body weight of atherogenic diet induced obese rats at different day's interval

	Group 1	Group 2	Group 3	Group 4	Group 5
Initial	158.64±2.1	159.02±1.25	157.70±2.09	158.16±2.58	157.89±2.8
1st week	160.33±3.01	171.86±1.41*	160.68±2.26	163.91±1.74	160.74±2.17
2nd week	162.44±2.54	184.9±3.8***	167.44±2.48*	169.02±3.54*	167.65±2.48**
3rd week	163.92±3.54	207.68±2.11***	174.51±4.25***	181.19±3.78**	174.69±2.39***
4th week	167.71±4.12	221.62±2.41***	180.78±2.95***	190.28±3.69**	181.98±2.25***
5th week	173.78±5.13	232.44±3.14***	182.27±3.24***	200.89±1.78***	188.48±2.36***
6th week	178.44±2.64	237.17±4.78***	185.46±2.72***	214.99±2.48**	195.84±1.96***

Values are Mean±SEM for six groups of six animals each, Values are statistically significant at *p<0.05, **p<0.01 and ***p<0.001when group 2 compared with group 1 and groups 3-5 were compared with group 2

Table 2: Effect of Methanol extract of *Tabernaemontana divaricata* on body temperature of atherogenic diet induced obese rats at different time interval on day 41

		Time after drug administration			
Groups	Before drug admin	30 min	60 min	90 min	120 min
Group 1	33.29± 0.08	33.53±0.12	33.23±0.06	33.16±0.03	33.43±0.03
Group 2	311.89±0.2	31.1±0.56***	31.81±0.19**	31.53±0.21***	31.7±0.17***
Group 3	31.85±0.07	33.23±0.45**	33.2±0.17***	33.65±0.14**	33.48±0.28**
Group 4	32.59±0.65	32.67±0.12**	32.7±0.12***	32.78±0.52**	32.45±0.16***
Group 5	32.15±0.56	32.83±0.22**	32.9±0.15***	32.66±0.07***	33.24±0.03***

Values are Mean±SE for six groups of six animals each, Values are statistically significant at *p<0.05, **p<0.01,***p<0.001 when group 2 compared with group 1 and groups 3, 4 and 5 were compared with group 2

Table 3: Effect of methanol extract of *Tabernaemontana divaricata* on lipid profiles of atherogenic diet induced obese rats on day 42

Groups	Cholesterol (mg dL^{-1})	Triglycerides (mg dL^{-1})	HDL (mg dL^{-1})	LDL (mg dL^{-1})	VLDL (mg dL^{-1})
Group 1	126.15±4.57	104.47±4.67	58.702.25	46.045.2	21.782.44
Group 2	188.577.02***	294.675.51***	45.141.53**	83.075.87***	59.924.56***
Group 3	129.248.327***	138.407.55***	63.653.511***	38.412.76***	27.683.75***
Group 4	150.464.13**	176.744.73***	46.772.49	68.724.15	33.783.42**
Group 5	130.843.71***	150.604.10***	55.602.19*	42.563.69***	30.692.70***

Values are Mean±SEM for six groups of six animals each, Values are statistically significant at *p<0.05, **p<0.01, ***p<0.001 when group 2 compared with group 1 and groups 3, 4 and 5 were compared with group 2

Effect of METD on lipid profile: Group 2 (Obese control group) animals fed with AD exhibited a significant (p<0.001) increase in Total Cholesterol (TC), Triglycerides (TG), LDL and VLDL when compared with group I (normal group) animals. Administration of METS (200 mg kg^{-1}) and sibutramine shows a noteworthy reduction (p<0.001) in TC, TG, LDL and VLDL when compared with the group 2 animals, whereas decreased HDL levels noted in group 2 animals were significantly (p<0.05) increased in group 4 (Table 3).

Atherogenic index (AI) and percentage protection: Decline in Atherogenic Index was observed in all the treated groups (group 3 to 4). Percentage defense for METS (100 and 200 mg kg^{-1}) was 24.63 and 48.30%, respectively and 49.51% for sibutramine treated group. (Table 4).

Effect of METD on liver function tests: Levels of SGOT, SGPT and total protein increased significantly (p<0.001) in group II animals. Group 3 and 4 exhibited a significant (p<0.001) decrease when compared with group 2 animals (Table 5).

Table 4: Effect of methanol extract of *Tabernaemontana divaricata* on atherogenic index and percentage protection of various groups

Groups	Atherogenic index (AI)	Protection (%)
Group 1	2.38±0.12	-
Group 2	4.14±0.38	-
Group 3	2.09±0.07	49.51
Group 4	3.12±0.01	24.63
Group 5	2.14±0.09	48.30

Effect of METD on blood glucose and urea: Major reduction of urea and lift up in blood glucose levels was observed in obese control animals (group 3). METS (200 mg kg^{-1}) shows a significant decrease in blood glucose (p<0.01) and increase in urea levels (p<0.001) when compared to group 2 (Table 5).

Effect of METD on inner organ weight: Feeding AD for six weeks twisted a significant increase in the weight of liver, heart and both of the kidneys. Treatment with METS significantly reduced the weight of liver, heart and kidneys (Table 6).

DISCUSSION

High proportion of fat in artherogenic diet (Cholesterol 1%) is considered to be an important factor inthe development of obesity, leading to the accretion of

Table 5: Effect of Methanol extract of *T.stans* on SGOT, SGPT, total protein, urea and blood glucose levels of Atherogenic diet induced obese rats on day 42

Groups	SGOT (IU L^{-1})	SGPT (IU L^{-1})	Total protein (gm dL^{-1})	Urea (mg dL^{-1})	Blood glucose (mg dL^{-1})
Group 1	163.464.31	58.702.10	6.210.15	41.510.90	82.841.445
Group 2	230.835.91***	127.426.16***	9.740.11***	24.270.81***	91.402.21**
Group 3	166.405.47***	62.542.12***	6.360.37***	32.671.74***	82.431.63**
Group 4	207.635.58*	98.432.51***	7.470.65**	39.702.80***	88.401.40
Group 5	168.404.54***	70.112.62***	6.40.33***	38.471.31***	82.361.21**

Values are Mean±SE for six groups of six animals each, Values are statistically significant at *p<0.05, **p<0.01, ***p<0.001when group 2 compared with group 1 and groups 3, 4 and 5 were compared with group 2

Table 6: Effect of methanol extract of *T.sans* on inner organ weights of atherogenic diet induced obese rats on day 42

			Kidney (g)	
Groups	Liver (g)	Heart (g)	Left	Right
Group I	5.22±0.30	0.63±0.14	0.55±0.01	0.56±0.20
Group II	8.62±0.14***	1.08±0.11***	0.85±0.03*	0.87±0.02**
Group III	5.12±0.14***	0.58±0.65***	0.56±0.02**	0.54±0.02***
Group IV	6.84±0.22***	0.67±0.21**	0.63±0.01*	0.66±0.02*
Group V	5.25±0.04***	0.65±0.077***	0.61±0.15*	0.60±0.10**

Values are Mean±SE for six groups of six animals each, Values are statistically significant at *p<0.05, **p<0.01, ***p<0.001 when group 2 compared with group 1 and groups 3, 4 and 5 were compared with group 2

body fat. The present tudy showed that the administration of AD for six weeks in rats shaped obesity-like conditions, with augment in body weight, parametrial adipose tissue mass and organ mass and serum lipid levels. It also induces to the amassing of hepatic triglycerides, leading to the hepatic failure causing boost in SGOT and SGPT levels in the serum. In obesity, there will be diminish in the diet induced thermogenisis, due to lessen in sympathetic activation of brown adipose tissue. Neuropeptide-Y (NPY), which synthesized in the brain causes increase in food intake and also inhibits thermogenisis by plummeting sympathetic activation of brown adipose tissue[2]. Treatment with METS at doses of 100 and 200 mg kg^{-1}, significantly abridged the increased body weight induced by AD, which shows a clear indication of an antiobesity effects.

In fatness there will be an increase in serum lipids, such as Total Cholesterol (TC), Triglycerides (TG), LDL-C and VLDL-C were pragmatic in humans and also a diminution in HDL-C levels. Variation in lipid levels is also painstaking as an index of obesity[13]. Low plasma HDL-C is a risk factor for cardiovascular diseases and is often found in hypertension and diabetes mellitus[14,16]. Administration of METS caused a significant correction of elevated TC, TG, LDL-C and VLDL-C and increases the serum HDL-C shows that, METS has a agreeable antihyperlipedimic activity. Lipids are mostly consumed in the form of neutral fats, which are also acknowledged as Triglycerides (TG). TGs form major constituents in food of animal derivation and fewer in food of plant source. Saturated fats increase blood cholesterol and thereby increase risk of atherosclerosis and coronary heart diseases, abnormal lipoprotein metabolism, obesity, insulin resistance and diabetes mellitus[15,17].

Atherogenic index is the powerful indicator of the risk of heart disease: the higher the value, the higher the risk of developing cardiovascular disease and vice versa[18,19]. In this study we observed that the METS significantly reduced atherogenic index, indicating the fortification against cardiovascular diseases[20]. The capacity of the hepatocytes in obese rats to produce urea from precursors is decreased and the uptake of amino acids by liver and the hepatic activity of the enzymes of the urea cycle are also decrease[21]. Hence, there will be a lesson in the urea level in obese rats and the METS treated animals showed a significant reverse activity. The liver uses transaminase enzymes, ALT (SGPT) and AST (SGOT) to metabolize amino acids and to build proteins. When liver cells get dented, ALT and AST leak into the blood stream. Fatty liver is also a reason for the hepatic damage and frequent causes of fatty liver are Diabetes, Obesity and alcohol abuse (www.medicinenet. com). Also, obesity is related with the increase adipose tissue buildup in the abdominal region. It is reported that METS produced decrease in the weight of liver, heart and kidney similar to that of the standard drug sibutramine[22].

Further investigation involving measure of enzymes in lipid pathways and harmones would ascertain the exact mechanism and figure out the therapeutic potential of *Tecoma stans* in the treatment of hyperlipedimia and obesity. However further studies under progress to isolate and characterize the phytoconstituents responsible for the above activities.

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