



CODEN [USA]: IAJPBB
7750

ISSN : 2349-

INDO AMERICAN JOURNAL OF PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

<https://doi.org/10.5281/zenodo.22997507>

Available online at: <http://www.iajps.com>

Research Article

EXPLORING THE ANTIDIABETIC POTENTIAL OF *CROSSANDRA INFUNDIBULIFORMIS* FLOWER EXTRACT IN STREPTOZOTOCIN-INDUCED DIABETES

Chandana A^{*1}, Mrs. Ahalyadevi K H², Dr. Suresha B S³, Dr. T balasubramanian⁴

¹Department Of Pharmacology, Bharathi College Of Pharmacy,
Bharathinagara, Karnataka, India.

²Asst.professor, Department Of Pharmacology, Bharathi College Of Pharmacy,
Bharathinagara, Karnataka, India.

³Professor And Head, Department Of Pharmacology, Bharathi College Of Pharmacy,
Bharathinagara, Karnataka, India.

⁴Principal, Department Of Pharmacology, Bharathi College Of Pharmacy,
Bharathinagara, Karnataka, India.

Abstract:

Aim: The present study was undertaken to evaluate the antidiabetic potential of the ethanolic flower extract of *Crossandra infundibuliformis* (CIFEE) in streptozotocin-induced diabetic Wistar albino rats.

Materials and Methods: The flowers of *Crossandra infundibuliformis* were extracted with ethanol and evaluated for acute oral toxicity according to OECD guideline 423. Diabetes was induced in overnight-fasted Wistar albino rats by a single intraperitoneal injection of streptozotocin (45 mg/kg). The animals were divided into normal control, diabetic control, CIFEE-treated groups receiving 200 and 400 mg/kg, and a standard drug group receiving glibenclamide (5 mg/kg). Treatments were administered orally for 21 days. Fasting blood glucose and body weight were recorded during the experimental period. At the end of treatment, serum total cholesterol, triglycerides, HDL, LDL and VLDL levels were estimated.

Results: The acute oral toxicity study showed no mortality or apparent signs of toxicity up to 2000 mg/kg, indicating an acute oral LD₅₀ greater than 2000 mg/kg under the conditions of the study. CIFEE produced a progressive reduction in fasting blood glucose levels over the 21-day treatment period. On day 21, blood glucose levels were reduced to 157.3 ± 10.26 mg/dL and 124.6 ± 9.83 mg/dL with CIFEE at 200 and 400 mg/kg, respectively, compared with 258.3 ± 15.82 mg/dL in diabetic control rats. CIFEE also improved the diabetes-associated lipid abnormalities by reducing total cholesterol, triglycerides, LDL and VLDL levels while increasing HDL levels. The 400 mg/kg dose generally produced greater improvement than the 200 mg/kg dose. The effect on body weight was not consistently dose dependent.

Conclusion: The findings demonstrate that the ethanolic flower extract of *Crossandra infundibuliformis* possesses promising antihyperglycaemic and lipid-modulating activity in streptozotocin-induced diabetic rats, with the 400 mg/kg dose showing greater effects across most biochemical parameters. Further studies are warranted to elucidate the underlying mechanisms and identify the active phytoconstituents responsible for these effects.

Keywords: *Crossandra infundibuliformis*, ethanolic flower extract, antidiabetic activity, streptozotocin, fasting blood glucose, lipid profile.

Corresponding author:

Chandana A*,

Contact no:8660556463

E-mail Id: chandana718@gmail.com

QR CODE



Please cite this article in press Chandana A et al., Exploring The Antidiabetic Potential Of *Crossandra Infundibuliformis* Flower Extract In Streptozotocin-Induced Diabetes., Indo Am. J. P. Sci, 2026; 13(09).

INTRODUCTION:

Diabetes mellitus is a multifaceted and chronic metabolic condition characterised by elevated blood glucose levels. This occurs due to the body's impaired ability to produce or effectively use insulin, a hormone essential for regulating blood sugar. The condition encompasses three main types: type 1, type 2, and gestational diabetes, each with distinct characteristics and onset patterns. Type 2 diabetes, the most prevalent form, typically develops in adulthood and is strongly associated with lifestyle factors such as obesity and physical inactivity.

Type 1 diabetes is an autoimmune disorder often diagnosed in childhood, where the immune system attacks insulin-producing cells in the pancreas. Gestational diabetes occurs during pregnancy when hormonal changes impair insulin function, leading to elevated blood glucose levels. While it typically resolves after childbirth, it increases the risk of developing type 2 diabetes later in life.

Diabetes can lead to various complications, including cardiovascular disease, kidney damage, nerve damage (neuropathy), and eye disorders. These complications arise from prolonged high blood sugar levels damaging blood vessels and nerves throughout the body. Effective management of diabetes is crucial to prevent or delay these complications.

Treatment strategies for diabetes are multifaceted and tailored to the individual's needs. They may include pharmacological interventions such as oral medications or insulin therapy, dietary modifications to regulate blood sugar levels, regular physical activity to improve insulin sensitivity, and consistent monitoring of blood glucose levels. A comprehensive approach involving healthcare professionals, lifestyle changes, and patient education is essential for optimal diabetes management.^[1]

Crossandra infundibuliformis, a member of the Acanthaceae family, is a well-known tropical ornamental plant commonly called the “Firecracker flower”. Because of its medicinal properties, different parts of this plant are used in the treatment of various diseases^[2]. *Crossandra infundibuliformis* (L.) is a perennial flowering shrub widely used for ornamental purposes, including pot cultivation, flower beds, and loose flowers, and it also has applications in the pharmaceutical field^[3]. The term *Crossandra* originates from the Greek words “krossoi” meaning fringe and “aner” meaning male, referring to the plant’s fringed stamens. Commercial cultivation of *crossandra* is influenced by several factors, including climatic conditions, fertilizer application, and plant spacing. It includes five cultivars—orange, yellow, red, deep orange, and

bluish-flowered types—and the flowers are non-fragrant^[4]. *Crossandra* is often referred to as the butterfly plant because it is a heat-loving tropical species that adds vibrant colour to gardens during the warm months^[5]. It can tolerate high temperatures, enabling it to thrive even under conditions of very high humidity^[6]. It is an erect, evergreen subshrub that grows up to about one metre (3 ft 3 in) tall, bearing glossy leaves with wavy margins and fan-shaped flowers that may appear throughout the year. The flowers are distinctly shaped, with three to five asymmetrical petals, and are borne on quadrangular, pedunculate spikes with tubular stalks about $\frac{3}{4}$ inch long. Flower colours range from the commonly seen orange to salmon-orange, apricot, coral, red, yellow, and even turquoise^[7]. Plants have long served as a valuable source of inspiration for new drug compounds, and plant-based medicines have made significant contributions to human health and well-being^[8].

METHODOLOGY:**EVALUATION OF ANTIDIABETIC ACTIVITY:****Experimental animals:**

Healthy Wistar albino male rats, weighing 180-200g and Healthy Swiss female mice, weighing 20-30g were taken for evaluating antidiabetic activity study. The animals were procured from Vertebrates., Bengaluru. The animals were acclimatized by keeping them in animal house facility of Bharathi College of Pharmacy, Bharathinagara. They were housed in polypropylene cages containing bedding material as husk and maintained under standard husbandry conditions and 12hrs light and 12hrs dark cycle. They were fed with commercial pelleted rat chow with water ad. libitum. The animals were maintained in accordance with CPCSEA guidelines. The Antidiabetic activity studies were conducted after obtaining the approval from Institutional Animal Ethical committee (IAEC) with a reference no. BCP/IAEC/2025/01 dated 12/07/2025.

1.ACUTE ORAL TOXICITY STUDY:

The LD₅₀ value of extract was determined as per OECD Guidelines 423, fixed dose procedure. Sighting study was performed using 1mice for each dose level (5, 50, 300 and 2000 mg/kg). Using the results of sighting study, the starting dose for main study were made. In main study, the test substance was given at one of the four fixed-dose levels (5, 50, 300, and 2000 mg/kg) to five female mice. Based on the derived LD₅₀ value two dose levels (low and High) were taken for the further study to establish antidiabetic activity.

Mode of administration:

The test substance was administered in a single dose by gavage using specially designed mice oral needle.

Animals were fasted 3 h prior to dosing (only food was withheld for 3 h but not water).

Administration of doses:

Paragraph 16 of OECD guideline 423 suggests that the test substance is administered in a single dose by gavage using a stomach tube or a suitable intubation canula. In the unusual circumstance that a single dose is not possible, the dose may be given in smaller fractions over a period not exceeding 24 hours. Paragraph 16 of OECD guideline 423 suggests that Animals should be fasted prior to dosing (e.g. with the rat, food but not water should be withheld over night, with the mouse, food but not water should be withheld for 3-4 hours). Following the period of fasting, the animals should be weighed and the test substance administered. After the substance has been administered, food may be withheld for a further 3-4 hours in rats or 1-2 hours in mice. Where a dose is administered in fractions over a period it may be necessary to provide the animals with food and water depending on the length of the period.

Test substance administration volume:

The administration volume was 1ml/kg body weight of the animal. Based on the body weight of the animal on the day of treatment, the quantity of the test substance was calculated.

Number of animals and dose levels:

Paragraph 18 of OECD guideline 423 suggests that three animals are used for each step. The dose level to be used as the starting dose is selected from one of four fixed levels, 5, 50, 300 and 2000 mg/kg body weight. The starting dose level should be that which is most likely to produce mortality in some of the dosed animals, the procedure that should be followed for each of the starting doses. Paragraph 19 of OECD guideline 423 suggests that when available information suggests that mortality is unlikely at the highest starting dose level (2000 mg/kg body weight), then a limit test should be conducted. When there is no information on a substance to be tested, for animal welfare reasons it is recommended to use the starting dose of 300 mg/kg body weight. Paragraph 20 of OECD guideline 423 suggests that the time interval between treatment groups is determined by the onset, duration, and severity of toxic signs. Treatment of animals at the next dose, should be delayed until one is confident of survival of the previously dosed animals. Paragraph 21 of OECD guideline 423 suggests that exceptionally, and only when justified by specific regulatory needs, the use of additional upper dose level of 5000 mg/kg body weight may be considered. For reasons of animal welfare concern, testing of animals in GHS Category 5 ranges (2000-5000mg/kg) is discouraged and should only be considered when there is a strong likelihood that results of such a test have a direct

relevance for protecting human or animal health or the environment.

Methodology:

Paragraph 22 of OECD Guideline 423 suggests two types of acute oral toxicity tests i.e. limit test and main test. The limit test is primarily used in situations where the experimenter has information indicating that the test material is likely to be nontoxic, i.e., having toxicity below regulatory limit doses. However, in those situations where there is little or no information about its toxicity, or in which the test material is expected to be toxic, only the main test should be performed. Paragraph 23 of OECD Guidelines suggests a limit test at one dose level of 2000 mg/kg body weight may be carried out with six animals (three animals per step). Exceptionally a limit test at one dose level of 5000 mg/kg may be carried out with three animals. If test substance-related mortality is produced, further testing at the next lower level may need to be carried out.

Observation period:

Animals were observed individually after at least once during the first 30 min, periodically during the first 24 h, with special thereafter, for a total of 14 days. All the rats were observed at least twice daily with the purpose of recording any symptoms of ill-health or behavioural changes. Direct observation parameters include tremors, convulsions, salivation, diarrhoea, lethargy, sleep and coma. Skin and fur, eyes and mucous membrane, respiratory, circulatory, autonomic and central nervous systems, somatomotor activity and behavior pattern are the other parameters observed. The time of death, if any, was recorded. After administration of the test substance, food was withheld for further 1-2 h. The number of survivors was noted after 24 h and then these were maintained for a further 14 days with a daily observation.

Test Procedure followed:

Prior to the dosing, the animals were fasted overnight for 24 hours. Following the period of fasting, the fasted body weight of each animal was determined as stated in paragraph 26 of OECD Guidelines 423 and the dose was calculated according to the body weight as per OECD Guidelines 423 and as stated in Paragraph 23 of OECD Guidelines 423. The starting dose of 5 mg/kg body weight of an animal was used. Ethanolic extract of *Crossandra infundibuliformis* flower was orally administered, animals were observed keenly for about 48 hours, within the first 30 minutes time period no morbidity of animals was observed and in the next 4 hours there is also no death of the animals were found in the ethanolic extract of *Crossandra infundibuliformis* flower, all three animals were survived. But there is morbidity in the extracts of *Crossandra infundibuliformis* flower. As there is no

mortality was indexed in the ethanolic extracts of *Crossandra infundibuliformis* flower at the dosage of 5 mg/kg body weight of an animal, the same procedure was again followed with the next three animals, and the results were found same. Since then the dose was brought up to the higher limit and a dose of 2000 mg/kg body weight of an animal was introduced into the second selected group under same laboratory conditions and were fasted for overnight and the dose was given.

2. Induction of diabetes:

Rats were made diabetic with streptozotocin. Diabetic was induced to overnight fasted Wistar Albino rats by single intraperitoneal injection of 45mg/kg of streptozotocin (STZ), freshly dissolved in cold citrate buffer, pH 4.5. Control animals received only citrate buffer. After 5 days of STZ injection, animals with fasting blood glucose above 250 mg/dl will be considered as diabetic and included in the studies [9].

3. Experimental design:

GROUP	TREATMENT
Group 1:	Normal control
Group 2:	Diabetic control (Streptozotocin 45mg/kg)
Group 3:	Diabetic + CIFEE (low dose 200mg/kg)
Group 4:	Diabetic + CIFEE (high dose 400mg/kg)
Group 5:	Diabetic + Standard control (Glibenclamide 5mg/kg)

4. Preparation of Standard drug solution for administration:

The Glibenclamide (5mg/kg) was suspended in distilled water and administered every morning for 21 days by gastric incubation with an oral gavage. During this period the animals in all groups had free access to standard diet and water [10].

5. Measuring fasting blood glucose:

Fasting blood glucose was measured with Control D select simple glucometer after the collection of blood from the tail vein method from overnight fasted rats on day 1st, 7th, 14th and 21st day.

6. Determination of Body weight of rats:

Body weight gain or lost in each experimental rat was measured and recorded on before treatment and after treatment with triple balance.

7. Estimation of Serum biochemical parameters:

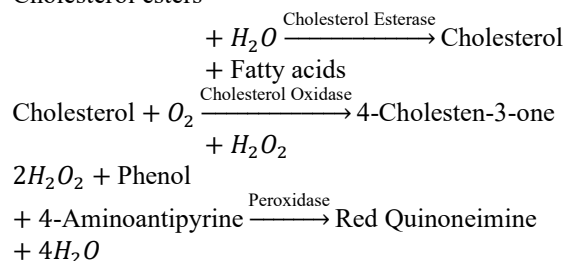
At the end of the experimental period (on 21st day), all five groups of rats were sacrificed after overnight fasting, by anesthetizing with diethyl ether and then blood was collected by cardiac puncture. Serum was separated after coagulated at room temperature for 30 mins and centrifuged at 3000 rpm for 10 mins, which was stored at -20°C until biochemical parameters were determined. Total cholesterol, Serum Triglycerides, High density Lipoprotein, Low density lipoprotein and very low-density lipoprotein level was calculated using Fried Wald equation.

7.1 Estimation Of Serum Total Cholesterol: [11]

Method: Enzymatic, CHOD- PAP Method, End point, single reagent chemistry.

Principle: Cholesterol esterase hydrolyses cholesterol esters into cholesterol and fatty acids.

Cholesterol esters



Reagent: The reagent and standard are ready to use and are stable at 2-8°C up to the expiry date mentioned on the label.

Reagent 1: Buffered enzymes

Standard: Cholesterol (200mg/dl)

Components of the Reagent:

Pipes buffer: 50 mmol/l

Phenol: 24 mmol/L

Sodium Cholate: 0.5mmol/L

Cholesterol Esterase: >180 U/L

Cholesterol Oxidase: > 200 U/L

Peroxidase: >1000 U/L

4-Amino antipyrine: 0.5 mmol/L

Assay procedure:

Wavelength: 505 nm & 630 nm

Path length: 10 mm

Incubation time: 5 min at 37°C.

Measure against reagent blank. One standard and one blank are sufficient for each assay procedures.

Table 1: Serum cholesterol working assay.

Test	Blank	Standard	Sample
Reagent	1000 µL	1000 µL	1000 µL
Standard	-	10 µL	-
Sample	-	-	10 µL

Mix, well and incubate for 5 min at 37 °C. Read absorbance of sample and absorbance of 10 µL standard against reagent blank.

Calculation:

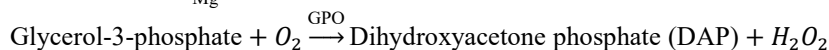
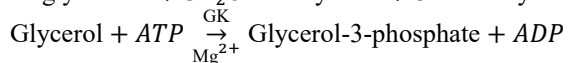
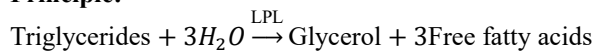
Concentration [C] of Cholesterol in the sample:

$$C = \text{Absorbance of sample} / \text{Absorbance of standard} * 200 \text{ mg/dl}$$

7.2 Estimation Of Serum Triglycerides:

Method: Colorimetric, enzymatic method.

Principle:



Reagent composition:

Buffer pipes (pH -7.0) – 30 mmol/L

4-Aminoantipyrine (4-AAP) – 0.9 mmol/L

ATP – 3.15 mmol/L

Mg+2 – 17 mmol/L

TOPS – 5.3 mmol/L

Potassium ferrocyanates – 10 mmol/L

Glycerol kinase (GK) > 450 U/L

Glycerol-3-Phosphate oxidase (GPO) > 3500 U/L

Peroxidase (POD) – >450 U/L

Lipoprotein lipase (LPL) – 1800 U/L

Triglyceride standard – 200mg/dl

Assay procedure:

Wavelength: 505nm & 630nm

Table 2: Serum triglyceride working assay.

Test	Blank	Standard	Sample
Reagent	1000 µL	1000 µL	1000 µL
Standard	-	10 µL	-
Sample	-	-	10 µL

Mix, well and incubate for 5 min at 37°C. Read absorbance of sample and absorbance of standard against reagent blank.

Calculation:

$$\text{Triglycerides (mg/dl)} = \text{Absorbance of test} / \text{Absorbance of Standard} * \text{Conc. Of Standard (mg/dl)}.$$

7.3 Estimation Of Serum HDL Cholesterol:

Method: Photometric test method

Principle: The reaction between cholesterol other than HDL, and the enzyme for cholesterol assay is suppressed by the electrostatic interaction between polyanions & cationic substances. Hydrogen peroxide is formed by the free cholesterol in HDL by cholesterol oxidase. Oxidative condensation of EMSE and 4-AA is caused by hydrogen peroxide in the presence of peroxidase, and the absorbance of the resulting red-purple Quinone is measured to obtain the cholesterol value in HDL.

Reagent:

Reagent 1 – Enzyme reagent

Reagent 2 – Developer reagent

Calibrator – Lyophilized human serum

Table 3: Serum HDL working assay.

Test	Blank	Callibrator	Sample
Reagent 1	450 µL	450 µL	450 µL
Callibrator	-	5 µL	-
Sample	-	-	5 µL
Mix and incubate for 5 mins at 37°C			
Reagent 2	150 µL	150 µL	150 µL

Mix and incubate for 5 min at 37°C and read absorbance of calibrator & sample against reagent black at 576 & 630nm.

Calculation:

HDL Chol (mg/dl) = Absorbance of Sample / Absorbance of Calibrator * Conc. Of Calibrator (mg/dl).

7.4 Estimation Of Serum LDL Cholesterol:

The LDL levels can be determined by using the following formula:

$$\text{LDL-C} = 0.7516 \times (\text{TC} - \text{HDL-C})$$

7.5 Estimation Of Serum VLDL Cholesterol: [12]

The VLDL (Very Low-Density Lipoprotein) formula is a mathematical equation used to estimate VLDL cholesterol levels based on the values obtained from a lipid profile test. It plays a significant role in assessing cardiovascular health.

Calculation:

$$\text{VLDL Cholesterol} = \text{Triglycerides} / 5$$

STATISTICAL ANALYSIS:

All the values were expressed as mean $\pm$ S.E.M and statistical significance is analyzed using one-way ANOVA followed by Dunnett's multiple comparison test. P values <0.001 were considered as highly significant, <0.01 were considered as moderately significant and <0.05 were considered as significant.

RESULT:

1.Acute oral toxicity study:

The present study conducted as per the OECD guidelines 423 revealed that the extracts did not

produce any mortality throughout the study period of 14 days even when the limit dose was maintained at 2000mg/kg body weight. The oral LD50 was determine being in excess of 2000 mg/kg body weight. So, testing the extracts at a higher dose may not be necessary. All the parameter were observed normal in the ethanolic extract of *Crossandra infundibuliformis*. The animals were orally administered a single dose of 5, 50, 300, 2000 mg/kg body weight. Signs of toxicity and mortality were noted after 1, 4 and 24h of administration of the extract for 14 days. The highest dose administered (2000 mg/kg body weight) did not produce mortality or changes in general behavior of the test animals and reported in **Table**. The medium lethal dose (LD50) of the extracts is higher than 2000 mg/kg body weight and hence, in a single dose administration, the flower extracts had no adverse effect.

LD50 Value: The acute oral toxicity study of the ethanolic flower extract of *Crossandra infundibuliformis*, conducted according to OECD guideline 423, revealed no mortality or apparent signs of toxicity at doses of 5, 50, 300 and 2000 mg/kg body weight during the 14-day observation period. Since no mortality was observed even at the limit dose of 2000 mg/kg body weight, the acute oral LD50 of the extract was considered to be greater than 2000 mg/kg body weight under the conditions of the present study. Based on these observations, the extract demonstrated a favourable acute oral safety profile and the doses selected for the subsequent pharmacological study were considered appropriate.

Table 4: Acute oral toxicity according to OECD-423.

Sl. No	Dose (mg/kg)	Leathality (Ethanolic extract of <i>crossandra infundibuliformis</i> flower)
1.	5mg/kg	0/3
2.	50mg/kg	0/3
3.	300mg/kg	0/3
4.	2000mg/kg	0/3

2.Fasting blood glucose level:

Streptozotocin treatment in rats results in raised blood glucose level which were evident by increase in blood glucose. The diabetic groups treated with Glibenclamide and ethanol extract for 21 days shows a significant dose dependent beneficial effect, when compared with the diabetic control rats.

Group 1: Normal control

Group 2: Diabetic control (Streptozotocin 45 mg/kg)

Group 3: Diabetic + CIFEE (Low dose 200mg/kg)

Group 4: Diabetic + CIFEE (High dose 400mg/kg)

Group 5: Diabetic + Standard control (Glibenclamide 5mg/kg)

Table 5: Effect of CIFEE on fasting blood glucose level in streptozotocin induced diabetic rats.

Group	Blood glucose levels (mg/dL) (Mean $\pm$ SEM)			
	1 st Day	7 th Day	14 th Day	21 st Day
Group 1	84.12 $\pm$ 1.58	83.26 $\pm$ 1.72	84.91 $\pm$ 1.24	85.18 $\pm$ 2.31
Group 2	244.6 $\pm$ 8.72	249.1 $\pm$ 5.34 ^a	251.6 $\pm$ 7.86 ^a	258.3 $\pm$ 15.82 ^a
Group 3	250.8 $\pm$ 6.41	226.4 $\pm$ 7.62 ^c	202.6 $\pm$ 11.84 ^c	157.3 $\pm$ 10.26 ^c
Group 4	249.3 $\pm$ 6.18	215.7 $\pm$ 6.84 ^b	181.9 $\pm$ 10.72 ^b	124.6 $\pm$ 9.83 ^b
Group 5	253.1 $\pm$ 5.76	209.8 $\pm$ 6.15 ^b	174.5 $\pm$ 9.43 ^b	112.8 $\pm$ 8.74 ^b

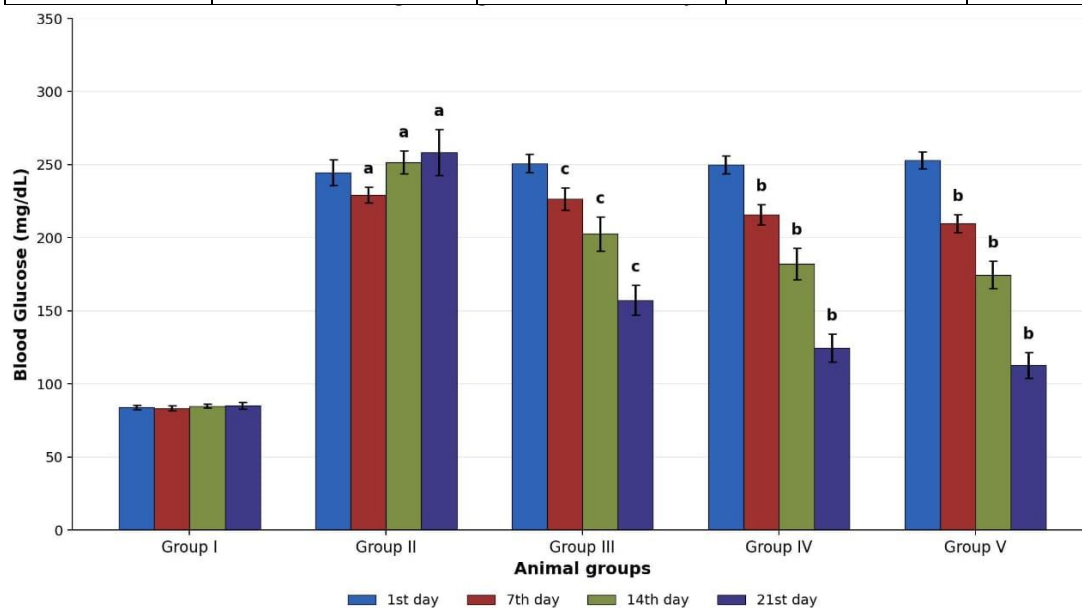


Figure 1: Effect of CIFEE on fasting blood glucose level in Streptozotocin treated diabetic rats.

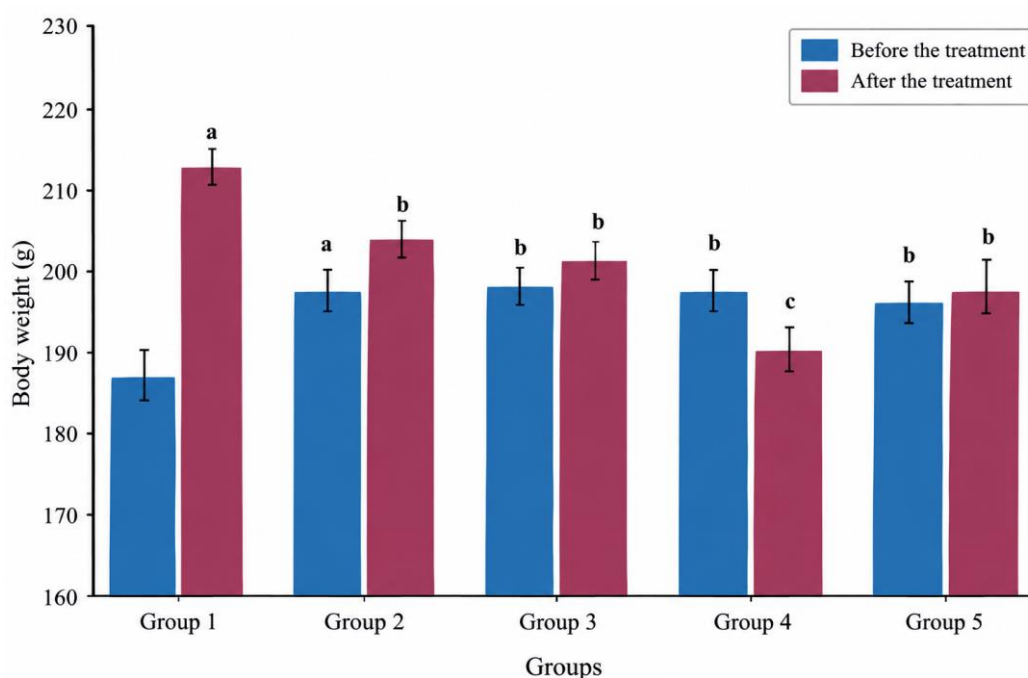
Values are expressed as mean $\pm$ SEM (n=6). The data were statistically analyzed by One way ANOVA followed by Dunnett's test. When compared with normal control, **c** represents significant at $p \leq 0.05$, **b** represents moderate significant at $p \leq 0.01$ and **a** represents highly significant at $p \leq 0.001$.

3.Body weight:

The effect of streptozotocin-induced diabetes and treatment with the ethanolic flower extract of *Crossandra infundibuliformis* on body weight was evaluated before and after the treatment period. The diabetic control group showed a increase in body weight from 196.1 $\pm$ 1.02 g before treatment to 203.7 $\pm$ 1.44 g after treatment. The low-dose extract-treated group (200 mg/kg) showed a slight increase in body weight from 197.2 $\pm$ 1.31 g to 201.0 $\pm$ 1.36 g. In contrast, the high-dose extract-treated group (400 mg/kg) showed a reduction in body weight from 196.3 $\pm$ 1.20 g to 190.2 $\pm$ 0.52 g. The standard-treated group receiving glibenclamide showed a slight increase from 195.0 $\pm$ 1.25 g to 197.1 $\pm$ 1.05 g. Thus, the body-weight response was not consistently dose dependent, with an increase observed in the low-dose group and a decrease observed in the high-dose group.

Table 6: Effect of CIFEE on Body weight on Streptozotocin induced diabetic albino rats.

Group	Mean body weight (g) (mean $\pm$ SEM)	
	Before the treatment	After the treatment
Group 1	186.4 $\pm$ 2.65	212.6 $\pm$ 2.58
Group 2	196.1 $\pm$ 1.02 ^a	203.7 $\pm$ 1.44 ^b
Group 3	197.2 $\pm$ 1.31 ^b	201.0 $\pm$ 1.36 ^b
Group 4	196.3 $\pm$ 1.20 ^b	190.2 $\pm$ 0.52 ^c
Group 5	195.0 $\pm$ 1.25 ^b	197.1 $\pm$ 1.05 ^b

**Figure 2: Effect of CIFEE on Body weight on Streptozotocin induced diabetic albino rats.**

Values are expressed as mean $\pm$ SEM (n=6). The data were statistically analyzed by One way ANOVA followed by Dunnett's test. Where, c represents significant at $p \leq 0.05$, b represents moderate significant at $p \leq 0.01$ and a represents highly significant at $p \leq 0.001$.

4.SERUM BIOCHEMICAL PARAMETERS:

Rats treated with Streptozotocin developed a significant diabetic stage observed as elevated serum levels like TC, TGs, LDL and VLDL when compared to normal control and HDL level where decreased. Treatment with Glibenclamide and ethanol extracts showed a significant dose dependent beneficial effect on lipid profile.

Table 7: Effect of CIFEE on lipid profile on Streptozotocin induced diabetic albino rats.

Group	Biochemical parameters (mg/dl)				
	TC	TG	HDL	LDL	VLDL
Group 1	128.72 $\pm$ 10.64	118.46 $\pm$ 7.42	72.23 $\pm$ 2.03	44.51 $\pm$ 7.68	23.69 $\pm$ 1.47
Group 2	224.41 $\pm$ 14.38 ^a	186.57 $\pm$ 6.93 ^a	56.12 $\pm$ 2.18 ^a	127.39 $\pm$ 11.13 ^a	37.31 $\pm$ 1.28 ^a
Group 3	165.29 $\pm$ 11.27 ^b	144.68 $\pm$ 8.21 ^b	65.14 $\pm$ 1.89 ^b	73.64 $\pm$ 9.14 ^b	28.92 $\pm$ 1.63 ^b
Group 4	146.83 $\pm$ 9.72 ^c	128.35 $\pm$ 7.68 ^c	68.92 $\pm$ 1.78 ^c	56.31 $\pm$ 7.42 ^c	25.67 $\pm$ 1.21 ^c
Group 5	139.27 $\pm$ 8.91 ^c	121.62 $\pm$ 6.34 ^c	70.38 $\pm$ 2.04 ^c	49.72 $\pm$ 6.51 ^c	24.32 $\pm$ 1.18 ^c

4.1 Estimation of serum total cholesterol:

Diabetic control rats showed a serum total cholesterol (TC) level of 224.41 ± 14.38 mg/dL measured on day 21. This was significantly higher ($P \leq 0.001$) when compared with the serum TC level of normal control rats (128.72 ± 10.64 mg/dL).

Diabetic rats treated with the standard drug Glibenclamide (5 mg/kg) showed a serum TC level of 139.27 ± 8.91 mg/dL when measured on day 21. This was significantly lower ($P \leq 0.001$) when compared with the serum TC level of diabetic control rats (224.41 ± 14.38 mg/dL).

Treatment with ethanolic extract of *Crossandra infundibuliformis* flower at doses of 200 mg/kg and 400 mg/kg p.o., once daily, showed serum TC levels of 165.29 ± 11.27 mg/dL and 146.83 ± 9.72 mg/dL, respectively, when measured on day 21. The reduction in serum TC was significant ($P \leq 0.01$ and $P \leq 0.001$, respectively) when compared with diabetic control rats (224.41 ± 14.38 mg/dL).

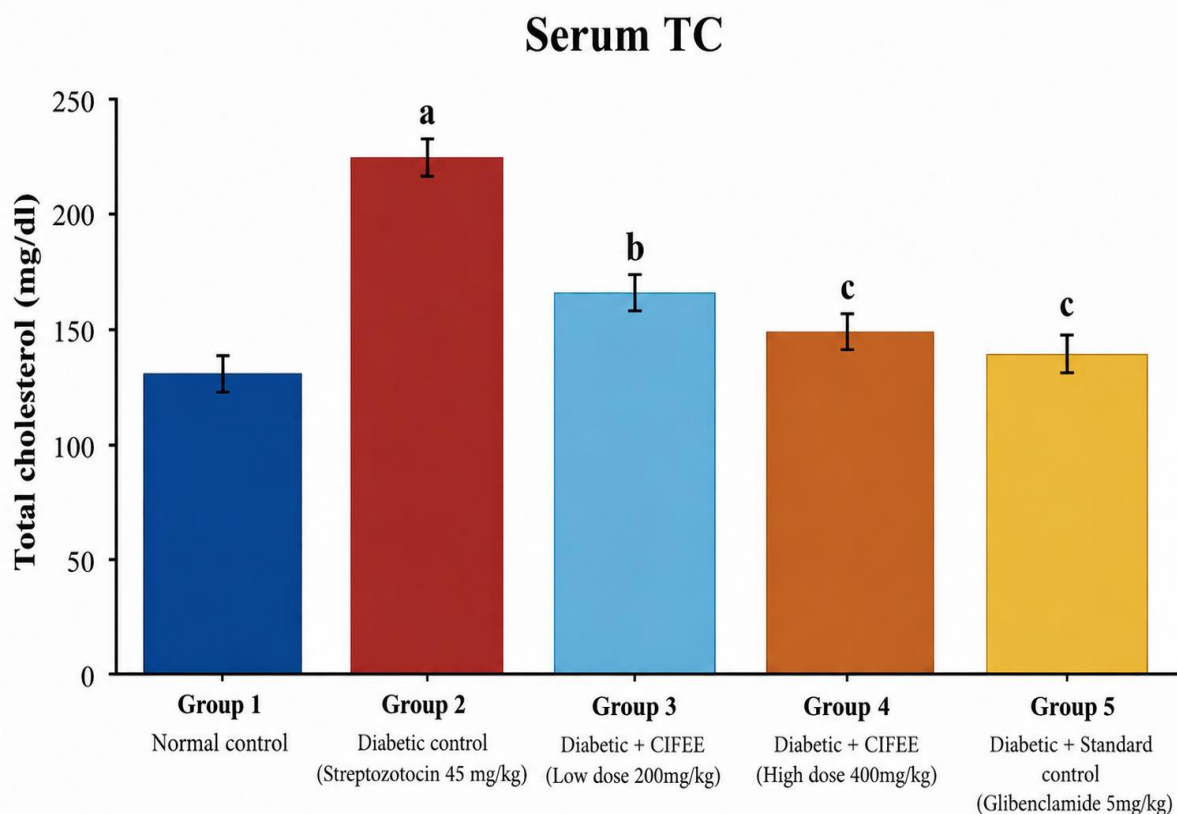


Figure 3: Effect of CIFEE on serum TC level in Streptozotocin treated diabetic rats.

Where, **c** represents significant at $p \leq 0.05$, **b** represents moderate significant at $p \leq 0.01$ and **a** represents highly significant at $p \leq 0.001$.

4.2 Estimation of serum triglycerides:

On day 21, the diabetic control rats (Group II) showed a markedly elevated serum triglyceride level of 186.57 ± 6.93 mg/dL, which was significantly higher ($P \leq 0.001$) compared with the normal control rats (Group I), which showed a serum TG level of 118.46 ± 7.42 mg/dL.

The standard-treated rats (Group V), administered Glibenclamide (5 mg/kg, p.o.), showed a serum TG level of 121.62 ± 6.34 mg/dL on day 21. This was significantly lower ($P \leq 0.001$) compared with the diabetic control group (186.57 ± 6.93 mg/dL).

The rats treated with ethanolic extract of *Crossandra infundibuliformis* at a low dose (Group III) showed a serum TG level of 144.68 ± 8.21 mg/dL, whereas those treated with the high dose (Group IV) showed a serum TG level of 128.35 ± 7.68 mg/dL on day 21. Both treatment groups exhibited a significant reduction in serum TG levels compared with the diabetic control group. The reduction was moderately significant ($P \leq 0.05$) in the low-dose group and highly significant ($P \leq 0.01$) in the high-dose group.

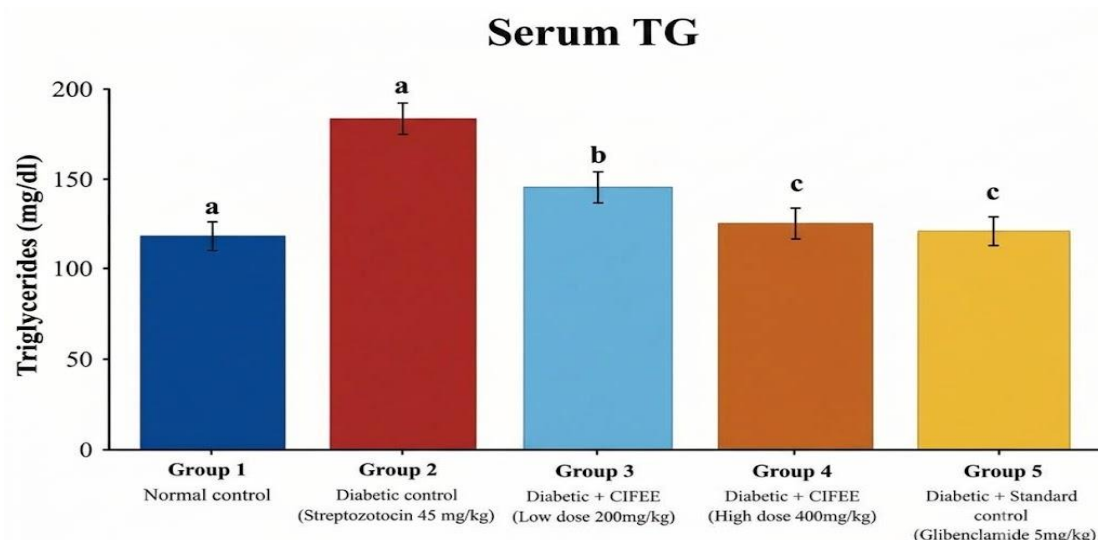


Figure 4: Effect of CIFEE on serum TG level in Streptozotocin treated diabetic rats.

Where, **c** represents significant at $p \leq 0.05$, **b** represents moderate significant at $p \leq 0.01$ and **a** represents highly significant at $p \leq 0.001$.

4.3 Estimation of serum HDL cholesterol:

On day 21, the diabetic control rats (Group II) showed a serum HDL level of 56.12 ± 2.18 mg/dL, which was significantly lower ($P \leq 0.001$) compared with the normal control rats (Group I), which showed a serum HDL level of 72.23 ± 2.03 mg/dL.

The standard-treated rats (Group V), administered Glibenclamide (5 mg/kg, p.o.), showed a serum HDL level of 70.38 ± 2.04 mg/dL on day 21. This was significantly higher ($P \leq 0.001$) compared with the diabetic control group (56.12 ± 2.18 mg/dL).

The rats treated with ethanolic extract of *Crossandra infundibuliformis* at a low dose (Group III) showed a serum HDL level of 65.14 ± 1.89 mg/dL, whereas the high-dose group (Group IV) showed a serum HDL level of 68.92 ± 1.78 mg/dL on day 21. Both treatment groups showed a significant increase in serum HDL levels compared with the diabetic control group. The increase was significant ($P \leq 0.05$) in the low-dose group and highly significant ($P \leq 0.01$) in the high-dose group.

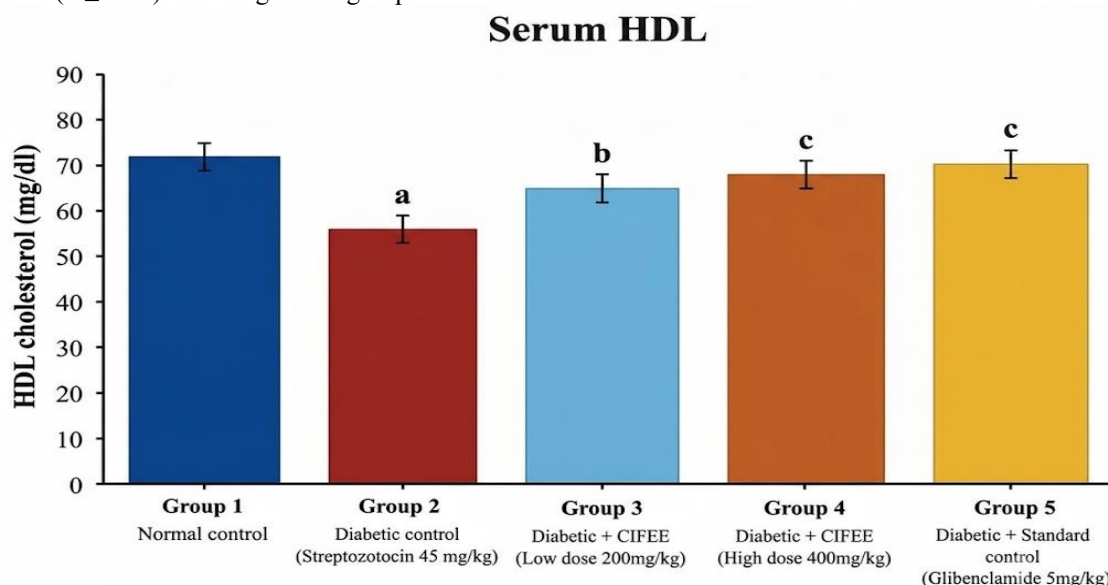


Figure 5: Effect of CIFEE on serum HDL level in Streptozotocin treated diabetic rats.

Where, **c** represents significant at $p \leq 0.05$, **b** represents moderate significant at $p \leq 0.01$ and **a** represents highly significant at $p \leq 0.001$.

4.4 Estimation of serum LDL cholesterol:

On day 21, the diabetic control rats (Group II) showed a markedly elevated serum LDL level of 127.39 ± 11.13 mg/dL, which was significantly higher ($P \leq 0.001$) compared with the normal control rats (Group I), which showed a serum LDL level of 44.51 ± 7.68 mg/dL.

The standard-treated rats (Group V), administered Glibenclamide (1 mg/kg, p.o.), showed a serum LDL level of 49.72 ± 6.51 mg/dL on day 21. This was significantly lower ($P \leq 0.001$) compared with the diabetic control group (127.39 ± 11.13 mg/dL).

The rats treated with ethanolic extract of *Crossandra infundibuliformis* at a low dose (Group III) showed a serum LDL level of 73.64 ± 9.14 mg/dL, whereas the high-dose group (Group IV) showed a serum LDL level of 56.31 ± 7.42 mg/dL on day 21. Both treatment groups exhibited a significant reduction in serum LDL levels compared with the diabetic control group. The reduction was significant ($P \leq 0.01$) in the low-dose group and highly significant ($P \leq 0.001$) in the high-dose group.

Serum LDL

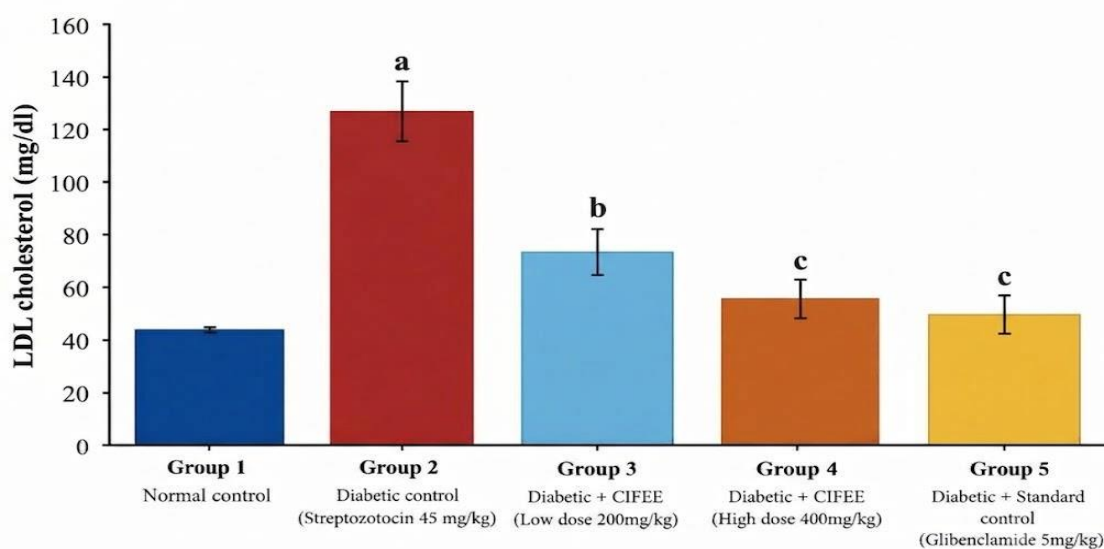


Figure 6: Effect of CIFEE on serum LDL level in Streptozotocin treated diabetic rats.

Where, **c** represents significant at $p \leq 0.05$, **b** represents moderate significant at $p \leq 0.01$ and **a** represents highly significant at $p \leq 0.001$.

4.5 Estimation of serum VLDL cholesterol:

On day 21, the diabetic control rats (Group II) showed a markedly elevated serum VLDL level of 37.31 ± 1.28 mg/dL, which was significantly higher ($P \leq 0.001$) compared with the normal control rats (Group I), which showed a serum VLDL level of 23.69 ± 1.47 mg/dL.

The standard-treated rats (Group V), administered Glibenclamide (5 mg/kg, p.o.), showed a serum VLDL level of 24.32 ± 1.18 mg/dL on day 21. This was significantly lower ($P \leq 0.001$) compared with the diabetic control group (37.31 ± 1.28 mg/dL).

The rats treated with ethanolic extract of *Crossandra infundibuliformis* at a low dose (Group III) showed a serum VLDL level of 28.92 ± 1.63 mg/dL, whereas the high-dose group (Group IV) showed a serum VLDL level of 25.67 ± 1.21 mg/dL on day 21. Both treatment groups exhibited a significant reduction in serum VLDL levels compared with the diabetic control group. The reduction was significant ($P \leq 0.05$) in the low-dose group and highly significant ($P \leq 0.01$) in the high-dose group.

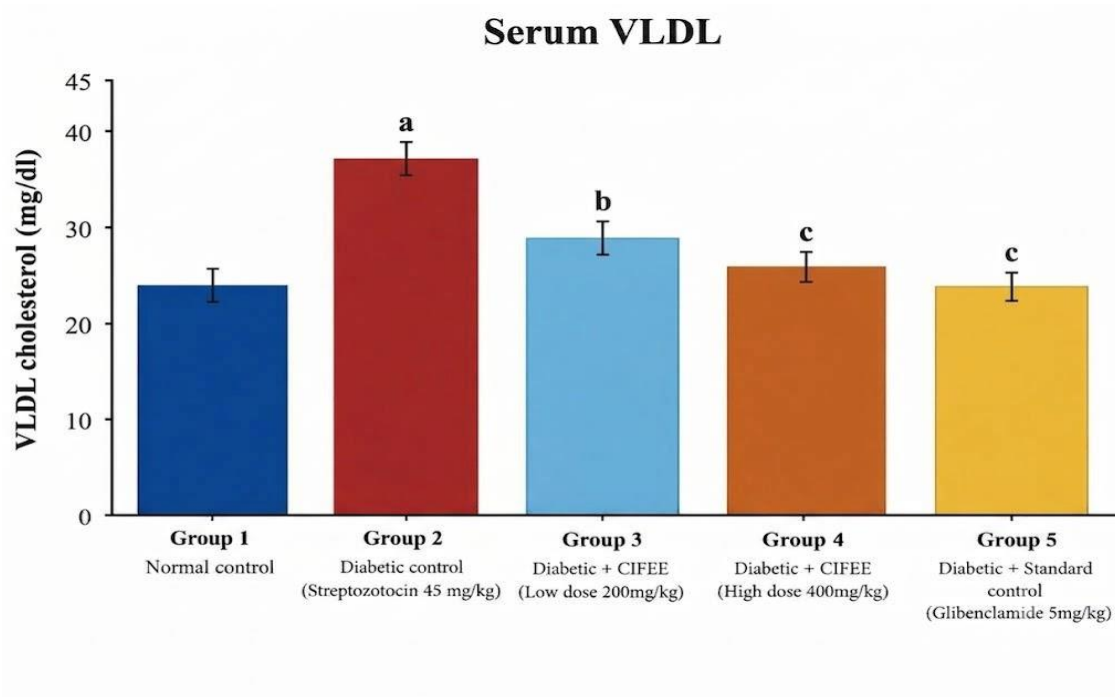


Figure 7: Effect of CIFEE on serum VLDL level in Streptozotocin treated diabetic rats.

Where, **c** represents significant at $p \leq 0.05$, **b** represents moderate significant at $p \leq 0.01$ and **a** represents highly significant at $p \leq 0.001$.

DISCUSSION

The present study was undertaken to evaluate the antidiabetic potential of the ethanolic flower extract of *Crossandra infundibuliformis* (CIFEE) in streptozotocin-induced diabetic rats. The study evaluated the acute oral safety of the extract, its effect on fasting blood glucose, body weight, and serum lipid parameters following 21 days of treatment. The findings demonstrated that CIFEE produced beneficial effects on glycaemic status and diabetes-associated alterations in lipid metabolism. The acute oral toxicity study conducted according to OECD guideline 423 demonstrated that CIFEE was well tolerated at the tested doses. No mortality or apparent signs of toxicity were observed at doses of 5, 50, 300 and 2000 mg/kg body weight during the 14-day observation period. Since no mortality was observed even at the limit dose of 2000 mg/kg, the acute oral LD₅₀ was considered to be greater than 2000 mg/kg under the conditions of the present study. These findings indicate a favourable acute oral safety profile of the extract and provided a basis for selecting the experimental doses used in the subsequent pharmacological study.

Streptozotocin administration produced a marked elevation in fasting blood glucose in the diabetic control group throughout the experimental period. The diabetic control group showed an increase in blood glucose from 244.6 ± 8.72 mg/dL on day 1 to 258.3 ± 15.82 mg/dL on day 21, confirming the development and persistence of the diabetic state. In contrast, treatment with CIFEE produced a progressive reduction in fasting blood glucose. The

200 mg/kg dose reduced the glucose level from 250.8 ± 6.41 mg/dL on day 1 to 157.3 ± 10.26 mg/dL on day 21, whereas the 400 mg/kg dose reduced it from 249.3 ± 6.18 mg/dL to 124.6 ± 9.83 mg/dL. The standard drug glibenclamide produced a reduction to 112.8 ± 8.74 mg/dL. Thus, CIFEE demonstrated a dose-related improvement in fasting blood glucose, with the 400 mg/kg dose showing a greater reduction than the 200 mg/kg dose.

The reduction in fasting blood glucose observed following CIFEE treatment suggests that the extract possesses antihyperglycaemic activity in streptozotocin-induced diabetic rats. The progressive response observed over the 21-day treatment period further supports the beneficial effect of repeated administration. The higher-dose group showed a greater reduction in blood glucose than the low-dose group, indicating a dose-associated response within the tested dose range. However, the present findings establish the observed pharmacological effect without determining the precise molecular mechanism responsible for the antihyperglycaemic activity.

Body weight was also evaluated as an additional parameter of the diabetic condition and treatment response. The normal control group increased in body weight from 186.4 ± 2.65 g to 212.6 ± 2.58 g during the study period. The diabetic control group increased from 196.1 ± 1.02 g to 203.7 ± 1.44 g. The 200 mg/kg CIFEE-treated group showed a slight increase from 197.2 ± 1.31 g to 201.0 ± 1.36 g. In contrast, the 400 mg/kg group showed a reduction from 196.3 ± 1.20 g to 190.2 ± 0.52 g, while the

glibenclamide-treated group showed a slight increase from 195.0 ± 1.25 g to 197.1 ± 1.05 g. Therefore, the body-weight response to CIFEE was not consistently dose dependent, and the reduction observed in the 400 mg/kg group should not be interpreted as weight gain.

Diabetes induced by streptozotocin was also associated with substantial alterations in serum lipid parameters. The diabetic control group exhibited increased total cholesterol, triglycerides, LDL and VLDL levels, together with a reduction in HDL compared with the normal control group. On day 21, total cholesterol increased from 128.72 ± 10.64 mg/dL in the normal control group to 224.41 ± 14.38 mg/dL in the diabetic control group. Treatment with CIFEE reduced total cholesterol to 165.29 ± 11.27 mg/dL at 200 mg/kg and 146.83 ± 9.72 mg/dL at 400 mg/kg. The standard-treated group showed a value of 139.27 ± 8.91 mg/dL. These findings indicate that CIFEE improved the elevated total cholesterol associated with the diabetic state, with a greater reduction observed at the higher dose.

A similar pattern was observed for serum triglycerides. The diabetic control group showed a markedly elevated triglyceride level of 186.57 ± 6.93 mg/dL compared with 118.46 ± 7.42 mg/dL in the normal control group. Following CIFEE treatment, triglyceride levels decreased to 144.68 ± 8.21 mg/dL at 200 mg/kg and 128.35 ± 7.68 mg/dL at 400 mg/kg. The standard-treated group showed a triglyceride level of 121.62 ± 6.34 mg/dL. Thus, both doses of CIFEE reduced the elevated triglyceride concentration, with the higher dose producing a greater reduction.

The HDL findings are particularly important because the diabetic control group showed a decrease in HDL compared with the normal control group. HDL decreased from 72.23 ± 2.03 mg/dL in normal rats to 56.12 ± 2.18 mg/dL in diabetic control rats. Treatment with CIFEE increased HDL to 65.14 ± 1.89 mg/dL at 200 mg/kg and 68.92 ± 1.78 mg/dL at 400 mg/kg. The glibenclamide-treated group showed an HDL level of 70.38 ± 2.04 mg/dL. Therefore, CIFEE produced an improvement in the reduced HDL concentration associated with diabetes, with the higher dose producing a greater increase.

The LDL concentration was markedly elevated in the diabetic control group, increasing from 44.51 ± 7.68 mg/dL in normal rats to 127.39 ± 11.13 mg/dL in diabetic rats. CIFEE treatment reduced LDL to 73.64 ± 9.14 mg/dL at 200 mg/kg and 56.31 ± 7.42 mg/dL at 400 mg/kg. The standard-treated group showed an LDL concentration of 49.72 ± 6.51 mg/dL. The reduction in LDL following CIFEE treatment was therefore more pronounced at the higher dose and approached the value observed in the normal control and standard-treated groups.

The VLDL concentration also showed a similar pattern. Diabetic control rats exhibited an increased

VLDL level of 37.31 ± 1.28 mg/dL compared with 23.69 ± 1.47 mg/dL in normal control rats. Treatment with CIFEE reduced VLDL to 28.92 ± 1.63 mg/dL at 200 mg/kg and 25.67 ± 1.21 mg/dL at 400 mg/kg. The standard-treated group showed a value of 24.32 ± 1.18 mg/dL. These observations indicate that CIFEE attenuated the diabetes-associated elevation in VLDL, with the higher dose producing a greater reduction.

Overall, the findings demonstrate that 21-day administration of CIFEE produced improvements in fasting blood glucose and several serum lipid abnormalities in streptozotocin-induced diabetic rats. The extract reduced total cholesterol, triglycerides, LDL and VLDL while increasing the reduced HDL concentration observed in diabetic animals. The higher dose of 400 mg/kg generally produced a greater improvement than the 200 mg/kg dose across the biochemical parameters evaluated. The findings therefore indicate that the ethanolic flower extract of *Crossandra infundibuliformis* possesses promising antihyperglycaemic and lipid-modulating activity in the experimental diabetic model used in the present study. Further studies involving larger sample sizes, mechanistic investigations and isolation of active phytoconstituents would be useful to establish the mechanisms underlying these observed effects.

SUMMARY:

The present study was undertaken to evaluate the antidiabetic potential of the ethanolic flower extract of *Crossandra infundibuliformis* (CIFEE) in streptozotocin-induced diabetic rats. The acute oral toxicity study conducted according to OECD guideline 423 showed that the extract did not produce mortality or apparent signs of toxicity at doses up to 2000 mg/kg body weight during the 14-day observation period, indicating an acute oral LD50 greater than 2000 mg/kg.

Administration of streptozotocin produced a marked diabetic condition, as evidenced by elevated fasting blood glucose and adverse changes in serum lipid parameters. Treatment with CIFEE at doses of 200 and 400 mg/kg for 21 days produced a progressive reduction in fasting blood glucose levels. The reduction was greater with the 400 mg/kg dose, which decreased blood glucose to 124.6 ± 9.83 mg/dL compared with 157.3 ± 10.26 mg/dL at 200 mg/kg, while the glibenclamide-treated group showed 112.8 ± 8.74 mg/dL.

The effect of CIFEE on body weight was not consistently dose dependent. The 200 mg/kg-treated group showed a slight increase in body weight, whereas the 400 mg/kg group showed a reduction in body weight during the treatment period. Therefore, the body-weight findings should be interpreted separately from the dose-dependent biochemical effects observed in the study.

The extract also improved the altered lipid profile associated with streptozotocin-induced diabetes. CIFEE treatment reduced total cholesterol, triglycerides, LDL and VLDL levels compared with the diabetic control group. The higher dose of 400 mg/kg generally produced a greater reduction than the 200 mg/kg dose. In addition, the decreased HDL level observed in diabetic control rats was increased following treatment with CIFEE, with the higher dose producing a greater improvement.

Overall, the findings indicate that the ethanolic flower extract of *Crossandra infundibuliformis* exhibited a favourable acute oral safety profile and demonstrated antihyperglycaemic and lipid-modulating effects in streptozotocin-induced diabetic rats. The observed improvements were more pronounced at the 400 mg/kg dose, suggesting that CIFEE has potential as a source of bioactive constituents with beneficial effects against experimental diabetes. Further studies are required to establish the mechanisms responsible for these effects and to identify the active phytoconstituents.

CONCLUSION:

The present study demonstrated that the ethanolic flower extract of *Crossandra infundibuliformis* (CIFEE) possesses promising antidiabetic activity in streptozotocin-induced diabetic rats. The extract showed a favourable acute oral safety profile, with no mortality or apparent signs of toxicity observed up to 2000 mg/kg body weight, indicating an acute oral LD₅₀ greater than 2000 mg/kg under the conditions of the study.

Treatment with CIFEE at 200 and 400 mg/kg for 21 days produced a marked reduction in fasting blood glucose levels, with the higher dose showing a greater reduction. The extract also improved diabetes-associated lipid abnormalities by reducing total cholesterol, triglycerides, LDL and VLDL levels, while increasing the reduced HDL level observed in diabetic control rats.

Overall, the findings suggest that *Crossandra infundibuliformis* flower extract has potential antihyperglycaemic and lipid-modulating effects in experimental diabetes. The effects observed at 400 mg/kg were generally more pronounced than those at 200 mg/kg. Further investigations are warranted to determine the active phytoconstituents and underlying mechanisms responsible for these pharmacological effects and to establish the therapeutic potential of the extract.

REFERENCES:

- Nadhiya J, Vijayalakshmi MK, Showbarnikhaa S. A Brief Review on Diabetes Mellitus. Journal of Pharma Insights and Research. 2024;2(1):117-21.

- Pulipati S, Vagdevi G, Sai Prudhvi D, Srinivasa Babu P. Evaluation of Phytochemical And Antimicrobial Properties Of Crossandra Infundibuliformis (L) Nees Flower Extract. International Journal of Biological & Pharmaceutical Research.4(8);2013:588-591.
- Mahesh Reddy D, Safeena SA, Chandrashekar N, Srinivas PT, Naveen Kumar P, Arivalagan M, Sonavane P. Deciphering genetic diversity and population structure in Crossandra (Crossandra infundibuliformis L.) genotypes based on SSR markers. Genetic Resources and Crop Evolution. 72(8);2025:9985-10000.
- Beese S, Sarvanan SS. Studies on effect of plant growth regulators on plant growth and flower yield of crossandra (Crossandra infundibuliformis L.) var. Arka ambara. Int J Chem Stud. 8(6);2020:1560-1567.
- Vasantha G, Bhargavi D, Yashodha A, Sharmila Roy N, Shaik SA. A plant review on Crossandra infundibuliformis. 52(1);2022:375-383.
- Sharmila N, Gomathi N. Antibacterial, Antioxidant activity and Phytochemical studies of Crossandra infundibuliformis leaf extracts. International Journal of Phytomedicine. 3(2);2011:151.
- Satheesh KG, Reddy GS, Mujahid SK, Ashwini T. Extraction, Phytochemical Studies and In-Vitro Screening of the Leaves and Flowers of Crossandra infundibuliformis against Mycobacterium tuberculosis. Asian Journal of Research in Pharmaceutical Science. 8(4);2018:247-252.
- Kumar SA, Sumalatha K, Lakshmi S. Aphrodisiac Activity of Crossandra infundibuliformis (L.) on Ethanol induced Testicular Toxicity in male rats. Pharmacologyonline. 2;2010:812-817.
- Pandit R, Phadke A, Jagtap A. Antidiabetic effect of Ficus religiosa extract in streptozotocin-induced diabetic rats. Journal of ethnopharmacology. 2010;128(2):462-466.
- Mutalik S, Udupa N. Formulation development, in vitro and in vivo evaluation of membrane controlled transdermal systems of glibenclamide. J Pharm Pharm Sci. 2005;8(1):26-38.
- VLDL Cholesterol Calculator <https://www.mdapp.co/vldl-cholesterol-calculator-452/>
- Munshi RP, Joshi SG, Rane BN. Development of an experimental diet model in rats to study hyperlipidemia and insulin resistance, markers for coronary heart disease. Indian j pharmacol. 2014;46(3):270-276.