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RESEARCH ARTICLE

Unravelling The Hypolipidemic and Anti-Inflammatory Potential of *Caralluma Fimbriata*: A Biochemical and Histological Study in a Rat Model

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A B S T R A C T

Hyperlipidemia is a major cause of the global health burden in terms of cardiovascular diseases. The minimal efficacy and potential adverse effects of conventional therapeutic treatments have triggered a growing interest in phytotherapeutic alternatives. *Caralluma fimbriata*, a succulent plant recognized for its bioactive constituents, has been historically utilized for its metabolic regulation properties. This research was conducted to evaluate the therapeutic potential of *C. fimbriata* extract (CFE) in a rat model of hyperlipidemia. Forty male Sprague-Dawley rats were randomized into four groups (n=10/group), and a 60-day bio-efficacy trial was performed. The induction of hyperlipidemia was done by feeding a high-fat and high-cholesterol (HFHC) diet for 22 days. The GI (negative control), GII (positive control group), GIII (atorvastatin-treated, 10mg/kg body weight), and GIV (CFE-treated, 250mg/kg body weight) were the experimental groups. Physical, biochemical, and histological biomarkers were analyzed. Findings indicated that CFE supplementation (GIV) led to significant improvements in metabolic parameters compared to the positive control and with effects comparable to those of atorvastatin. CFE significantly diminished levels of total cholesterol, triglycerides, low-density lipoprotein, and very low-density lipoprotein, and simultaneously increased high-density lipoprotein concentrations ($P<0.05$), compared to the positive control. Moreover, body weight gain and feed intake were markedly reduced. There were significant improvements in biomarkers of liver and kidney function, along with hematological indices. In the treated groups, reduced hepatic and renal necrosis were revealed by histopathological analysis. These results support the therapeutic potential of CFE as a natural lipid-lowering agent and its role as an alternative and adjunct to other lipid-lowering measures in the management of hyperlipidemia and cardiovascular consequences.

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INTRODUCTION

Hyperlipidemia is defined by the disruption of the metabolism of lipids, which is followed by an increase in the amount of one or more lipids in the blood. Increased total serum cholesterol (TC), triglycerides (TAGs), and low-density lipoproteins (LDL) or reduced levels of high-density lipoproteins (HDL) are common symptoms of dyslipidemia (Subaş *et al.,* 2025). Globally, hyperlipidemia is observed in more than a third of adults, with low HDL in 38.4% that may result in serious cardiovascular disorders (CVDs), such as coronary and atherosclerotic cardiovascular disease (Ballena-caicedo et al., 2025; WHF, 2025). Worldwide, CVDs are the main cause of mortality and morbidity, accounting for 19.1 million deaths in 2022. Global health burden major drivers are metabolic disorders like obesity, diabetes, and dyslipidemia. This trend is especially worrisome in the developing world, such as South Asia, where urbanization, poor dietary habits, and sedentary lifestyles

have contributed to the rising number of non-communicable diseases (Sarfaraz *et al.,* 2021). Hyperlipidemia is characterized by the pathophysiological mark of lipid metabolism disruption, such as lipid synthesis, absorption, transportation, and excretion. The dysregulation of any of these steps can lead to the aberrant lipid accumulation in the blood (Fularski *et al.,* 2024). The World Health Organization (WHO) estimates that over 2.6 million deaths occur annually due to hypercholesterolemia (Iqbal *et al.,* 2024). Despite advances in treatment, associated risks of hyperlipidemia continue to rise, highlighting the dire need for both preventive and long-term management measures (Kushner, 2018).

Pharmaceutical intervention is necessary when lifestyle changes are no longer effective. Traditional lipid-lowering medications include statins, fibrates, nicotinic acids and cholesterol absorption inhibitors. While these drugs demonstrate clinical efficacy, prolonged administration of statins has been linked to various side effects such as hepatic and renal impairment, gastrointestinal disturbances, and other adverse reactions (Parhofer & Laufs, 2023). Consequently, the desire for natural, plant-derived alternatives has increased significantly. WHO estimates that over 80% of the global population continues to rely on herbal remedies for primary healthcare concerns (Xie *et* al., 2024; Khan *et al.,* 2025;). Phytochemicals are gaining attention due to their favourable safety profile and potential medicinal benefits (Ullah R, 2024; Matra *et al.,* 2025; Qadeer *et a*l., 2025; Subaş *et al.,* 2025).

Several plant-based supplements can help lower blood cholesterol and TAGs levels, thereby reducing the risk of CVDs with minimal adverse effects. Among these wild edible plants stands out for its accessibility and therapeutic potential. One such valuable indigenous plant is *Caralluma fimbriata*, a wild edible succulent native to Asia and Southeast Europe. It belongs to the *Asclepiadaceae* family, traditionally known as "chong/choongan" in Pakistan and India (Gujjala *et al.,* 2019). Historically, it was utilized by Indian tribal communities to alleviate their thirst and hunger, termed as "famine food." The phytochemical profile of *C. fimbriata* extract (CFE) contains pregnane glycosides, flavonoids, terpenoids, tannins, saponins, phenolic compounds, and ascorbic acid (Jaswanth *et al.,* 2025). Pregnane glycosides, a class of steroidal chemicals conjugated with sugar moieties, are particularly important for regulating lipid metabolism through the inhibition of fatty acid production (Padwal *et al.,* 2016; Anwar *et al.,* 2022). Previous studies on CFE have reported antihyperglycemic, antioxidant, hepatoprotective, and appetite-suppressing effects attributed to its hypothalamic modulation and cortisol-regulating mechanism (Ashwini and Anitha, 2017*;* Gujjala *et al.,* 2017; Malladi *et al.,* 2017). Furthermore, its anti-obesogenic properties (Kamalakkannan *et al.,* 2010) may lead to a reduced risk of CVDs (Rao *et al.,* 2021). However, there is a lack of comprehensive data exploring the direct hypolipidemic and anti-inflammatory effects of *C. fimbriata* in a well-characterised in vivo model. The novelty of the present study lies in three aspects: evaluation of anti-inflammatory end points, histopathological assessment, and use of high-fat and high-cholesterol (HFHC) to induce hyperlipidemia. Therefore, the study is designed to test the mechanistic hypothesis that HFHC induced metabolic stress promotes hepatic injury and inflammation, and that CFE treatment can attenuate these effects by modulating inflammatory markers and improving histological outcomes. Therefore, the present study aims to explore the therapeutic potential of CFE in a HFHC diet-subjected hyperlipidemic rat model, providing novel insights into its role as a natural intervention for managing hyperlipidemia.

MATERIALS AND METHODS

Procurement of raw material and preparation of *C. fimbriata* extract (CFE): *C. fimbriata* was obtained from the local market in the Kamra Tehsil of Attock, Punjab, Pakistan, and was transferred to the food analysis laboratory at the National Institute of Food Science and Technology, University of Agriculture, Faisalabad, for preservation and further analysis. *C. fimbriata* was cleaned, chopped into pieces, and subsequently ground into a fine powder following an 8-hour drying process at 50 °C in a dehydrator (Harvest Saver dehydrator, model R 5A, USA). The resultant *C. fimbriata* powder was thereafter stored in polyethylene bags until further examination. The analytical-grade chemicals and reagents used in our study were acquired from reputable suppliers such as Sigma-Aldrich (St. Louis, MO, USA) and Merck KGaA, Darmstadt, Germany. The extract of *C. fimbriata* was prepared using a protocol with slight modifications (Rajaram & Suresh Kumar, 2011). The dried *C. fimbriata* (30g) was subjected to successive extraction with 300 mL of ethanol on a magnetic stirrer for 3 hours at ambient temperature. Thereafter, the extract was filtered through Whatman filter paper no. 2, and the extraction process was repeated once with the remaining residue to ensure maximum yield (Shivakumara *et al.,* 2025). The extraction yield was 6.5g from 30g of plant powder (21.67% w/w). The extract was stored at -20°C in airtight amber vials until further use. The extract was concentrated at 40°C for 4 hours to a minimal volume through a rotary evaporator (EYELA Rotary Vacuum Evaporator N-N Series, Tokyo, Japan).

Bioethical compliance and animal study: The hypolipidemic potential of CFE was investigated in a rat model, 40 Sprague-Dawley rats (195-225g) were procured from the Pakistan Council of Scientific and Industrial Research, located in Lahore, Pakistan. Rats were provided with a standard laboratory feed comprising flour (80%), casein (5%), corn oil (10%), minerals (3%), and vitamins (2%) throughout the experiment period. The animals were kept in the controlled room at the National Institute of Food Science and Technology, University of Agriculture, Faisalabad, Pakistan. They were provided a basal diet for the 15-day acclimatization period with environmental surroundings maintained at a temperature of 25±2°C, humidity of 55±5%, and a 12-hours light-dark cycle. Rats had ad libitum access to water and feed throughout the study (AlMasoud *et al.,* 2024). The animals were housed in groups of 5 per cage under controlled conditions. Feed intake was measured at the cage level, and therefore, the

cage was considered the experimental unit for feed intakes and feed efficiency ratio (FER) calculations. Body weight and other biochemical parameters were recorded individually for each rat. CFE was administered once daily via oral gavage in the morning (between 9:00-10:00 am) using distilled water as a vehicle. The gavage volume was maintained at 1mL/100g body weight to ensure uniformity of dosage. The administered dosage was adjusted according to the body weight of each rat, recorded weekly to maintain accurate dose normalization across the whole study. The entire efficacy trial spanned 60 (22 days of induction period and 38 days of treatment) days. The ethical guidelines approved by the Institutional Bio-safety and Bioethics Committee (D#6895/ORIC) on 28-10-2022 were followed during the efficacy trial in accordance with the National Institutes of Health's (NIH Publications No. 8023, amended 1978) guidelines for the use and care of laboratory animals.

Rats were randomly assigned to four experimental groups (n=10/group). The experimental design with animal groups undergoing various dietary interventions is depicted in Fig. 1. The GI (negative control) received a regular diet throughout the trial. Meanwhile, groups GII, GIII, and GIV were fed HFHC diet containing 45% fat and 2% cholesterol. Experimental diets were modified with oil substitutions as shown in Table 1, and administered for 22 days to induce hyperlipidemia (Gujjala *et al.,* 2019). After the induction period, all the HFHC groups were switched back to a regular chow diet. GII (positive control) continued to regular chow diet; GIII (standard drug group) received atorvastatin (10mg/kg body weight), along with the regular diet, and GIV (treatment group) was administered CFE (250mg/kg body weight, orally) alongside the regular diet. Table 1 shows the composition of experimental diets (A. ingredients and B. nutritional composition).

Assessment of physical indicators: Weekly measurements of body weight and feed intake were recorded to evaluate growth performance. Lee index and body mass index (BMI) were calculated accordingly (Rabail *et al.,* 2025). After decapitation of the animals, vital organs such as the heart, kidney, liver, and spleen were excised and weighed. Moreover, the feed efficiency ratio (FER%), along with BMI, and Lee Index, were computed using the formulas as follows

$$FER\% = \frac{\text{Body weight gain (g)}}{\text{Food intake (g)}} \times 100$$

$$BMI = \frac{\text{Body weight (g)}}{\text{Length (cm)}^2}$$

$$\text{Lee index} = \frac{\text{Body weight (g)}^{1/3}}{\text{Body length (cm)} \times 10^3}$$

Assessment of biochemical indicators: At the end of the experiment, rats were anesthetized with isoflurane (2-3%) to induce a deep plane of anesthesia and minimize pain and distress. While under deep anesthesia, blood was collected via cardiac puncture. Immediately following blood collection, euthanasia was completed by decapitation, in accordance with the AVMA Guidelines for Euthanasia of Animals (2020). Blood samples were collected for comprehensive biochemical and hematological analysis. For hematological parameters, samples were stored in EDTA-containing tubes. Serum samples were obtained by collecting blood in serum-separating gel tubes without anticoagulant and allowing them to clot at room temperature for 30 minutes, followed by centrifugation at 4°C for 10 minutes (Karabekir *et al.,* 2024). The investigation comprised an intricate examination of blood and serum samples to assess serum lipid profile, and serum leptin, and blood glucose levels. Furthermore, the liver and renal function tests, as well as inflammatory markers, were performed.

Table 1: Composition of experimental diets a: Ingredients (g/kg)

Ingredients	Basic Chow Diet (g/kg)	HFHC Diet (g/kg)	HFHC (%)
Soybean meal	180	—	—
Maize	620	—	—
Full-fat soya	130.5	—	—
Wheat offal	40	—	—
Bone meal	20.5	—	—
Lysine	3	—	—
Salt	4	—	—
Methionine	2	—	—
Basic chow diet	—	700	70
Cholesterol	—	22	2.2
Vanaspati ghee	—	278	27.8
Total	1000	1000	100

b: Nutritional Composition

Components	Basic Chow (g/kg)	Basic Chow (%)	HFHC(g/kg)	HFHC(%)
Fat	20	2	450	45
Protein	220	22	150	15
Cholesterol	0	0	20	2
Fiber	60	6	40	4
Moisture	120	12	80	8
Ash	80	8	55	5.5
Energy (kcal/kg)	2900	—	4730	—
Energy (kcal/100 g)	29	29	47.3	47.3

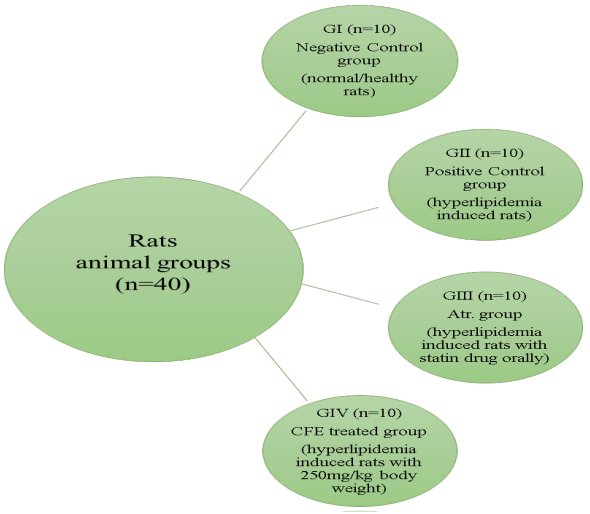

Fig. 1: A diagram illustrating the experimental setup with different rat groups, Atr.: Atorvastatin.

Assessment of lipidemic profile: The serum lipid profiles were evaluated utilizing commercial kits from Sigma Aldrich (St. Louis, Mo, USA) including TAGs, TC, LDL, VLDL, and HDL. A UV spectrophotometer (Perkin Elmer Lambda 40 UV/VIS Spectrophotometer Waltham, MA, USA) measured the samples' absorbance at 505/670 nm,

with values reported in mg/dL (Freidwald *et al.,* 1972). LDL and VLDL cholesterol were determined using the following formulas (Rabail *et al.,* 2022).

$$LDL = TC - HDL - VLDL$$

$$VLDL = \frac{TAGs}{5}$$

Assessment of blood glucose and serum leptin: Fasting blood glucose and serum leptin were assessed via commercially available kits (Gluco- assay kit, Sigma Aldrich, catalog#gago20, St. Louis, MO, USA, and rat leptin ELISA kit Abcam, catalog#ab10884; Cambridge, UK) (Kamalakkannan *et al.,* 2010; Sultan *et al.,* 2012).

Assessment of liver and renal function indicators: Aspartate transaminase (AST), alanine transaminase (ALT), albumin (ALB), and bilirubin were among the liver function parameters measured using Sigma Aldrich kits; St. Louis, MO, USA, following the manufacturer's instructions. Renal function tests, including albumin, creatinine, and blood urea nitrogen (BUN) were also evaluated by using Ogunlana's technique (Ogunlana, 2012).

Assessment of hematological indicators: The impact of CFE consumption on several hematological parameters, including red blood cells (RBCs), white blood cells (WBCs), hemoglobin concentration (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and platelet count, was assessed using an automated hematological analyzer (Mindray B.C-10, Mindray Medical International, China) (Filho *et al.,* 2011; Delwatta *et al.,* 2018). All samples were analyzed in triplicate to ensure reproducibility and standard quality control materials.

Assessment of inflammatory markers: Inflammatory markers, specifically IL6 (interleukin 6) and CRP (C-reactive protein), were assessed using commercially available ELISA kits (IL-6: Sigma-Aldrich, Catalog #RAB0319; CRP: Abcam, Catalog #ab260058) according to the manufacturers' method (Karbiner *et al.,* 2013). Serum dilution of samples was done at 1:2 for IL6 and 1:10 for CRP. The assays were based on Sandwich ELISA principle, and absorbance was measured at 450 nm with microplate reader (BioTek ELx800, USA). All samples were performed in triplicate, with kit-provided quality controls included to ensure assay accuracy and reproducibility.

Assessment of cardiovascular risk indices: The atherogenic, coronary, and cardiovascular risk index was calculated using the following formulas (Famurewa *et al.,* 2017).

$$\text{Atherogenic index (AIP)} = \text{LDL cholesterol/ HDL} - \text{C}$$

$$\text{Coronary index (CRI)} = \text{Total cholesterol/ HDL} - \text{C}$$

$$\text{Cardiovascular index (CVDI)} = \text{Triglyceride/ HDL} - \text{C}$$

Histopathological examination: Upon the decapitation of experimental rats, organs like the liver and kidney were preserved in a 10% formalin solution for structural examination of the tissues. Histological examination of the organs was conducted using the method with some modifications (Ibrahim *et al.,* 2018). The liver and kidney specimens were carefully sectioned into 5-µm-thick slices and affixed onto glass slides. Subsequent staining of the tissue samples was carried out by employing hematoxylin-eosin (H&E), as the sections were swiftly passed through an alcohol series after H&E staining. The resulting slides were examined under a light microscope (MCX 100, Micros Austria).

Statistical Analysis: All measurements were performed in triplicate to get mean values±standard deviation (SD) All the data obtained from single endpoint measurements were subjected to One-way ANOVA followed by Tukey post hoc test to perform a comparison of means at a 95% ($P<0.05$) confidence level using SPSS-16 (IBM, Chicago, IL, USA) (Montgomery, 2017). For repeated measures (body weight and feed intake) a repeated measures ANOVA was performed to account correlations within subjects over time period. The Omni online percentage increase calculator was used to determine the percentage increase or decrease.

$$\text{Effect} = [(\text{Day 38} - \text{Day 1}) \times 100] \div \text{Day 1}$$

RESULTS

The primary outcomes of current research were to analyze the antihyperlipidemic potential of CFE using an animal model, focusing on its ability to lower lipid profile and manage hyperlipidemia, as well as to mitigate inflammatory markers caused by free radicals.

Physical indicators: The efficacy of CFE and Atr. for the various physical parameters (weight gain, feed intake, FER, and organ weights) was evaluated and compared to both negative and positive control groups (Table 2). A significant increase in total body weight gain was observed in the positive control group (85.80±3.45g) compared to the negative control group (49.34±2.50g), representing a 73.89% rise. Treatment with Atr. and CFE significantly reduced weight gain (52.20±2.81g and 48.80±2.78g, respectively), showing reductions of 39.16% and 43.12% relative to the positive control group. Results show that CFE has stronger anti-obesogenic potential associated with the diseased model of the positive control group.

Daily feed intake was highest in the positive control (32.80±1.99g/day), significantly surpassing the negative control (25.06±1.09g/day). Atr. administration reduced feed intake to 26.94±1.26 g/day, indicating a 17.85% decrease, while the group receiving CFE showed a more pronounced reduction (24.65±1.18g/day), corresponding to a 24.86% decrease as compared to the positive control. A similar trend was observed in FER. The positive control group exhibited the highest FER value (6.89±0.32%), indicating improved feed-to-weight conversion. Treatment with Atr. (5.10±0.16%) and CFE (5.21±0.37%) significantly decreased FER values by 25.97% and 24.38%, respectively, further corroborating the mitigating effects of Atr. and CFE on excessive weight gain.

No statistically significant difference ($P>0.05$) was found among groups for the Lee index and BMI, although

slight variations were present. The naso-anal length showed a maximum increase in the positive control group (307.7±14.92), indicating a 7.96% increase compared to the negative control (285.0±9.59). Treatment with Atr. and CFE resulted in a moderate reduction (297.9±18.05 and 294.6±11.73) in the Lee index, corresponding to 3.18% and 4.25% decreases, respectively. BMI showed a non-significant decrease in the treatment groups compared to the positive control. The heart-weight and heart percentage of body weight ratio were significantly increased in the positive control group (1.29±0.30g and 0.49±0.12%, respectively). Treatments with Atr. and CFE significantly reduced heart weights (0.83±0.17g and 0.73±0.08g) and heart weight percentage ratio (0.35±0.64% and 0.26±0.30%, respectively).

Liver weights and liver-to-body weight percentage were also significantly higher in the positive control group (5.05±0.27g and 1.66±0.08%, respectively), compared to the negative control (2.78±0.51g and 1.14±0.25%), Atr. and CFE significantly reduced liver weights (2.89±0.21g and 3.07±0.216g), and liver percentage (1.08±0.07% and 1.12±0.08%, respectively).

Kidney weight increased slightly in the positive control group (0.30±0.03g) compared to the negative control (0.29±0.04g), while treatment with Atr. and CFE reduced kidney weights (0.26±0.06g and 0.25±0.01g, respectively). Similarly, kidney-to-body weight percentage was significantly reduced by both treatments compared to the positive control. The spleen weight and its relative weight were comparatively higher in the positive control group than in the negative control. In contrast, CFE treatment notably decreased spleen weight (0.14±0.02g) and spleen percentage of body weight (0.04±0.007%) compared to all other groups *(*P<*0.01*). Overall, the HFHC diet induced significant physical changes, including increased weight gain, FER %, and organ hypertrophy. However, treatment with Atr. and CFE successfully alleviated these alterations, significantly improving metabolic indices. These findings suggest a potential preventive effect of CFE against obesity-related physiological dysfunction.

Biochemical indicators

Serum lipid profiles: The results illustrate various lipid profile parameters (mg/dL) of the rat's blood across different treatment groups (Table 3), highlighting their significant variations between the groups *(*P<0.05*)*. The positive control group revealed significantly elevated TC levels (200.03±8.83mg/dL) compared to the negative control (129.05±5.57mg/dL), indicating higher cholesterol in the hyperlipidemic rats. Both, Atr. group and CFE-treated group showed significant reductions in TC levels (133.95±6.02mg/dL and 139.45±6.50mg/dL, respectively) compared to the positive control group.

Evaluating the outcomes for TAGs of rats subjected to various treatments, the positive control group exhibited significantly elevated TAGs levels compared to the negative control group (251.96±11.89mg/dL vs. 191.44±8.05mg/dL), (P<0.05), indicating the onset of hyperlipidemia. However, both the Atr. and CFE treatment groups showed significant reductions in TAGs levels, (187.51±6.19mg/dL and 193.71±8.67mg/dL, respectively), compared to hyperlipidemic rats.

The results for HDL and LDL showed that the positive control group (GII) had significantly lower HDL levels than the normal rat group (21.34±1.20mg/dL vs. 30.17±1.50mg/dL), indicating the variation in the diseased group of rats. The Atr. group fed with the standard drug had improved lower levels of HDL (28.27±1.8mg/dL). The CFE-treated group significantly increased the level of HDL (26.27±1.22mg/dL) compared to the positive control suggesting the potential of the drug and CFE. Likewise, regarding LDL levels, the positive control group displayed considerably higher levels than the negative control (128.66±5.39mg/dL and 65.59±2.84mg/dL, respectively). However, the Atr. and CFE-treated groups demonstrated a significant decrease in LDL levels (68.18±2.64mg/dL and 74.44±3.7mg/dL) compared to the positive control group. The results demonstrated the effectiveness of Atr. and CFE supplementation in lowering LDL levels.

Consistent with the other lipid parameters, VLDL cholesterol levels were significantly elevated in the positive control group compared to the negative control group (50.39±2.37mg/dL vs. 38.28±0.41mg/dL), indicating dyslipidemia in the diseased rats. VLDL levels were lower in the conventional drug group (37.50±1.24mg/dL) and treatment group (38.74±1.43mg/dL) compared to the positive control group. Overall, the lipid profiles of hyperlipidemic rats were considerably improved by both atorvastatin and CFE interventions, with the effects of the standard medication group being somewhat more noticeable.

Table 2: Efficacy results (mean±SD) for physical parameters of all groups

Physical Parameters	Neg. Control	Pos. Control	Atr.	CFE	F Value	Effect[1]	Effect[2]	Effect[3]
Total wt. gain (g)	49.34±2.50^{a}	85.80±3.45^{c}	52.20±2.81^{b}	48.80±2.78^{a}	363.40**	^73.89	v43.12	v39.16
Wt. gain/day (g)	1.29±0.09^{a}	2.25±0.09^{c}	1.37±0.04^{b}	1.28±0.07^{a}	364.00**	^74.41	v43.11	v39.11
Food intake (g/day)	25.06±1.09^{b}	32.80±1.99^{c}	26.94±1.26^{b}	24.65±1.18^{a}	130.33**	^30.88	v24.84	v17.86
FER %	5.01±0.49^{a}	6.89±0.32^{b}	5.10±0.16^{a}	5.21±0.37^{a}	64.79**	^37.52	v24.38	v25.97
Lee Index	285.0±9.59^{a}	307.7±14.92^{b}	297.9±18.05^{ab}	294.6±11.73^{ab}	4.508NS	^7.96	v4.25	v3.18
BMI	0.180±0.007^{a}	0.207±0.007^{b}	0.202±0.03^{b}	0.197±0.009^{b}	4.712NS	^0.027	v4.83	v2.41
Heart wt. (g)	0.80±0.05^{a}	1.29±0.30^{b}	0.83±0.17^{a}	0.73±0.08^{a}	19.40**	^61.25	v43.41	v35.65
Heart % of body wt.	0.32±0.02^{ab}	0.49±0.12^{c}	0.35±0.64^{b}	0.26±0.30^{a}	16.64**	^53.12	v46.93	v28.57
Liver wt. (g)	2.78±0.51^{a}	5.05±0.27^{c}	2.89±0.21^{ab}	3.07±0.216^{b}	270.69**	^81.65	v39.20	v42.77
Liver % of body wt.	1.14±0.25^{a}	1.66±0.08^{b}	1.08±0.07^{a}	1.12±0.08^{a}	141.77**	^45.614	v32.53	v34.93
Kidney wt. (g)	0.29±0.04^{bc}	0.30±0.03^{c}	0.26±0.06^{ab}	0.25±0.01^{a}	20.35**	^3.448	v35.89	v33.33
Kidney % of body wt.	0.12±0.01^{b}	0.100±0.01^{a}	0.09±0.02^{a}	0.09±0.07^{a}	7.38*	v16.66	v32.33	v32.33
Spleen wt. (g)	0.16±0.03^{b}	0.19±0.02^{b}	0.15±0.02^{a}	0.14±0.02^{a}	7.53**	^18.75	v21.05	v26.31
Spleen % of body wt.	0.06±0.01^{c}	0.09±0.006^{b}	0.05±0.007^{ab}	0.04±0.007^{a}	9.18**	^50.00	v44.44	v55.55

Neg. Control = Negative control, Pos. Control = Positive control, Atr. = Atorvastatin, CFE= *C. fimbriata* extract; Wt. = weight, FER- Food Efficacy Ratio = (Wt. gain/day ÷ Food intake/day) ×100; Body mass index (BMI), Lee index (LI); Effect= [(D38-D1) ÷D1] ×100; ^- % Increase; v- % Decrease, Effect1 (Percentage ^ or v between Neg. and pos. control group), Effect2 (Percentage ^ or v between pos. control group and Atr. group), Effect3 (Percentage ^ or v between pos. control group and CFE group). Means subscripted with the identical letters in columns are not significantly different from each other. *= significant at P<*0.05*. ** = highly significant at P<*0.01*; NS, non-significant at P>*0.05*.

Fasting blood glucose and serum leptin: The positive control group GII showed the highest fasting blood glucose level (99.89±4.28mg/dL) compared to the negative control group GI (81.75±2.94mg/dL), demonstrating hyperglycemia caused by the HFHC diet. Additionally, rats administered atorvastatin (GIII) and CFE supplementation (GIV) had considerably lower blood glucose levels (85.31±3.79mg/dL and 82.45±3.41mg/dL, respectively). These results imply that both treatments effectively reduced hyperglycemia and possess antidiabetic potential.

Similarly, the positive control group (GII) had significantly higher serum leptin concentrations (2.42±0.22ng/mL) than the negative control group (GI) (0.66±0.50ng/mL), indicating increased adiposity. But atorvastatin (GIII) and CFE (GIV) therapy significantly decreased leptin levels (1.66±0.50ng/mL and 1.39±0.20ng/mL, respectively). These findings imply that CFE supplementation may provide a protective effect against leptin dysregulation and glucose, comparable to conventional medication therapy.

Liver and renal function parameters: Table 5 summarizes the results of liver and renal function parameters for the various groups. Significant intergroup differences in ALT and AST levels suggested the changes in liver enzyme levels in response to dietary intervention. The positive control group (GII) exhibited elevated AST and ALT levels (109.18±4.83U/L and 62.94±1.48U/L), as compared to normal rats (GI) (68.36±1.38U/L and 36.74±1.27U/L). However, the standard drug group (GIII) and the CFE-treated group (GIV) had the lowest AST (80.97±3.42U/L and 58.29±1.38U/L), and ALT levels (83.87±4.21U/L and 59.09±1.51U/L, respectively) compared to hyperlipidemic rats. The protective benefits of CFE intervention proved beneficial against liver injury. Additionally, the positive control group (GII) had the highest creatinine level (0.94±0.01mg/dL), indicating renal dysfunction in the absence of intervention, compared to healthy rats (GI), (0.61±0.03mg/dL). The standard drug group (GIII) and the CFE-treated group (GIV) showed decreased creatinine concentrations (0.74±0.02mg/dL and 0.72±0.01mg/dL, respectively). Moreover, albumin levels were significantly lower in GIII (4.21±0.32g/dL) and GIV (3.91±0.43g/dL), in contrast to the positive control group (5.09±0.17g/dL). These results show better renal and liver functions following treatment. Likewise, the positive control group had the greatest BUN concentration (18.45±1.23mg/dL), whereas GIII had the lowest BUN level (15.58±0.34mg/dL), followed closely by GIV (16.04±0.40mg/dL).

Hematological parameters: Table 6 showed significant variations among experimental groups in several blood parameters, including red blood cells (RBCs), hemoglobin (Hb) concentration, hematocrit (Hct), platelet count, mean platelet volume (MPV), white blood cells (WBCs), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). Remarkably, there were no discernible variations in the mean corpuscular volume (MCV) between the groups, indicating that this parameter remained constant throughout the investigation. Hematological parameters, including Hb, RBCs, and HCT, were reduced in the positive control group. Both treatments significantly improved these markers. CFE was particularly effective, increasing Hb levels (13.57 ± 1.12g/dL) compared to the Atorvastatin group (11.77 ± 1.52g/dL) and the positive control (9.97 ± 1.03g/dL) F = 14.26, P<*0.01*). Notably, the positive control group (GII) showed a significant decrease in RBCs (5.20±0.72×106/µL), in contrast to the negative control group (7.65±0.68×106/µL). The RBCs counts in the atorvastatin-treated group (GIII) showed a moderate restoration (7.25±0.61×106/µL), while CFE therapy exhibited the highest RBCs concentration (7.42±0.61×106/µL). This finding highlights that CFE may increase Hb levels, enhancing the blood's capacity to carry oxygen. Moreover, the differences between GII and GIV highlight the beneficial effect of CFE in restoring normal Hb concentrations in rats with induced dyslipidemia. The Hct values of the positive control group were higher (37.64±3.11%). However, the Atr. and CFE-treated groups had Hct values of (46.82±7.73% and 45.47±5.82%, respectively). These findings suggest that although CFE and atorvastatin treatments can lower Hct, the impact is stronger in the CFE-treated group, suggesting a possible role in controlling blood viscosity or enhancing blood flow. Platelet counts were significantly decreased in the positive control group (680±17.34×10³/µL), while Atorvastatin and CFE restored levels (882±21.11×10³/µL and 941±26.49×10³/µL, respectively). MCV showed no significant differences across groups (F = 2.21, ns), indicating no marked impact on red cell volume.

Table 3: Efficacy results (mean±SD) for the serum lipid profile of all rat groups

Parameters	Neg. Control	Pos. Control	Atr.	CFE	F value	Effect[1]	Effect[2]	Effect[3]
TC (mg/dL)	129.05±5.57[a]	200.03±8.83[c]	133.95±6.02[b]	139.45±6.50[b]	1703.4**	^55.00	v33.03	v30.28
HDL (mg/dL)	30.17±1.50[d]	21.34±1.20[a]	28.27±1.81[b]	26.27±1.22[b]	59.62**	v29.26	^32.47	^23.10
LDL (mg/dL)	65.59±2.84[a]	128.66±5.39[c]	68.18±2.64[b]	74.44±3.74[b]	1157.9**	^96.15	v47.00	v42.14
VLDL (mg/dL)	38.28±0.41[a]	50.39±1.37[b]	37.50±1.24[a]	38.74±1.43[a]	637.41**	^31.63	v25.58	v23.11
TAGs (mg/dL)	191.44±8.05[a]	251.96±11.89[b]	187.51±6.19[a]	193.71±8.67[a]	636.85**	^31.61	v25.57	v23.11

Neg. Control = Negative control, Pos. Control = Positive control, Atr. = Atorvastatin, CFE= *C. fimbriata* extract, total cholesterol (TC), triglycerides (TAGs), high-density lipoproteins (HDL), low-density lipoproteins (LDL), very low-density lipoproteins (VLDL), D=Days; Effect= [(D38-D1) ÷D1] ×100; ^- % Increase and v- % Decrease. Effect1 (Percentage ^ or v between Neg. and pos. control group), Effect2 (Percentage ^ or v between pos. control group and Atr. group), Effect3 (Percentage ^ or v between pos. control group and CFE group). Means subscripted with the identical letters in columns are not significantly different from each other. *= significant at P<*0.05*. ** = highly significant at P<*0.01*; NS, non-significant at P>*0.05*.

Table 4: Efficacy results (mean±SD) for glucose and serum leptin of all groups

Parameters	Neg. Control	Pos. Control	Atr.	CFE	F value	Effect[1]	Effect[2]	Effect[3]
Glucose (mg/dL)	81.75±2.94[a]	99.89±4.28[c]	85.31±3.79[b]	82.45±3.41[b]	137.83**	^14.59	v17.45	v22.18
SL (ng/mL)	0.66±0.50[a]	2.42±0.22[c]	1.66±0.35[b]	1.39±0.20[b]	92.91**	v31.40	v42.56	^266.66

Neg. Control = Negative control, Pos. Control = Positive control, Atr. = Atorvastatin, CFE= *C. fimbriata* extract, Serum leptin (SL), D= Days; Effect = [(D38-D1) ÷D1] ×100; ^- % Increase; v- % Decrease. Effect1 (Percentage ^ or v between Neg. and pos. control group), Effect2 (Percentage ^ or v between pos. control group and Atr. group), Effect3 (Percentage ^ or v between pos. control group and CFE group). Means subscripted with the identical letters in columns are not significantly different from each other. *= significant at P<*0.05*. ** = highly significant at P<*0.01*; NS, non-significant at P>*0.05*.

Table 5: Efficacy results (mean±SD) for liver and renal function parameters of all groups

Parameters	Neg. Control	Pos. Control	Atr.	CFE	F value	Effect[1]	Effect[2]	Effect[3]
AST (U/L)	68.36±1.38[a]	109.18±3.83[d]	80.97±1.42[b]	83.87±1.47[c]	461.31**	^59.7	v26.10	v23.45
ALT (U/L)	36.74±1.27[a]	62.94±1.48[c]	58.29±1.38[b]	59.09±1.51[b]	1027.4**	^71.31	v7.38	v6.11
Creatinine (mg/dL)	0.61±0.03[a]	0.94±0.01[d]	0.74±0.02[b]	0.72±0.01[c]	327.6**	^54.09	v21.27	v23.40
Albumin g/dL	3.02±0.01[a]	5.09±0.17[c]	4.21±0.32[b]	3.91±0.43[b]	61.08**	^68.54	v17.28	v23.18
BUN (mg/dL)	9.58±0.59[a]	18.45±1.23[c]	15.58±0.34[b]	16.04±0.40[b]	460.35**	^92.58	v15.55	v13.06

Neg. Control = Negative control, Pos. Control = Positive control, Atr. = Atorvastatin, CFE= *C. fimbriata* extract, blood urea nitrogen (BUN), alanine transaminase (ALT), aspartate transaminase (AST), D-Days; Effect= [(D38-D1) ÷D1] ×100; ^- Percentage Increase; v- Percentage Decrease. Effect1 (Percentage ^ or v between Neg. and pos. control group), Effect2 (Percentage ^ or v between pos. control group and Atr. group), Effect3 (Percentage ^ or v between pos. control group and CFE group). Means subscripted with the identical letters in columns are not significantly different from each other. *= significant at P<*0.05*. ** = highly significant at P<*0.01*; NS, non-significant at P>*0.05*.

Table 6: Efficacy results (mean±SD) for hematological parameters of all groups

Parameters	Neg. Control	Pos. Control	Atr.	CFE	F value	Effect[1]	Effect[2]	Effect[3]
RBCs (10^6/µL)	7.65±0.68[b]	5.20±0.72[a]	7.25±0.61[b]	7.42±0.61[b]	5.33*	v32.02	^39.42	^42.69
MCV (fL)	56.21±1.07[a]	55.10±1.95[a]	56.39±1.95[a]	54.88±0.98[a]	2.21NS	v1.97	^2.34	v0.39
HCT/PCV (%)	43.09±5.40[a]	37.64±3.11[c]	46.82±7.73[b]	45.47±5.82[b]	23.08**	^18.32	^24.38	^20.80
Platelets (10^3/µL)	1154±24.29[d]	680±17.34[a]	882±21.11[b]	941±26.49[c]	1098**	v41.07	^29.70	^38.38
Hb (g/dL)	12.69±0.92[ab]	9.97±1.03[c]	11.77±1.52[a]	13.57±1.12[b]	14.26**	v21.43	^18.05	^36.10
MCH (pg)	20.28±0.96[a]	22.38±1.05[b]	19.18±2.09[a]	20.11±1.55[a]	8.22**	^10.35	v14.29	v10.14
MCHC (g/dL)	31.75±1.71[ab]	33.86±0.83[d]	32.45±1.19[c]	30.95±0.87[a]	16.48**	^6.64	v4.16	v8.59
WBC (10^3 mm^3)	8.37±0.43[a]	12.94±0.96[c]	9.91±1.14[b]	8.85±1.39[a]	38.21**	^54.59	v23.41	v31.60

Neg. Control = Negative control, Pos. Control = Positive control, Atr. = Atorvastatin, CFE= *C. fimbriata* extract, hemoglobin (Hb), red blood cells (RBCs), hematocrit concentration (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), D- Days; Effect= [(D38-D1) ÷D1] ×100; ^- % Increase; v- % Decrease. Effect1 (Percentage ^ or v between Neg. and pos. control group), Effect2 (Percentage ^ or v between pos. control group and Atr. group), Effect3 (Percentage ^ or v between pos. control group and CFE group). Means subscripted with the identical letters in columns are not significantly different from each other. *= significant at P<*0.05*. ** = highly significant at P<*0.01*; NS, non-significant at P>*0.05*.

Table 7: Efficacy results (mean±SD) for cardiovascular risk indices of all groups

Parameters	Neg. Control	Pos. Control	Atr.	CFE	F value	Effect[1]	Effect[2]	Effect[3]
AIP Index	2.18±0.20[a]	6.06±0.39[d]	2.42±0.23[b]	2.84±0.18[c]	438.9**	^177.98	v60.06	v53.13
CRI Index	4.46±0.30[a]	9.43±0.47[b]	4.75±0.31[b]	5.32±0.25[c]	433.3**	^111.43	v49.62	v43.58
CVDI Index	6.36±0.41[a]	11.86±0.54[c]	6.65±0.43[a]	7.39±0.35[b]	324.4**	^86.47	v44.07	v37.84

Atherogenic index (AIP Index), Coronary risk index (CRI Index), Cardiovascular index (CVDI Index) * D- Days; Effect= [(D38-D1) ÷D1] ×100; ^- % Increase; v- % Decrease. Effect1 (Percentage ^ or v between Neg. and pos. control group), Effect2 (Percentage ^ or v between pos. control group and Atr. group), Effect3 (Percentage ^ or v between pos. control group and CFE group). Means subscripted with the identical letters in columns are not significantly different from each other. *= significant at P<*0.05*. ** = highly significant at P<*0.01*; NS, non-significant at P>*0.05*.

Cardiovascular risk indices: The cardiovascular risk indicators, such as the atherogenic index of plasma (AIP), coronary risk index (CRI), and cardiovascular risk index (CVDI), were examined across the experimental groups (Table 7). The positive control group revealed elevated values of all three indices compared to the negative control group, suggesting a higher risk of cardiovascular disease. Specifically, AIP increased by 177.9 8%, CRI by 111.43%, and CVDI by 86.47%, respectively. By day 38, treatment groups showed significant improvements. In the Atr. group, AIP dropped by 60.06%, followed by 53.13% in the CFE-treated group relative to the positive control group. A similar trend was observed for the CRI, reduced by 49.62% in the standard drug group and 43.58% in the CFE-treated group. Meanwhile, the CVDI decreased by 44.07% in the Atr. group and 37.84% in the CFE-treated group, respectively, compared to the hyperlipidemic rat group. These results support that Atr. and CFE effectively mitigate cardiovascular risk indices.

Inflammatory indicators

Serum IL-6 and CRP: Fig. 2 illustrates the serum concentrations of interleukin-6 (IL-6) and C-reactive protein (CRP) among the experimental groups (P<*0.05*). The positive control group demonstrated elevated concentrations of IL-6 (1.63±0.06pg/mL) and CRP (5.16±0.22mg/L), indicating a heightened inflammatory response. In contrast, the treatment group receiving CFE exhibited significantly reduced levels of IL-6 (0.88±0.03pg/mL) and CRP (4.45±0.04mg/L).

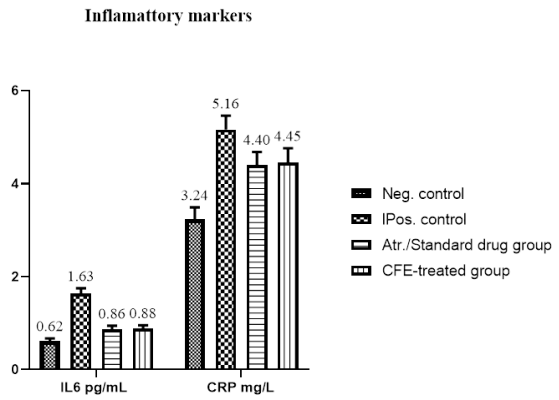

Fig. 2: Effect of inflammatory markers on all groups. Data are presented as a mean value; n=10 rats/group. Neg. Control = Negative control group, Pos. Control = Positive control group, Atr. /Standard drug group=Atorvastatin, CFE-treated group= *C. fimbriata* extract.

Histopathological examination: Histopathological analysis of hepatic tissues (Fig. 3) unveiled that the structural organization of hepatocytes in rats fed a standard diet in GI showed normal liver histology, devoid of pyknotic nuclei, inflammation, and vascular impairment. On the contrary, evaluation of rats in GII revealed cytoplasmic vacuolation, considerable vascular congestion, centrilobular necrosis, and pyknotic nuclei, accompanied by sinusoidal congestion, all of which are indications of hepatocellular damage. Conversely, rats treated with atorvastatin (GIII) exhibited slight

congestion, pyknotic nuclei, and moderate sinusoidal congestion. The treatment group rats (GIV) also displayed a decrease in sinusoidal congestion, vacuolation, and the restoration of hepatocytic architecture.

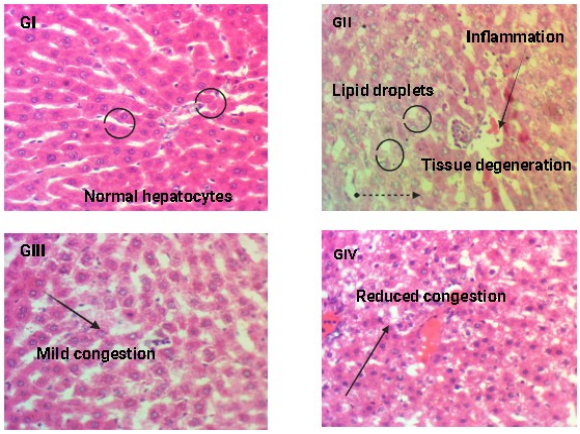

Fig. 3: Liver histology of experimental rat groups. Representative (H & E) stained liver sections from each group. GI (Negative control group), GII (Positive control group), GIII (Atr. /Standard drug group), GIV (CFE-treated group). Images are representative of each group, evaluated in a blinded manner. Scale bar = 50 µm; magnification = 40X.

Fig. 4 illustrates the histopathological alterations in the rat's kidneys in the negative control and dietary treatment groups, indicating that the negative control group (GI) fed a standard diet exhibited normal renal parenchyma architecture. Conversely, rats in the positive control group (GII) exhibited structural changes including glomerular inflammation, vacuolated epithelial linings in glomeruli and renal tubules, and varying degrees of congestion in glomerular capillaries, accompanied by interstitial edema. The renal parenchyma of the Atr. group (GIII) showed moderate glomerular capillary congestion, epithelial vacuolation in renal tubules, and disruptions in Bowman's capsule. The administration of CFE reversed glomerular atrophy and capillary inflammation, although mild glomerular congestion and pyknotic nuclei were observed along with mild shrinkage of the Bowman's capsule.

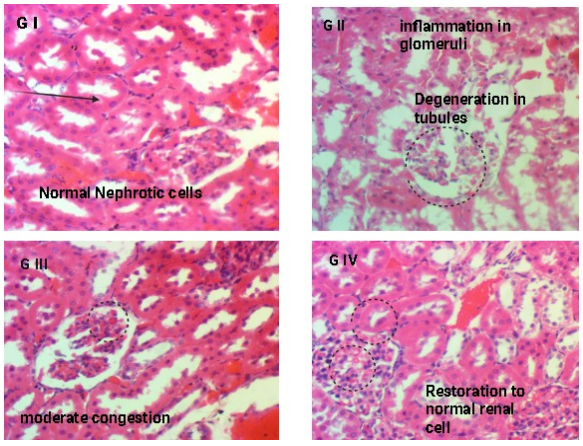

Fig. 4: Kidney histology of experimental rat groups. Representative (H & E) stained kidney sections from each group. GI (Negative control group), GII (Positive control group), GIII (Atr. /Standard drug group), GIV (CFE-treated group). Images are representative of each group, evaluated in a blinded manner. Scale bar = 50 µm; magnification = 40X.

DISCUSSION

The current study systematically assessed the potential of CFE as a treatment for hyperlipidemia in Sprague-Dawley rats fed a HFHC diet. CFE improved physical indicators, lipid profiles, glycemic control, liver and kidney functions, and inflammatory markers. These findings closely paralleled the effects observed in the atorvastatin group, underscoring CFE's promise as a natural alternative to conventional treatments.

In our results, feed intake and weight gain were both significantly reduced in the CFE-treated group compared to the positive control group. This decrease indicates the anorectic potential of CFE. This reduction may be attributed to the presence of pregnane glycosides in CFE, which act on the hypothalamus to regulate appetite by inhibiting ghrelin secretion and Neuropeptide-Y levels (De Leo *et al.,* 2005; Abdel-Sattar & Ali, 2022). A similar reduction in food intake has also been reported in Prader-Willi syndrome rodents administered CFE (Griggs *et al.,* 2018). Likewise, previously published findings also documented comparable appetite-suppressing effects of CFE (Vitalone *et al.,* 2017). The observed decrease in liver weights and improvement in hepatic parameters further support antiobesogenic effects of CFE (Kamalakkannan *et al.,* 2010). These findings may suggest that CFE influences its anti-obesity properties via the modulation of appetite and enhancement of hepatic functionality.

In our results, CFE supplementation significantly improved dyslipidemia by reducing serum TAGs, LDL, and TC levels. These results mirrored the effects of atorvastatin, thereby validating the model and supporting CFE's role in restoring normal lipid profiles. This hypolipidemic effect may be attributed to the presence of pregnane glycosides in CFE, which alter food intake, enhance lipid metabolism, and reduce intestinal fat absorption. By reducing intestinal fat absorption, CFE prevents the accumulation of excessive fat, resulting in decreased levels of TC, LDL, and TAGs (Anwar *et al.,* 2022).

Although the precise mechanisms remain to be fully elucidated, it is proposed that CFE may inhibit citrate lyase, an enzyme involved in fatty acid synthesis activity, thereby reducing malonyl-CoA production (Topiwala & Krishnamurthy, 2013).This pathway is also inhibited and probably promotes the mobilization of existing fat reserves and increases lipid catabolism (Rauf *et al.,* 2022). This effect is similar to that of *Garcinia cambogia*, which also acts on ATP-citrate lyase and its active ingredient, hydroxycitric acid, to lower the availability of acetyl-CoA to de novo lipogenes, and malonyl-CoA mediated inhibition of fatty acid oxidation. CFE and *Garcinia cambogia* are therefore both fat catabolic rather than fat synthesis, which helps to improve lipid profiles and weight management (Sudhakara *et al.,* 2014).

The hypolipidemic effect is correlated with that of Ambadasu, who showed that TC, TAGs, and LDL levels decreased significantly after CFE treatment. Likewise, Gujjala, reported that CFE inhibited lipid abnormalities in HFD-fed Wistar rats (Gujjala *et al.*, 2016). Akram *et al.,* (2023) have also found that CFE has lipid-lowering effects, as he reported *Caralluma edulis* extract in better

serum lipid markers (Akram *et al.*, 2023). Moreover, CFE includes pregnane glycosides that could have a direct effect on adipose tissue by inhibiting the proliferation and maturation of adipocytes (Kamalakkannan *et al.,* 2010). Therefore, these results indicate that CFE pregnane and steroidal glycosides can counteract the negative metabolic consequences caused by the HFHC diet.

In the present study, administration of CFE significantly reduced blood glucose levels in rats fed a 16-week HFHC. This hypoglycemic effect may be attributed to the presence of pregnane and steroidal glycosides, which are known to increase insulin secretion and restrict intestinal glucose absorption (Abdel-Sattar and Ali, 2022; Rao *et al.,* 2021). These findings are consistent with previous research demonstrating the antidiabetic potential of CFE (Gujjala *et al.,* 2016; Ashwini and Anitha, 2017). Supporting this, Poodineh and Nakhaee reported a similar antidiabetic effect using *Caralluma tuberculate* in diabetic rat models (Poodineh and Nakhaee, 2016). Collectively, these findings suggest that phytochemicals such as pregnane glycosides may play a role in enhancing glycemic control and insulin sensitivity, although more mechanistic studies are required to confirm these effects.

Our study revealed that CFE supplementation also reduced serum leptin levels. This finding is consistent with prior research in both animal and human studies (Astell *et al.,* 2013; Sudhakara *et al.,* 2014). Leptin plays a key role in regulating appetite through neural pathways, and the reduction in serum leptin in the current study may be due to enhanced leptin sensitivity induced by pregnane and steroidal glycosides. The observed phenomena support the role of CFE in regulating energy homeostasis and reducing adiposity.

The results of this study show that the CFE exhibited pronounced hepatoprotective effects, as evidenced by a decrease in AST and ALT compared to the positive control group. The hepatoprotective effects may be attributed to the capacity of CFE to reduce LDL cholesterol and inflammatory cytokines, thereby preventing liver damage caused by HFHC diets. These results are consistent with previous research on *Caralluma umbellata*, which indicated a reduction in hepatic injury and oxidative stress (Shanmugam *et al.*, 2013). Furthermore, our results demonstrated CFE renoprotective properties by enhancing serum creatinine, urea, and albumin concentrations. The presence of phytochemicals exhibiting antioxidant and anti-inflammatory properties, including steroidal and pregnane glycosides, may account for these observed effects. These observations are consistent with prior findings (Gujjala *et al*., 2016), which illustrated that CFE mitigated the elevation of plasma urea and creatinine levels induced by the HFHC dietary regimen. The accumulation of lipids and fatty substances in arterial walls affects vital organs, including the kidneys, liver, and aorta, contributing to AIP. Increased AIP values indicate a heightened risk of injury to these organs (Qanwil *et al.,* 2025). The noted decrease in CVDI, AIP, and CRI index relative to the positive control group aligns with previous findings (Gujjala *et al.,* 2016), who found that CFE reduced the AIP in hyperlipidemic rats by 18.2%. This major reduction indicates that certain of the pharmacologically active constituents of *C. fimbriata* might play a role in its therapeutic efficacy in the prevention of atherosclerosis. This is probably because of its ability to lower lipid and anti-inflammatory effects, especially pregnane glycosides.

CFE also had a positive effect on hematological parameters in the present study as compared to the positive control group. The results align with the earlier works on the application of *Caralluma tuberculata* in diabetic rats, as they have demonstrated a significant change in the parameters of RBCs. Such results can be attributed to flavonoids which promote erythropoietin and inhibit systemic inflammation (Poodineh and Nakhaee, 2016). The levels of inflammatory factors, i.e., CRP and IL-6, were also significantly decreased in the CFE-treated group, which supports the previous research that *Caralluma tuberculata* can reduce the concentration of such pro-inflammatory factors as cyclooxygenase enzyme, IL-1b, IL-6 and TNF-a (Haider *et al.,* 2022). The reverse mechanism of CFE is attributed to saponin glycosides, which inhibit cyclooxygenase activity, thereby contributing to its antinociceptive and anti-inflammatory properties (Saini *et al.,* 2025).

Previous literature confirmed a positive association between hypercholesterolemia and hepatocytic injury (Csonka *et al.,* 2017). Histopathological analyses revealed improved architecture with reduced lipid deposition in the CFE group as compared to the positive control group, supporting previously documented findings. Likewise, previous results have been reported that highlight the protective effect of CFE in mitigating cholesterol-induced histological changes (Latha *et al.*, 2014). The hepatoprotective effect is attributed to synergistic effects of phenolic compounds, glycosides, polysaccharides, and saponins (Gujjala *et al.,* 2017; Akram *et* al., 2023) This research work supports CFE's multi-target therapeutic potential, including antihyperlipidemic, antihyperglycemic, hepatoprotective, renoprotective, and anti-inflammatory pathways. The synergistic action of bioactive components, including pregnane glycosides and flavonoids, is responsible for its diverse bioactivity, which could be a beneficial dietary intervention. Future investigation may also integrate computational and in silico modelling to better predict the systemic effects of bioactive compounds from *C. fimbriata*. Recent studies have demonstrated the effectiveness of complex biological models and simulation approaches in analyzing advanced biochemical and CVD's pathways (Amilo *et al*., 2025a; Amilo *et al.,* 2025b). Such models could complement in vivo experiments and accelerate translational research (Amilo *et al.,* 2025). However, the present study employed only male rats, which may limit the generalizability of findings as sex related differences in lipid metabolism and hormonal regulation could influence the response to CFE treatment. To give a deeper insight on its therapeutic effectiveness, studies that involve both sexes should therefore be conducted in the future.

Conclusions: CFE portrayed potential beneficial effects in metabolic disorders associated with hyperlipidemia. As a post-induction therapy, CFE was associated with lower feed intake and controlled body weight gain. Furthermore, improvements were observed in hepatic, renal and serum lipid profiles with cholesterol lowering effects comparable

to conventional pharmacological interventions. This data highlights the promise of CFE as a natural treatment method in the management of hyperlipidemia and prevention of cardiovascular diseases. The understanding of the particular mechanism of action, molecular studies, and clinical effectiveness of the findings in human trials should be further elaborated, which will improve the translational value of the results. Additionally, future research should focus on bioactivity-based fractionation of the extract to isolate and determine the active components that confer the extract its lipid-lowering effects. A clear understanding of the exact metabolic routes under the influence of these substances will provide greater understanding of the therapeutic potential of *C. fimbriata*. This research is a foundation to develop CFE as a potential complementary or alternative intervention to hyperlipidemia that requires more research in the preclinical and clinical settings.

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Informed consent statement: Not applicable

Data availability statement: Data will be available on request. More enquiries can be forwarded to the corresponding author; the article contains the original contributions made throughout the study.

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REFERENCES

Abdel-Sattar E & Ali DE, 2022. Russelioside B: a pregnane glycoside with pharmacological potential. Revista Brasileira de Farmacognosia 32(2):188-200.

Akram A, Jamshed A, Anwaar M, *et al.,* 2023. Evaluation of Caralluma edulis for its potential against obesity, atherosclerosis and hypertension. An International Journal 21(1):1-12.

AlMasoud N, Rabail R, Alomar T, *et al.,* 2024. Therapeutic Impact of Bitter Gourd Seed-fortified Crackers on Alloxan-induced Diabetic Rats. Pakistan Veterinary Journal 44(3):629-636.

Amilo D, Sadri K, Hincal E, *et al.,* 2025a. Dual approach artificial neural networks-fractional order operator to enhancing in vitro fertilization predictions and success measure. Modeling Earth Systems and Environment 11(4):1-27.

Amilo D, Sadri K, Suleiman I, *et al.,* 2025b. A study on fractional-order lung cancer model under different internal influences with time delays analysis and modeling. Network Modeling Earth Systems and Environment 11(4):1-27.

Anwar R, Rabail R, Rakha A, *et al.,* 2022. Delving the role of caralluma fimbriata: An edible wild plant to mitigate the biomarkers of metabolic syndrome. Oxidative Medicine and Cellular Longevity 2022:5720372.

Ashwini S & Anitha R, 2017. Antihyperglycemic activity of Caralluma fimbriata: An in vitro approach. Pharmacognosy Magazine 13(51): 499-504.

Astell KJ, Mathai ML, McAinch AJ, *et al.,* 2013. A pilot study investigating the effect of Caralluma fimbriata extract on the risk factors of metabolic syndrome in overweight and obese subjects: A randomised controlled clinical trial. Complementary Therapies in Medicine 21(3):180-189.

Ballena-caicedo J, Zuzunaga-montoya FE & Loayza-castro JA, 2025. Global prevalence of dyslipidemias in the general adult population : a systematic review and meta-analysis. Journal of Health, Population and Nutrition 44 (1):308-319.

Csonka C, Baranyai T, Tiszlavicz L, *et al.,* 2017. Isolated hypercholesterolemia leads to steatosis in the liver without affecting the pancreas. Lipids in Health and Disease 16(1):1-14.

De Leo M, De Tommasi N, Sanogo R, *et al.,* 2005. New pregnane glycosides from Caralluma dalzielii. Steroids 70(9):573-585.

Delwatta SL, Gunatilake M, Baumans V, *et al.,* 2018. Reference values for selected hematological, biochemical and physiological parameters of Sprague-Dawley rats at the Animal House, Faculty of Medicine, University of Colombo, Sri Lanka. Animal Models and Experimental Medicine 1(4):250-254.

Famurewa AC, Nwankwo OE, Folawiyo AM, *et al.,* (2017). Repeatedly heated palm kernel oil induces hyperlipidemia, atherogenic indices and hepatorenal toxicity in rats: the beneficial role of virgin coconut oil supplementation. Acta Scientiarum Polonorum Technologia Alimentaria 16(4):451-460.

Filho LHG, Ferreira NL, Carvalho RB, *et al.,* 2011. Experimental model of myocardial infarction induced by isoproterenol in rats. Brazilian Journal of Cardiovascular Surgery 26(3):469-476.

Freidwald WT, Levy RI & Fredrickson DS 1972. Estimation of the Concentrationof low-Density lipoprotein cholesterolin plasma,without use of the preparative ultracentrifuge. Clinical Chemistry 18(6):499-502.

Fularski P, Hajdys J, Majchrowicz G, *et al.,* 2024. Unveiling Familial Hypercholesterolemia-Review, Cardiovascular Complications, Lipid-Lowering Treatment and Its Efficacy. International Journal of Molecular Sciences 25(3):1637.

Griggs JL, Mathai ML & Sinnayah P, 2018. Caralluma fimbriata extract activity involves the 5-HT2c receptor in PWS Snord116 deletion mouse model. Brain Behavior 8(12):1-11.

Gujjala S, Putakala M, Bhusana S, *et al.,* 2019. Preventive effect of Caralluma fimbriata against high-fat diet induced injury to heart by modulation of tissue lipids, oxidative stress and histological changes in Wistar rats. Archives of Physiology and Biochemistry 2(2), 474-482.

Gujjala S, Putakala M, Nukala S, *et al.,* 2017. Modulatory effects of Caralluma fimbriata extract against high-fat diet induced abnormalities in carbohydrate metabolism in Wistar rats. Biomedicine and Pharmacotherapy 92:1062-1072.

Gujjala S, Putakala M, Nukala S, *et al.,* 2016. Renoprotective effect of Caralluma fimbriata against high-fat diet-induced oxidative stress in Wistar rats. Journal of Food and Drug Analysis 24(3):586-593.

Haider SI, Asif A, Rasheed HMF, *et al.,* 2022. Caralluma tuberculata exhibits analgesic and anti-arthritic potential by downregulating pro-inflammatory cytokines and attenuating oxidative stress. Inflammopharmacology *30*(2):621-638.

Ibrahim KE, Al-Mutary MG, Bakhiet AO, *et al.,* 2018). Histopathology of

the liver, kidney, and spleen of mice exposed to gold nanoparticles. Molecules 23(8):1848.

Iqbal T, Sohaib M, Iqbal S, *et al.,* 2024. Exploring therapeutic potential of *Pleurotus ostreatus* and *Agaricus bisporus* Mushrooms against Hyperlipidemia and Oxidative Stress Using Animal Model. Foods 13(5):709.

Jaswanth BK, Vijaya P, Reddy B, *et al.,* 2025. In vitro Strategies for the Production of Bioactive Therapeutics from Caralluma Species. Asian Journal of Biological Life Sciences 14(1):1-7.

Kamalakkannan S, Rajendran R, Venkatesh RV, *et al.,* 2010. Antiobesogenic and antiatherosclerotic properties of Caralluma fimbriata extract. Journal of Nutrition and Metabolism 10:1-29.

Karabekir SC, Gultekin B, Ayan IC, *et al.,* 2024. Protective Effect of Astaxanthin on Histopathologic Changes Induced by Bisphenol A in the Liver of Rats. Pakistan Veterinary Journal 44(2):244-251.

Karbiner MS, Sierra L, Minahk C, *et al.,* 2013. The role of oxidative stress in alterations of hematological parameters and inflammatory markers induced by early hypercholesterolemia. Life Sciences *93*(15):503-508.

Khan A, Khan I, Khan B, *et al.,* 2025. Caralluma-enhanced bread : A novel approach to combat advanced glycation end products and metabolic syndrome-related enzymes. World Journal of Biology Pharmacy and Health Sciences 21(1):1-12.

Kushner RF, 2018. Weight loss strategies for treatment of obesity: lifestyle management and pharmacotherapy. Progress in Cardiovascular Diseases 61(2):246-252.

Latha S, Rajaram K, & Suresh Kumar P, 2014. Hepatoprotective and antidiabetic effect of methanol extract of Caralluma fimbriata in streptatozocin induced diabetic albino rats. International Journal of Pharmacy and Pharmaceutical Sciences 6(1):665-668.

Malladi S, Ratnakaram VN, Babu KS *et al.,* 2017. Phytochemical screening of Caralluma lasiantha isolation of C21 pregnane steroid. Orient Journal of Chemistry 33(2):963-967.

Matra M, Phupaboon S, Totakul P, *et al.,* 2025. Microencapsulated-Bioactive compounds from medicinal leaf extracts used as feed supplements: effects on in vitro rumen fermentation, microbial population, and methane mitigation. International Journal of Agriculture and Biosciences 14(2): 258-264.

Montgomery DC, 2017. *Design and analysis of experiments*. Wiley, New York, USA.

Ogunlana 2012. Phytochemical, biological and toxicological studies of the extracts of young twigs and leaves of gray nicker nut (*Caesalpinia bonduc* (Linn)) Roxb. Covent University, Otawa Nigeria 1-327.

Padwal AD, Varpe SN & Waman MB, 2016. Phytochemical and nutritional analysis of *Caralluma Fimbriata* L. International Journal of Researches in Biosciences and Agriculture Technology 1(7):1-4.

Parhofer KG & Laufs U, 2023. Lipid Profile and Lipoprotein(a) Testing. Deutsches Arzteblatt International 120(36):582-588.

Poodineh J & Nakhaee A, 2016. Hypoglycemic and hypolipidemic effects of Caralluma tuberculata and its safety on liver and kidneys of diabetic rats. Turkish Journal of Biochemistry 41(3):136–143.

Qadeer I, Aslam HKW, Tayyib M, *et al.,* 2025. Ultrasound applications in bioactive peel compounds: Enhancing gut, food, and plant health. Journal of Global Innovations in Agricultural Sciences 13:1245-1256.

Qanwil T, Malik A, Mushtaq A, *et al.,* 2025. Hypolipidemic and vasoprotective potential of caralluma edulis: a histological and biochemical study. Jordan Journal of Pharmaceutical Sciences 18(1):21–35.

Rabail R, Rauf A, Mousavi A, *et al.,* 2025. Biosafety assessment of edible oil blended from flax , coconut , sunflower , and olive oils in healthy Sprague Dawley rats. Journal of Agriculture and Food Research 20:101768.

Rabail R, Shabbir MA, Ahmed W, *et al.,* 2022. Nutritional, functional, and therapeutic assessment of muffins fortified with garden cress seeds. Journal of Food Processing and Preservtion 46(7):1-11.

Rajaram K & Suresh Kumar P, 2011. Phytochemical studies and Gc-Ms analysis of Caralluma fimbriata wall. International Journal of Pharmaceutical Research and Developpement 3(0974):105-110.

Rao A, Briskey D, dos Reis C, *et al.,* 2021. The effect of an orally-dosed Caralluma Fimbriata extract on appetite control and body composition in overweight adults. Scientific Reports 11(1):1-10.

Rauf A, Akram M, Anwar H, *et al.,* 2022. Therapeutic potential of herbal medicine for the management of hyperlipidemia: latest updates. Environmental Science and Pollution Research 29(27):40281-40301.

Saini I, Kumar P & Kumar A, 2025. Anti-inflammatory and analgesic properties of caralluma fimbriata: a comprehensive study. Journal of Population Therapeutics & Clinical Pharmacology 32(05):927-935.

Sarfaraz S, Ikram R, Munawwar R, *et al.,* 2021. Rising trend of Nutraceuticals : Evaluation of lyophilized beetroot powder at different doses for its hypolipidemic effects. Pakistan Journal of Pharmaceutical Sciences 34(4):1315-1322.

Shanmugam G, Ayyavu M, Dowlathabad MR, *et al.,* 2013). Hepatoprotective effect of Caralluma umbellate against acetaminophen induced oxidative stress and liver damage in rat. Journal of Pharmacy Research 6(3):342-345.

Subaş T, Badem M, Kanbolat Ş, *et al.,* 2025. Lipid Metabolism-Related Enzyme Inhibition and Antioxidant Potential of the Extracts and Phytochemical Compounds from Trachystemon orientalis (L.) D.Don. Plant Foods for Human Nutrition 80(2):114.

Sudhakara G, Mallaiah P, Sreenivasulu N, *et al.,* 2014. Beneficial effects of hydro-alcoholic extract of Caralluma fimbriata against high-fat diet-induced insulin resistance and oxidative stress in Wistar male rats. Journal of Physiology and Biochemistry *70*(2):311-320.

Sultan MT, Butt MS, Ahmad RS, *et al.,* 2012. Supplementation of Nigella sativa fixed and essential oil mediates potassium bromate induced oxidative stress and multiple organ toxicity. Pakistan Journal of Pharmaceutical Sciences 25(1):175-181.

Topiwala B & Krishnamurthy R, 2013. Hoodia gordonii (African plant), caralluma fimbriata and achyranthes aspera (Indian plants): An appetite suppressant. Biotechnology: An Indian Journal *7*(8):285-290.

Ullah R, 2024. The therapeutic potential of aromatic plants: a new frontier in bioactive compound research. Trends in Animal and Plant Sciences 4:112-117.

Shivakumara P, Sumalatha KR and Sushmitha S, 2023. A comparative study on wet and dry extracts of Caralluma fimbriata for phytochemicals and evaluation of therapeutic activity. Biological Forum 15(8A):238-251.

Vitalone A, Di Sotto A, Mammola CL, *et al.,* 2017. Phytochemical analysis and effects on ingestive behaviour of a Caralluma fimbriata extract. Food and Chemical Toxicology 108:63-73.

Xie J, Chen X, Tan Y, *et al.,* 2024. Anti-Hyperlipidemic Components of the Leaves of Synsepalum dulcificum (Miracle Fruit). Plant Foods for Human Nutrition 79(2):451-459.