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Antihyperlipidemic Activity of *Michelia champaca* L. In Triton WR 1339 Induced Albino Rats

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Abstract: The hypolipidemic activity of *Michelia champaca* extract was studied on triton WR 1339 induced models of hyperlipidemia in rats. Hyperlipidemia in experimental rats evidenced by an enhancement in the levels of Cholesterol, Triglycerides, LDL,VLDL, HDL and Oxidative stress markers (MDA,GSH). Methanolic extract of flowers showed significant reduction in the level of serum cholesterol, triglycerides, LDL, VLDL,MDA,GSH and increase in HDL level which was similar to the standard drug atrovastatin. Preliminary phytochemical analysis revealed the presence of phytoconstituents such As Tannins, Saponins, Steroids, Terpenoids, Flavonoids, Carbohydrates, Anthroquinone, Polyphenol And Glycosides.
Key words: *Michelia champaca*, Hyperlipidemia, Triton, LDL,VLDL.

Introduction:

Hyperlipidemia has been ranked as one of the greatest risk factors contributing to prevalence and severity of coronary heart diseases [1]. Coronary heart disease, stroke, atherosclerosis and hyperlipidemia are the primary cause of death [2]. Hyperlipidemia characterized by elevated serum total cholesterol and low density and very low density lipoprotein cholesterol and decrease high density lipoprotein are the risk factor for coronary heart diseases. Hyperlipidemia associated lipid disorders are considered to cause the atherosclerotic cardiovascular disease [3]. Among these hypercholesterolemia and hyper triglyceridemia are closely related to ischemic heart disease [4]. The main aim of treatment in patients with hyperlipidemia is to reduce the risk of developing ischemic heart disease or the occurrence of further cardiovascular or cerebrovascular disease [5]. Currently available hypolipidemic drugs have been associated with number of side effects [6]. The consumption of synthetic drugs leads to hyperuricemia, diarrhoea, nausea, myositis, gastric irritation, flushing, dry skin and abnormal liver function [7]. Medicinal plants are used for various research purposes. It has been reported that traditional systems have immune potential against various diseases. More than thirteen thousand plants have been studied for various pharmacological properties. An herbal treatment for hypercholesterolemia has no side effects and is relatively cheap, locally available. They are effective in reducing the lipid levels in the system [8]. Hyperlipidemia was classified into primary and a secondary type clearly indicates the complexities associated with disease. The primary disease may be treated baker's yeast anti-lipidemic drugs but the secondary type originating from diabetes, renal lipid nephrosis or hypothyroidism demands the treatment of original disease rather than hyperlipidemia [9]. Consumption of much fat may lead to the production of extra VLDL, resulting in the formation of large amounts of LDL which may stick to the walls of the blood vessels if the quantity of HDL is insufficient, causing blockages for the normal flow of blood.

Michelia champaca L. (Magnoliaceae) commonly known as Svarna champa, a tall handsome tree with yellow fragrant blossoms, is commonly used by many traditional herbal preparations and it is also reported to have significant wound healing[10], antimicrobial[11], antidiabetic [12], antitumor [13], anti-inflammatory [14], antioxidant [15] and anti infective [16] properties.

Materials and Methods:

Collection of Plant materials:

The fully mature flowers of *M. champaca* (MC) were procured from a local florist shop and authenticated by the Professor of Dr. S. John Britto, Botany, St. Joseph's College, Trichy.

Preparation of methanolic extract:

Flowers were shade dried and were finely powdered. The powder was loaded into Soxhlet extractor in batches of 150 g each and was subjected to extraction for 30-40 hours with 70 % methanol. After extraction, the solvent was distilled off and concentrated on a water bath at a temperature below 50º C to syrup consistency. Then it was dried and stored in desiccators.

Animals:

Male albino rats of Wistar strain approximately weighing 150-180g were used in this study. They were healthy animals from animal house, Annamalai University, Chidambaram. The animals were housed in spacious polypropylene cages bedded with rice husk. The animal room was well ventilated and maintained under standard experimental conditions (Temperature 27 ± 2º C and 12 hour light/dark cycle) throughout the experimental period. All the animals were fed with standard pellet diet and water were provided *ad libitum*. They were acclimatized to the environment for one week prior to experimental use. The animal feed composition is crude protein (22.3%), crude oil (4.01%), crude fiber (4.02%), Ash (8.02%) and sand silica (1.02%).

Chemicals:

Triton WR-1339, Thiobarbituric acid (TBA), 2,4, Dinitrophenylhydrazine (DNPH), reduced glutathione and Triton WR 1339 were purchased for sigma chemical company, Mumbai. All other chemicals and reagents used in this study were of analytical grade with high purity and were obtained from Glaxo laboratories and Sisco Research laboratories, Mumbai, India.

Phytochemical screening:

To determine the presence of Tannins, Flavonoids, Steroids, Saponins, Cardiac Glycosides, Terpenoids, Phlobatannins, Alkaloids, Triterpenoids, Anthroquinones, Carbohydrate, a preliminary phytochemical study (color reaction) with various plant extracts were performed [17].

Experimental Design:

The animals were divided into four groups of six animals each. First were given standard pellet diet water and orally received with 5% CMC. Second group were given a single dose of triton (350 mg/kg) was administered intraperitoneally . After 72 hours of triton injection received a daily dose of 5% CMC (p.o) for 14 days. Third group was administered a daily dose of *Michelia champaca* methanolic flower extract 500mg/kg suspended in 5% CMC (p.o) for 14 days, after inducing hyperlipidemia.

Collection of blood:

On the 15th day the blood was collected by retro orbital sinus puncture, under mild ether anesthesia. The collected samples were centrifuged for 10 minutes. Then serum samples were collected and it is used for various biochemical experiments.

Biochemical Analysis:

The serum samples were analyzed spectro photometrically for total serum of Total cholesterol (TC), triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C), LDL,VLDL and oxidative stress markers (MDA,GSH) by using suitable standard methods [18],[19], [20],[21] &[22].

Statistical Analysis:

The results were presented as mean ± SD. Data was statistically analysed using student 't' test. P value set as lower than 0.05 was considered as statistically significant.

Results and Discussion:

Phytochemical screening:

The preliminary phytochemical screening of *Michelia champaca* in methanolic extract showed the presence of tannin, phlobatanin, saponin, flavonoids, steroids, terpenoids, triterpenoids, carbohydrates, anthroquinone, polyphenol and glycosides (Table 1).

Effects of *Michelia champaca* on serum lipids:

A marked increase in the level of serum cholesterol, triglycerides, LDL, VLDL and HDL levels were decreased in triton induced animals. Administrations of methanol extract at the dose of 500mg/kg showed significant reduction in the level of serum cholesterol triglyceride LDL, VLDL and increased in the HDL level which was similar to the standard atrovastatin and are almost near the levels of normal control.

A significant percentage reduction of serum cholesterol, triglyceride, LDL, VLDL and increase in HDL percentage were observed in test extract was also comparable with standard. A potent hypolipedemic effect of mehanolic extract was evident by a significant reduction in the level of serum cholesterol, LDL, VLDL and triglycerides in the Triton treated animals and also marked in the increase in the HDL (Table 2)

Table 1: Phytochemical screening of *Michelia champaca* L. flowers

Phytochemical tests	Observation
Tannin	+
Phlobotannins	+
Saponini	+
Flavonoids	+
Steroids	+
Terpinoids	+
Alakloids	-
Carbohydrates	+
Protein	-
Anthroquinone	+
Polyphenol	+
Glycoside	+

+ indicates presence; whereas – indicates absence

Table 2 : Effect of *Michelia champaca* on serum lipid profile of control and experimental rats

Parameters	Group I	Group II	Group III	Group IV
Cholesterl (mg/dl)	116.66 ± 62.36	255.55 ± 72.00	127.77 ± 77.22	194.44 ± 77.21
Triglycerides (mg/dl)	92.55 ± 11.62	157.86 ± 21.90	94.88 ± 6.44	103.70 ± 19.21
LDL-Cholesterol (mg/dl)	41.7 ± 2.93	60.32 ± 6.58*	42.7 ± 2.81**	44.29 ± 3.06**
VLDL-Cholesterl (mg/dl)	31.4 ± 2.93	51.31 ± 6.14*	32.84 ± 5.81**	32.84 ± 5.81**
HDL – Cholesterl (mg/dl)	36.45 ± 10.68	16.66 ± 5.43*	36. ± 11.53**	30.41 ± 4.92**

Values were expressed as mean ± SD for six rats in each group.* Significantly different from Group I,III.IV

Cholesterol is a waxy substance produced by the liver and supplied in the diet. It is vital for the body to function properly (i.e., for hormone and bile acid production). Most of the body's cholesterol is made in the liver, with excess production occurring when the diet is rich in saturated (mainly animal) fats. Excess cholesterol can accumulate and form deposits, called plaques, on artery walls. This can lead to atherosclerosis (hardening of the arteries).As plaques continue to grow; blood flow in affected arteries may slow (or) even stop. There is also a risk that a plaque can trigger local clotting (or) that part of a plaque can become dislodged leading to an ischemic event. Blood is mainly made up of water. Because cholesterol, a fat, is water insoluble it is carried in the blood bound to different lipoproteins. These lipoprotein packages transport the cholesterol around the body. TC is a measure of the total lipoprotein – cholesterol content in the blood [23].

Triglycerides are composed of fatty acids and glycerol. Like cholesterol, they circulate in the blood but are stored in body fat. When a fatty meal is eaten, triglyceride (and glucose) levels increase significantly. Gradually as the body processes the fat efficiently the level of triglycerides will decrease [24].

About 65 percent of TC is carried by low density lipoproteins. LDL cholesterol (known as "bad" cholesterol) is potentially harmful, becoming dangerous when it is oxidized. It is deposited onto the walls of arteries (eg.coronary arteries) to form atheromatous plaques. Particle size is important because large particles are less dangerous than small ones, which readily penetrate the arterial wall and are more easily oxidized (leading to endothelial dysfunction and atheromatous plaque formation) [25].

VLDL cholesterol is composed mostly of cholesterol, with little protein. VLDL cholesterol is also often called "bad cholesterol" because it, too deposits cholesterol on artery walls. Increased levels of VLDL cholesterol are associated with atherosclerosis and coronary heart disease.

However, the risk of CVD cannot be judged on TC alone. Other factors make a significant difference. Cholesterol carried by HDL has been removed from the walls of blood vessels. HDL cholesterol is known as "good" cholesterol because it helps to clear excess lipids from the arteries[26].

Effect of *Michelia champaca* on Oxidative stress markers:

Triton induced hyperlipidemic rats showed a significant increased in the level of MDA when compared to control. Triton induced hyperlipidemic rats treated with *Michelia champaca* (500mg/kg bwt) significantly decreased in the level of MDA when compared to triton induced rats. Atrovastatin treated rats also decreased significantly.

Triton induced hyperlipidemic rats showed a significant decreased in the level of GSH when compared to control rats. Triton induced hyperlipidemic rats treated with *Michelia champaca* 500mg/kg significantly increased in the level of GSH as compared to triton induced rats. Atrovastatin treated rats increased significantly (Table 3).

Table 3: Effect of *Michelia champaca* on MDA and GSH in experimental rats

Parameters	Group I	Group II	Group III	Group IV
MDA (nmol/L)	2.72± 1.44	7.11± 3.10	3.40± 0.84	3.10 ±1.47
GSH (mg/dl)	3.15 ± 0.67	1.32 ± 0.34	2.92 ± 0.89	3.07 ± 0.59

Values were expressed as mean ?SD for six rats en each group

Oxidative stress is believed to be a primary factor in various diseases as well as in the normal process of aging [27]. Free radicals and reactive oxygen species (ROS) are well known inducers of cellular and tissue pathogenesis leading to several human diseases such as cancer, inflammatory disorders, atherosclerosis and cardiovascular diseases [28]. Cardiovascular diseases are the most common cause of death in the industrialized countries [29]. Many epidemiological and experimental studies have shown that the polyphenol intake is inversely correlated with atherosclerosis development and related cardiovascular events. The beneficial effect of polyphenols is associated with a multitude of biological activities, including antioxidant and free radical-scavenging properties, anti-platelet aggregation and inhibition of vascular smooth muscle cell proliferation, all these effects might interfere with atherosclerotic plaque development and stability. These observations might explain their cardio-vascular protective properties. On the other hand, it is now established that hyperlipidaemia represents a major risk factor for the premature development of atherosclerosis and its cardiovascular

complications. A logical strategy to prevent or treat atherosclerosis and reduce the incidence of cardiovascular disease events is to target the hyperlipidaemia and oxidative stress by diet and/or drug intervention [30].

The study of lipid peroxidation is attracting much attention in recent years due to its role in disease processes. Membrane lipids are particularly susceptible to LPO due to the presence of polyunsaturated fatty acids. It has been implicated in the pathogenesis of a number of diseases and clinical conditions[31]. Malondialdehyde (MDA), a commonly used biomarker of lipid peroxidation, belongs to the group of aldehydes arising mainly from lipid perioxidation in the body. Measured levels of MDA can be considered an direct index of oxidative injuries associated with lipid peroxidation[32]. In this context a marked increase in the concentration of LPO was observed in triton induced hyperlipidemic rats when compared to control rats. Administration of *Michelia champaca* significantly decreased the level of LPO in Triton induced hyperlipidemic rats.

GSH is a major non- protein thiol in living organism, which plays a central role of co-ordinating the body's antioxidant defense process. It is implicated in the cellular defense against xenobiotics and naturally occurring deleterious compounds such as free radicals. Glutathione status is a highly sensitive indicator of cell functionality and viability. Perturbation of GSH status of a biological system has been reported to lead to serious consequences [33]. In the present study, declined level of GSH was observed in Triton induced hyperlipidemic rats when compared to control rats. The decrease in GSH level represents increased utilization for neutralizing free radicals generated from Triton induced hyperlipidemic rats. Administration of *Michelia champaca* to Triton induced hyperlipidemic rats attained near normal level.

Conclusion

Thus, our study concluded that administration of methanolic flower extract of 500mg/kg b/wt. *Michelia champaca* was more effective to manage hyperlipedemia. The active ingredients present here may recover the disorders in lipid metabolism noted in hyperlipidemic state.

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