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EVALUATION OF ETHANOLIC EXTRACT OF CORCHORUS TRILOCULARIS LINN FOR ANTIHYPERLIPIDEMIC ACTIVITY

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ABSTRACT: The aim of the present study is to investigate the hypolipidemic effect of Corchorus trilocularis leaves extracts in high cholesterol diet induced hyperlipidemia. Aqueous and ethanolic extracts of leaves of Corchorus trilocularis were administered in doses of 200mg/kg/day p.o. each for 14 days. Simultaneous administration of Corchorus trilocularis leaves extracts significantly ($p<0.001$) prevent the rise in serum levels of total cholesterol, triglyceride, LDL-C,VLDL-C and Atherogenic index whereas significant ($p<0.01$) increases in the level of HDL-C. The Corchorus trilocularis showed protective action at a dose of 200mg/kg and demonstrated a significant decrease in the raised diet induced levels of serum TC, LDL-C and triglycerides. At a dose of 200mg/kg, effects were comparable with that of the standard drug atorvastatin. Thus, the results of the present study demonstrated that administration of Corchorus trilocularis at dose level 200mg/kg was effective as hypolipidemic agent.

KEYWORDS: Corchorustrilocularis, LDL, hypolipidemic effect, HDL, triglycerides, Extraction

INTRODUCTION

Hyperlipidemia is a highlypredictive risk factor for atherosclerosis, coronary arterydiseases and cerebral vascular diseases. Coronary heart disease, stroke, atherosclerosis and hyperlipidemia are the primary cause of death. Hyperlipidemia is characterized by elevated serum total cholesterol and low density and very low-density lipoprotein cholesterol and decreased high density lipoprotein levels. Hyperlipidemia associated lipid disorders are considered to cause atherosclerotic cardiovascular disease. Atherosclerosis (Sclrero-hardening) of arteries is a generalized disease of arterial network known as a progressive and silent killer disease characterized by the formation of lesions called atherosclerosis plaques in the walls of large and or medium sized coronary arteries and reduces blood flow to the myocardium called coronary artery diseases (CAD). Hyperlipidemia is classified

into a primary and a secondary type, which indicates the complexities associated with disease. The primary disease may be treated using anti-lipidemic drugs but the secondary type originating from diabetes, renal lipid nephrosisorhypothyroidism demands the treatment of the original disease rather than hyperlipidemia. 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.

Hyperlipidemia is defined as an elevation of lipids in plasma. Several studies have showed that an intimate correlation exists between coronary heart diseases and hyperlipidemia, consequently a rational approach to the treatment and prevention of coronary heart diseases could be by decreasing any elevated levels of lipids in plasma. For that purpose, many studies have been conducted to evaluate the potential hypolipidemic effects of synthetic and naturally occurring compounds. Triton WR-1339-induced hyperlipidemic rats are a globally accepted model used to evaluate potential hypolipidemic drugs. Triton WR-1339 is a nonionic detergent that prevents catabolism of triacylglycerol-rich lipoproteins by lipo-protein lipase andis commonly used for *in vivo* determination of triacylglycerol production, and very low density lipoprotein (VLDL) secretion or clearance rate. Treatment with fibrates, a widely used class of lipid-modifying agents, results in a significant decrease in plasma triglycerides (79%) and is usually associated with a decrease in low density lipoprotein (LDL), cholesterol (11%), and an increase in high density lipoprotein (HDL)- cholesterol concentrations (27%). The major pharmacological mechanism of fibrates, including bezafibrate, is by the induction of lipoprotein lipase and reduction of a polipoprotein C-III synthesis leading to increased hydrolysis of triglycerides (TG). Some indole derivatives are well-known for their diverse pharmacological effects including a hypolipidemic effect. Although studies haveshown the potential role for indole-2- carboxamide derivatives as anti-allergics, and antioxidants to thebestofourknowledge *N*-(benzoylphenyl)-5-fluoro-1*H*-indole-2- carboxamide derivatives have not been investigated as potential lipid-lowering agents. In the present study, we aimed to synthesize a new series of ethyl-5- fluoro-1*H*-indole-2-carboxamide derivatives and to investigate their hypolipidemic activity using Triton WR-1339 induced hyperlipidemic rats as a model.

Definition

Hyperlipidemia is an excess of fatty substances called lipids, largely cholesterol andtriglycerides, in the blood. It is also called hyperlipoproteinemia because these fatty substances travel in the blood attached to proteins. This is

the only way that these fatty substances can remain dissolved while in circulation.

Hyperlipidemia, in general,can be divided into two subcategories:

- hypercholesterolemia, in which there is a high level of cholesterol
- hypertriglyceridemia, in which there is a high level of triglycerides, the most commonform of fat

Causes: Common secondarycauses of hypercholesterolemia (specifically, high LDL cholesterol) include hypothyroidism (that is, low thyroid hormone levels), pregnancy, and kidney failure. Common secondary causes of hypertriglyceridemia include diabetes, excess alcohol intake, obesity, and certain prescription medications (such as glucocorticoids and estrogen). Hyperlipidemia, along with diabetes, hypertension (high blood pressure), positive familyhistory, and smoking are all major risk factors for coronary heart disease.

Symptoms: Hyperlipidemia usually has no noticeable symptoms and tends to be discovered during routine examination or evaluation for atherosclerotic cardiovascular disease. However, deposits of cholesterol (known as xanthomas) may form under the skin (especially around the eyes or along the Achilles tendon) in individuals with familial forms of the disorder or in those with veryhigh levels of cholesterol in the blood. Individuals with hypertriglyceridemia may develop numerous pimple-like lesions across their body. Extremely high levels of triglycerides may also result in pancreatitis, a severe inflammation of the pancreas that may be life-threatening.

Diagnosis: Diagnosis is typically based on medical history, physical examination, and blood tests (doneafter overnight fasting) in order to determine the specific levels of LDL cholesterol, HDL cholesterol, and triglycerides. Simple blood tests are done to check blood lipid levels. The National Cholesterol Education Program recommends that people be tested every 5 years after age 20. A lipoprotein test, also called a fasting lipid test, is commonly performed as part of a routine medical examination. The test measures lipid levels and usually reports on four groups:

- Total cholesterol (normal:100-199mg/dL)
- LDL (normal: less than100mg/dL)
- HDL (normal: 40-59 mg/dL)
- Triglycerides (normal:less than150mg/dL)

A total cholesterol value greater than 200 mg/dL is indicative of a greater risk for heart disease. However, LDL levels are a better predictor of heart disease, and they determine how your high cholesterol should be treated.

Prevention of hyperlipidemia

A. First level Prevention of hyperlipidemia

a. Health examination regularly, high-risk population must monitor lipid level regularly.

High-risk population includes:

--Middle-old aged men

--Postmenopausal women

--Healthy people with familial history of hyperlipidemia, coronary heart disease,cerebrovascular disease
--Various yellow tumor patients and over weight or obese people.

b. High-risk population should do self-health-care. Learning health-care knowledge, taking part in sport activities, improving diet structure, controlling heat intake. Obese patients should lose weight actively and scientifically.
c. Actively treat diseases that may cause lipidemia, such as nephrotic syndrome, diabetes, liver and gall disease, hypothyroidism,etc.

B. Second level Prevention of hyperlipidemia

a. Diet treatment.

--All hyperlipidemic patients should do diet treatment first.

--Most light or middle level patients can get good control by diet treatment.

--Severe hyperlipidemic patients or those who have no effect after six months diet therapy, should combine medical treatment.

b. Medical treatment, we don't include it in this website. Please consult your doctor.

c. Appropriate exercise. Keep regularly sport activities during diet and medical treatment.

C. Third level Prevention of hyperlipidemia

Those who are with syndrome such as coronary heart disease, pancreatitis, cerebrovascular disease must do active prevention and treatment.

Therapy

Generally, drug therapy is considered when:

- the LDLcholesterol is190mg/dL or higher.
- the LDL cholesterol is160mg/dL or higher and there is one risk factor for heart disease.
- The LDL cholesterol is130mg/dL or higher and there are two risk factors for heart disease or diabetes.
- The LDL cholesterol is100 mg/dL or higher and there is heart disease.
- The LDL cholesterol is greater than70mg/dL and there is recent heart disease along with diabetes, smoking, high blood pressure, or high triglycerides, low HDL, and obesity.

There are several types of drugs available to help lower blood cholesterol levels, and they workin different ways. Some are better at lowering LDL cholesterol, some are good at lowering triglycerides, while others help raise HDL cholesterol. Lipid-lowering medications include:

- Statin drugs, such as lovastatin,that prevent the liver from manufacturing cholesterol;
- Bile acid resins, such as cholestyramine and colestipol, that prevent the body from reabsorbing the cholesterol present in bile;
- Fibrates, such as bezafibrate, fenofibrate, or gemfibrozil, particularly effective in treating high triglyceride levels;
- Niacin (vitaminB_5)

Treatment

Treatment depends on lipid levels, the presence of risk factors for heart disease, and general health. When lipid levels are not balanced, the goal is to bring them under control and this isdone with changing dietary habits. Hyperlipidemia is accordingly first treated by modifying eating habits:

- Reducing saturated fat intake to 7% of the daily intake of calories.
- Reducing total fat intake to 25-35% of the daily intake of calories.
- Limiting the dietary cholesterol to less than 200 mg per day.
- Ensuring the intake of 20-30g a day of soluble fiber.
- Ensuring the intake of plant sterols to2-3 g daily

MATERIAL&METHODS

Collection & Authentification of plant

The plant material was collected from local area of Bhopal in March 2011 and was authenticated at the

Department of Botany, Barkatullah University bhopal. A voucher specimen number or the herbarium number is Bot/Her/Bl763 has been deposited.

Preparation of the extract of leaves

The preparation of extract was carried out according to the leaves of *Corchorus trilocularis* was shade dried after collection for 5 days and was powdered. Approximately 0.95 kg of powdered drug material was extracted using 99% pure ethanol in the ratio of 1:2 (w/v) in a air tight container. The extract obtained was dried in a steam bath and the dried mass was weighed and recorded. The percentage of yield was calculated. The weight of dried crude extract obtained was approximately 0.16 g which commemorated with the percentage yield of 17.16%.

Method

The process consist of keeping the crude drug in intimate contact with whole of the menstrum in a closed vessel with occasionally shaking for 7 days, straining, pressing the marc. Mixing the liquid, & finally clarifying by subsidence or filtration. The drug should be properly communicated. The cellular structure get penetrated & the soluble portion are softening & dissolved. Occasionally shaking bring about a rapid equilibrium between the intra and extracellular fluid. A closed vessel is recommended so as to prevent loss of menstrum. As the degree of pressing the marc may very the final product in not adjusted to any complete extraction. The drug menstum ratio is 1:10. a sediment may form on standing for a few day before use. Maceration process is very simple & does not require a skilled operator.

Drugs &Chemicals

Attorvastatin (PLEOSTIN-10) was obtained from Mano Pharma Chemical & Pharmaceuticals Ltd. Chennai ,Triton was purchased from Neon Laboratories Ltd., Mumbai, ethanol were obtained from Merck Ltd., The other chemicals and solvents used were of analytical grade.

Atherogenic Diet

Diet Components	**5 kg.**	**10 kg.**
Dairy Butter	922.5 g.	1845 g.
Corn Oil	100 ml.	200 ml.
Sucrose	2500 g.	5000 g.
Cellulose (Alphacel)	203.5 g.	407 g.
Casein-Vit.Free	1000 g.	2000 g.
Cholesterol	48 g.	96 g.
Sodium Cholate (Cholic Acid)	25 g.	50 g.
Ain 76 Mineral Mix	250 g.	500 g.

Ain 76 Vitamin Mix	50 g.	100 g.
DL-Methionine	15 g.	30 g.
DL-a-Tocopheol	6.5 g.	13 g.
Choline Chloride(0.5gr./ml.)	100 ml.	200 ml.
Distilled Water	+/-175ml.	+/-350ml.

Experimental animals

Wistar rats weighing 130-165g were used in the present study. The experimental animals were maintained under standard laboratory conditions in an animal house approved by the committee for the purpose of control and supervision on experiments on animals (CPCSEA) under 12 h light/dark cycle and controlled temperature (24 ± 2°C) and fed with commercial pellet diet and water *ad libitum*. All animals were acclimatized to the laboratory environment for at least one week before the commencement of experiment. The experimental protocol was approved by the Institutional Animal Ethical Committee, Millennium College of Pharmacy, Bhopal, Madhya Pradesh, India.

Screening Models

1. Diet-induced hyperlipidemic model

The animals were selected, weighed then marked for individual identification. Rats were made hyperlipidemic by the oral administration of atherogenic diet for 20 days. The rats were then given plant extracts suspended in 2% acasia at the dose of 200mg/kg b.w. once daily in the morning through gastric intubation for 14 consecutive days.

During these days, all the groups also received atherogenic diet inthe same doseas given earlier. The control animals received the hyperlipidemic diet and the vehicle. At the end of treatment period, the animals were used for various biochemical parameters. Blood was collected by heart puncturing of rat under ether anesthesia and centrifuged by using centrifuge at 2000 rpm for 30 minute to get serum.

Experimental Design

Table 1.Groups & Doses schedule for Diet-induced hyperlipidemic model

S. NO	GROUP	TREATMENT	ANIMAL USED
1	I	2%acacia + atherogenic diet for14 days	6
2	II	Positive control received standard drug Atorvastatin (10mg/kg/ day p.o.) for14 days	6
3	III	Aq. Extract (200mg/kg/day) fine suspension of 2% acasia +atherogenic Diet for 14days	6

4	IV	Ethanol Extract (200mg/kg/day) fine Suspension of 2% acasia+atherogenic diet for 14 days	6

2. Triton-induced hyperlipidemic model

Animals kept for fasting for 18 h, will be injected a saline solution of Triton (Triton x-100) at the dose of 100mg/kg b.w. intra-peritoneally. The plant extracts, at the dose of 200mg/kg b.w., was administered orally through gastric intubation. The first dose being given immediately after triton injection and second dose 20 h later and continue the extraction process for 7 days. After 7 days dose the animals were used for various biochemical parameters. Blood was collected by heart puncturing of rat under ether anesthesia and centrifuged by using centrifuge at 2000 rpm for 30 minute to get serum.

Experimental Design

Table 2. Groups & Doses schedule for Triton-induced hyperlipidemic model

S. NO	GROUP	TREATMENT	ANIMALUSED
1	I	Control received 2% acasia+ triton (100mg/kg) for one days (p.o.).	6
2	II	After 18 hrs. of triton positive control received standard drug atorvastatin (10mg/kg/ day p.o.) for 7 days.	6
3	III	After 18 hrs. of triton Aq. Extract (200mg/kg/day) Fine suspension of 2% acasia was given for 7 days.	6
4	IV	After 18 hrs. of triton Ethanol Extract (200mg/kg/day) fine suspension of 2% acasia was given for 7 days.	6

Collection of Blood Samples

On 8th day of Triton & 21 st day of Hyperlipidemic treatment, the blood was collected by Heart puncture, under mild ether anesthesia in tubes. Serum obtained by immediate centrifugation of blood samples using Remi ultra cooling centrifuge at 2000 rpm for 30 minutes at room temperature and directly used for estimating serum lipid profiles (TC, TG, LDL,VLDL and HDL).

Statistical Analysis

The results were expressed as mean ± SEM. Statistical analysis was carried out using One-way ANOVA followed by Tukey test with the help of Graph pad instant software. Values of $P<0.05$ were considered statistically significant.

RESULTS & DISCUSSION

Table 3. Effect of Corchorustrilocularis on serum biochemical parameter in diet induced hyperlipidemic model on rat.

GROUP	DOSE	TC (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
1.Group (vehicle)	1ml/kg	120.61±1.2	105.13±2.9	48.45±2.6	51.14±0.01	21.02±0.00
2.Group (diet)	1.5ml/kg	250.21±1.3 a***	210.35±2.0 a***	38.31±2.5	169.83±0.01 a***	42.07±0.01 a***
3.Group (std.+diet)	10mg/kg	135.44±2.5 a**,b***	130.41±2.3 a***,b***	75.10±1.6 a***,b***	34.26±0.07 a***,b***	26.08±0.02 a***,b***
4.Group (aqs.+diet)	200mg/kg	215.33±2.5 a***,b***, c***	202.25±1.4 a***,c***	65.33±3.1 a***,b***	109.55±0.08 a***,b***, c***	40.45±0.01 a***,b***, c***
5.Group (etoh.+diet)	200mg/kg	178.35±3.7 a***,b***, c***,d***	165.33±1.6 a***,b***, c***	68.45±2.4 a***,b***	76.84±0.00 a***,b***, c***,d***	33.06±0.01 a***,b***, c***,d***

The data obtained were analyzed by one way ANOVA followed by Tukey Multiple Comparisons Test. Each values represent themean ± SEM; n=6. **p< 0.01*p< 0.05, p< 0.001***

a- Significant difference as compare to negative control group.

b- Significant difference as compare to control group.

c- Significant difference as compare to standard group.

d- Significant difference as compare to aquous group.

Table 4. Effect of Corchorustrilocularis on serum biochemical parameter in triton induced hyperlipidemia on rat.

GROUP	DOSE	TC (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
1.Group (vehicle)	1ml/kg	110.34±1.1	90.15±2.7	45.34±2.2	46.97±0.00	18.03±0.01
2.Group (triton)	100mg/kg	152.51 +4.3 a***	153.24+4.0 a***	27.65+1.6 a**	94.21±0.06 a***	30.62±0.02 a***

3.Group (std.+triton)	10mg/kg	120.15± 2.3 b***	90.44 + 7.5 b***	55.84+1.1 b***	46.26±0.00 a***,b***	18.05±0.00 b***
4.Group (Aqs.+triton)	200mg/kg	135.26 +2.1 a***,b*** , c**	132.37+5.4 a***,b* , c***	35.56 + 3.2 c***	73.23±0.00 a***,b***, c***	26.47±0.00 a***,b***, c***
5.Group5 (Etoh.+triton)	200mg/kg	122.10 +1.1 a*,b***, d**	104.55+3.1 a***,b***, d**	50.22+5.1 b***,d*	50.96±0.01 a***,b***, c***,d***	20.92±0.00 a***,b***, c***,d***

The data obtained were analyzed by one way ANOVA followed by Tukey Multiple Comparisons Tests. Each values represent the mean±SEM; n=6.**p<0.01*p<0.05,ns$p$>0.05.p< 0.001***

a. Significant difference as compare to negative control group.
b. Significant difference as compare to control group.
c. Significant difference as compare to standard group.
d. Significant difference as compare to aquous group.

SUMMARY & CONCLUSION

Natural remedies have been investigated for centuries for a wide variety of ailments. Corchorus trilocularis has received special attention for its beneficial effects, but until recently there has been little scientific support for its therapeutic and pharmacological properties. In the present study, Corchorus trilocularis was selected to screen for its antihyperlipidemic activity in Triton X-100 (100 mg/kg) induced hyperlipidemic rats & diet induced hyperlipidemic rats. The present studywas designed to investigate the hypolipidemic effect of Corchorus trilocularis leaves extracts in high cholesterol diet induced hyperlipidemia &Triton induced hyperlipidemia. In this study firstly we choose this plant because it having antioxidant activity after that rat were divided in to 5 group. Then the vehicle are given for the 1st group, high cholesterol diet for the2nd attorvastatin for the 3rd group & aquous ethanolic extract was given for the 4th and 5th group till the end of 20th days. At the end of 20th days or atthe end of the experimental period Blood was withdrawn from Heart puncturing of rat under ether anesthesia and centrifuged at 2000 rpm for 30min so at to get serum. After obtaining the blood various biochemical estimation were performed like total cholesterol, triglyceride HDL, LDL, was estimated by using span diagnostic kits. Thus to conclude that the study showed that administration of Corchorus trilocularisat dose level 200mg/kg was effective as hypolipidemic agent. Chemical studies on Corchorustrilocularishave reported the presence of lignans, alkaloids and flavonoids as main chemicals constituents and were confirmed by phytochemical screening. As for the phytochemical result the flavonoid may be responsible for the anti-hyperlipidemic activity and this antioxidant properties are useful for further

various study. In this study, we concluded that both aquous & ethanolic extract of Corchorus trilocularishave significant anti-hyperlipidemic activity, as compared to atorvastatin in group 1st& 2nd similar Finally we observed that the aquous & ethanolic extract of Corchorustrilocularis are show similar effect as compare to atorvastatin in group 1st& 2nd.

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