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RESEARCH ARTICLE

A STUDY OF ANTI-HYPERLIPIDEMIC ACTIVITY OF MARKETED FORMULATIONS OF *TERMINALIA ARJUNA* POWDER USING EXPERIMENTAL ANIMAL MODEL

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ABSTRACT

Hyperlipidemia is a disorder of lipid metabolism which is major risk of coronary heart disease. Now a day's synthetic drugs have been associated with number of side effects but herbal medicines have lipid lowering and antioxidant activities without any side effects. Some traditionally herbs like: - *Commiphora mukul (Gugglul), Terminalia Arjuna (Arjun), Picrorrhiza Kurroa(Kutki), Allium Sativum (Lasuna),* etc. are used as Antihyperlipidemic drug in ayurvedic literature. Hence the present study was undertaken to investigate the antihyperlipidemic effect of marketed formulations of *terminalia arjuna* against Triton WR-1339 induced hyperlipidemia in rats at 200 and 400 mg/kg dose inhibited the elevation of serum cholesterol and triglyceride levels in hyperlipidemic rats. Marketed formulations also significantly decreased 3-hydroxy-3-methylglutaryl- CoA reductase (HMG-CoA reductase) activity at the dose of 200mg/kg and 400mg/kg; p.o. showed good antihyperlipidemic activity in Triton WR-1339 induced hyperlipidemic rats. The probable mechanism of action of the marketed formulations may be inhibition of HMG-CoA reductase enzyme pathway.

Key Words: Antihyperlipidemic activity, marketed formulations, Triton WR 1339, HMG-CoA reductase, Sprague–Dawley rats.

INTRODUCTION:

Hyperlipidemia is a disorder of lipid metabolism produced by elevation of plasma concentration of the various lipid and lipoprotein fractions, which cause the cardic disease.[1] Hyperlipedemia is define in a simple way by increase serum TC, TG, VLDL, LDL and IDL which are responsible for various complications like: heart attack, premature coronary artery disease, stroke, atherosclerosis, myocardial infarction and pancreatitis.[2] The aim of treatment of hyperlipidemia is to reduce the risk of heart disease or cardiovascular or cerebrovascular disease.[3] Now a day's therapy includes statins and fibrates which correct the blood lipid profile by inhibiting the biosynthesis of cholesterol. The use of synthetic hypolipidemic drugs having various adverse effects like: nausea, vomiting, diarrhea, gastric irritation, hyperuricemia, dry skin and abnormal liver function.[4] The use of indigenous plants as an alternative medicine which is use to increased the desired activity and minimizes the unwanted side effects of synthetic drugs adopted by the world health organization.[5-6] Research work was done on various plants. About 12000 plants have been studied for various pharmacological actions. Hyperlipidemia can be either primary or secondary type, the primary disease may be treated by hypolipidemic drugs, but the secondary type induced by diabetes, hypothyroidism or renal lipid nephrosis that treated by treating the original disease rather than hyperlipidemia.[7-8] Terminalia arjuna is a famous Indianfolk plant used as a cardiotonic in ischaemic cardiomyopathy, heartfailure, atherosclerosis andmyocardium necrosis. It contains essential ingredient of many Ayurvedic preparations which are sold as cardiotonics. It use in the treatment of, ulcers, fractures, blood diseases. Terminalia arjuna contain tannin, ellagic acid, ester, phytosterols sugar, steroids, arjunolone, triterpenoid, saponins (e.g., arjunic acid and derivatives), gallic acid, flavonoids (arjunone, luteolin), polyphenols, calcium, magnesium and zinc.

The present rsearch was undertaken to investigate the antihyperlipidemic effect of Two different marketed formulations of *terminalia arjuna* against Triton WR-1339 induced hyperlipidemia in rats at 200 and 400 mg/kg dose inhibited the elevation of serum cholesterol and triglyceride levels in hyperlipidemic rats.

MATERIAL AND METHODS

Collection of Marketed Formulation

Two samples of *Terminalia arjuna,* was purchased. **Sample 1st** was purchased from Chakrapani Ayurveda

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Clinic & Research Center, jaipur and **Sample 2nd** was purchased from Divya Pharmacy, Haridwar, Uttarakhand, India.

Induction of Hyperlipidemia

Hyperlipidemia was induced in the experimental rats by a ip injection of triton WR 1339 (300 mg/kg b.w.) and after 48 h rats depicted elevated levels of cholesterol and triglyceride in serum.

Experimental Animals

Adult Sprague–Dawley rats (200-250 gms) were maintained under good hygienic conditions in the departmental animal house of Jaipur College of Pharmacy. Animals were maintained under standard environmental conditions (18-26°C, 60-70% relative humidity, 12 hr L-D cycle) and fed with standard feed and water *ad libitum.* The experimental protocol was approved by the Institutional Animal Ethics Committee (Registration No. 931/po/ac/06/CPCSEA). Animals were allowed to acclimatize to experimental conditions by housing them for 8-10 days period prior to experiments.

Chemicals and Drugs

Tyloxapol (Triton WR-1339, Sigma Aldrich, USA)
Atorvastatin (Cipla Ltd, Baddi, HP)

Experimental Design

The use of Triton WR 1339 induced hyperlipidaemia through accelerated hepatic cholesterol synthesis is suggested as an important approach to screen the action of hypolipidaemic drugs. Male Sprague–Dawley rats weighing 200- 250 gm, were divided into 7 groups of 6 animals each. The first group (Normal control) received normal saline orally for one week. The second group (Triton positive control) received Triton WR-1339 dissolved in 0.9% saline (400 mg/kg bodyweight) by i.p. route. The third and fourth groups were treated with Sample 1st (200 mg/kg and 400mg/kg, p.o.) respectively, once a day for one week. The fifth and sixth group was treated with Sample 2nd (200 mg/kg and 400mg/kg, p.o.) respectively, once a day for one week.[10] The seventh group was treated with Atorvastatin suspension prepared with 0.5% CMC (10mg/kg, p.o.), once a day for one week. On the 7th day, the animals were fasted for 18 hrs (had only access to water) and 400 mg/kg Triton WR 1339 was injected (i.p), to all the four groups of rats immediately after drug administration. On the 8th day, blood was collected by retro-orbital sinus puncture, under mild ether anaesthesia. The collected blood samples were centrifuged for 10 minutes at 2000 r.p.m. and serum samples so collected were used for various biochemical tests.

The treatment schedule was followed:

Group I: normal control
Group II: Triton positive control
Group III: Triton treated + S 1 (200mg/kg)
Group IV: Triton treated + S 1 (400mg/kg)
Group V: Triton treated + S 2 (200mg/kg)
Group VI: Triton treated + S 2 (400mg/kg)
Group VII: Triton treated + Atorvastatin

ACUTE TOXICITY STUDIES

Acute toxicity studies for the marketed formulations of *terminalia arjuna* powder were conducted as per OECD guidelines 423 using Sprague–Dawley rats[9]. Each animal was administered the marketed formulations of *terminalia arjuna powder suspension* by oral route. The animals were observed for mortality up to 72 hours. The marketed formulations of *terminalia arjuna* was found to be safe up to 2000mg/kg body weight.

BIOCHEMICAL ANALYSIS OF SERUM

Serum samples were analysed for total cholesterol, triglyceride levels and high-density lipoproteins using laboratory testing. Low density lipoprotein (LDL) and Very low density lipoprotein (VLDL) were calculated according to Friedwald formula.[11] LDL = TC – HDL – VLDL VLDL cholesterol = Triglycerides / 5. Atherogenic index (A.I) was also calculated as AI = (TC − HDL)/HDL Per formula.[12]

3 Results

Table 1: Effect of oral administration of marketed formulations of *terminalia arjuna* on serum Cholesterol, Triglyceride, HDL, LDL, VLDL and Atherogenic index.

Treatment	TC (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)	A.I
NC	51.19±1.98	70.80±2.19	23.25±1.05	33.93±2.39	15.34±0.73	1.20±0.21
TP	157.59±3.27	139.54±3.05	19.47±1.02	110.50±3.79	29.87±0.86	7.09±4.88
T+ S-1 (200 mg/kg)	110.47±2.69	117.71±2.54	22.38±0.90	63.65±2.54	24.42±0.55	3.93±1.17
T+ S-1 (400 mg/kg)	95.56±2.08	93.59±2.11	24.38±1.13	53.59±1.23	19.40±0.37	2.91±1.12
T+ S-2 (200 mg/kg)	108.98±2.31	115.62±2.47	23.89±1.17	65.53±2.07	23.32±0.67	3.56±0.93
T+ S-2 (400 mg/kg)	94.44±1.89	91.59±2.01	25.55±0.97	55.41±1.87	18.08±0.43	2.69±0.19
T+ At	84.20±2.24	89.14±2.17	26.77±1.28	45.62±1.33	17.79±0.52	2.14±0.21

Values are as mean ± SEM from 6 animals in each group. P value: P ≤ 0.001, P ≤ 0.05 compared with normal group; P ≤ 0.001, P ≤ 0.05 compared with control group Triton WR treated rats.

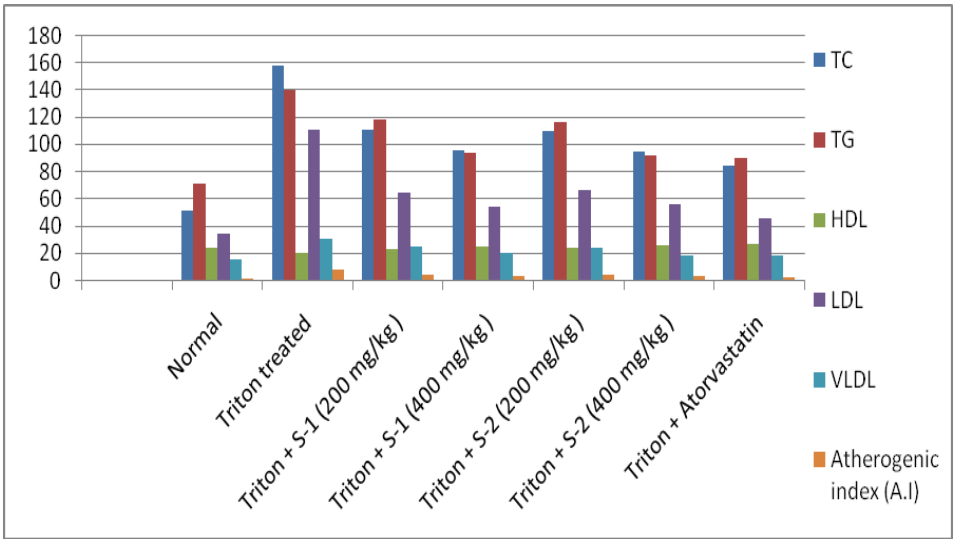

Figure 6.1: Effect of Marketed formulation of Terminalia Arjuna Powder on Serum Cholesterol in Triton induced hyperlipidemic rats.

Effect of marketed formulations of *terminalia arjuna* powder on Lipid Profile in Serum of Triton Induced Hyperlipidemic Rats:

Oral administration of marketed formulations of *terminalia arjuna* (200 mg/kg and 400mg/kg, p.o.) to Triton induced hyperlipidemic rats, significantly reduced the serum cholesterol (TC), triglyceride (TG), low density lipoprotein-cholesterol (LDL-C), VLDL-cholesterol levels and atherogenic index. Levels of serum HDL-cholesterol were significantly increased in rats treated with marketed formulations of *terminalia arjuna* as compared to Triton treated rats (Table 1).

4. DISCUSSION

Triton WR-1339, has been widely used to block the uptake of triacyl glycerol-rich lipoproteins from plasma by peripheral tissues in order to produce acute hyperlipidemia in animal models which are often used for a number of objectives, in particular for screening natural or chemical hypolipidemic drugs[13.14] With this objective, many medicinal plants, such as Commiphora mukul (Gugglul), Picrorrhiza Kurroa(Kutki), Allium Sativum (Lasuna), have been assessed for their anti-hyperlipidemic activity against Triton WR-1339-induced hyperlipidemia. In our study, this model gave similar plasma lipid profile changes, at 24 h after Triton WR-1339 injection in rats. This result demonstrates the feasibility of using Triton induced hyperlipidemic rats as an experimental model to investigate the hypolipidemic effect of marketed formulations of *terminalia arjuna*. Our study clearly shows that the large increase in serum levels of cholesterol and triglycerides due to Triton WR-1339 injection results mostly from an increase of VLDL secretion by the liver accompanied by a strong reduction of VLDL and LDL catabolism.[15, 16] The reduction of total cholesterol by the marketed formulations of *terminalia arjuna* was associated with a decrease of its LDL fraction in serum, which is the target of several hypolipidemic drugs. Report of a study suggests that cholesterol lowering activity of the marketed formulations of *terminalia arjuna* could be the result of the rapid catabolism of LDL cholesterol through its hepatic receptors for final elimination in the form of bile acids, as demonstrated.[17-19] Increased level of serum LDL-cholesterol results in increased risk for the development of atherosclerosis. It is well known that HDL-Cholesterol levels have a protective role in coronary artery disease.[20] HDL-cholesterol is reported to have a preventive function against atherogenesis since an independent inverse relationship between blood HDL-C levels and cardiovascular risk incidence has been reported.[21] Atherosclerotic index (A.I) is believed to be an important risk factor for diagnosis of atherosclerosis. The marketed formulations of *terminalia arjuna* reduced atherogenic index which is one of the most important risk factors of atherosclerotic plaques. Similar results were reported by others when studying the hypolipidemic effect of natural products.[22] which has a number of pharmacological properties such as binding bile acid and lowering plasma cholesterol.[23-25] *Terminalia arjuna* contains saponins which are part of sugar chains which attach themselves to a sterol or triterpene. Saponins are known to form complexes with cholesterol by binding plasma lipids, thereby altering cholesterol metabolism.[26] *contains* saponins and tannins which inhibit lipid absorption.[27-28] Thus all these constituents present in marketed formulations of *terminalia arjuna* may be responsible for its hypolipidemic activity.

5. CONCLUSION

Thus it can be concluded that marketed formulations of *terminalia arjuna* at the dose of 200mg/kg and 400mg/kg

showed good anti-hyperlipidemic action in Triton WR-1339 and High cholesterol diet induced hyperlipidemia model. The probable mechanism of action of marketed formulations of *terminalia arjuna* may be inhibition of HMG-CoA reductase enzyme pathway.

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