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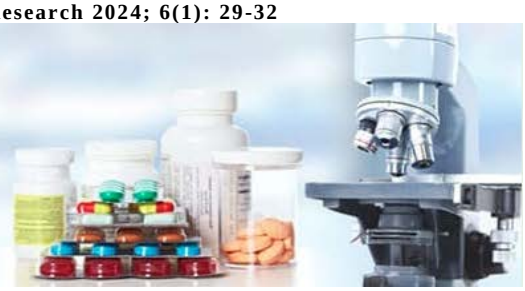

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Anti-hyperlipidemic activity of ethanol extract of *Simarouba amara* Aubl in high-fat diet-induced hyperlipidemia in rats

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Abstract
Hyperlipidemia is a term that encompasses various genetic and acquired disorders that describe elevated lipid levels within the body. Lipoprotein lipase deficiency (type I a), due to a deficiency of Lipoprotein lipase (LPL) or altered apolipoprotein C2, resulting in elevated chylomicrons, the particles that transfer fatty acids from the digestive tract to the liver is called primary hyperlidimia: Lipoprotein lipase deficiency (type I a), due to a deficiency of Lipoprotein lipase (LPL) or altered apolipoprotein C2, resulting in elevated chylomicrons, the particles that transfer fatty acids from the digestive tract to the liver. There are various medicinal plants has been used for the treatment of hyperlipidemia. In view of this, in present study we have to evaluate Anti-hyperlipidemic activity of ethanol extract of *Simarouba amara* Aubl in High-fat diet-induced hyperlipidemia in rats**.** High fat diet induced hyperlipidemia; Male Wistar rats (18-weeks-old), housed in a room maintained at 12 h light–dark cycles and a constant temperature of 22±2 °C, were fed laboratory chow enriched with 2% cholesterol, 1% cholicacid, 20% Dalda and 6% Coconut oil for 4 weeks Hyperlipidemia was confirmed by measuring the levels of serum lipids and lipoproteins in the rats. After 4-week induction of hyperlipidemia the standard drug (Atorvastatin) and test drug (*Simarouba amara* Aubl ethanol extraction) is treated for two weeks after the experimentation the animals are anesthetized and carried for biochemical and hematological evaluation. The ethanolic extract has shown a significant reduction in serum cholesterol and TGs level indicating anti hyperlipidemic potentials.

Keywords: Hyperlipidemia, high fat diet, *Simaroba amara* Aubl

Introduction
Hyperlipidemia is a family of disorders characterized by abnormally high levels of lipids in Hyperlipidemia is a family of disorders characterized by abnormally high levels of lipids in the blood. While fat plays a major role in the body's metabolic process high blood fat increases the risk of coronary heart disease (CHD).

Lipoprotein lipase deficiency (type I a), due to a deficiency of Lipoprotein lipase (LPL) or altered apolipoprotein C2, resulting in elevated chylomicrons, the particles that transfer fatty acids from the digestive tract to the liver Familial apoprotein CII deficiency (type 1b), a condition caused by a lack of lipoprotein lipase activator. Chylomicronemia due to circulating inhibitor of lipoprotein lipase (type I c). The individual may see an increased incidence of xanthomas with each decade, and Achilles tendinitis and accelerated Atherosclerosis will occur. The receptor defect is an autosomal recessive mutation or polymorphism. Lipoprotein levels are normal or increased a little. Treatment includes diet control, Fibrates, and Niacin. Statins are not better than fibrates when lowering triglyceride levels [1, 2]. Peroxisome Proliferator-Activated Receptors (PPARs), specifically PPARα, decrease free fatty acid Production. Statin drugs, especially the synthetic Statins (Atorvastatin and Rosuvastatin) can decrease LDL levels by increasing hepatic reuptake of LDL due to increased LDL-receptor expression [3].

Table 1: Types of hyperlipidemia

Class	Increased lipoprotein	Synonym
Type 1	↑ chylomicrons	Familial chylomicronemia
Type 2 a 2 b	↑ LDL ↑ LDL and VLDL	Familial hypercholesterolemia Familial combined hyperlipidemia
Type 3	↑ IDL	Familial dysbetalipoproteinemia
Type 4	↑ VLDL	Familial hypertriglyceridemia
Type 5	↑ VLDL and chylomicrons	Familial mixed hyperlipidemia

Pathophysiology

The pathophysiology of primary hyperlipidemia involves idiopathic hyperchylomicronemia in which a defect in lipid metabolism leads to hypertriglyceridemia and hyperchylomicronemia caused by a defect in lipoprotein lipase activity or the absence of the surface apoprotein CII31. In secondary hyperlipidemia, the postprandial absorption of chylomicrons from the gastrointestinal tract occurs 30-60 min after ingestion of a meal containing fat that may increase serum triglycerides for 3-10 hours. Here we x-rayed the root causes of various hyperlipidemia, their clinical manifestation, and possible treatments ranging from pharmacological to change in dieting. An improved lifestyle or healthy lifestyle may be a possible way out from lipid-related diseases [4].

Materials and Methods

Collection and preparation of plant material

The roots of the plant Simarouba amara Abul were collected and their size was reduced into small pieces and shadow dried [5]. The dried materials were coarsely powdered before extraction, and used for further detailed studies.

Extraction

Preparation of the extracts About 100 gm of Simarouba amara Abul air-dried powdered material was taken in 1000 ml Soxhlet apparatus and extracted with ethanol as a solvent, for 72 hrs. The temperature was maintained at 55 - 65 °C. The extracts were concentrated by distillation and the solvents were removed by distillation under reduced pressure. The extracts were dried and stored in desiccators. A Greenish-yellow residue was obtained. The percentage yield was calculated [6, 7].

Selection of animal model

Healthy young Wister albino rats weighing 100-150 gm (8 to 12 weeks old) were selected for toxicology study. The rats were kept in property-numbered large polypropylene cages with stainless steel top grills having facilities and given a standard diet and water ad libitum throughout the experimental period. The animals were maintained for12 hours. Light and dark cycleat 22 °C (±3 °C 0 in a well-ventilated animal house under natural conditions, they were acclimatized to laboratory conditions for 10 days before the commencements of the experiments. Paddy husk was used as breeding material and changed twice a week. The institutional animal ethics committee has approved the experimental protocol [8].

Induction disease

High-fat diet-induced hyperlipidemia: Male Wistar rats (18 weeks old), housed in a room maintained at 12 h light-dark cycles and a constant temperature of 22±2 °C, were fed laboratory chow enriched with 2% cholesterol, 1% cholic acid, 20% Dalda, and 6% Coconut oil for 4 weeks Hyperlipidemia was confirmed by measuring the levels of serum lipids and lipoproteins in the rats [9].

Treatment group: The selected animals were grouped randomly irrespective of six into five groups. In the first group, only water was administered without a hyperlipidemic diet The Group (2, 3, 4, 5) group received a control diet. The hyperlipidemic diet included hydrogenated vegetable oil (Vanaspati Ghee), and made into 20% of coconut oil (parachute coconut oil), The suspension was administered in adose of 0.1 ml/100 g body weight of rats, respectively, 4 weeks to the rats of (2, 3, 4, 5) groups. Concomitantly, the second group was treated with a marketed test drug (atorvastatin) whereas group (3, 4, 5) was treated with Simarouba amara Aubl ethanol extraction. After a 4-week induction of hyperlipidemia, the standard drug (atorvastatin) and test drug (Simarouba amara Aubl ethanolextraction) is treated for two weeks after the experimentation the animals are anesthetized and carried out for biochemical and hematological evaluation [10].

Blood was withdrawn by the supraorbital plexus and sent to a biochemical laboratory for biochemical estimations. Then, the rats were sacrificed by cervical dislocation, and important organs like the liver, kidney, aorta, and heart were dissected. The liver, kidney, and heart were weighed and they were (including the aorta) transferred to a fixing solution (10% formalin) for histopathological examinations. Biochemical parameters like serum total cholesterol, serum triglyceride, serum HDL cholesterol, and serum (LDL + VLDL) cholesterol were studied. Serum (LDL + VLDL) was calculated by subtracting HDL cholesterol value from total cholesterol instead of using both values separately, in rats [11, 12].

Table 2: Ethanolic extract of plant Simarouba amara Aubl and standard drug (Atorvastatin) by using number of animals

Group	Drug and Dose	Number of animals used
I	Normal control	3
II	Disease control (High fat diet)	3
III	Standard treatment: HFD + Atorvastatin	3
IV	Ethanolic extract of Simarouba amara Aubl (low dose 200 mg oral) HFD + Extract	3
V	Ethanolic extract of Simarouba amara Aubl (High dose 400 mg oral) HFD + Extract	3

Results and discussion

Table 3: Phytoconstituents present in the plant extract of Simarouba amara Aubl

S. No.	Chemical constituents	Extract (Ethanol)
1.	Alkaloids	Present
2.	Carbohydrates	Present
3.	Glucosides	Present
4.	Steroids	Negative
5.	Tannins	Present
6.	Aminoacids	Negative
7.	Flavanoids	Present
8.	Saponins	Negative
9.	Fixedoil	Present
10.	Triterpenoids	Present

Table 4: Effect of total cholesterol in the plant extract of Simarouba amara Aubl

S. No.	Groups	Total cholesterol (mg/)
I	Normal (Saline)	89.25±4.76
II	Disease Control (High fat diet)	153.8±4.49 ***
III	Standard (Atorvastatin)	91.00±1.95 **
IV	Test 200 mg/kg (Simarouba amara Aubl ethanolic extract)	82.75±4.99 *
V	Test 400 mg/kg (Simarouba amara Aubl ethanolic extract)	92.50±2.39 **

All values expressed as mean± SEM and n=3 indicates significance difference $p<0.001$ ****

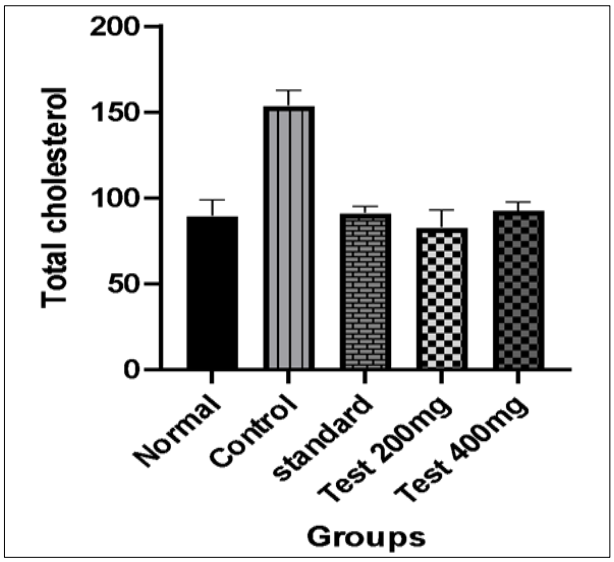

Fig 1: Total cholesterol

Table 5: Effect of triglycerides in the plant extract of Simarouba amara Aubl

S. No.	Groups	Triglycerides
I	Normal (Saline)	107.3±1.79
II	Disease Control (High fat diet)	131.5±2.10 *
III	Standard (Atorvastatin)	123.3±2.21 **
IV	Test 200 mg/kg (Simarouba amara Aubl ethanolic extract)	86.25±1.88 ***
V	Test 400 mg/kg (Simarouba amara Aubl ethanolic extract)	106.0±2.67 **

All values expressed as mean±SEM and n=3 indicates significance difference $p<0.0002$

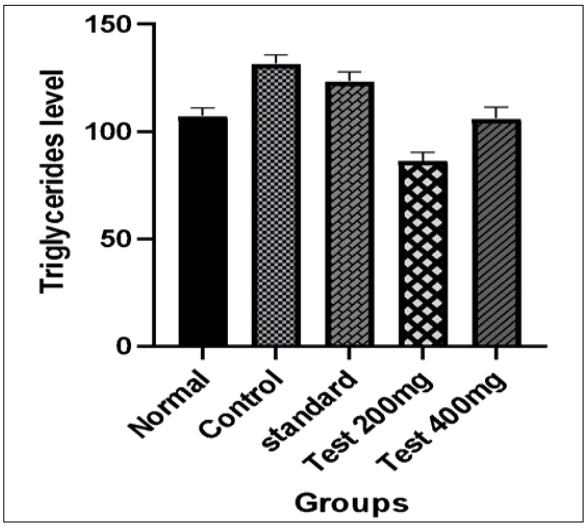

Fig 2: Triglycerides

Table 6: Effect of LDL/HDL ratio in the plant extract of Simarouba amara Aubl

S. No.	Group	HDL/LDL ratio (mg/dl)
I	Normal (Saline)	0.39±0.06
II	Disease Control (High fat diet)	4.82±0.11 ***
III	Standard (Atorvastatin)	0.17±0.01 **
IV	Test 200 mg/kg (Simarouba amara Aubl ethanolic extract)	0.36±0.02 **
V	Test 400 mg/kg (Simarouba amara Aubl ethanolic extract)	0.89±0.02 **

All values expressed as mean± SEM and n=3 indicates significant difference $p<0.05$ *

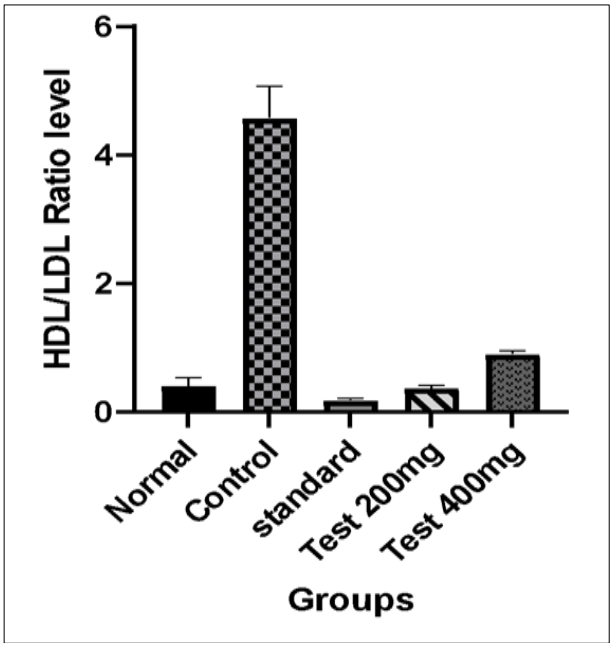

Fig 3: HDL / LDL

Results and Discussion

In this hyperlipidemic activity evidence have shown that flavonoids have diverse beneficial effect including antioxidant activity decreasing LDL, increasing HDL. Flavanoids are potent free radical scacengers and are known to modulate the activities of various system. The weight gain in high cholesterol diet group of rats was significantly higer than the normal control group reflecting the influence of high cholesterol diet. In the present study hyperlipidemia was induced by giving high cholesterol dietto rats for 14 days [13, 14]. Treatment with ethanolic extract of Simarouba amara Aubl non significantly prevent the increased body weight, thus showing a protective effect in weight gain. Clinical evaluation also has shown that the accumulation of fat on liver and aorta was reduced by treatment with atorvastatin.

Hyperlipidemic rats has shown significant increase in levels of TC. TGs, LDL, VLDL and decrease in HDL-C levels. The high cholesterol circulated in bloodwhich is leads CHD. Treatment with atorvastatin significantly decreased the TC, TGs, LDL, VLDL levels when compared to negative control group. The ethanolic extract of Simarouba amara Aubl showed a significant anti hyperlipidemic activity in cholesterol induced hyperlipidemic rats, which was almost comparable to the standard drug atorvastatin(10 mg/kg) p.o used in the treatment [15, 16].

The result in present study showed a decreased level of LDL by the standard drug which may also have reduced serum TC levels during the treatment with the test extract. The ethanolic extract Simarouba amara Aubl was increased serum HDL level in the hyperlipidemic models which is prove beneficial in lipd disorder and also serve as a cardio protective factor [17, 18].

Conclusion

The findings of the present study provide evidence that Simarouba amara Aubl ethanolic extract of 200 mg and 400.o respectively have potential anti-hyperlipidemic effects in high-fat diet-induced hyperlipidemic rats [19, 20]. It also inhibit lipoprotein factors (LDL, VLDL) in various concentrations. The plant Simarouba amara Aubl contains powerful antihyperlipidemic therapy.

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