Hypolipidemic and Vasoprotective Potential of *Caralluma edulis*: A Histological and Biochemical Study

Tayyaba Qanwil[1], Abdul Malik[1]*, Aamir Mushtaq[2]*, Alamgeer[3], Muhamad Fayyaz Ur Rehman[4], and Umar Farooq Gohar[5]

[1] College of Pharmacy, University of Sargodha, Sargodha, Pakistan
[2] Department of Pharmaceutical Sciences, Government College University, Lahore, Pakistan
[3] Punjab University College of Pharmacy, University of the Punjab, Lahore, Pakistan
[4] Institute of Chemistry, University of Sargodha, Sargodha, Pakistan
[5] Institute of Industrial Biotechnology, Government College University, Lahore, Pakistan

ABSTRACT

Caralluma edulis (Apocynaceae) is well known for its medicinal properties, including antioxidant, anti-inflammatory, antimicrobial, and hypoglycemic activities, and has been used as a valuable remedy in various cultures. This scientific study aimed to validate the efficacy of *C. edulis* in lowering lipid profiles using two hyperlipidemic animal models: lipofundin-induced rabbits and fructose-induced rats. Lipofundin was administered intravenously at 2 mL/kg for 23 days, while fructose (25% w/v) was given for 28 consecutive days by dissolving it in drinking water to induce dyslipidemia and vascular dysfunction. The hydroalcoholic extract of *C. edulis* was orally administered (250 and 500 mg/kg) to experimental groups, while atorvastatin (10 mg/kg p.o.) was given only to the standard control group. Blood samples were collected to assess various biochemical parameters. Furthermore, histological examinations of liver and thoracic aorta tissues from fructose-fed rats were conducted, along with an evaluation of their vasorelaxant properties. The hydro-methanolic extract of *C. edulis* demonstrated dose-dependent hypolipidemic effects, significantly reducing serum cholesterol, triglycerides, and low-density lipoproteins at a dose of 500 mg/kg in both models, comparable to atorvastatin. Additionally, the hydroalcoholic extract exhibited significant endothelium-dependent vasorelaxant activity and hepatoprotective effects in fructose-fed rats. *C. edulis* also displayed antioxidant potential through free radical scavenging activity. These findings suggest that *C. edulis* possesses hypolipidemic and vasoprotective properties, likely attributed to its active pharmacological constituents, supporting its traditional use.

Keywords: Lipofundin; fructose-induced hyperlipidemia; atorvastatin; vasorelaxant studies; serum cholesterol.

1. INTRODUCTION

Cardiovascular diseases are the prominent cause of death in human being throughout the world [1] and is estimated to cause more or less 16.7 million deaths per year. In Pakistan, cardiovascular arterial disease affects 26.9% of the population, with a more pronounced incidence among women at 30% compared to men at 23.7% [2]. The prevalence of these diseases can be recognized by a number of factors such as alcohol consumption, smoking, sedentary lifestyle, consumption of high-calorie diets, aging, and genetic predisposition [3]. These factors contribute to the development of lipid and lipoprotein abnormalities, including deficiencies or overproduction. The relationship between elevated risks of

Corresponding author:
Abdul Malik: abdul.malik@uos.edu.pk
Aamir Mushtaq: aamir.mushtaq@gcu.edu.pk
Received: 11/03/2024 Accepted: 18/07/2024.
DOI: https://doi.org/10.35516/jjps.v18i1.2464

coronary heart disease (CHD) and serum cholesterol levels was initially established in 1984, highlighting that a mere 1% reduction in serum cholesterol levels could potentially reduce the risk of CHD by 2% [4].

Hyperlipidemia stands as the primary cause of mortality in both developing and developed nations [5]. Plasma cholesterol levels exceeding >200 mg/dL serve as a significant risk factor, contributing to approximately 4.4 million deaths annually. Data from the National Health and Nutrition Examination Survey (NHANES) suggests that 11.7% of individuals aged 20-39 and 41.2% of those aged 40-64 exhibit elevated LDL levels. Moreover, hyperlipidemia affects 10.6% of individuals aged 20-39 and 47.7% of those aged 40-64 [6].

When lifestyle modifications prove ineffective in managing hyperlipidemia, pharmacological intervention becomes necessary to attain lipid-lowering objectives. Findings from a national survey (NEPTUNE II, 2003) indicated that 67% of 4885 hyperlipidemic patients successfully achieved their cholesterol-lowering targets. Moreover, data from national health and nutrition examination surveys revealed a decrease in the prevalence of hyperlipidemia, with statistics ceindicating that by 2002, no more than 17% of American patients would have elevated cholesterol levels [7]. Several lipid-lowering medications are available in the market to address hyperlipidemia. Currently, five primary classes of drugs are utilized in the management of this condition.

Research studies have shown that fructose consumption can lead to hypertension, insulin resistance, and hypertriglyceridemia. Upon ingestion and absorption in the gastrointestinal tract (GIT), fructose undergoes metabolism in hepatocytes to form acetyl CoA and glycerol-3 phosphate. Subsequently, the metabolites contribute to triglyceride synthesis, accelerating lipogenesis and resulting in the production and accumulation of VLDL (very low-density lipoproteins) and hepatic TG (triglycerides). Consequently, this process reduces insulin sensitivity and induces hepatic insulin resistance [8].

Synthetic drugs often pose a challenge due to their potential side effects outweighing their benefits. The initiation of drug therapy with HMG Co-A reductase inhibitors or fibric acid derivatives, which are inhibitors of CYP3A4 isozymes, has been linked to increased hospitalizations and gastrointestinal (GIT) issues [9]. Furthermore, the use of statins and fibrate combinations has been associated with elevated risks of renal failure and hepatic injury [10].

In contrast, herbal medicinal products constitute a significant portion, accounting for 57% of complementary medicine sales. A survey conducted in England in 1998 revealed that 22.1% of 5010 adults had purchased over-the-counter (OTC) herbal drugs [11]. Plants such as musli, pipal, palash, mulethi, amaltas, kesraj, and bottle gourd exhibit substantial lipid-lowering activities. Numerous studies have reported that the use of nutraceuticals and herbs like artichoke leaf extract, garlic, soluble fibers, nuts, and orange juice leads to a notable reduction in plasma lipid levels [7].

Belonging to the Asclepiadaceae family, Caralluma is commonly known as the milkweed family. While approximately 200 genera and 2500 species have been documented within the Asclepiadaceae family. Advanced genetic and molecular studies propose Asclepiadaceae as a subfamily in the Apocynaceae family [12]. Caralluma plants boast numerous medicinal properties, with applications in Arabic traditional herbs and Indian conventional medicines for managing cancer, tuberculosis, inflammation, skin problems, diabetes mellitus, and more. Pharmacological studies on Caralluma species have demonstrated anticancer [13], anti-eczemic, anti-inflammatory, antioxidant, antifungal, antidiabetic, and antimalarial activities [12].

Caralluma edulis, a medicinal plant, has garnered significant attention due to its therapeutic potential. Its traditional use in treating various ailments has spurred scientific investigations into its pharmacological properties. Among the numerous health benefits attributed

to *C. edulis*, its hypolipidemic and vasoprotective effects have garnered particular interest. This study aims to explore the hypolipidemic and vasoprotective potential of *C. edulis* through biochemical and histological analysis, offering promising avenues for the development of novel therapies for hyperlipidemia treatment.

2. MATERIALS AND METHODS

2.1. Chemicals

The chemicals of analytical grade were utilized in this study, including Atorvastatin (MediPak Pvt Ltd), Lipofundin (B. Braun), Fructose 25% w/v (Sigma Aldrich), Sodium Phenobarbital, Potassium chloride, Phenylephrine, Ketamine chloride and Acetylcholine, (Sigma Aldrich).

2.2. Equipment

The following equipment was employed: Tissue organ bath, Centrifuge machine Lab Chart 6.0 (AD instruments), Lyophilizer (Christ alpha 1-4 LD, Germany), Rotary evaporator (Stuart, Bibby Steriline Ltd. UK), and Power lab Data Acquisition System, Model No. ML865 (AD instruments).

2.3. Animal models

In this study we used local breed of rabbits of either sex (1-1.5 Kg) and male adult Wister Albino rats (150-200 g). All the animals were housed in the animal facility of the Pharmacology Department of College of Pharmacy, University of Sargodha. They were supplied with a regular pellet diet and tap water *ad libitum* and kept under standard environmental conditions (humidity; 50% ± 5%), (room temperature; 22 ± 2 ºC), and light and dark period of 12-hour each, following the guidelines of NIH (National Institute of Health) regarding the use and care of the animals. The experimental procedures and animal handling were carried out by following the rules and regulations of the National Research Council (NRC., 1996). The ethical approval for the use of laboratory animals were obtained by institutional animal ethical committee vide letter no 33637/AE.

2.4. Plant collection and identification

In this study, the succulent stems of *C. edulis* were utilized. Around 14 kg of *C. edulis* stems were gathered in November 2022 from the local market of District Malakand, KPK, Pakistan. Authentication was conducted by an Associate Professor, Dr. Hassan Sher, from Department of Plant Science, Swat University, Pakistan**.**

2.4.1. Preparation of plant extract

The hydro-methanolic extract of *C. edulis* or *C. edulis* methanolic extract was obtained using the cold maceration technique. First, the stems of the plant were collected, washed thoroughly to remove any dirt or impurities, and then shade dried. Once dried, they were powdered into coarse particles. Approximately 2 kg of the powdered material was weighed out and soaked in a mixture of 70% distilled water and 30% methanol, totaling 5 L, at room temperature for 3 days, with occasional shaking. After the maceration period, the material was filtered first through muslin cloth and then through Whatman No. 1 filter paper. The residue was subjected to another round of maceration for an additional 3 days, followed by filtration. The filtrate obtained was then processed using a rotary evaporator under controlled conditions: speed set at 55–60 rpm, temperature maintained at 35 ± 5 °C, and pressure adjusted to 45-50 Torr. This process yielded a semi-solid, thick paste-like extract, which was carefully removed from the rotary flask and weighed. The percentage yield was calculated to be 17%. Lastly, the extract was poured in a dry glass jar and stored at -8 °C in a refrigerator.

2.5. Experimental procedures

2.5.1. Lipofundin induced dyslipidemia

Initially, a Rabbit model was employed for the hypolipidemic study. The animals were randomly divided into five groups, each comprising six rabbits. Group-I was designated as the normal control. Group-II, the disease control, received intravenous lipofundin for eight consecutive days at a dose of 2 mg/Kg. Group-III served as the standard control, initially receiving intravenous lipofundin (2 mg/Kg) for eight days, followed by oral administration of atorvastatin (10 mg/Kg) for the subsequent 15 days. Similarly, Group-IV and Group-V

were experimental controls. They initially received intravenous lipofundin at a dose of 10 mg/Kg for eight consecutive days. Subsequently, they were orally administered with methanolic extract of *C. edulis* at doses of 250 mg/Kg and 500 mg/Kg, respectively, for the next eight consecutive days.

Upon completion of the experiment, the animals underwent overnight fasting. On the 24th day, we collected blood (approximately 3 mL) from the jugular vein of each rabbit. It was then centrifuged for ten minutes at 3000 rpm to get serum for the estimation of biochemical parameters. Then biochemical studies were performed on the serum to assess TG (Triglyceride), TC (Total Cholesterol) and HDL (High-Density Lipoprotein) and commercial kits of Human Germany were used for the analysis. The other parameters like AI (atherogenic index), CRI (Coronary Risk Index), LDL (Low Density Lipoprotein) and VLDL (Very Low Density Lipoprotein) levels were estimated from TG, TC and HDL values by using the following formulas [14]:

Estimation of VLDL = TG/5

Estimation of AI = TC-HDL/HDL

Estimation of LDL = TC-(HDL + VLDL)

Estimation of CRI = TC/HDL

2.5.2. Fructose induced hyperlipidemia

Adult male Wistar Albino rats weighing between 100-150g were randomly allocated into five groups, with six rats in each group. Rats in Group-I were fed a standard diet and served as the normal control. Group-II, designated as the disease control group, received oral administration of fructose (25% w/v) in their drinking water for 28 consecutive days to induce hyperlipidemia. Similarly, hyperlipidemia was induced in Groups III, IV, and V by orally administering fructose (25% w/v) in their drinking water for 14 consecutive days. Starting from the 15th day until the 28th day, Group-III was orally treated with 10 mg/Kg of atorvastatin two hours prior to fructose feeding. Likewise, Groups IV and V received oral doses of hydro-methanolic extract of *C. edulis* at doses of 250 mg/Kg and 500 mg/Kg, respectively, also two hours before fructose feeding from the 15th to the 28th day. After the completion of the experiment, the animals underwent overnight fasting. On the following day, blood samples were collected via cardiac puncture from each rat after euthanization. The blood samples were then centrifuged to obtain serum.

Then biochemical studies were performed on the serum to assess triglyceride (TG), Total cholesterol (TC) and high-density lipoprotein (HDL) and commercial kits of Human Germany were used for the analysis. The other parameters like AI (atherogenic index), CRI (coronary risk index), LDL (low density lipo protein) and VLDL (very low density lipoprotein) levels were estimated as indicated in section 2.5.1 [14]

2.5.3. Fructose-induced vascular dysfunction

In vitro vascular reactivity assessments were conducted on fructose-fed rats to evaluate endothelial integrity. The thoracic aorta of the rats was carefully dissected and cut into 3 mm long rings, with meticulous measures taken to prevent any damage to the endothelium. These rings were suspended in organ baths using two stainless steel wires inserted into the lumen between a clip and a force-displacement transducer. A resting tension of 2 g was applied to aid in achieving isometric force. The organ chamber was filled with 10 mL of oxygenated Krebs's Henseleit buffer solution (95% oxygen and 5% carbon dioxide), maintained at 37°C. The preparations were allowed to equilibrate with continuous exchange of Krebs's solution for approximately 1 hour. After the equilibration period, the ring segments were pre-contracted with KCl, and the active muscle tone of the ring segments was then contracted with 10-6 M phenylephrine. Upon reaching a stable contraction plateau, the relaxation response to cumulative acetylcholine concentrations (10^{-9} to 10^{-4} mole per liter) was measured [15].

2.6. Histopathological analysis of liver in fructose-fed rats (FFR)

The livers from both the normal control and treated rats were carefully extracted, washed with a normal saline

solution, and then fixed in a 10% buffered formalin solution for preservation. Subsequently, they underwent processing for histological studies. Histopathological examination was conducted on liver sections of 5-micron thickness, which were prepared by processing the liver tissues with paraffin and staining them with Hematoxylin and Eosin (H&E). The tissue samples were then examined under a light microscope to analyze the cellular structure and identify any pathological changes. Photomicrographs were captured using a Kodak digital 10-megapixel camera. Notable alterations in histopathological parameters, such as hepatic steatosis, areas of necrosis, vacuoles of varying sizes, and fatty degeneration, were observed in the liver sections of normal, control, and treated rats, enabling the assessment of significant structural changes in hepatic tissue architecture [16,17].

2.7. Free radical scavenging activity

The antioxidant capacity of the *C. edulis* extract was evaluated using the stable free radical scavenger DPPH. This involved assessing the rate of bleaching of the stable free radical at a specific absorption wavelength of 517 nm, where its absorption decreases upon reduction by a radical or antioxidant species. The methodology included preparing various concentrations of the hydro-methanolic extract of *C. edulis* (125-100 µg/mL) in methanol. Additionally, a 0.1 mM DPPH solution was prepared in methanol. Subsequently, 1 mL of the prepared DPPH solution was added to 3 mL of the different concentrations of plant extract solutions. The reaction mixture was then incubated for 30 minutes at room temperature (28 ± 2ºC). The absorbance of the reaction mixture was measured at a wavelength of 517 nm using a spectrophotometer. A control solution containing 100 µL of methanol in the DPPH solution was also prepared, and its absorbance was measured. The assay was conducted in triplicate. L-ascorbic acid was used as a reference. A higher radical scavenging capacity of the reaction mixture was indicated by a lower absorbance value [18]. The DPPH free radical scavenging capacity of the plant extract was calculated based on the ability to scavenge the DPPH radical by the following equation:

$$\text{DPPH scavenging effect (\%)} = [(A_{\text{Control}} - A_{\text{Sample}}/A_{\text{Control}}) \times 100]$$

Whereas:

A_{Control} is the absorbance of the control reaction; A Sample is the absorbance in the presence of a sample (plant extract).

2.8. Statistical analysis

The data were presented as means ± S.E.M. Statistical analysis was performed using GraphPad Prism 5. For all experiments, two-way ANOVA and Bonferroni's posttest were utilized. A significance level of $p < 0.05$ (95% confidence interval) was considered statistically significant.

3. RESULTS

3.1. Hypolipidemic activity of hydro-alcoholic extract of *C. edulis* in lipofundin-induced dyslipidemia

3.1.1. Effect on lipid profile

In the LIPO group, rats showed elevated levels of TC, TG, LDL, and VLDL. On the 23rd day, the LIPO group exhibited a significant increase ($P<0.05$) in TC (84.33 ± 4.25 mg/dL) and serum TG ($P<0.001$) to (112 ± 6.24 mg/dL) compared to the control group values (65 ± 2.8, 72.66 ± 4.33 mg/dL). The *C. edulis* hydro-methanolic extract demonstrated dose-dependent hypolipidemic effects. At a dosage of 500 mg/Kg, it notably attenuated the elevation of TC, TG, and LDL compared to the LIPO group on the 23rd day, while the reduction in HDL and VLDL was not statistically significant. *C. edulis* hydro-methanolic extract significantly ($P<0.001$) decreased serum TC to (59.33 ± 2.96 mg/dL) compared to the LIPO 23rd group (84.33 ± 4.25 mg/dL) and serum TG ($P<0.001$) to (81 ± 4.93 mg/dL) compared to the LIPO 23rd group (112 ± 6.24 mg/dL). Furthermore, it markedly reduced serum LDL levels to (12.80 ± 1.33 mg/dL) compared to the LIPO group on the 23rd day (29.93 ± 4.47 mg/dL), as illustrated in Table 1.

3.1.2. Effect on the atherogenic and coronary risk index

The 70% methanolic extract of *C. edulis* at a dosage of 500 mg/Kg exhibited a significant ($P<0.01$) reduction in

the values of the Atherogenic index (AI) compared to the LIPO 23rd day control group, from (1.63 ± 0.15 mg/dL) to (0.97 ± 0.11 mg/dL). Similarly, in the case of the coronary risk index (CRI), *C. edulis* at a dosage of 500 mg/Kg demonstrated a significant (P<0.01) decrease in CRI (1.97±0.11 mg/dL) compared to the diseased group (2.63±0.15 mg/dL), as outlined in Table 1.

Table 1: Effect of *C. edulis* extract on serum lipid profile, atherogenic (AI) and coronary risk index (CRI)

No	Parameter	Animal Groups					
		G-I (Control)	**G-II** (LIPO 8th day)	**G-II** (LIPO 23rd day)	**G-III** (ATOR)	**G-IV** (CE 250)	**G-V** (CE 500)
I	Serum TC (mg/dL)	65.00±2.8	86.6±4.40**	84.33±4.25*	61.00±4.93[b]	73.67±6.17	59.33±2.96[a]
II	Serum TG (mg/dL)	72.66±4.33	118.3±7.26***	112.0±6.24***	72.66±4.33[a]	96.00±12.42[c]	81.00±4.93[a]
III	HDL (mg/dL)	33.00±3.21	31.33±1.85	32.00±0.57	35.33±3.71	34.33±3.38	30.33±3.18
IV	VLDL (mg/dL)	14.53±0.86	23.66±1.45	22.4±1.24	14.53±0.86	19.20±2.48	16.2±0.98
V	LDL (mg/dL)	18.46±3.37	32.00±0.2	29.93±4.47	11.33±2.02[c]	20.13±3.57	12.80±1.33[c]
VI	AI (mg/dL)	1.007±0.24	1.76±0.03**	1.63.0±0.15*	0.73±0.06[a]	1.16±0.18	0.97±0.11[b]
VII	CRI (mg/dL)	2.007±0.24	2.76±0.03**	2.63±0.15*	1.73±0.06[a]	2.16±0.18	1.97±0.11 [b]

G-I= Normal Control, G-II = Disease Control (lipofundin 2 mg/Kg), G-III = Standard Control (Atorvastatin 10 mg/Kg), G-IV = *C. edulis* hydro-methanolic extract at dose 250 mg/Kg, G-V = *C. edulis* hydro-methanolic extract at dose 500 mg/Kg. Data are expressed as Mean ± SEM and two-way ANOVA was applied as statistical tool by using Graphpad Prism-7. The level of significance was denoted as: *P<0.05, **P<0.01, ***P<0.001 (compared with normal control). [a] P<0.001, [b] P<0.01, [c]P<0.05 (as compared to LIPO 23rd day control).

3.2. Antihyperlipidemic effect of hydro-methanolic extract of *C. edulis* in fructose-induced hyperlipidemia and vascular dysfunction

3.2.1. Effect on serum lipid profile

In the FFR group, rats exhibited increased levels of serum TC, TG, VLDL, and LDL. The FFR group demonstrated a significant (P<0.001) elevation in TC (106.66 ± 6.76 mg/dL) and TG (196.66 ± 7.26 mg/dL) compared to the control group (71 ± 2.30 mg/dL, 91.66 ± 6.00 mg/dL) for TC and TG, respectively. *C. edulis* hydro-methanolic extract demonstrated dose-dependent hypolipidemic effects. At a dosage of 500 mg/Kg, it significantly attenuated the rise in serum TC, TG, and VLDL compared to the FFR group, while the reduction in HDL and LDL was not significant. *C. edulis* at 500 mg/Kg significantly (P<0.001) reduced serum TC and TG to (73.33 ± 3.52 mg/dL) and (95.66 ± 7.21 mg/dL), respectively, in contrast to the FFR group (106.66 ± 6.76 mg/dL, 196.66 ± 7.26 mg/dL). Furthermore, FFR + CE 500 (*C. edulis* 500 mg/Kg) also significantly (p<0.01) decreased serum VLDL (19.13 ± 1.44 mg/dl) compared to the FFR group (39.33 ± 1.45 mg/dL). Additionally, FFR+

ATOR group significantly (p<0.001) decreased TC, TG, and VLDL levels (63.33 ± 4.63 mg/dL, 72.66 ± 4.33 mg/dL, 14.53 ± 0.86 mg/dL) compared to the FFR group (106.66 ± 6.76 mg/dL, 196.66 ± 7.26 mg/dL, 39.33 ± 1.45 mg/dL), respectively (Table 2).

3.2.2. Effect on Atherogenic (AI) and Coronary risk index (CRI)

The CE 500 group (*C. edulis* hydro-methanolic extract at dose 500 mg/Kg), demonstrated a significant (p<0.01) decrease in the Atherogenic index (0.84 ± 0.125 mg/dL) compared to the FFR (Fructose Fed Rats) group (1.43 ± 0.127 mg/dL). Moreover, the FFR + CE 500 group (group administered with fructose 25% w/v and *C. edulis* hydro-methanolic extract at dose 500 mg/Kg) also exhibited a significant (p<0.01) decrease in Coronary risk index (1.84 ± 0.125 mg/dL) compared to the FFR group (2.43 ± 0.127 mg/dL), as depicted in Table 2.

Table 2: Effect of hydro-methanolic extract of *C. edulis* on serum lipid profile, atherogenic (AI) and coronary risk index (CRI)

No.	Parameter	Animal Groups				
		G-I (Normal Control)	G-II (FFR)	G-III FFR+Ator	G-IV FFR+CE 250	G-V FFR+CE 500
I	Serum TC	71.0±2.30	106.66± 6.76***	63.33±4.63[a]	89±4.35[c]	73.33±3.52[a]
II	Serum TG	91.66±6.00	196.66±7.26***	72.66±4.33[a]	111.66±4.40[a]	95.66±7.21[a]
III	HDL	36.66±2.40	44.33±5.36	33.33±4.91	44.00±3.05	40.00±2.88
IV	VLDL	18.33±1.20	39.33±1.45**	14.53±0.86[a]	22.33±0.88[c]	19.13±1.44[b]
V	LDL	16.00±0.57	23.0±2.88	15.46±2.14	22.66±2.02	14.2±2.69
VI	AI	0.97±0.066	1.43±0.127*	0.93±0.14[c]	1.03±0.08[c]	0.84±0.125[b]
VII	CRI	1.97±0.06	2.43±0.127*	1.93±0.14[c]	2.03±0.08 [c]	1.84±0.125[b]

G-I= Normal Control, G-II = Disease Control (fructose (25% w/v)), G-III = Standard Control (fructose 25% w/v+Atorvastatin 10 mg/Kg), G-IV = fructose 25% w/v+ *C. edulis* hydro-methanolic extract at dose 250 mg/Kg, G-V = fructose 25% w/v+ *C. edulis* hydro-methanolic extract at dose 500 mg/Kg. Data are expressed as Mean ± SEM and two-way ANOVA was applied as statistical tool by using Graphpad Prism-7. The level of significance was denoted as: *P<0.05, **P<0.01, ***P<0.001 (compared with normal control). [a] P<0.001, [b] P<0.01, [c]P<0.05 (as compared to Fructose control). FFR stands for fructose fed rat and CE stands for *C. edulis*, hydro-methanolic extract.

3.3. The vasorelaxant effect of *C. edulis* extract on fructose-induced vascular dysfunction

Ach (10^{-9} to 10^{-4} M) elicited concentration-dependent relaxation in pre-constricted abdominal aorta rings treated with 10^{-6} M phenylephrine. Fructose-fed rats displayed a significant (P<0.001) impairment in maximum endothelium-dependent vascular relaxation compared to the Control group. Hydro-methanolic extract of *C. edulis* demonstrated a dose-dependent effect on endothelium-dependent vasorelaxation. Both CE 500 mg/Kg and atorvastatin effectively mitigated the impairment of vascular endothelial function induced by fructose administration. Notably, the highest dose of the plant extract (CE 500 mg/Kg) exhibited superior efficacy in preserving vascular endothelial integrity (Fig. 1).

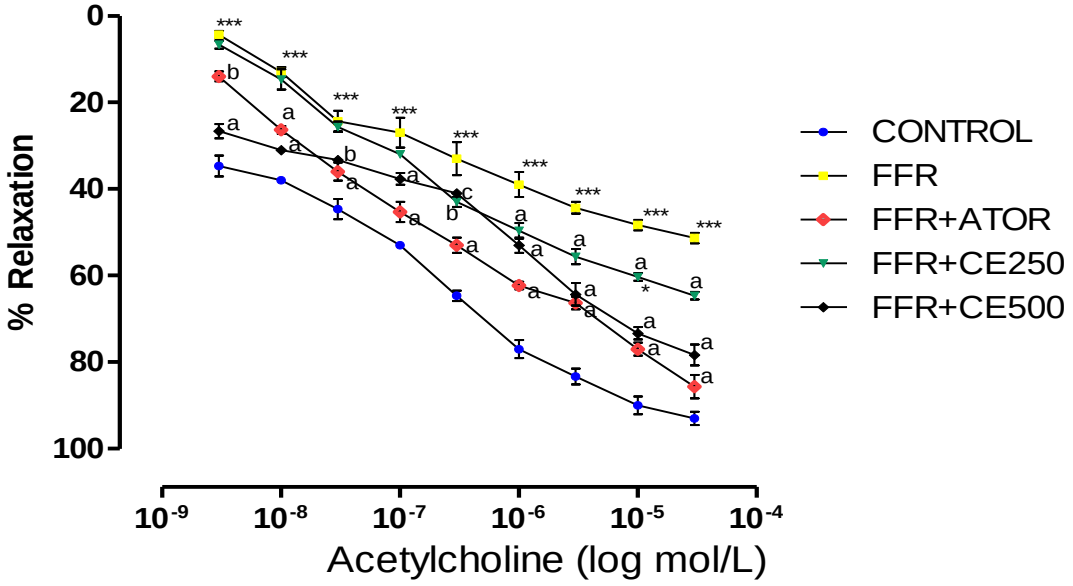

Fig 1: Endothelium-dependent vascular relaxations by Ach in rat thoracic aorta rings.

Data are expressed as Mean ± SEM and two-way ANOVA was applied as statistical tool by using Graphpad Prism-7. The level of significance was denoted as: *P<0.05, **P<0.01, ***P<0.001 (compared with normal control). [a] P<0.001, [b] P<0.01, [c] P<0.05 (as compared to Fructose control). FFR stands for fructose fed rat and CE stands for *C. edulis*, hydro-methanolic extract.

3.4. Hepatoprotective activity of hydro-methanolic extract of *C. edulis* in fructose-fed rats

Histopathological examination of normal rat liver sections revealed an intact hepatic architecture. Conversely, liver sections from fructose-fed rats exhibited significant alterations, including focal necrosis, steatosis, and congestion of the central hepatic vein. Treatment with the highest dose of CE (500 mg/Kg) markedly ameliorated these histopathological changes compared to the lower dose of CE (250 mg/Kg), which still exhibited signs of steatosis and hepatic architectural damage. Rats treated with *C. edulis* hydro-methanolic extract at 500 mg/Kg, as well as those treated with atorvastatin, demonstrated hepatoprotective effects, characterized by reduced hepatocellular necrosis, diminished fatty degeneration, and decreased central vein congestion, in contrast to fructose-fed rats (Fig.2).

3.5. The Antioxidant potential of *C. edulis* extract by DPPH scavenging capacity

The increase in the DPPH scavenging capacity of *C. edulis* was observed in a dependent manner (Table 3).

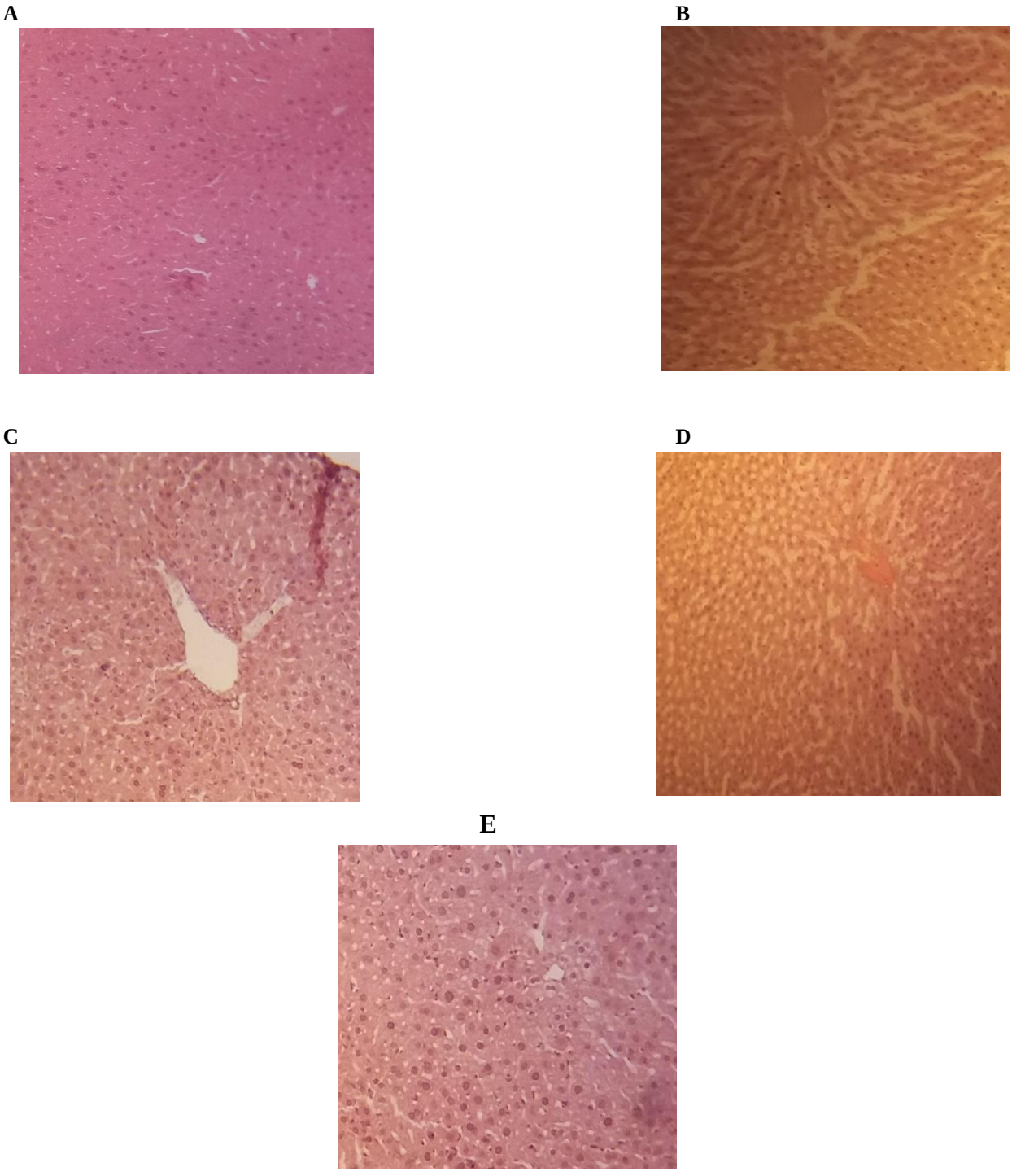

Fig 2: Histopathological examination of rat liver sections

(H and E x 200); A = Normal Group; B = Fructose fed group; C = Standard group; D = CE 250 mg/Kg; E = CE 500 mg/Kg.

Table 3: The antioxidant potential of *C. edulis*

Concentration (ug/mL)	% Antioxidant potential	
	Ascorbic acid	CE
125	80.74±0.026	32.14±0.007***
250	83.45±0.018	40.43±0.018***
500	86.64±0.012	50.45±0.020***
10	88.53±0.023	64.24±0.026***

Values were expressed as Mean ± SEM. Data were evaluated by means of two-way ANOVA. *P<0.05, **P<0.01, ***P<0.001

DISCUSSION

The condition of hyperlipidemia, characterized by elevated plasma lipid levels and altered lipoprotein profiles, significantly contributes to the development of atherosclerosis and cardiovascular diseases [19]. The World Health Organization (WHO) has projected a substantial increase in cardiovascular-related deaths globally, underscoring the urgency of addressing this health concern [20]. Hyperlipidemia often arises from dietary factors, sedentary lifestyles, and genetic predispositions, among other factors, and is exacerbated by various diseases such as diabetes and hypothyroidism [19]. Liver enzymes, particularly 3-hydroxy-3-methylglutaryl (HMG-CoA reductase), play a crucial role in cholesterol synthesis, making them key targets for therapeutic intervention [5]. Currently, anti-hyperlipidemic treatment primarily involves the use of various pharmaceutical agents such as HMG-Co-A reductase inhibitors (statins), fibrates, cholesterol absorption inhibitors, and bile acid sequestrants. While these medications effectively target cholesterol synthesis and lipid metabolism, they often come with cost-related challenges and significant long-term side effects. Consequently, there has been a growing interest in alternative therapies, particularly herbal medicines, which offer a cost-effective and safer approach with lower toxicity compared to synthetic drugs. The World Health Organization (WHO) has also advocated for the use of herbal medicine as an alternative therapy in developing countries [21].

In this study, we utilized the hydro-methanolic extract of *C. edulis* stems to evaluate its anti-hyperlipidemic properties in models of hyperlipidemia induced by lipofundin and fructose, as well as vascular dysfunction in rabbits and rats. Administration of lipofundin 20% for eight consecutive days led to elevated serum levels of triglycerides (TG), total cholesterol (TC), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL). Lipofundin, containing long-chain triglycerides derived from soybean oil, has previously been associated with fat accumulation and alterations in aortic architecture, contributing to the development of atherosclerotic lesions in rabbits. These effects may be attributed to the generation of systemic lipid peroxidation (LPO) products, leading to oxidative stress and depletion of antioxidants [22]. The *C. edulis* hydro-methanolic extract demonstrated significant reductions in serum cholesterol, triglycerides, and LDL levels in rabbits, comparable to the effects of atorvastatin administered at a dose of 500 mg/Kg orally. This hypocholesterolemic activity of the plant extract may be attributed to the inactivation of the HMG-Co-A reductase enzyme, potentially mediated by the phosphorylation of protein kinase (PKA) [23].

Our experimental plant extract, *C. edulis*, contains abundant glycosides, primarily flavone and megastigmane glycosides [12]. The lipid-lowering potential of this extract may be attributed to the presence of polyphenols, which are known for their ability to limit the incidence of atherosclerosis and other cardiovascular diseases by neutralizing oxidizing free radicals [24]. Previous studies have also reported that polyphenolic compounds, such as

flavonoids, exhibit strong antioxidant potential [25]. To assess the antioxidant capacity of our plant extract, we performed a DPPH radical scavenging assay. The hydro-methanolic extract of *C. edulis* exhibited robust antioxidant activity, which may contribute to the neutralization of oxidant species causing oxidative damage to lipid membranes and the reduction of peroxide radicals through its glycoprotein scavenging activity [23].

Various research findings suggest several mechanisms of fructose-induced hyperlipidemia. Previous studies have indicated that fructose alters enzyme activities that regulate hepatic carbohydrate metabolism, thereby impacting lipid metabolism and leading to hepatic insulin resistance [26]. In our study, we utilized a 25% w/v fructose solution in drinking water for 28 days to induce hyperlipidemia and vascular dysfunction. Fructose administration resulted in elevated levels of serum total cholesterol (TC), triglycerides (TG), very low-density lipoproteins (VLDL), and low-density lipoproteins (LDL), along with a significant impairment in endothelium-dependent vascular relaxation [27]. These findings align with previous research indicating that fructose administration is associated with insulin resistance, hypertriglyceridemia, hypercholesterolemia, and vascular dysfunction. Additionally, other studies have reported that fructose intake leads to impaired endothelial vascular relaxations, with insulin resistance contributing to compromised endothelial function [28]. This aligns with research indicating that the conversion of fructose carbon atoms into glycerol 3-phosphate may contribute to increased triglyceride levels in fructose-fed rats [26]. Our study found that the hydro-methanolic extract of *C. edulis* exhibited strong therapeutic potential against hyperlipidemia at a dose of 500 mg/Kg. This extract significantly reduced serum cholesterol, triglycerides, and LDL levels in fructose-fed rats. Elevated levels of cholesterol, triglycerides, LDL, and low levels of HDL are associated with the development of cardiovascular diseases. The plant may exert its antihyperlipidemic activity by modulating phosphofructokinase enzyme activity, which is crucial for lipogenesis [29]. The significant reduction in triglyceride levels observed with the hydro-methanolic extract of *C. edulis* suggests a potential mechanism involving the inhibition of chylomicron-triglyceride complex discharge into the lymph by the plant extract. Additionally, the study suggests that the plant's anti-hyperlipidemic activity could be associated with increased lecithin acyl transferase activity on HDL [30]. It's likely that the hydro-methanolic extract of *C. edulis* contains saponins, tannins, and triterpenoids, similar to other species of the Caralluma genus like *Caralluma tubercala*, which possess saponins[31]. Studies indicate that saponins in plant extracts form complexes with cholesterol, thereby modifying cholesterol metabolism. Furthermore, the presence of saponins, tannins, and triterpenoids in plant extracts is associated with hypolipidemic activity, suggesting that the reduction in serum lipid levels observed with *C. edulis* may be attributed to these active phytoconstituents, as observed in other species like *Caralluma adcendens* and *Caralluma fimbriata* [32].

Previous research indicates that endothelial damage plays a crucial role in the progression of vascular diseases [33]. Hyperlipidemia often contributes to endothelial impairment, leading to reduced availability of nitric oxide (NO) and consequent vascular dysfunction. The hydro-methanolic extract of *C. edulis* significantly mitigated vascular damage induced by fructose administration and demonstrated a dose-dependent improvement in endothelium-dependent vascular relaxation in response to Ach (10^{-9} to 10^{-4} M) in pre-constricted abdominal aorta rings with 10^{-6} M phenylephrine, particularly at the highest dose (500 mg/Kg), yielding results comparable to atorvastatin. The restoration of vascular endothelial damage by the plant extract may be attributed to enhanced NO availability and inhibition of endothelial nitric oxide synthase (eNOS) activity [34].

The effectiveness of *C. edulis* against hypertension, atherosclerosis, obesity and hyperlipidemia has also been

scientifically proved. But the current study conducted on the same plant is different in the sense that two animal models; rat model and rabbit model, have been used here. Furthermore, the detailed vasoprotective effects of the *C. edulis* have been reported in this study [35-36]. The previous studies have indicated that high levels of fructose (25% w/v) can lead to increased liver weight in animals. Administration of high doses of fructose to the liver may result in rapid lipogenesis, accumulation of triglycerides, and fat in hepatocytes [5,37]. In our study, histopathological examinations of isolated rat liver sections were conducted to evaluate the hepatoprotective effects of the plant. These examinations revealed that fructose administration caused structural damage to hepatocytes, potentially associated with steatosis or increased hepatic cholesterol synthesis due to elevated hepatic HMG Co-A reductase activity [29]. However, the hydro-methanolic extract of *C. edulis* demonstrated hepatoprotective activity, significantly improving hepatic architecture when administered at a dose of 500 mg/Kg/p.o.

Hyperlipidemia poses a significant risk factor for the development of atherosclerosis, which can lead to coronary heart disease and other vascular conditions [23]. Atherogenic and coronary risk indexes are crucial determinants in assessing the risk of atherosclerotic plaque formation. The atherogenic index reflects the deposition of fatty substances and lipids in arterial walls, impacting vital organs such as the aorta, liver, and kidneys. Higher values of the atherogenic index indicate an increased risk of damage to these organs [5,38,39]. In our study, the hydro-methanolic extract of *C. edulis* (administered at 500 mg/Kg/p.o) significantly reduced both atherogenic and coronary risk indexes ($P<0.01$) compared to both lipofundin-administered rabbits and fructose-fed rats. This substantial reduction suggests that certain pharmacologically active components present in *C. edulis* may contribute to its therapeutic potential in preventing atherosclerosis.

CONCLUSIONS

The findings indicate that the hydro-methanolic extract of *C. edulis* exhibits dose-dependent hypolipidemic activity, as well as antioxidant and vasoprotective properties. This suggests that specific active constituents within the plant extract may be responsible for its lipid-lowering effects. Further research is needed to fractionate the extract based on its activity, which would facilitate the identification and characterization of these constituents. Understanding their precise mode of action in experimental models could provide valuable insights into the therapeutic potential of *C. edulis*.

FUNDING

Authors received no funding for this study from any source.

COMPETING INTERESTS

No competing interests were declared by authors.

REFERENCES

1. Goff Jr D.C., Bertoni A.G., Kramer H., Bonds D., Blumenthal R.S., Tsai M.Y. and Psaty B.M., Dyslipidemia prevalence, treatment, and control in the multi-ethnic study of atherosclerosis (MESA) gender, ethnicity, and coronary artery calcium. *Circulation*. 2006; 113(5):647-656.
2. \Jafar T.H., Jafary F.H., Jessani S. and Chaturvedi N., Heart disease epidemic in Pakistan: women and men at equal risk. *Am. Heart J*. 2005; 150(2):221-226.
3. Valenzuela P.L., Ruilope L.M., Santos-Lozano A., Wilhelm M., Kränkel N., Fiuza-Luces C. and Lucia A., Exercise benefits in cardiovascular diseases: from mechanisms to clinical implementation. *Eur. Heart J*. 2023; 44(21):1874-1889.

4. Al-Rawi N.H. and Shahid A.M., Oxidative stress, antioxidants, and lipid profile in the serum and saliva of individuals with coronary heart disease: is there a link with periodontal health. *Minerva Stomatol*. 2017; 66(5):212-25.
5. Dhingra D., Lamba D., Kumar R., Nath P. and Gauttam S., Antihyperlipidemic activity of Aloe succotrina in rats: possibly mediated by inhibition of HMG-CoA Reductase. *ISRN Pharmacol*. 2014; 2014.
6. Navar-Boggan A.M., Peterson E.D., D'Agostino Sr R.B., Neely B., Sniderman A.D. and Pencina M.J., Hyperlipidemia in early adulthood increases long-term risk of coronary heart disease. *Circulation*. 2015; 131(5):451-458.
7. Nelson R.H., Hyperlipidemia as a risk factor for cardiovascular disease. *Prim. Care*. 2013; 40(1):195-211.
8. Abdelrahman A.M., Al Suleimani Y.M., Ashique M., Manoj P. and Ali B.H., Effect of infliximab and tocilizumab on fructose-induced hyperinsulinemia and hypertension in rats. *Biomed. Pharmacother*. 2018; 105:182-186.
9. Schelleman H., Bilker W.B., Brensinger C.M., Wan F., Yang Y.-X. and Hennessy S., Fibrate/Statin initiation in warfarin users and gastrointestinal bleeding risk. *Am. J. Med*. 2010; 123(2):151-157.
10. Akoglu H., Yilmaz R., Kirkpantur A., Arici M., Altun B. and Turgan C., Combined organ failure with combination antihyperlipidemic treatment: a case of hepatic injury and acute renal failure. *Ann. Pharmacother*. 2007; 41(1):143-147.
11. Thomas K.J., Nicholl J. and Coleman P., Use and expenditure on complementary medicine in England: a population based survey. *Complement Ther. Med.* 2001, 9(1)2-11.
12. Adnan M., Jan S., Mussarat S., Tariq A., Begum S., Afroz A. and Shinwari Z.K., A review on ethnobotany, phytochemistry and pharmacology of plant genus C aralluma R. Br. *J. Pharm. Pharmacol*. 2014; 66(10):1351-1368.
13. Waheed A., Barker J., Barton S.J., Khan G.-M., Najm-us-Saqib Q., Hussain M., Ahmed S., Owen C. and Carew M.A., Novel acylated steroidal glycosides from Caralluma tuberculata induce caspase-dependent apoptosis in cancer cells. *J. Ethnopharmacol*. 2011; 137(3):1189-1196.
14. Ghuffar A., Ahmad T. and Mushtaq M.N., Antihyperlipidemic effect of Berberis orthobotrys in hyperlipidemic animal models. *Bangladesh J. Pharmacol*. 2014; 9(3):377-382.
15. Chou C.-L., Pang C.-Y., Lee T.J. and Fang T.-C., Direct renin inhibitor prevents and ameliorates insulin resistance, aortic endothelial dysfunction and vascular remodeling in fructose-fed hypertensive rats. *Hypertens. Res*. 2013; 36(2):123-128.
16. Pramyothin P., Samosorn P., Poungshompoo S. and Chaichantipyuth C., The protective effects of Phyllanthus emblica Linn. extract on ethanol induced rat hepatic injury. *J. Ethnopharmacol*. 2006; 107(3):361-364.
17. Apaydin F.G., Baş H., Kalender S. and Kalender Y., Bendiocarb induced histopathological and biochemical alterations in rat liver and preventive role of vitamins C and E. *Environ. Toxicol. Pharmacol*. 2017; 49:148-155.
18. Sirivibulkovit K., Nouanthavong S. and Sameenoi Y., based DPPH assay for antioxidant activity analysis. *Anal. Sci*. 2018; 34(7):795-800.
19. Lu Y., Cui X., Zhang L., Wang X., Xu Y., Qin Z., Liu G., Wang Q., Tian K. and Lim K.S., The functional role of lipoproteins in atherosclerosis: Novel directions for diagnosis and targeting therapy. *Aging Dis*. 2022; 13(2):491.
20. Balakumar P., Maung-U K. and Jagadeesh G., Prevalence and prevention of cardiovascular disease and diabetes mellitus. *Pharmacol. Res*. 2016; 113:600-609.
21. Lai P., Du J.-R., Zhang M.-X., Kuang X., Li Y.-J., Chen Y.-S. and He Y., Aqueous extract of Gleditsia sinensis Lam. fruits improves serum and liver lipid profiles and attenuates atherosclerosis in rabbits fed a high-fat diet. *J. Ethnopharmacol*. 2011; 137(3):1061-1066.

22. Roche L.D. and Pérez Á.F., Protective Effects of Mangifera indica L. Extract Against Lipofundininduced Oxidative Stress in Rats. *Pharm. Crop*. 2012; 3(1).
23. Ali I., Ahmed W., Tariq M., Asghar R. and Hussain M.A., 10. Therapeutic potential of ethanolic extract of Solanum nigrum for lipofundin-induced hyperlipidemia in Rabbits. *Pure Appl. Biol.*. 2021; 5(1):85-90.
24. Pandey K.B. and Rizvi S.I., Plant polyphenols as dietary antioxidants in human health and disease. *Oxid. Medi and Cell. Longev*. 2009; 2:270-278.
25. Arulmozhi V., Krishnaveni M., Karthishwaran K., Dhamodharan G. and Mirunalini S., Antioxidant and antihyperlipidemic effect of Solanum nigrum fruit extract on the experimental model against chronic ethanol toxicity. *Pharmacogn. Mag.*. 2010; 6(21):42.
26. Subasini U., Thenmozhi S., Sathyamurthy D. and Rajamanickam G.V., Attenuation of fructose induced hyperlipidemia of Enicostemma axillare. *Int. J. Pharm. Phytopharmacol. Res*. 2012; 1(5):306-312.
27. Huang F., Lezama M.A.R., Ontiveros J.A.P., Bravo G., Villafaña S., del-Rio-Navarro B.E. and Hong E., Effect of losartan on vascular function in fructose-fed rats: the role of perivascular adipose tissue. *Clin. Exp. Hypertens*. 2010; 32(2):98-104.
28. Katakam P.V., Ujhelyi M.R., Hoenig M.E. and Miller A.W., Endothelial dysfunction precedes hypertension in diet-induced insulin resistance. *Am. J. Physio*. 1998; 275(3):R788-R792.
29. Kumar N., Mudgal J., Parihar V.K., Nayak P.G., Kutty N.G. and Rao C.M., Sesamol treatment reduces plasma cholesterol and triacylglycerol levels in mouse models of acute and chronic hyperlipidemia. *Lipids*. 2013; 48:633-638.
30. Abdel-Sattar E., Harraz F.M., Ghareib S.A., Elberry A.A., Gabr S. and Suliaman M.I., Antihyperglycaemic and hypolipidaemic effects of the methanolic extract of Caralluma tuberculata in streptozotocin-induced diabetic rats. *Nat. Prod. Res*. 2011; 25(12):1171-1179.
31. Rauf A., Jan M., Rehman W. and Muhammad N., Phytochemical, phytotoxic and antioxidant profile of Caralluma tuberculata NE Brown. *Wudpecker Journal of Pharmacy and Pharmacology*. 2013; 2(2):21-25.
32. Maheshu V., Priyadarsini D.T. and Sasikumar J.M., Antioxidant capacity and amino acid analysis of Caralluma adscendens (Roxb.) Haw var. fimbriata (wall.) Grav. & Mayur. aerial parts. *J. Food Sci Technol*. 2014; 51:2415-2424.
33. Tao X., Jing-Bo P., Wen-Tong Z., Xin Z., Tao-Tao Z., Shi-Jun Y., Lei F., Zhong-Mei Z. and Da-Yong C., Antiatherogenic and anti-ischemic properties of traditional Chinese medicine Xinkeshu via endothelial protecting function. *Evid. Based Complement Alternat. Med*. 2012; 2012.
34. Jamshed H. and Gilani A.H., Almonds inhibit dyslipidemia and vascular dysfunction in rats through multiple pathways. *J. Nutr*. 2014; 144(11):1768-1774.
35. Akram A., Jamshed A., Anwaar M., Rasheed H.F.M., Haider S.I. Aslam N. and Jabeen Q., Evaluation of Caralluma edulis for its potential against obesity, atherosclerosis and hypertension. *Dose Response*. 2023; 12(21): 1-12.
36. Ashfaq A., Khan A.U., Minhas A.M., Aqeel T., Asseri A.M.,and Bukhari I.A., Anti-hyperlipidemic effects of Caralluma edulis (Asclepiadaceae) and Verbena officinalis (Verbenaceae) whole plants against high-fat diet-induced hyperlipidemia in mice. *Trop. J. Pharm. Res.* 2017; 16(10): 2417-2423.
37. Pavithra K. and Manimaran V., A Review of Safety, Quality, Regulation, and Delivery Approaches for Phytopharmaceuticals. *JJPS.* 2024: 17(2): 316-332.
38. AlKhoury R. and AlKhatib R., Rumex conglomeratus Murr. Grown Wild in Syria: Phytochemical Analysis and in Vitro Antioxidant Activities of Aerial Parts and Rhizomes Extracts. *JJPS.* 2024; 17(4):659-674.
39. Abu-Darwish D., Shibli R. and Al-Abdallat A.M., Phenolic Compounds and Antioxidant Activity of Chiliadenus montanus (Vhal.) Brullo. grown in vitro. *JJPS.* 2024; 17(3):611-628.

نقص شحميات الدم وإمكانية حماية الأوعية الدموية في *Caralluma edulis* دراسة نسيجية وكيميائية حيوية

طيبة قنوي[1]، عبد الملك[1*]، عامر مشتاق[2*]، الامجير[3]، محمد فياض الرحمن[4]، عمر فاروق جوهر[5]

[1]كلية الصيدلة، جامعة سرجودا، سرجودا، باكستان

[2]قسم العلوم الصيدلانية، جامعة الكلية الحكومية، لاهور، باكستان

[3]كلية الصيدلة بجامعة البنجاب، جامعة البنجاب، لاهور، باكستان

[4]معهد الكيمياء، جامعة سرجودا، سرجودا، باكستان

[5] معهد التكنولوجيا الحيوية الصناعية، جامعة الكلية الحكومية، لاهور، باكستان

ملخص

(Apocynaceae**)** معروف جيدًا بخصائصه الطبية، بما في ذلك الأنشطة المضادة للأكسدة والالتهابات والمضادة للميكروبات وخافضة السكر في الدم، وقد تم استخدامه كعلاج قيم في مختلف الثقافات. يهدف هذا العمل العلمي إلى التحقق من فعالية C. edulis في خفض مستوى الدهون باستخدام نموذجين حيوانيين لارتفاع نسبة الدهون في الدم: الأرانب التي يسببها الليبوفوندين والفئران التي يسببها الفركتوز. تم إعطاء الليبوفوندين عن طريق الوريد بمعدل 2 مل / كجم لمدة 23 يومًا، في حين تم إعطاء الفركتوز (25٪ وزن / حجم) لمدة 28 يومًا متتالية عن طريق إذابته في مياه الشرب لتحفيز اضطراب شحوم الدم واختلال وظائف الأوعية الدموية. تم إعطاء المستخلص المائي الكحولي لـ C. edulis عن طريق الفم (250 و 500 مجم / كجم) للمجموعات التجريبية، بينما تم إعطاء أتورفاستاتين (10 مجم / كجم ص) لحيوانات المجموعة الضابطة القياسية فقط. تم جمع عينات الدم لتقييم المعايير البيوكيميائية المختلفة. علاوة على ذلك، تم إجراء الفحص النسيجي لأنسجة الكبد والشريان الأورطي الصدري من الجرذان التي تتغذى على الفركتوز، إلى جانب تقييم خصائصها المرخية للأوعية الدموية. أظهر المستخلص المائي الميثانولي لـ C. edulis تأثيرات خافضة للدهون تعتمد على الجرعة، مما يقلل بشكل كبير من نسبة الكوليسترول في الدم والدهون الثلاثية والبروتينات الدهنية منخفضة الكثافة بجرعة 500 ملغم / كغم في كلا النموذجين، مقارنة بأتورفاستاتين. علاوة على ذلك، أظهر المستخلص المائي الكحولي نشاطًا كبيرًا يعتمد على ارتخاء الأوعية الدموية وتأثيرات وقائية للكبد في الجرذان التي تتغذى على الفركتوز. أظهر C. edulis أيضًا إمكانات مضادة للأكسدة من خلال نشاط مسح الجذور الحرة. تشير هذه النتائج إلى أن C. edulis يمتلك خصائص خافضة لشحوم الدم وواقية للأوعية الدموية، والتي تعزى على الأرجح إلى مكونات دوائية نشطة محددة، مما يدعم استخدامه التقليدي.

الكلمات الدالة: ليبوفوندين، فرط شحميات الدم الناجم عن الفركتوز، أتورفاستاتين، دراسات مرخيات الأوعية، الكولسترول في الدم.

المؤلف المراسل:

عبد الملك: abdul.malik@uos.edu.pk

عامر مشتاق: aamir.mushtaq@gcu.edu.pk

تاريخ استلام البحث 2024/03/11 وتاريخ قبوله للنشر 2024/07/18.