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EVALUATION OF HYPOGLYCEMIC AND HYPOLIPIDEMIC ACTIVITY OF 50% HYDRO ETHANOLIC LEAF EXTRACT OF *BARLERIA CRISTATA* L. IN ALLOXAN INDUCED DIABETIC AND HIGH LIPID DIET FED RATS.

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Keywords:

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ABSTRACT: The present study was carried out to evaluate the hypolipidemic and hypoglycemic effects of the plant *Barleria cristata L*. Phytochemical screening of crude powdered leaf extract of *Barleria cristata* L. revealed the presence of various bioactive phytoconstituents. An acute toxicity study of 50% hydroethanolic leaf extract of *Barleria cristata* L. reported that at all normal therapeutic doses, the test sample was safe for oral treatment. There was no significant change in the bodyweight of rats. Diabetes was induced in experimental rats by the intraperitonial injection of Alloxan. The 50% hydroethanolic extract of *Barleria cristata* L effectively lowered the blood glucose level in diabetic rats which was equal to glibenclamide treated rats. The plant extract treated HLD rats showed a dose related hypolipidemic activity. All the lipid components - TC, TG, LDL-C, VLDL-Cholesterol levels were reduced significantly, and HDL-C, protective cholesterol level was increased. The present study clearly indicated that 50% hydroethanolic extract of *Barleria cristata* L. leaf had produced a hypoglycemic and hypolipidemic effect on both diabetic and HLD fed rats.

INTRODUCTION: Diabetes mellitus is a group of metabolic disorders characterized by increased blood glucose levels due to the absence of insulin secretion or peripheral insulin resistance. Impaired metabolism of a number of biomolecules such as glucose, lipids, proteins and glycoproteins has been reported in diabetes mellitus. Type 1 and type 2 diabetes mellitus are the most common forms of diabetes mellitus [1].

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It is becoming a worldwide public health problem leading to macro and microvascular complications [2]. Diabetic patients in the age group between 20 and 79 years are predicted to increase to 700 million by 2045 [3]. The primary medication for diabetes mellitus is oral hypoglycemic drugs and insulin injections.

The available antidiabetic drugs have various side effects and are not suitable for use during pregnancy. The usage of sulfonyl drugs induces *β*-cell death in isolated rodent and human islets, while glucagon-like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors have potential risks for pancreatitis, pancreatic and thyroid cancers.

Globally, health expenditure for the management of diabetes is expected to reach USD 490 billion in 2030 [4]. Therefore novel antidiabetic medicines are necessary [5]. Another approach to the treatment of diabetes is the application of medicinal plants with phytochemicals that cause beta-cell regeneration leading to normal blood glucose in animals and humans [6].

Phytoconstituents protect cellular antioxidant defense mechanisms from oxidative stress, stimulate insulin signaling pathways and regulate transcription factors, hormones, peptides and inflammatory pathways to manage hyperglycemic conditions and diabetes-associated complications. 45,000 plant species have records of widespread usage in treating diabetes mellitus in the world [7].

Herbal therapies are proven safe and effective for healing diseases and have been the potential source for developing new drugs. A majority of people in the world rely on herbal therapy. Phytotherapy is the antecedent of modern drugs and one-third of the top-selling drugs in the world plant origins [8]. Plants rich in polyphenolics have been given attention due to their therapeutic benefits [9]. Hyperlipidemia is one of the important risk factors for cardiovascular diseases and conditions [10, 11].

Barleria cristata L. is a shrub found widely in subtropical Himalaya, Sikkim, and Central and South India. It has various medicinal and therapeutic uses. Different parts of the plant have been used in the treatment of various diseases like anemia, toothache, and cough [12, 13].

Decoction of root is used for treating rheumatism and pneumonia. Oil from leaf extract is used for ear and eye oinments. In the present study, efforts have been made to establish the scientific validity of this plant's hypoglycemic and hypolipidemic properties.

MATERIALS AND METHODS:

Plant Collection and Authentication: The plant *Barleria cristata* L. commonly known as Kodilkannu (in Southern India) was collected from the rural area around Erode district, Tamil Nadu in December. A complete plant with flowers of *Barleria cristata* L. was identified by the Botanical Survey of India (BSI), Tamil Nadu Agricultural University (TNAU), Coimbatore, Tamil Nadu, India (N.BSI/SC/5/23/08-09/Tech.175).

Fresh leaves were washed, shade dried, and then homogenized into fine powder by mixer grinder and used for further studies.

Phytochemical Screening of Plant Sample: The plant material was subjected to Soxhlet extraction with different solvents such as ethanol, acetone, chloroform, distilled water, petroleum ether, and benzene for 18 hours. The extracts were condensed and used to screen phytochemicals using standard procedures.

50% Hydroethanolic Extract preparation: About 5 kg of freshly collected leaves were shade dried and powdered. Then cold macerated with ethanol for 3 days with occasional stirring. The suspension was filtered through a fine muslin cloth. The water portion of the sample was evaporated at low temperature (approximately at 40 °C) under reduced pressure in a rotary evaporator. Dark brown coloured crystals obtained were stored in an air-tight desiccator. Whenever needed, the residues were dissolved in distilled water, filtered (Whatman No.1 filter paper), and used for the studies.

Experimental Animals: Male albino rats of Wistar strain weighing 120 – 150 g were procured from the animal house, PSG Institute of Medical Science and Research (No: 158/1999/CPCSEA), Coimbatore, India.

The rats were grouped and housed in polyacrylic cages and maintained under standard conditions (25 ± 2°C) with 12 ± 1 h dark/light cycle. The animals were fed with rat pellet (Hindustan Lever Ltd., Bangalore, India) and water *ad libitum.*

All the experimental procedures were conducted after the approval of the ethical committee and were in strict accordance with institutional animal ethical committee guidelines.

Acute Toxicity Study: The 50% hydroethanolic extracts of *Barleria cristata* L. leaf were tested for its acute toxicity in Wistar albino rats by the method described by Miller and Tainter [14]. Overnight fasted rats weighing between 120-150g were divided into 6 groups, containing 5 animals each. Test samples were administered separately in various doses by oral route. The toxicity determinations were done for the doses of 2, 4, 6, 8,

10 g/kg b.w. The LD_{50} was calculated graphically and theoretically using the formula;

$$0\% \text{ death} = (0.25 / n) \times 100$$

$$100\% \text{ death} = (n - 0.25) / n \times 100,$$

Where n – number of animals in each group. The corrected percentage was then transformed into probit values by referring to the table to transform percentage to probit.

A plot of log dose (on X-axis) vs. % mortality (on Y-axis) was plotted, and a line was obtained.

The log dose corresponding to probit 5 was determined, and its corresponding antilog value was computed, taken as the LD_{50} value.

Hypoglycemic and Hypolipidemic Study:

Induction of Diabetes: Alloxan monohydrate was used to induce diabetes mellitus in normoglycemic rats.

Animals were allowed to fast for 18 hours and were injected intraperitoneally with freshly prepared alloxan monohydrate in sterile normal saline in a dose of 120 mg/kg body weight. After 72 h of injection, the rats with fasting blood glucose levels greater than 350 mg/dl were considered diabetic and were selected for the study.

Induction of Hyperlipidemia: High lipid diet was prepared by mixing 50 g fat as dalda, 32 g whole wheat flour, 16 g of whole milk powder, 1g NaCl, 1g cholesterol, 0.2 mg thiamine, 0.25 mg riboflavin and 3 mg niacin.

Rats were fed with HLD for 30 days, and their serum cholesterol levels were checked after 30 days. When the cholesterol level reached 350 – 400 mg/dl, the rats were subjected to treatment.

Experimental Design: The overnight fasted rats were divided into 6 groups of 6 animals each.

Group I: Normal healthy controls and received standard rat pellet for 28 days.

Group II: Diabetic control rats.

Group III: Diabetic rats received glibenclamide (600 µg/kg body weight) drug for 28 days served as drug control.

Group IV: High Lipid Diet (HLD) Control rats fed with high lipid diet for 28 days.

Group V: HLD rats received 50% hydroethanolic leaf extract of *Barleria cristata* L. (200 mg/kg b.w) for 28 days.

Group VI: HLD rats received 50% hydroethanolic leaf extract of *Barleria cristata*L. (400 mg / kg b.w) for 28 days.

Group VII: Diabetic rats received 50% hydroethanolic leaf extract of *Barleria cristata* L. (500 mg / kg b.w) for 28 days.

To all the groups plant extract were administered orally once a day. The blood samples were drowned on 0^{th}, 7^{th}, 14^{th}, 21^{th} and 28^{th} day by retro-orbital route under mild anaesthesia. At the end of treatment period blood samples were (1 – 1.5 ml) collected after mild chloroform anaesthesia and by the cardiac puncture. Serum was collected from blood by centrifuging at 3000 rpm for 20 min. The body weight of different animals was measured before and after treatment.

Biochemical Analysis: The serum was used to analyze fasting Blood Glucose [15], Total cholesterol [16], Triglyceride [17], HDL cholesterol [18]. The LDL and VLDL cholesterol values were calculated by Friedewalds formula [19].

Statistical Analysis: Data were reported as means ± SD by using the statistical package of social sciences (SPSS). Data were analyzed using analysis of Variance (ANOVA), and the group means were compared by Duncan's Multiple Range Test (DMRT). Values were considered statistically significant when $P<0.05$.

RESULTS:

Phytochemical Screening of *Barleria cristata* L. Leaf: The phytochemical screening of *Barleria cristata* L. leaf extract revealed the presence of alkaloids, flavonoids, glycosides, phenols, saponins, tannins, carbohydrates and protein, and showed absence of safronins. These phytochemicals possess good antioxidant properties and have exhibited multiple biological effects, including anti-inflammatory and antitumor activities [20].

TABLE 1: QUALITATIVE PHYTOCHEMICAL EVALUATION OF PLANT CRUDE POWDER EXTRACT

	Extracts					
Constituents	**Alcohol**	**Acetone**	**Chloroform**	**Distilled water**	**Petroleum ether**	**Benzene**
Alkaloids	+ + +	+ + +	+ + +	+ + +	- - -	- - -
Flavonoids	+	+	+	+	-	-
Phenols	+	+	+	+	+	+
Tanins	+ +	+ +	- -	+ +	- -	- -
Glycosides	+ +	+ +	- -	+ +	- -	- -
Saponins	+ +	+ +	- -	+ +	- -	- -
Safronins	-	-	-	-	-	-
Carbohydrate	+ +	+ +	+ +	+ +	+ +	+ +
Total protein	+ +	+ +	- +	+ +	- -	- -
Steroids	+	+	+	+	-	-
Thiols	+	-	-	+	-	-

+, - symbols indicate the presence and absence of phytochemicals, respectively.

Preparation of 50% Hydroethanolic Extract of Plant Sample: From the phytochemical screening tests, it was clear that water and ethanol extract of plant sample showed the presence of biologically important phytoconstituents.

Hence, in the present study, 50% hydroethanolic extract of plant samples was chosen that could provide information related to constituents available from the plant.

Acute Toxicity Study of 50% Hydroethanolic Leaf Extract of *Barleria cristata* L.: The results for acute toxicity studies were tabulated as shown in **Table 2.**

TABLE 2: ESTIMATION OF LD50 FOR 50% HYDROETHANOLIC LEAF EXTRACT

Groups	Dose (g/kg b.w)	Log Dose	Dead Total	% Dead	Corrected %	Probit
Group-I	2	0.3010	0	0	5	3.36
Group-II	4	0.6020	0	0	5	3.36
Group-III	6	0.7781	1	20	20	4.16
Group-IV	8	0.9030	2	40	40	4.75
Group-V	10	1.0000	3	60	60	5.25

The LD_{50} values of *Barleria cristata* L. leaf sample was found to be 0.94 g /kg b.w.

Effect on Body Weight: All the animals from treated groups did not show any significant decrease in body weight following 28 days of treatment as compared with 0-day treatment. The experimental animals showed a slight increase in body weight which was statistically insignificant **Table 3.** From the result of this study, it was observed that the test sample was considered safe for long-term oral treatment at all normal therapeutic doses.

TABLE 3: CHANGE IN BODY WEIGHT OF RATS FOLLOWING TEST SAMPLE

Groups	*Barleria cristata* L.	
	Before Treatment	**After Treatment**
Control	128.16±5.00	125.70±10.20
Group-I	125.00±16.0	152.00±3.16*
Group-II	122.10±07.00	135.00±1.50*
Group-III	136.21±11.61	148.00±4.08*
Group-IV	138.40±09.00	152.00±3.16*
Group-V	132.09±18.02	150.00±0.72*

P<0.05 when comparing treatment to corresponding control groups. *-statistically not significant.

Hypoglycemic and Hypolipidemic Study:

Effect on Body Weight: Normal control rats showed no change in their body weight during the treatment, but diabetic (G II) rats showed a significant reduction in body weight.

TABLE 4: EFFECT OF PLANT EXTRACT ON BODY WEIGHT

Groups	Body Weight (gms)	
	Before Treatment	**After Treatment**
Group-I	90.00 ± 8.16	93.00±1.63
Group-II	170.00±0.00	146.67±2.84
Group-III	131.67±6.94	155.00±9.43
Group-IV	140.00±6.72	168.00±0.19
Group-V	156.00±9.43[ab]	125.00±12.75[ab]
Group-VI	160.00±8.16[ab]	129.67±2.05[ab]
Group-VII	169.18±1.1 [a]	155.00±2.15[ac]

Values are expressed as mean ± SD of six rats on each group, P<0.05. a - comparison between normal control with treatment groups I, II, and III is significant at 5% level. b - comparison between HLD control with treatment groups I and II is significant at 5% level. c - Comparison between diabetic control with treatment group III is significant at 5% level.

Weight gain was observed in HLD control rats. Significant (P<0.05) decrease in body weight of plant extract treated HLD rats (G V and G VI) were observed but were not significant in dose-dependent manner **Table 4**. The alloxan mediated bodyweight reduction was significantly improved by the 50% hydroethanolic extract (500 mg/kg b.w.) treatment.

Effect on Fasting Blood Glucose: A marked increase in fasting blood glucose level was observed in diabetic control rats. In HLD fed rats, the effect of plant extract at a dose of 400 mg/kg b.w was highly significant than the 200 mg/kg b.w dose **Table 5.**

The 500 mg/kg b.w. dose level restored the fasting blood glucose level of diabetic rats to G I rats level.

Glibenclamide produced a significant reduction in blood glucose levels.

TABLE 5: EFFECT OF PLANT EXTRACT ON FASTING BLOOD GLUCOSE (mg/dl)

Groups	0 day	7th day	14th day	21st day	28th day
Group-I	89.0 ± 12.0	92.0 ± 7.5	90.0 ± 4.01	91.0 ± 5.02	90.0 ± 4.58
Group-II	382.52 ± 7.5	398.0 ± 13.0	367.03 ± 5.02	386.0 ± 11.23	342.0 ± 9.14
Group-III	400.0 ± 5.1	331.67 ± 2.62	265.33 ± 4.11	218.33 ± 7.36	180.8 ± 5.60
Group-IV	185.0 ± 9.1	177.67 ± 7.33	190.80 ± 5.60	186.67 ± 7.33	192.32 ± 7.19
Group-V	201.67 ± 9.6^{ab}	195.0 ± 4.9^{ab}	182.67 ± 4.9^{ab}	177.67 ±7.0^{ab}	157.67 ± 7.3^{ab}
Group-VI	208.0 ± 2.9^{ab}	182.0 ± 9.42^{ab}	156.67 ±7.0^{ab}	117.51 ± 7.5^{ab}	95.82 ± 5.36^{ab}
Group-VII	380.11 ± 8.2^{ac}	321.02 ± 1.6^{ac}	270.0 ± 4.0^{ac}	193.0 ± 3.27^{ac}	115.57 ± 4.0^{ac}

Values are expressed as mean ± SD of six rats on each group, P<0.05. a - comparison between normal control with treatment groups I, II and III is significant at 5% level. b - comparison between HLD control with treatment groups I and II is significant at 5% level. c - Comparison between diabetic control with treatment group III is significant at 5% level.

The plant extract effectively lowered the blood glucose level in diabetic and HLD fed conditions equal to glibenclamide treated and normal control animals. The results of this study are in accordance with the earlier reports on *Lannea edulis* [21], *Hibiscus rosasinensis* flower [22], *C. batatas* [23], *Cynodon dactylon pers* [24].

Effect of Plant Extract on Lipid Parameters:

Effect on Total Cholesterol: The diabetic control rats showed a significant (P<0.05) increase in Total Cholesterol (TC) level **Fig. 1**. There was a reduction in cholesterol levels in glibenclamide-treated animals (G III).

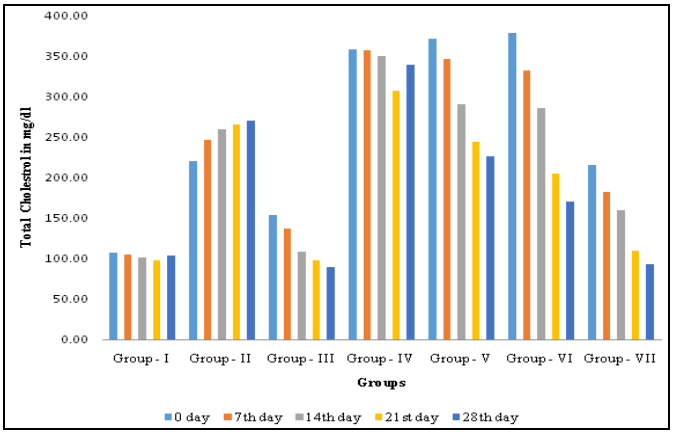

FIG. 1: EFFECT OF PLANT EXTRACT ON TOTAL CHOLESTEROL (mg/dl)

HLD Treatment groups at a dose of 200 and 400 mg/kg b.w showed a significant reduction of cholesterol levels in a dose-dependent manner.

The oral administration of 500 mg/kg b.w. dose to diabetic rats decreased the cholesterol level by 15%, 26%, 49% and 51% at each weekly interval. At the 3rd week of treatment, about 50% reduction in cholesterol level was observed in 500 mg/kg b.w plant extract treated diabetic, and 400 mg/kg b.w treated HLD rats.

Effect on Triglyceride: The diabetic rats showed a significant (P<0.05) increase in Triglyceride (TG) level throughout the experimental period. In glibenclamide and 500 mg/kg b.w. plant extract treated diabetic rats (G III) TG level was reduced to below the normal rats (GI) level **Fig. 2**.

There was no considerable difference in TG levels found in HLD control rats. In 200 mg/kg b.w dose-treated HLD rats significant (P<0.05) reduction of TG level was found in the first two weeks (17, 47%), but later days of treatment would not reduce TG level much significantly, whereas 400 mg/kg b.w plant extract treated HLD rats showed drastic lowering of (27%, 52%, 63%) TG level up to 3 weeks of treatment.

On 4th week the extracts had produced a significant lowering effect on TG level when compared to the previous weeks effect. Plant extract dose of 400 mg/kg b.w. restored the TG level of group VI rats to the level seen in normal control rats (G I).

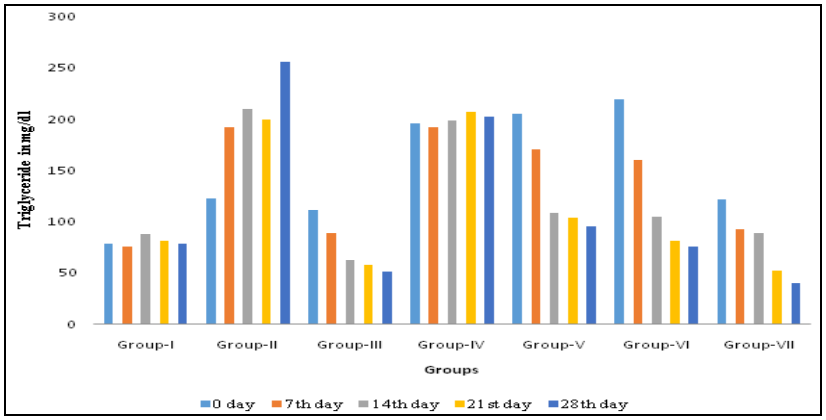

FIG. 2: EFFECT OF PLANT EXTRACT ON TRIGLYCERIDE (mg/dl)

Effect on HDL-Cholesterol: Glibenclamide treated animals (G III) showed improvement in HDL-C levels after the treatment period **Table 6**. In 200 and 400 mg/kg b.w. treated HLD rats, the HDL-C level was increased on 2nd, 3rd and 4th weeks (57%, 65%, 77%, and 74%, 85%, 111%), respectively. 500 mg/kg b.w. dose treatment to diabetic rats, the HDL-C level increased significantly (24%, 45%, 67%, and 100%).

TABLE 6: EFFECT OF PLANT EXTRACT ON HDL-CHOLESTEROL (mg/dl)

Groups	Day-0	Day-7	Day-14	Day-21	Day-28
Group-I	41.0 ± 1.00	39.0 ± 1.00	38.0 ± 0.0	36.0 ± 0.0	38.0 ± 1.7
Group-II	16.5 ± 2.50	15.0 ± 0.0	14.0 ± 0.0	12.0 ± 0.0	10.0 ± 1.7
Group-III	19.0 ± 5.35	24.33 ± 4.92	39.0 ± 7.79	53.0 ± 2.16	46.0 ± 0.0
Group-IV	20.07 ± 0.00	19.52 ± 0.172	18.15 ± 0.19	22.75 ± 0.10	21.55 ± 1.0
Group-V	19.0 ± 1.70 [a]	19.83 ± 3.30 [a]	30.67 ± 0.94[ab]	31.33 ± 2.49 [ab]	33.6 ± 3.09 [ab]
Group-VI	18.0 ± 2.45 [a]	21.0 ± 5.72 [ab]	31.33 ± 3.30 [ab]	33.33 ± 3.09 [ab]	38.0 ± 2.52 [ab]
Group-VII	16.82 ± 1.41 [a]	20.82 ± 0. 15 [ab]	24.4 ± 1.96 [ab]	28.0 ± 1.00 [ab]	33.6 ± 0.28 [ab]

Effect on VLDL-Cholesterol: Administration of plant extract to HLD fed rats, and diabetic rats showed a lowering of VLDL-C level in animals. A similar effect was also found in glibenclamide-treated animals. Treatment with 400 mg/kg b.w. dose produced a marked reduction of 200 mg/kg b.w. dose in HLD fed rats **Table 7**. In normal control rats (G I), no alteration in VLDL-C level was observed throughout the study.

TABLE 7: EFFECT OF PLANT EXTRACT ON VLDL-CHOLESTEROL (mg/dl)

Groups	Day-0	Day-7	Day-14	Day-21	Day-28
Group-I	24.80 ± 1.60	26.30 ± 2.10	23.40 ± 3.80	23.60 ± 2.00	24.00 ± 2.30
Group-II	30.60 ± 1.20	32.40 ± 3.00	36.00 ± 4.00	440.00 ± 4.10	43.20 ± 4.16
Group-III	22.40 ± 4.55	20.87 ± 2.62	17.60 ± 1.53	12.60 ± 1.53	10.53 ± 2.47
Group-IV	33.91 ± 1.00	34.86 ± 0.183	34.00 ± 6.61	35.60 ± 4.20	34.12 ± 4.17
Group-V	34.93 ± 2.38 [a]	32.13 ± 3.89 [a]	26.00 ± 2.27[ab]	20.73 ± 1.64 [ab]	19.20 ± 2.07 [ab]
Group-VI	35.00 ± 4.67 [a]	30.13 ± 7.59 [ab]	21.67 ± 3.18 [ab]	16.33 ± 1.70 [ab]	15.20 ± 2.34 [ab]
Group-VII	30.00 ± 0.65 [a]	27.20 ± 5.10 [ab]	22.40 ± 0.12 [ab]	18.40 ± 1.83 [ab]	15.20 ± 2.34 [ab]

Effect on LDL-Cholesterol: The dose of 500 and 400 mg/kg b.w of plant extract produced significant ($P<0.05$) decrease in LDL-C level when compared to glibenclamide and 200 mg/kg b.w dose of plant extract, respectively **Table 8**. In diabetic control (G II) rats increase in LDL-C level was found. Similar kind of lipid component TC, TG, LDL-C, VLDL-C lowering effect and HDL-C improving effect was also reported with other plants such as *Sphaeranthus indcus* Linn [25], *Syzygium cumini* and *Cinnamon zeylanicum* [26], *Lannea edulis* [21].

TABLE 8: EFFECT OF PLANT EXTRACT ON LDL-CHOLESTEROL (mg/dl)

Groups	Day-0	Day-7	Day-14	Day-21	Day-28
Group-I	44.20 ± 0.0	39.70 ± 5.10	38.60 ± 6.20	32.90 ± 3.50	39.00 ± 2.25
Group-II	137.10 ± 8.90	166.6 ± 10.55	173.00 ± 9.68	213.00 ± 6.49	236.80 ± 6.75
Group-III	51.93 ± 22.97	43.47 ± 26.64	38.40 ± 9.60	26.47 ± 9.92	22.47 ± 7.92
Group-IV	303.0 ± 4.18	306.15 ± 14.58	290.0 ± 9.20	297.89 ± 5.48	292.00 ± 1.00
Group-V	307.07 ± 29.1[ab]	294.87 ± 22.3[ab]	268.3 ± 17.99[ab]	232.27 ± 23.2[ab]	192.8 ± 8.94[ab]
Group-VI	349.33 ± 16.7[ab]	279.53 ± 35.8[ab]	232.33 ± 23.1[ab]	158.0 ± 17.11[ab]	116.8 ± 5.46[ab]
Group-VII	130.25 ± 0.12[a]	123.60 ± 3.56[ac]	115.0 ± 6.52[ac]	81.30 ± 0.82[ac]	78.72 ± 0.09[ac]

DISCUSSION: Medicinal plants play an important role in developing potent therapeutic agents. Plant-derived drugs came into use in modern medicine through the uses of plant material as an indigenous cure in folklore or traditional systems of medicine [27]. The phytochemical screening of crude extract of *Barleria cristata* L. leaf revealed the presence of various bioactive components. The disease-curing properties of medicinal plants are due to various secondary metabolites. Thus, the preliminary screening tests are useful in detecting bioactive principles and may lead to the discovery and development of new drugs. This plant's antidiabetic and antilipidemic activity may be due to the presence of different phytochemicals [1].

An acute toxicity study of 50% hydroethanolic extract did not show any significant signs (or) symptoms of toxicity in normal rats proving their high safety for long-term oral treatment. Alloxan was one of the usual substances used for the induction of diabetes mellitus. It has a destructive effect on the β cells of the pancreas. Glibenclamide was an oral sulphonylurea antidiabetic preparation and was widely used as a standard drug in antidiabetic studies. Administration of plant extract to diabetic and HLD rats reduced the body weight confirming its lowering effects on lipid content. Plants with hypoglycemic activity act through multiple mechanisms, such as improving insulin sensitivity and insulin secretion. Administration of *Barleria cristata* L. leaf extract to diabetic and HLD fed rats showed a significant reduction in blood glucose level and lipid parameters, which confirms its hypoglycemic and hypolipidemic activity. The abnormally high level of serum lipid is mainly due to a decrease in lipolytic hormones' action on fat depots. In normal conditions, insulin activates the enzyme lipoprotein lipase, which hydrolyses triglycerides. However, in diabetic state, lipoprotein lipase is not activated due to insulin deficiency resulting in hypertriglyceridemia [28,] and insulin deficiency is also associated with hypercholesterolemia due to metabolic abnormalities. In the present study, the diabetic rats showed hypercholesterolemia and hyper-triglyceridemia compared with those in normal rats. In the plant extract treated diabetic and HLD fed animal groups, TC and TG levels were significantly ($P<0.05$) decreased [29]. It is known that the level of glycemic control is the major determinant of serum TG level. Several investigators demonstrated that near normalization of blood glucose level resulted in a significant reduction in plasma cholesterol and triglycerides levels [30].

In-plant extract-treated HLD rat's lipid components, TC, TG, LDL-C levels were reduced significantly. Similarly, HDL-C, a protective cholesterol level, was increased. These effects may be due to the low activity of cholesterol biosynthetic enzymes or increased lipolysis. In the present study significant decrease in serum fasting blood glucose and lipid components – TC, TG, VLDL – C, LDL – C with an increase in body weight and HDL – C levels were observed. The high lipid diet-fed animals produced a dose-related hypolipidemic effect.

CONCLUSION: The present study results showed that hydroethanolic leaf extract of *Barleria cristata* L. had produced better antihyperglycemic and antihyperlipidemic activity.

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