Research Article

Evaluation of Hypolipidemic Activity of *Cleome gynandra* L. against Dexamethasone Induced Hyperlipidemia in Rats

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Received: 01-04-2018; **Revised:** 26-04-2018; **Accepted:** 08-05-2018.

ABSTRACT

The global prevalence of obesity is increasing rapidly with high dietary fat intake as a major risk factor for the development of obesity. The present study was aimed at investigating hypolipidemic activity of *Cleome gynandra* L. by in vivo animal model. Hyperlipidemia model was induced by administering dexamethasone (10mg/kg, b.wt.,s.c.) in rats with significant imbalance in the in serum lipid profiles such as TC, TG, VLDL-C, LDL-C, HDL-C levels along with increase in atherogenic index. Treatment with hydroalcoholic extract of leaves of *Cleome gynandra* L. (200 and 400mg/kg,b.wt.,p.o) has shown significant amelioration of altered serum lipid profile reducing atherogenic index as evidenced by histopathological examinations compared to the standard treatment (atorvastatin, 10mg/kg, b.wt. p.o.).

Keywords: Hypolipidemic activity, Dexamethasone, Lipid profile, *Cleome gynandra* L.

INTRODUCTION

Hyperlipidemia is a highly predictive risk factor for atherosclerosis, coronary artery diseases and cerebral vascular diseases.[1] Coronary heart disease, stroke, atherosclerosis and hyperlipidemia are the primary cause of death.[2] Hypercholesterolemia enhances the free radical generation in various ways and eventually the formation of oxygen free radicals in the human cellular system .[3] The World Health Organization (WHO) predicted that heart disorders and stroke are becoming deadly, with a projected combined deaths of 24 million by 2030.[4] However, consumption of synthetic drugs has been associated with muscle toxicity, rhabdomyolysis, psychiatric adverse reactions which include depression, memory loss, confusion and aggressive reactions.[5,6]

Medicinal plants are an indispensable part of the traditional medicine practiced all over the world due to low costs; easy access and ancestral experience. 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.[7]*Cleome gynandra Linn* belongs to Cleomaceae family commonly known as Spider plant, African spider flower or cat's whiskers, comprising 150-200 species of which 50 were indigenous to Africa.[8] The plant reported to have rubefacient, vesicant, antiseptic, anti-inflammatory, anthelminthic, Immunomodulatory effects and analgesic properties. The extract of this plant possesses anticancer, antibacterial, antimycotic and antioxidant properties.[9,10,11] In Ayurveda it is used as an Anthelmentic, in ear diseases, pruritis and several other diseases like gastro intestinal disorders and gastrointestinal infections etc.[12] The plant also used in the treatment of malaria, piles, rheumatism and in tumour. The decoction of the root is used to treat fevers. A decoction or infusion of boiled leaves and or roots is administered to facilitate childbirth in pregnant women, treat stomach-ache and constipation, treat conjunctivitis, treat severe thread-worm infection and relieve chest pains.[13]

Based on the information, the current study was aimed at evaluating the Hypolipidemic activity of *Cleome gynandra* L. against dexamethasone induced hyperlipidemia in wistar rats.

MATERIALS AND METHODS

Identification, Authentication of plant materials

The leaves of *Cleome gynandra* L. were collected from Seshachalam Hills, Tirupati and was authenticated (Voucher No. 1968) by Dr. K. Madhava Chetty, Assistant Professor, Department of Botany, S.V. University, Tirupati, Andhra Pradesh, India.

Preparation of extract

The leaves of *Cleome gynandra* L. were dried under shade at room temperature for 7 days and powdered by pulverization and the powder was used for preparation of 70% ethanolic extract. The hydroalcoholic extract of *Cleome gynandra* (HACG) was prepared by maceration method for 72hrs and the obtained extract was concentrated by simple evaporation at room temperature.[14] Preliminary phytochemical screening of HACG was carried out for the detection of the various bioactive constituents.[15]

Animals

Albino Wistar male rats weighing 150-200gms were procured and acclimatized to the experimental area having a temperature of 24±2 °C, controlled humidity

conditions and 12:12 h light and dark cycle. Animals were kept in polypropylene cages and were fed with standard food pellets and water *ad libitum*. The study was approved by Institutional Animal Etical Committee (IAEC), Seven Hills College of Pharmacy, Tirupati, Andhra Pradesh, India (Registered No: 1995/PO/Re/S/17/CPCSEA).

Dose Preparation and Administration of Standard Atorvastatin

Standard atorvastatin at a dose of 10 mg kg^{-1}, b.wt. was prepared by suspending atorvastatin in aqueous 0.5%w/v carboxy methyl cellulose (CMC).[16]

Experimental Design

Dexamethasone-induced hyperlipidemia in rats

Hyperlipidemia was induced using dexamethasone: a glucocorticoid known to evoke plasma lipid elevation. Dexamethasone (10mg/kg/day, S.C) was administered to rats for 8 consecutive days to induce hyperlipidemia. The animals were divided into five groups each containing six rats.[17]

Grouping of animals

Control	Treatment & Route of Administration	Duration
Vehicle	0.5 ml normal saline p.o	8 Days
Hyperlipidemic	Dexamethasone (10 mg/kg, b.wt., s.c)	
Standard	Atorvastatin (10mg/kg, b.wt., po.)	
HACG-I	200 mg/kg, b.wt., p.o	
HACG-II	400 mg/kg, b.wt., po	

On the 9th day, the blood samples were collected by cardiac puncture under light ether anesthesia. Blood was centrifuged by using table top centrifuge at 2000rpm for 30 minutes so as to get serum. Serum samples were analyzed for total serum cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), very low density lipoprotein cholesterol (LDL-C) were estimated using diagnostic kits.[18] Atherogenic Index (AI) was calculated.[19] The liver was isolated, analyzed for the antioxidant[20,21] and pro-oxidant[22,23] studies along with histopathological examination.

Statistical Analysis

All the values were expressed as mean ± standard error mean. The data's were statistically analyzed by one-way ANOVA followed by Dunnet's *t*-test, and value $P < 0.05$ was considered to be significant.

RESULTS

Phytochemical screening

The phytochemical screening of HACG revealed the presence of Carotenoids, glycosides, Flavanoids, Saponins, alkaloids, Triterpenes, sugars, Tannins etc.

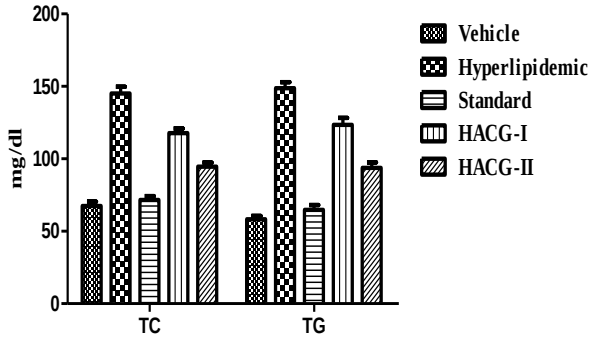
Table 1: Effect of HACG on serum lipid profile in dexamethasone induced hyperlipidemia in rats

Control	TC (mg/dL)	Triglycerides (mg/dL)	VLDL-C (mg/dL)
Vehicle (0.5ml of normal saline, p.o)	67.43 ± 2.98	58.17 ± 2.40	11.23 ± 1.16
Hyperlipidemic (10 mg/kg, b.wt. s.c)	145.13 ± 4.57	148.8 ± 4.18	39.67 ± 3.73
Standard (10 mg/kg, b.wt.p.o)	71.5 ± 2.73***	64.83 ± 3.31***	17.83 ± 1.51***
HACG-I (200 mg/kg, b.wt., p.o)	117.8 ± 3.16**	123.45 ± 4.74**	29.54 ± 1.79**
HACG-II (400 mg/kg, b.wt., p.o)	94.5 ± 2.88***	93.8 ± 3.76***	23.83 ± 1.18***

Data represents the Mean ± SEM values (n=6). Statistical significance: *P<0.05, **P<0.01, ***P<0.001 with respect to hyperlipidemic control on 8th day

(One Way Anova followed by Dunnett's: Compare all columns vs. hyperlipidemic control)

Graph 1: Effect of HACG on serum biochemical parameters in dexamethasone induced hyperlipidemia in rats



Graph 2: Effect of HACG on lipid profile in dexamethasone induced hyperlipidemia in rats

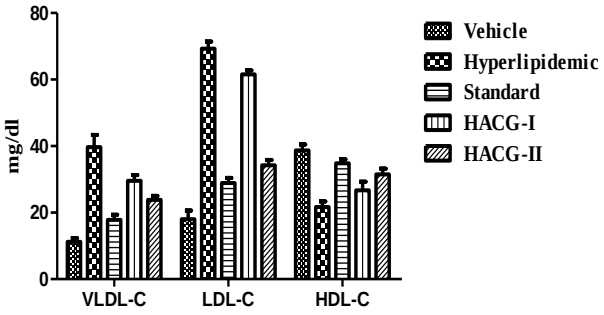


Table 2: Effect of HACG on serum lipid profile & atherogenic index in dexamethasone induced hyperlipidemia in rats

Control	LDL-C (mg/dL)	HDL-C (mg/dL)	Atherogenic index
Vehicle (0.5ml of normal saline, p.o)	18.00 ± 2.60	38.67 ± 1.80	1.85
Hyperlipidemic (10 mg/kg, b.wt. s.c)	69.3 ± 2.16	21.67 ± 1.67	4.32
Standard (10 mg/kg, b.wt.p.o)	28.90 ± 1.55***	34.83 ± 1.18***	2.12
HACG-I (200 mg/kg, b.wt., p.o)	61.57 ± 1.23**	26.67 ± 2.60*	3.52
HACG-II (400 mg/kg, b.wt., p.o)	34.23 ± 1.58***	31.5 ± 1.73***	2.67

Data represents the Mean ± SEM values (n=6). Statistical significance: *P<0.05, **P<0.01, ***P<0.001 with respect to hyperlipidemic control on 8th day

(One Way Anova followed by Dunnett's: Compare all columns vs. hyperlipidemic control)

Table 3: Effect of HACG on tissue parameters in dexamethasone induced hyperlipidemia in rats

Control	CAT	SOD	MDA
Vehicle (0.5ml of normal saline, p.o)	10.38 ± 0.81	6.87 ± 0.60	5.59 ± 0.91
Hyperlipidemic (10 mg/kg, b.wt. s.c)	5.31 ± 0.69	4.32 ± 0.61	10.83 ± 1.50
Standard (10 mg/kg, b.wt.p.o)	9.36 ± 0.64***	6.67 ± 0.72***	6.22 ± 0.55***
HACG-I (200 mg/kg, b.wt., p.o)	7.41± 0.75**	5.08 ± 0.77**	8.17 ± 0.58**
HACG-II (400 mg/kg, b.wt., p.o)	8.83± 0.60***	5.71 ± 0.63***	6.89 ± 0.73***

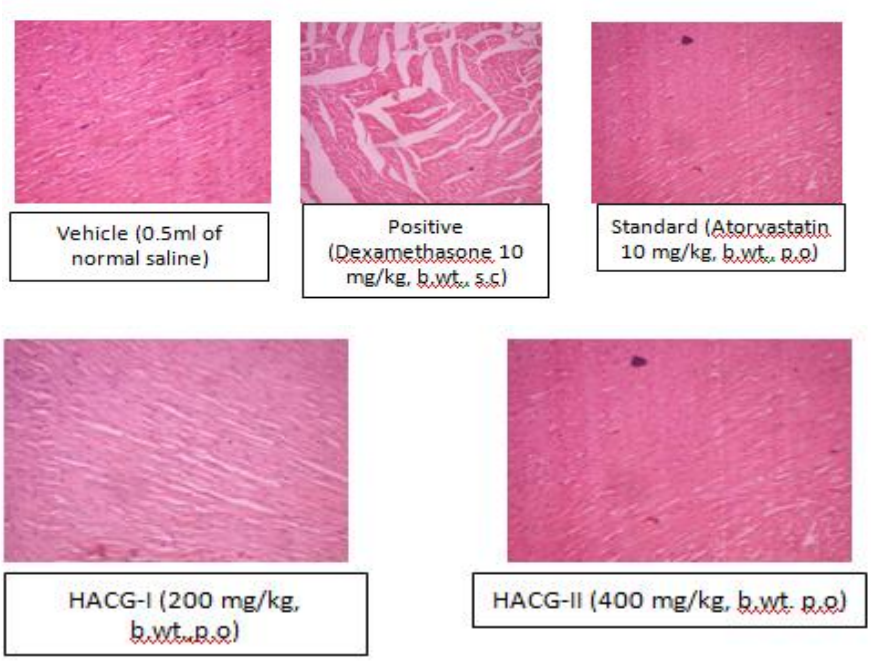
Data represents the Mean ± SEM values (n=6). Statistical significance: *P<0.05, **P<0.01, ***P<0.001 with respect to hyperlipidemic control on 8th day

(One Way Anova followed by Dunnett's: Compare all columns vs. Hyperlipidemic control)

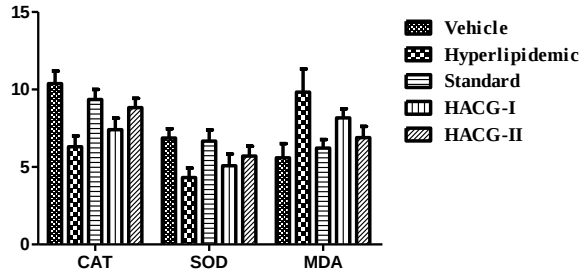
SOD-U/mg protein; **MDA**-µmoles of MDA/gm tissue/hr;

CAT-µmoles of H_2O_2/min/mg protein;

Histopathology:



Graph 3: Effect of HACG on Tissue parameters in dexamethasone induced hyperlipidemia in rats



SOD-U/mg protein
CAT-µmoles of H_2O_2/min/mg protein
MDA-µmoles of MDA/gm tissue/hr

DISCUSSION

Cardiovascular diseases are leading cause of death in both industrialized and developing nations. Disorders of lipid metabolism, following oxidative stress are the prime risk factors for initiation and progression of these diseases.[24] Hyperlipidemia is a major cause of atherosclerosis and the atherosclerosis-associated conditions, such as coronary heart disease, ischemic cerebro vascular disease and peripheral vascular diseases.

Dyslipidemia, including hyperlipidemia and hypercholesterolemia and low level of HDL-C are major causes of increased atherogenic risk; both genetic disorders and lifestyle diet high in calories, saturated fat, and cholesterol contribute to dyslipidemia seen in developed countries around the world.[25] However, we do not have satisfactory remedy for hyperlipidemia; most of the herbal drugs speed up the reduction of cholesterol by healthy dietary intake due to its rich therapeutic properties and being 100% natural.

The yield of HACG by maceration method for 25gms powder was 11.2%. The Preliminary phytochemical screening of the HACG revealed the presence of Carotenoids, glycosides, Flavanoids, Saponins, alkaloids, Triterpenes, sugars, Tannins etc. Based on the previous data of oral acute toxicity studies, the HACG was found safe up to a dose of 2000mg/kg, body weight.[26] The dried extract was suspended in 1%w/v CMC at a dose of 200mg/kg and 400mg/kg body weight for oral administration.

The present study carried out including dexamethasone (10mg/kg, b.wt.) for the experimental induction of hyperlipidemia in rats. Glucocorticoid hormonal level elevation includes the plasma lipid concentration but varies from species to species. Synthesis of triacylglycerol in the liver is stimulated by the injection of glucocorticoid in rats and consequently may lead to the accumulation of free fatty acids leading to hyperlipidemia.[27] The stimulation of the triglycerides (TG) production could lead to increased secretion of VLDL-C. Increasing VLDL-C secretion has been reported when dexamethasone is injected for several days in rats.[28,29]

TC and TG are present in dietary fat, FFAs combine with glycerol to form TG and cholesterol is esterified by ACAT to form cholesterol esters, storing in cells. Upon administration with dexamethasone resulted in increase in TC levels. The plasma cholesterol levels were reduced remarkably on treating the hyperlipidemic rats with HACG at both dose levels. The lipid lowering effects may be due to the presence of plant sterols. Plant sterols reduces the absorption of cholesterol and thus increases the fecal excretion of steroids that results in decrease of body lipids reduction reducing in CHD risk[30] compared to standard control treated with the atorvastatin at 10mg/kg b.wt.

Dexamethasone administration (10mg/kg body wt) increased the triglycerides levels, inducing imbalance in lipid metabolism leading to hyperlipidemia.[29,31] Upon treatment with HACG at both dose levels (200mg/kg body weight) significantly reduced the elevated TG levels with comparison to the standard treated animals.

The treatment is known to cause increased production of VLDL-C in the liver. In addition, corticoids may also stimulate VLDL-C formation in the intestine. The increase in the VLDL-C in dexamethasone induced hyperlipidemic rats was due to reduced lipoprotein lipase activity in the liver which could be responsible for high VLDL-C and triglyceride levels causing imbalance in lipid metabolism leading to hyperlipidemia.[32] Upon treatment with the HACG at both dose levels (200 & 400mg/kg, b.wt.) significantly ameliorated the elevated levels of VLDL-C compared to the standard treatment with atorvastatin.

The Mechanisms responsible for glucocorticoid induced dyslipidemia could be impaired catabolism of LDL-C, increase in the activity of lipoprotein lipase and subsequent increase in LDL-C[33] was observed in dexamethasone induced hyperlipidemia. Further treatment with the standard and HACG significantly reduced the abnormal levels of LDL-C.

HDL is a key lipoprotein involved in reverse cholesterol transport and transfer of cholesterol esters. It attracts cholesterol from cell membranes and free cholesterol to the core of the HDL particle, inhibiting the oxidation of LDL and by neutralizing the atherogenic effects of oxidizes LDL. The decreased levels of the HDL-C in dexamethasone induced hyperlipidemia[34] in rats was restored upon treatment with the standard and HACG when compared to the Hyperlipidemic control.

Oxidative stress is also considered as one of the main issues involved in the pathogenesis of cardiovascular disorders induced by glucocorticoids.[35] Over production of free radicals and hepatic oxidative damage has been reported in dexamethasone induced dyslipidemia.[36] Induction with the dexamethasone lowered the SOD & CAT levels attributing to the inactivation of enzyme by ROS bringing damage to proteins. Treatment with HACG have shown the strong antioxidant activity for *Cleome gynandra* extract which may include in its preventive

effects on hypolipidemic activity raising the levels of antioxidants.[37,13]

Lipid peroxidation is regarded as one of the basic mechanisms of tissue damage caused by free radicals. The dexamethasone treated rats significantly increased the lipid peroxidation which was measured by estimating MDA levels. The declined levels of lipid peroxidation in HACG treated rats contribute to the potential inhibitors of lipid peroxidation due to the presence of polyphenols like flavanoids, tannins and phenols as they are reported to exhibit antioxidant property. Presence of phenolic constituents have the ability to strongly inhibit the LPO process, and flavanoids act as potent antioxidants and free radical scavengers when compared to the standard treated animals.[38]

The histological studies reveals that the heart sections in the dexamethasone treated groups showed a marked fat cells in the heart when compare to normal control. Animals treated with atorvastatin showed a significant reversal of altered architecture of the heart where as animals treated with HACG restored the architecture of heart cells may be due to reducing the free fatty acid accumulations reducing the atherogenic index exhibiting antihyperlipidemic activity.

Some edible plants as a whole, or their identified ingredients with potent antioxidant properties, especially the predominant polyphenolics in *Cleome gynandra,* have substantial protective effects on human carcinogenesis, cardiovascular and renal disorders, memory and cognitive function, age-related neurological dysfunction such as Alzheimer's disease, diabetes, ulcers and several other human ailments.[39, 40, 41, 42]

CONCLUSION

Hyperlipidemia is a major cause of cardio vascular disorders. At present, the treatment of hyperlipidemia mainly involves a sustained reduction in lipid level with unwanted side effects, the efficacies of these compounds are debatable and there is a demand for new compounds for the treatment of hyperlipidemia. Fortunately the potency of herbal drugs is significant and they have negligible side effects. In the present Study, the HACG restored the altered lipid profile, with decrease in atherogenic Index as evidenced by Histopathological observations. The crude ethanolic extract and aqueous extracts of *Cleome gynandra* are a potential source of natural antioxidants like flavanoids. Further isolation & identification of active constituent from cleome gynandra, preparation of standardized dose & dosage regimen can play a significant role in improving the hypolipidemic action.

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Source of Support: Nil, **Conflict of Interest:** None.