WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.421
Volume 7, Issue 11, 1293-1305 Research Article ISSN 2278 – 4357

EFFECT OF *CLERODENDRUM PHILIPPINUM* LEAF EXTRACT ON RATS INDUCED WITH HYPERLIPIDEMIA

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Article Received on
08 September 2018,

Revised on 29 Sept. 2018,
Accepted on 19 Oct. 2018,

DOI: 10.20959/wjpps201811-12614

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ABSTRACT

Objective: The aim of the present study is to Effect of *Clerodendrum Philippinum* Leaf Extract on rats induced with hyperlipidemia. **Method:** Screening of antihyperlipidemia was done by using *clerodendrum* leaves. The leaf extract used for antihyperlipidemic activity at dose of 200mg/kg, 400mg/kg. Hyperlipidemia was administered in experimental animals using TritonX-100 by intraperitoneal administration at the dose of 100mg/kg. On 8th day blood was withdrawn through retro-orbital puncture, and evaluated estimation of lipid profiles. **Result:** Treatment with *clerodendrum philippinum* leaf extract at dose of 400mg/kg significantly ($p<0.01$) decrease the serum total cholesterol, triglycerides, and LDL-C, VLDL-C levels and increase in HDL-C levels when compared to hyperlipidemic control, and also the standard group i.e atorvastatin group significantly lower the serum lipid levels ($p<0.001$). **Conclusion:** The present finding suggest that the ethanolic extract of *clerodendrum philippinum*(EECP) 400mg/kg have definite anti hyperlipidemic activity in Triton X-100 induced hyperlipidemic model and which is equipotent activity when compared with Atorvastatin treated group.

KEYWORDS: Ethanolic Extract of *Clerodendrum philippinum*, Triton X-100, Atorvastatin, Hyperlipidemia.

INTRODUCTION

Hyperlipidemia is a condition in which there is characterized by high levels of lipids. That is Total cholesterol (TC), Triglycerides (TG), Very low density lipoproteins (VLDL), Low density lipoproteins (LDL) and along with decrease the high density lipoprotein levels. Hypercholesterolemia is a lifestyle disorder which seriously effect on human health. (Syed Safilullah Ghori et al., 2015) Lipids are fats in the blood stream and divided into cholesterol & triglycerides. Triglycerides are provide energy that is used directly or stored in fat cells. Cholesterol circulates in the blood stream and is elaborate in the structure and function of cells. (Dr. Arun kumar et al., 2013).

Hyperlipidemia is also called as dyslipidemia, hypercholesterolemia and hyperlipoprotenemia. (Pankti, P et al., 2014, Dr. Arun kumar et al., 2013) It contributes significantly to develop the atherosclerosis, coronary artery disease. (Arati Ramesh et al., 2015) Atherosclerosis is contributes the mortality and morbidity worldwide. (Varsha D et al., 2010) Approximately 12 million people reportedly die of cardio vascular diseases (CVD) each year worldwide. (R. Dhanalaksmi et al., 2014) It causes some factors like cholesterol diet high in saturated fats & family history, age, life style play, hypertension, (Varsha, D et al., 2010) genetic factors, microbiological aspect, medical illness. (P.K.Kasthuri et al., 2015) CVD like myocardial, angina pectoris, congestive heart failure, hypertension. (Syed Safilullah Ghori et al., 2015).

The main aim of treatment in patients with hyperlipidemia is to decrease the risk of developing ischemic heart disease or the occurrence of further CVD like cerebrovascular disease or atherosclerosis. (Nimmy Chacko et al., 2012) Currently available drug have been associated with number of side effects. The consumption of synthetic drugs leads to diarrhea, myositis, nausea, hyperuricemia, flushing, gastric irritation, abnormal liver function and dry skin. (S.S.Sudha et al., 2011).

Medicinal plants are used for various research. An herbal treatment for hyperlipoproteinemia has no side effect and is relatively locally, cheap available. They are effective in decreasing the lipid levels in the system. (A.Saravanakumar et al., 2010) The genus of *clerodendrum* has more than five hundred species very widely distributed in the world. Many species of this genus have been used in the medicines for the treatment of various life-threatening diseases. The *clerodendrum philippinum* presence of phytochemical viz.,cardio glycosides, alkaloids, flavanoids, saponins, steroids, protein, terpenoids, tannins and phenols. Family is Lamiaceae.

Clerodendrum common name of *clerodendrum philippinum schauer* and Chinese glory bower glory tree, stick bush. (T. Rajeswariet al., 2012) *Clerodedrum philippinum* have been used in the number of biological properties, mainly including anti-inflammatory and anti-oxidant, anti-nociceptive, antihypertensive, anti cancer, anti diarrheal, Anti microbial, hypoglycemic and hepatoprotective, hypolipidemic, neuroprotective, memory enhancing and other activities. (Mao-Xing Li et al., 2017) Medical plants have always been considered as healthy source of life for all people due to its rich therapeutic properties & being 100% natural. (P.Veeramani et al., 2015).

MATERIALS AND METHODS

Chemicals

Triton X-100 (a non-ionic detergent, iso octyl polyoxy ethylene phenol, formaldehyde polymer) was obtained from sisco research laboratory Hyderabad. Atorvastatin was obtained from Dr. Reddy's Hyderabad. All other chemical were of analytical grade & obtained locally.

Collection of Plant material & Authentification of plant material

Leaves collected from local areas of Rama Krishna colony, karimnagar, telangana, india. Authenticated by Botanical Survey of India, Deccan regional centre, Attapur, Hyderabad [authentication no: BSI\DRC\2017-18\Tech.\698].

Fig. 1: *Clerodendrum Philippinum.*

Plant Drying & Extraction

The leaves of *Clerodendrum philippinum* were dried under shade and then coarse powdered with a mechanical grinder. The powder was passed through sieve no. #30. Dried samples was extracted with ethanol using soxhlet process. (Gaurav k. soni et al., 2013) The % yield of *clerodendrum philippinum* was found to be 8.72%.

Preliminary Phytochemical Screening

Preliminary phytochemical analysis carried out by standard protocol methods. (T.Rajeswari et al., 2012).

Thinlayer Chromatography

TLC analysis of all the fractions using different solvent system followed by standard protocol methods. (Alebiosu c.o et al., 2015).

Experimental Animals

Healthy adult wistar rats of 8-10 weeks old with average weight in the range of 150-180gms were selected. Animals are housed 4 per cage in temperature controlled (27ºC±3ºC) room with light/dark cycle in a ratio of 12:12hrs is to be maintained. The animals are allowed to acclimatize to the environment for 7 days and are supplied with a standard diet and water ad libitum. The guidelines of committee for the purpose of control and supervision of experiments on animals (CPCSEA), Govt of India were followed and prior permission was sought from the Institutional Animal Ethics Committee (IAEC) for conducting the study.

Acute toxicity studies

Healthy adult female wistar albino rats starved over night were divided into eight groups, each containing of four rats and were orally feed with the test extracts in increasing dose levels of 500, 1000,2000 and 4000mg/kg body weight. The acute toxicity study was carried out according to OECD guidelines. The rats were observed continuously for 2hrs under the following profiles.

1. Behavioral profile: Alertness, restlessness, irritability, and fearfulness.
2. Neurological profile: Spontaneous activities, reactivity, touch response, pain response and gait.
3. Autonomic profile: Defecation and urination.

After a period of 24 hrs, 72hrs and 14 days, the rats were observed for any lethality or death. (Mihir K.Kar et al., 2015)

Experimental Animal Protocol

The rats were divided into 5 groups containing 4 animals in each group.

Group-I: Normal control.

Group-II: Hyperlipedemic control, (Triton X-100).

Group-III: Hyperlipedemic rats treated with EECP at dose of 200mg/kg p.o for 7 days.
Group-IV: Hyperlipedemic rats treated with EECP at dose of 400mg/kg p.o for 7 days.
Group-V: Hyperlipedemic rats treated with Atorvastatin at dose of 10mg/kg p.o for 7 days.

Hyperlipidemia was induced by single intraperitoneal injection of freshly prepared solution of Triton X-100 (100mg/kg) in physiological solution after overnight fasting for 18 hrs. All the groups receives single i.p injection of Triton X-100 at dose of 100mg/kg, simultaneously with Group-II, Group-III, Group-IV, Group-V, expect Group-I (Normal control). After 72hrs of Triton X-100 injection, the Group-V was administered with the standard atorvastatin at dose of 10mg/kg, p.o for 7 days. The group-III was administered at daily dose of EECP 200mg/kg orally for 7 days and group-IV was administered EECP at daily dose of 400mg/kg p.o for 7 days.

Blood Sample Collection and Analysis

The rats are anesthetized and then blood samples were collected on 8th day from retro-orbital plexus of rats of all the groups, and centrifugated at 3000rpm for 15 min so as to get serum. The serum is analyzed for total cholesterol, triglycerides and HDL levels using biochemical kits (diagnostic kits). According to that result LDL-C, VLDL-C calculated by using following formulas:

LDL-Cholesterol = Total cholesterol-HDL-TG/5

VLDL-C=TG/5 (Chakraborty Manodeep et al., 2012)

Statistical Analysis

The results were expressed as mean ± S.E.M. all the groups are compared with control. Statistical analysis was carried out by using ANOVA followed by dunnet's multiple comparison tests using Graph pad prism software version.

RESULTS

Preliminary Phytochemical Screening

Investigation revealed the presence of Alkaloid, Flavonoid, Phenols, Tannin, Terpenoids, Amino acid in Ethanolic extract of *Clerodendrum Philippinum.*

Fig. 2: preliminary phytochemical screening.

Thinlayer Chromatography

TLC analysis of all the fractions using diffent solvent system revealed the presence of promising spots like Flavonoid, Phenol, Alkaloid, Amino acid.

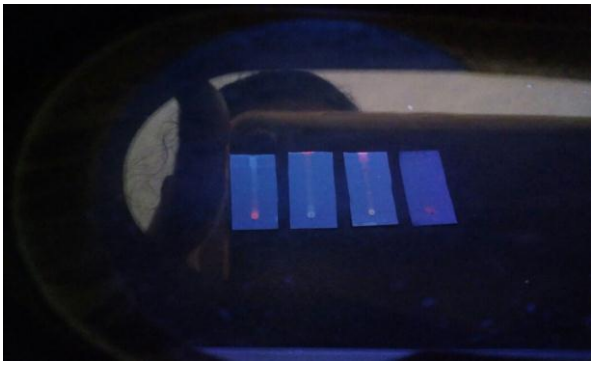

Fig. 3: Thinlayer Chromatography.

Table 1: Effect of Ethanolic Extract of *Clerodendrum Philippinum* on serum lipids.

SI. No.	Groups	TC	TG	HDL	LDL	VLDL
I	Normal control	63.52±5.97	75.68 ±4.60	36.48±3.70	14.81±5.23	15.13±1.84
II	Hyperlipidemic control	182.12±4.81	160.98±5.57	24.06 ±5.96	125.85±5.21	32.19±2.23
III	EECP 200 mg/kg	124.39±3.19*	105.05±5.65*	29.49±5.59**	74.03±5.19**	20.85±2.16*
IV	EECP 400 mg/kg	116.18±3.74**	98.24±3.37**	34.15±4.52***	62.37±5.76**	19.66±1.33*
V	Standard Atorvastatin 10 mg/kg	88.4±5.55***	93.88±3.88**	38.81±5.94***	46.27±8.12***	18.77±1.55**

All the data are expressed as MEAN ± S.D (n=4), *p=<0.05, **p=<0.01, ***p=<0.001.vs group-II.

Effect of Ethanolic Extract of *Clerodendrum Philippinum* on Total Cholesterol

In the normal rats the total cholesterol levels were found to be 63.52±5.97. Treatment with Triton X-100 caused a significant rise in the levels of cholesterol 182.12±4.81. Administration of various doses of the plant extract after the treatment with Triton X-100 resulted in the lowering of cholesterol levels in a dose dependant manner. The total cholesterol levels of group treated with 200, 400 mg/kg were 124.39±3.19, 116.18±3.74 respectively. In atorvastatin group the total cholesterol decrease to 88.4±5.55.

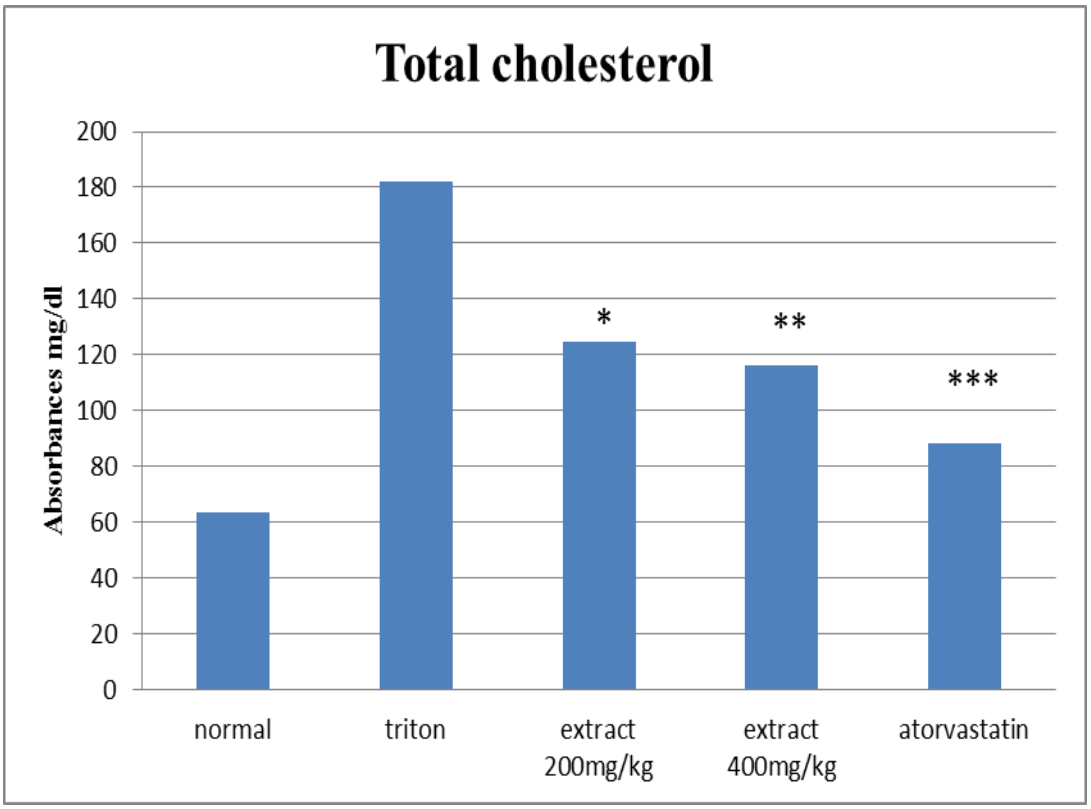

Fig. 4: Effect of Ethanolic Extract of *Clerodendrum Philippinum* on Total Cholesterol.

Effect of Ethanolic Extract of *Clerodendrum Philippinum* on Triglycerides

The triglycerides levels in normal rats were found to be 75.68±4.60. Administration of Triton X-100 resulted in a rise in triglycerides levels 160.98±5.57. In atorvastatin group the triglyceride was reduced to 93.88±3.88, were as groups treated with 200, 400 mg/kg of extract showed a dose dependant decrease in the triglyceride levels 105.05±5.65, 98.24±3.37 respectively.

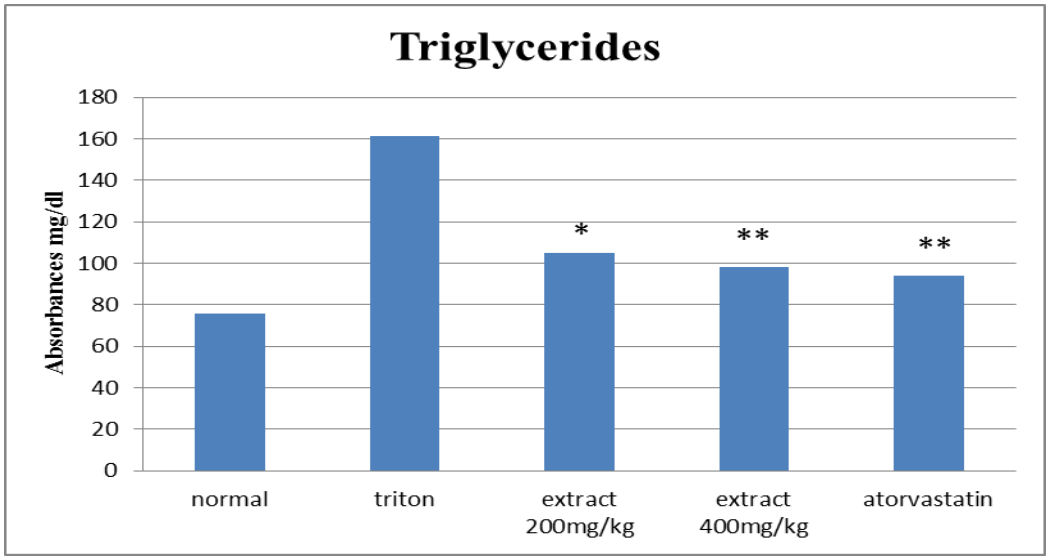

Fig. 5: Effect of Ethanolic Extract of *Clerodendrum Philippinum* on Triglycerides.

Effect of Ethanolic Extract of *Clerodendrum Philippinum* on LDL-C

In the normal rats the LDL levels were found to be 14.81±5.23. Induction of hyperlipidemia resulted in significantly raised LDL levels 125.85±5.21. Administration of various doses of the ethanolic extract of *clerodendrum philippinum* after the induction with Triton X-100 resulted in the decreasing of LDL levels. The LDL levels of groups treated with EECP at dose of 200, 400 mg/kg were 74.03±5.59 & 62.37±5.76 respectively. Lowering of LDL levels was dose dependent manner in EECP. In atorvastatin group the LDL levels was reduced to 46.27±8.12.

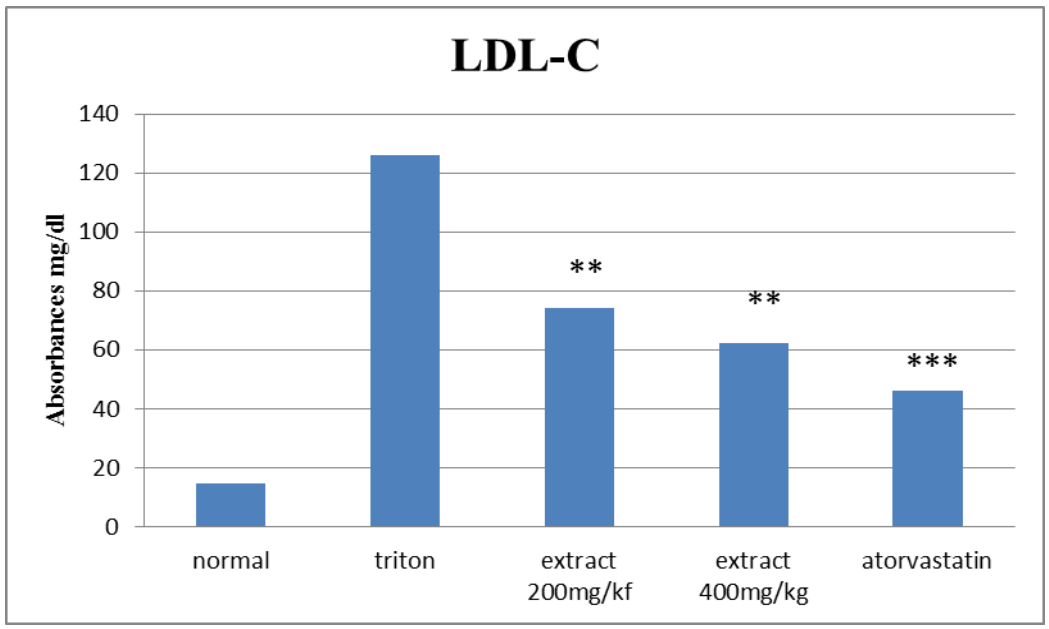

Fig. 6: Effect of Ethanolic Extract of *Clerodendrum Philippinum* on LDL-C.

Effect of Ethanolic Extract of *Clerodendrum Philippinum* on VLDL-C

The VLDL levels in normal rats were found to be 15.13±1.84. Administration of Triton X-100 resulted in a rise in VLDL levels 32.19±2.23. In atorvastatin group the VLDL was reduced to 18.77±1.55, were as group treated with 200, 400 mg/kg of extract showed a dose dependant decrease in the VLDL levels 20.85±2.16, 19.66±1.33 respectively.

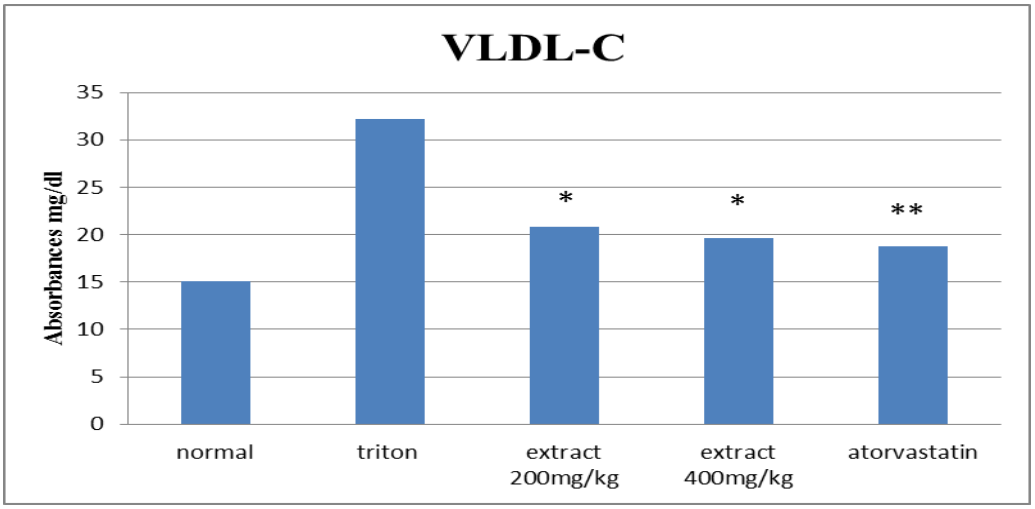

Fig. 7: Effect of Ethanolic Extract of *Clerodendrum Philippinum* on VLDL-C.

Effect of Ethanolic Extract of *Clerodendrum Philippinum* on HDL-C

The HDL levels in normal rats were found to be 36.48±3.70. Administration of Triton X-100 resulted in a fall in HDL levels 24.06±5.96. In atorvastatin group the HDL was elevated to 38.81±5.94, were as groups treated with 200, 400 mg/kg of extract showed a dose dependant increase in the HDL levels 29.49±5.59, 34.15±4.52 respectively.

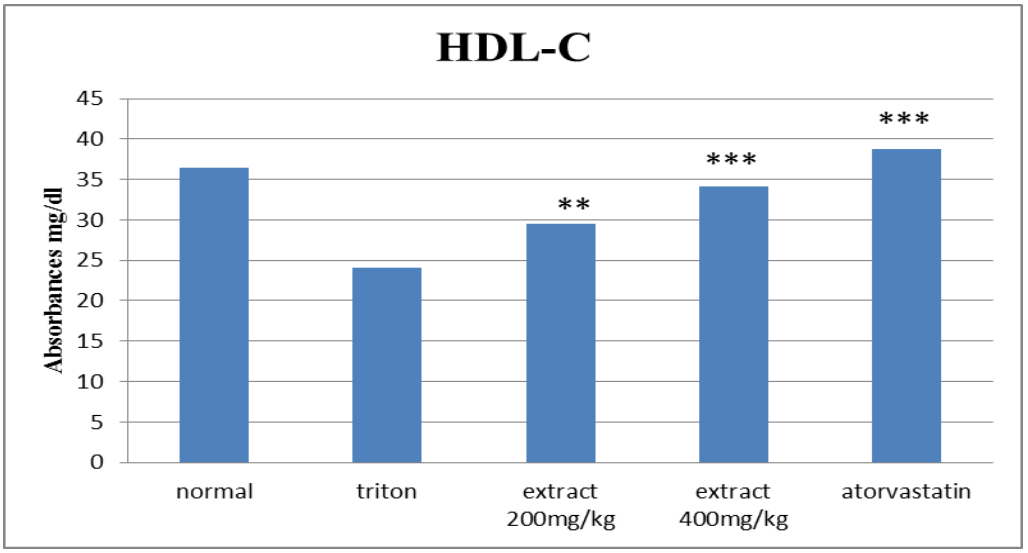

Fig. 8: Effect of Ethanolic Extract of *Clerodendrum Philippinum* on HDL-C.

DISCUSSION

According to the world health organization, about 80% of the world's population relies on traditional medicine. (Alebiosu c.o et al., 2015) Ayurvedic system of medicines is one of the oldest system of medicine having of more than 3500 years. Several prototype derived from these herbal medicines are in use for different kind of disease and disorders. It not only gives new molecule but also with newer mechanism of action, hence is called gold mine. (Vijay R et al., 2012).

The *clerodendrum philippinum* one of the medicinal plant. Mihir K. kar et al., has been reported to be evaluated the anti diabetic activity of *clerodendrum philippinum schauer* leaves using streptozotocin induced diabetic rats. B. Venkatanarasimman et al., demonstrated antibacterial activity of ethanolic leaf extract of *clerodendrum philippinum*. K. G. Lalitha et al., studied about ethanolic extract of *clerodendrum philippinum schauer* flower for anti anxiety and central nervous system depressant activities. So this study is being carried out to evaluate the *clerodendrum philippinum* towards anti hyperlipidemia.

The present study was designed to investigate the effect of *clerodendrum philippinum* leaf extract in triton X-100 induced hyperlipidemic rats. Phytochemical investigation revealed the presence of Alkaloid, Flavonoid, Phenol, Tannin, Terpenoid, Amino acid in ethanolic extract of *Clerodendrum Philippinum*.

Administration of Triton X-100 was chosen for the induction of hyperlipidemia. Triton X-100 model is usedas a acute model for induction of hyperlipidemia in rats. Rats given Triton X-100 (100mg/kg) intraperitoneally to all fasted rats showed significantly elevation of TG, TC, VLDL, and LDL & reduction of HDL levels. After 72 hrs of induction of Triton X-100 results in hyperlipidemia. Which is compared with normal control group which results in significantly increased serum lipid levels in hyperlidemic group.

The change in lipid levels in group number III, IV, were comparable with group of hyperlipidemic control i.e Triton X-100 group- II. The standard group i.e atorvastatin group significantly lower the serum lipid level. HMG coA reductas inhibitor has been used in the treatment of hyperlipidemia, and atorvastatin is one of the greatest prevalently used HMG coA reductas inhibitors. (Varsha D et al., 2010).

The results of study clearly indicate that Ethanolic Extract of *clerodendrum philippinum* extract at dose of 400mg/kg significantly lowered serum lipid levels of TC, triglycerides, LDL-C, VLDL-C ($p<0.01$). Antihyperlipidemic activity which was found to be more effective in higher dose of EECP as compared to lower dose of EECP when administered orally in Triton induced hyperlipidemic models.

Flavonoids are reported to increase HDL-C concentration and decrease in LDL and VLDL levels in hypercholestermic rats. (Varsha D et al., 2010) Flavonids found in our Ethanolic Extract of *Clerodendrum philippinum* could therefore be considered favorable in increasing HDL and decreasing LDL and VLDL in Ethanolic Extract of *Clerodendrum Philippinum* treated rats.

Thus the present result strongly suggests that the hyperlipidemic activity of this medicinal plant could be attributed to the presence of Flavonoids, Alkaloids, Phenols, Tannin, Terpenoids in the extract.

CONCLUSION

The result of present study revealed that the Ethanolic Extract of *Clerodendrum Philippinum* altered the serum lipid profile in rats. Leaf extract of *clerodendrum philippinum* proved to be effective at higher doses (400mg/kg) and atorvastatin standard drug shows better results in decreases TC, TG, LDL, VLDL levels and increase the HDL levels compare to hyperlipidemic rats. The results concluded that EECP (400mg/kg) have definite Anti Hyperlipidemic activity in Triton X-100 induced hyperlipidemic model and which is equipotent activity when compared with Atorvastatin treated group. The leaves extract of *clerodendrum philippinum* as anti hyperlipidemic agent having curative effect against hyperlipidemia.

ACKNOWLEDGEMENTS

I am thankful to Head of the department of Pharmacology, principal and management of Vaageswari College of Pharmacy, Karimnagar, Telangana, India for providing laboratory facilities to carry out this study successfully.

FUNDING SOURCE

No funding source has been provided for this research work.

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