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Research Article

EFFECT OF *VITIS VINIFERA* AGAINST TRITON X 100 INDUCED HYPERLIPIDAEMIA IN RATS

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ABSTRACT

To evaluate the effect of *Vitis vinfera* fruit juice (VVFJ) against Triton X 100 induced hyperlipidaemia. Wister strain rats were treated with atorvastatin (ATOR-10mg/kg, p.o.), low and high dose of *Vitis vinifera* fruit juice (VVFJ- 100 and 500mg/kg) orally for 0, 24 and 44 hours after treated with Triton X 100 (400mg/kg, p.o). 4 hour after the last dose, blood was collected from all the animals and the separated serum was subjected for the estimation of serum lipoproteins level such as Triglycerides (TGs), Total cholesterol (TC), High density lipoprotein-cholesterol (HDL-c), Low density lipoprotein-cholesterol (LDL-c), Very low density lipoprotein (VLDL) and serum glucose level and atherogenic index.

In hyperlipidemic control group Triton X 100 resulted in a significant increase in TG, TC, LDL, VLDL, atherogenic index and a significant decrease was found for HDL values compared with normal control. The treatment group of atorvastatin and *Vitis vinifera* fruit juice (100/500mg/kg, p.o.) showed significant decrease in TG, TC, LDL, VLDL, atherogenic index and serum glucose compared with hyperlipidemic control. Whereas for HDL values it was found to be a significant increase.

The study revealed that atorvastatin, low dose and high dose of *Vitis vinifera* fruit juice (100/500mg/kg, p.o.) possess significant antihyperlipidemic activity. Among all treated group high dose of *Vitis vinifera* fruit juice found to be more effective against Triton X 100 induced hyperlipidaemia.

KEY WORDS: Antihyperlipidemic effect, *Vitis vinifera*, Hyperlipidemia, Triton X 100.

INTRODUCTION

Hyperlipidemia is characterized by alteration occurring in serum lipid and lipoprotein profile due to increased concentration of Total cholesterol (TC), Low density lipoprotein cholesterol (LDL- C), Very low density lipoprotein cholesterol (VLDL-C) and Triglyceride (TG) with concominant decrease in concentration of High density lipoprotein cholesterol (HDL-C) in blood circulation[1]. Disorders of lipid metabolism, following oxidative stress are the prime risk factors for initiation and progression of these diseases[2].

Many researchers have documented that the action of herbal drug has shown promising effect. Medicinal plants play a major role in hypolipidemic activity, literature suggests that the lipid lowering action is mediated through, inhibition of hepatic cholesterol biosynthesis and reduction of lipid absorption in the intestine[3].

The *Vitis vinifera* is a fruit belongs to the family Vitaceae. Seed and skin contain several active components including flavonoids, polyphenols, anthocyanins, proanthocyanidins, procyanidines and the stilbene derivative resveratrol[4]. Grapevine seed extract in particular has been reported to possess a broad spectrum of pharmacological and therapeutic effects such as anticarcinogenic, antioxidative, anti-inflammatory and antimicrobial activities, as well as having cardioprotective, hepatoprotective, and neuroprotective effects[4]. As it is one of the herbs which possess large number of therapeutic efficacies, it was felt worthwhile to evaluate its role during hyperlipidaemia condition either alone or in presence of conventional antihyperlipidemic drug. The present research was designed to determine the antihyperlipidemic activity of *Vitis vinifera* fruit juice and its possible interaction with Atorvastatin in Triton X 100 induced hyperlipidemia.

MATERIALS AND METHODS

Chemicals

Triton X-100 was purchased from National chemicals, Vadodara, India. Triglycerides (TGs), Total cholesterol (TC), High density lipoprotein-cholesterol (HDL-c), Low density lipoprotein-cholesterol (LDL-c) and serum glucose kits were procured from Robonik India Pvt Ltd, Mumbai, India.

Experimental animals

Healthy adult female Sprague-Dawley (SD) rats weighing 175-250 g, housed in polypropylene cages, maintained under standardized condition (12 h L:D cycles, 28°±2°C) with paddy husk bedding at the Central Animal House, Shree Devi College of Pharmacy, Mangalore, India were provided with standard pellet food and had free access to purified drinking water. The guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Social Justice and Empowerment, Government of India were followed and prior permission was sought from the Institutional Animal Ethics Committee for conducting the study (SDCP/IAEC-10/2011-12).

Preparation of *Vitis vinifera* fruit juice

Vitis vinifera fruit commonly known as Red grapes was procured during the month of July 2012 from the local market of Mangalore. Fresh juice of *Vitis vinifera* fruit was prepared by homogenizing with blender mixer.

Phytochemical estimations of the extract[5,6]

Vitis vinifera fruit juice (VVFJ) was subjected to phytochemical analysis to investigate the presence of various constituents such as alkaloids, triterpenoids, steroids, carbohydrates, glycosides, polyphenols, proteins, saponins, tannins and flavonoids.

Acute toxicity study

The acute oral toxicity study was performed according to the Office of Prevention, Pesticide and Toxic Substance (OPPTS) guidelines following the limit test procedure. The animals were fasted overnight prior to the experiment. Test dose of 2 and 5 g/kg were given orally to mice. Both doses were found to be safe. Hence 1/10th and 1/50th of the

maximum safe dose corresponding to 500 and 100 mg/kg orally were selected as high and low doses respectively.

Standardization of hyperlipidemic dose of Triton X 100[7]

To induce the hyperlipidemia rats were kept in fasting for 18 hours with access of water and subjected to Triton X 100 at the dose of 300, 400, 500, 600 and 700 mg/kg p.o. and the levels of different lipoproteins was evaluated at 24, 48 and 72 hours. It was observed that Triton X 100 in the dose of 400 mg/kg p.o. can induce maximum hyperlipidemia after 48 hours. Hence 400 mg/kg p.o. was considered the ideal dose for induction of hyperlipidemia.

Experimental protocol

Animals were divided into seven different groups in each group 6 animals. Animals were kept for fasting 18h and injected Triton X 100 at the dose of 400 mg/kg p.o. prepared in saline solution. According to treatment protocol, the first dose of drug treatment was given immediately after triton administration to animals from group II to VII. Second and third dose was administered after 24h and 44 h respectively. After 4h of third dose, the animals were used for the study of various biochemical parameters. Blood was collected by retro orbital plexus of the rat under anaesthesia and centrifuge at 2000 rpm for 30 min to get the serum and analysed for lipoproteins like TGs, TC, HDL-c, LDL-c, VLDL, serum glucose level and atherogenic index were estimated.

Statistical analysis

Results are expressed as mean ± SE. Statistical significance was assessed using One-way Analysis of variance (ANOVA) followed by Tukey-Karmer multiple comparison tests. $P<0.05$ was considered significant by Instat graphpad 3.06 software.

Table 1: Effects of VVFJ and atorvastatin on different lipid and glucose parameters

TREATMENT	Serum HDL-C	Serum TC	Serum TG	Serum LDL-C	Serum VLDL-C	Serum Glucose	Atherogenic index
Normal Control	36.65±2.40	82.30±3.35	17.09±1.38	42.23±1.56	3.14±0.27	116.36±6.82	2.25±0.07
Hyperlipidemic Control	16.11±0.58***	123.10±2.44***	89.97±2.88***	89.00±3.05***	19.99±0.57***	236.66±3.52***	7.66±0.43***
ATOR	48.48±1.77^{**+++}	92.34±1.29^{+++}	38.33±1.76^{***+++}	35.20±2.71^{+++}	7.66±0.35^{***+++}	128.33±1.76^{+++}	1.90±0.07^{+++}
VVFJ-100	40.13±1.67^{+++}	105.70±6.79^{**+}	52.35±1.44^{***+++}	55.09±6.65^{+++}	10.46±0.29^{***+++}	152.00±5.85^{**+++}	2.64±0.20^{+++}
VVFJ-500	45.00±1.52^{+++}	81.77±2.98^{+++}	42.23±2.13^{***+++}	28.33±1.76^{+++}	8.44±0.42^{***+++}	127.00±4.16^{+++}	1.81±0.01^{+++}

All values are mean ± SEM, n=6, $^{*}P<0.05$, $^{***}P<0.01$ and $^{***}P<0.001$ when compared to normal control; $^{+}P<0.05$, $^{+++}P<0.001$ compared to TRITON control. VVFJ-100 (*Vitis vinifera* fruit juice-100mg/kg), VVFJ-500 (*Vitis vinifera* fruit juice-500mg/kg) and ATOR (Atorvastatin-10 mg/kg).

RESULTS

Preliminary phytochemical investigation

The preliminary phytochemical investigation of the VVFJ showed the presence of Polyphenols, carbohydrates, flavonoids, glycosides, proteins, saponnins, tannins and terpenoids.

Effect on serum HDL cholesterol (HDL-C): (Table 1)

There was an extremely significant ($P<0.001$) decrease in serum HDL cholesterol in hyperlipidemic control group compared to normal control. Atorvastatin-10mg/kg, low dose and high dose of *Vitis vinifera* fruit juice showed an extremely significant ($P<0.001$) increase in HDL-C compared to hyperlipidemic control group. *Vitis vinifera* fruit juice-500mg/kg found to be most protective group.

Effect on serum lipoproteins (TC, TGs, LDL-c, VLDL) level and atherogenic index: (Table 1)

There was an extremely significant ($P<0.001$) increase in serum TC, TG, LDL, VLDL and Atherogenic index in hypelipidemic control group compared to normal control. All the treated groups showed an extremely significant ($P<0.001$) decrease in serum TC, TGs, LDL-c, VLDL and Atherogenic index, but TC level in *Vitis vinifera* fruit juice -100 mg/kg showed significant ($P<0.05$) decrease compared to hyperlipidemic control group. Among all treated group *Vitis vinifera* fruit juice-500mg/kg possessed better antihyperlipidemic property.

Effect on serum Glucose level: (Table 1)

There was an extremely significant ($P<0.001$) increase in serum Glucose level of hyperlipidemic control animals compared to normal control animals. Atorvastatin, low dose and high dose of *Vitis vinifera* fruit juice treated animals showed extremely significant ($P<0.001$) decrease serum Glucose level compared to hyperlipidemic control animals. *Vitis vinifera* fruit juice-500mg/kg found to be most protective group in all groups.

DISCUSSION

The aim of the present study was to elucidate the role of *Vitis vinifera* fruit juice during hyperlipidemia induced by Triton X 100 in rat.

Triton X 100 was used to induce acute hyperlipidemia. It is well known that triton X-100 (a non-ionic detergent) elevates total TC and TG in blood by altering the hepatic lipid metabolism. This model has been used as a screening method for hyperlipidemic agents and also for elucidating lipid metabolism.

Moreover, this could be associated with a down regulation in LDL receptors by the cholesterol and saturated fatty acids in the diet, which could also explain the elevation of serum LDL-C levels either by changing hepatic LDL-R (LDL-receptor) activity, the LDL production rate or both.

The activity of cholesteryl ester transfer protein (CETP), a key enzyme in reverse cholesterol transport and HDL metabolism increase in high fat diet and mediates the transfer of cholesteryl esters from HDL-C to triglyceride-rich particles in exchange for triglycerides. This leads to increased plasma concentrations of TGs and decreased concentrations of HDL-C.

Lipid profile of hyperlipidemic control rats in our study revealed higher levels of serum triglycerides, cholesterol, LDL and VLDL accompanied by decrease of serum HDL-C as compared to controls.

Treatment hyperlipidemic rats with Atorvastatin, low dose and high dose of *Vitis vinifera* fruit juice (VVFJ-100 and 500mg/kg) showed a significant decrease of serum triglycerides, cholesterol, LDL and VLDL and significant increase of serum HDL-C levels compare to hyperlipidemia control.

The potential of protective effect may be due to the rich source of Polyphenols present as a chief chemical constituent but the exact mechanism is still not clear.

CONCLUSION

The findings of the present study revealed that *Vitis vinifera* fruit juice (VVFJ) in both low (100mg/kg) and high (500mg/kg) doses showed antihyperlipidemic activity against Triton X-100 induced hyperlipidemia. Among all treated group *Vitis vinifera* fruit juice-500mg/kg shown better protection.

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