

Original Article

THERAPEUTIC POTENTIAL OF *Clitoria ternatea* FLOWER NANOPARTICLES IN AMELIORATING DYSLIPIDEMIA, LIVER DYSFUNCTION, OXIDATIVE STRESS, AND SYSTEMIC INFLAMMATION IN RATS

Ayesha kousar ^{1,*}, Muhammad Naeem ², and Bushra Zaidi ³

¹Department of Graduate Institute of Acupuncture Science, China Medical University, Taiwan Province of China.

²Department of Zoology, Government College University Lahore, Pakistan.

³Department of Zoology, Bahauddin Zakariyah University Multan, Punjab, Pakistan.

*Corresponding author, E-mail: ayeshakousar415@gmail.com (Tel: +92-318-9479905)

ABSTRACT

Received
August 4, 2026

Accepted
August 23, 2026

Published
October 10, 2026

This study examines the therapeutic effects of *Clitoria ternatea* flower nanoparticles in ameliorating dyslipidemia, hepatic injury, oxidative stress, and inflammatory responses in hyperlipidemic rats. Sixty Wistar rats were randomly divided into four groups: normal control, high-fat diet control, and high-fat diet supplemented with *C. ternatea* nanoparticles at doses of 45 and 90 mg/kg administered orally for 60 days. Serum lipid profile, liver function biomarkers, oxidative stress indices, and inflammatory mediators were assessed using standard biochemical and ELISA techniques. High-fat diet Administration significantly $p = 0.005$ total cholesterol (181.51 ± 6.45), triglycerides (172.14 ± 5.72), LDL-C (34.14 ± 2.81), and VLDL-C (32.24 ± 1.13), while reducing HDL-C (27.53 ± 1.36) compared with the normal control group. Liver function markers including ALT (92.63 ± 3.54), AST (172.65 ± 5.72), ALP (227.34 ± 6.81), and total bilirubin (1.27 ± 0.08) were markedly increased in hyperlipidemic rats. Additionally, elevated malondialdehyde (6.82 nmol/mL) indicated enhanced lipid peroxidation, while antioxidant enzyme activities were reduced. Systemic inflammation was evidenced by increased TNF- α (46.23 ± 1.72), IL-6 (39.42 ± 1.54), IL-1 β (27.46 ± 1.23), and CRP (3.91 ± 0.18) in G2. Treatment with *C. ternatea* flower nanoparticles dose-dependently restored these alterations. The nanoparticles improved lipid homeostasis, preserved hepatic integrity, reduced oxidative damage, and suppressed pro-inflammatory cytokine production. These findings demonstrate that *C. ternatea* flower nanoparticles exert potent antihyperlipidemic, hepatoprotective, antioxidant, and anti-inflammatory effects.

Keywords: Hyperlipidemia, anthocyanins, *Clitoria ternatea*, cholesterol.

1. INTRODUCTION

Hyperlipidemia is a main factor for cardiovascular disease and a common disorder categorized by higher levels of cholesterol, which is also caused by fatty liver disease, obesity, and other metabolic disorders (Wazir *et al.*, 2023). Hyperlipidemia disrupts hepatic lipid absorption, leading to liver dysfunction, oxidative stress, and chronic inflammation (Cheng *et al.*, 2024). Excessive lipid accumulation contributes to disease progression and is involved in metabolic disturbances. Lipid abnormalities directly cause lipotoxicity-driven liver injury (Yuan *et al.*, 2016). The lipid abnormalities adversely affect the function of several organs and accelerate the development of atherosclerosis, a pathological process strongly associated with abnormal lipid accumulation, transport, and metabolism (Pacinella *et al.*, 2022).

Oxidative stress is a fundamental mechanism in the pathogenesis of hyperlipidemia and associated complications, causing cellular injury and playing a vital role in hyperlipidemia (Masenga *et al.*, 2023). Elevated malondialdehyde levels with reduced activities of antioxidant enzymes are commonly used as indicators of oxidative stress, which leads to mitochondrial dysfunction and promotes pro-

tein oxidation and oxidative damage (Arsova *et al.*, 2009). Simultaneously, increased synthesis of cytokines exacerbates hepatic injury and metabolic dysfunction, playing a pivotal part in initiation and development of metabolic infections (De Col *et al.*, 2024). The pro-inflammatory cytokines are recognized as major mediators that contribute to metabolic dysfunction, endothelial injury, and hepatic inflammation (Ullah *et al.*, 2024). C-reactive protein is also extensively used as a systemic marker of inflammation and is strongly related to cardiovascular risk and tissue damage (Amezcuca *et al.*, 2023).

Clitoria ternatea L. is a butterfly pea that is extensively used in traditional medicine throughout Asia (Oguis *et al.*, 2019). The flowers of *C. ternatea* are rich in anthocyanins, flavonoids, and phenoplast compounds which possess antioxidant and anti-inflammatory activities (Jamil *et al.*, 2018). Nanoparticle formulation stabilizes anthocyanins, enhances bioavailability, and improves tissue distribution of *C. ternatea* extracts. It also contains hepatoprotective, antihyperglycemic, and cardioprotective properties and has demonstrated its potential for treating metabolic disorders (Balogh *et al.*, 2023). Nanotechnology has appeared as an effective strategy for improving absorption and biological activity (Pateiro *et al.*, 2021). It increases the surface area of phytochemicals and improves tissue distribution,

Access this article online



DOI: <https://doi.org/10.25271/sjuoz.2026.14.4.1991>

Printed ISSN 2663-628X;
Electronic ISSN 2663-6298

Science Journal of University of Zakho
Vol. 14, No. 04, pp. 651-656, October -2026

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thereby enhancing therapeutic efficacy (Shah *et al.*, 2025). Plant-based nanotherapeutics offer clinical potential for managing metabolic syndrome and fatty liver disease (Wei *et al.*, 2018).

The dietary polyphenols and anthocyanins reduce hepatic lipid accumulation and play a role in lipid maintenance through regulating cholesterol biosynthesis, increasing fatty acid oxidation, and promoting cholesterol excretion (Chang *et al.*, 2013; Naeem *et al.*, 2026). These bioactive compounds protect cellular structures and strengthen endogenous antioxidant defense systems (Rao *et al.*, 2025). Their ability to suppress inflammatory signaling pathways contributes to curing metabolic syndromes (He *et al.*, 2020). The application of nanotechnology exhibits enhanced cellular uptake and tissue distribution, allowing lower therapeutic doses while diminishing undesirable effects. (Wei *et al.*, 2018). These advantages encouraged extensive research on plant-based nanoparticles for various chronic metabolic diseases (Zhang *et al.*, 2022; Abdulla *et al.*, 2023).

Despite increasing attention to plant-derived nanoparticles, limited studies are available regarding *Clitoria ternatea* flower nanoparticles. Therefore, the present study aimed to evaluate the potential protective effects of *C. ternatea* flower nanoparticles in hyperlipidemic rats by assessing serum lipid profiles, liver function biomarkers, oxidative stress indices, and systemic inflammatory mediators.

2. MATERIALS AND METHODS

Experimental Animals

Sixty healthy Wistar albino rats aged 8–10 weeks, weighing 250 ± 12 g were collected from different villages in Lahore, Punjab, Pakistan, and transferred to the Department of Zoology, Lahore College for Women University, Lahore, Pakistan. All the rats were housed in standard plastic laboratory cages and were acclimatized for one week before the commencement of the experiment. During the acclimatization period, the animals were maintained at a temperature of $23 \pm 3^\circ\text{C}$ and a relative humidity of $54 \pm 9\%$. Drinking water was provided ad libitum throughout the study period.

Ethical approval

This study was designed in accordance with the methods approved by the Animal Ethics Committee (LCWU/IAEC/2025/445) of the Department of Zoology.

Experimental Design

Sixty days experimental study with four groups (G1-G4) was designed in triplicate, and then all animals were distributed into all groups. Each replicate of each group contained 5 rats ($n = 15$ per group; each rat as independent unit). G1 was the control group, which received rodent pellet diet (Hi-Tech Feeds (Pvt.) Ltd., Lahore, Pakistan), G2 contained a diet with high-fat to bring hyperlipidemia in rats, G3 received a commercial diet with *Clitoria ternatea* flower nanoparticles at a low dose of 45 mg/kg; and G4 received a commercial diet with *Clitoria ternatea* flower nanoparticles at a high dose of 90 mg/kg. The nanoparticles were given daily by oral gavage using the Gavage needle (not mixed) for 60 days, and the health status and behavioral changes were checked during the experiment.

Synthesis of Nanoparticles

The flowers of *C. ternatea* were taken locally and washed with purified water. The flowers were dried out and crushed into a fine powder. The powder was taken out with 70% ethanol (10 : 1 solvent-to-powder ratio, 40°C , 4 hours), and then filtered. The extract was then used for nanoparticles by the ionic gelation method by the application of chitosan and sodium tripolyphosphate. After that, the

nanoparticles were collected by centrifugation, dried, and kept at 4°C till usage. Before use, nanopowder putted into the distilled water and vortex-mixed to get a suspension (Giang *et al.*, 2025).

Blood Collection and Serum Preparation

Before Blood collection, all the animals were fasted for about 12 h, then all the rats were anesthetized with ketamine and xylazine at about 80 and 10 mg/kg, respectively. Blood was taken and transferred into serum tubes and allowed to clot, the samples were subsequently centrifuged at 3,000 rpm for 10 min to separate the serum. The obtained serum was carefully transferred into labeled microcentrifuge tubes and stored at -20°C until biochemical analysis.

Determination of Serum Lipid Profile

The lipid parameters like Total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol HDL-C, low-density lipoprotein cholesterol LDL-C, and very low-density lipoprotein cholesterol (VLDL-C) were assessed by Mindray BS-120 semi-automated analyzer (China) as studied by Antonis (1967).

Assessment of Liver Function Biomarkers

The serum alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin, and aspartate aminotransferase (AST) were determined by use of a semi-automated analyzer, and all the measures were performed as described by Burtis and Bruns (2014).

Oxidative Stress Analysis

The oxidative stress indicators such as malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT) were determined by means of the assay kits (Elabsience Biotechnology Inc., Wuhan, China). The assays were performed by means of a microplate reader. All the measures were assessed following the protocol of Wang and Joseph (1999).

Determination of Inflammatory Biomarkers

Serum levels of tumor necrosis factor-alpha ($\text{TNF-}\alpha$), interleukin-1 beta ($\text{IL-1}\beta$), interleukin-6 (IL-6), and C-reactive protein (CRP) were assessed by the use kits of ELISA. The microplate reader was used to measure the absorbance at 450 nm. The standard curves were generated, and the concentrations were calculated according to the protocol of the kit as studied by Elswefy *et al.* (2016).

3. RESULTS

Table 1 showed the significant changes in all serum lipid parameters across all groups. Rats in G2 revealed advancement in total cholesterol (181.51 ± 6.45 mg/dL), 172.14 ± 5.72 mg/dL triglycerides, and VLDL-C (32.24 ± 1.13 mg/dL), with a reduction in HDL-C (27.53 ± 1.36 mg/dL) compared to G1. *Clitoria ternatea* flower nanoparticles improved lipid parameters in G3 which consisted of the low-dose group showing significant decreases in cholesterol, triglycerides, and VLDL-C, with a rise in HDL-C. The improvements were recorded in the G4 group, in which cholesterol, triglycerides, HDL-C, and VLDL-C values were nearly equal to the control animals, which represented the dose-dependent hypolipidemic effect of the nanoparticles. The LDL-C values also significantly changed in the groups in this study, demonstrating that *Clitoria ternatea* flower nanoparticles efficiently improved the changes in serum lipid digestion.

Table 1: Effect of *Clitoria ternatea* Flower Nanoparticles on Serum Lipid Profile.

Parameter (mg/dL)	G1	G2	G3	G4	p-value
Total Cholesterol (TC) mg/dL	82.21 ± 2.12 ^c	181.51 ± 6.45 ^a	132.45 ± 1.28 ^b	98.81 ± 3.36 ^c	0.005
Triglycerides (TG) mg/dL	72.33 ± 2.84 ^c	172.14 ± 5.72 ^a	122.82 ± 1.84 ^b	87.76 ± 3.67 ^c	0.006
HDL-C mg/dL	48.18 ± 1.84 ^a	27.53 ± 1.36 ^c	37.14 ± 1.72 ^b	44.81 ± 1.73 ^a	0.005
LDL-C mg/dL	21.1 ± 1.32 ^c	34.14 ± 2.81 ^a	72.36 ± 3.64 ^b	37.72 ± 1.28 ^c	0.006
VLDL-C mg/dL	13.34 ± 0.62 ^c	32.24 ± 1.13 ^a	25.39 ± 0.92 ^b	18.65 ± 0.81 ^c	0.005

Data = mean ± SEM (n = 15). Different superscripts (^{a,b,c}) differ significantly at p < 0.05. LDL-C and VLDL-C were calculated using Friedewald formula.

G2 group displayed the maximum ALT (92.63 ± 3.54), AST (172.65 ± 5.72), ALP (227.34 ± 6.81), and total bilirubin (1.27 ± 0.08) levels as compared to the control group which observed the corresponding values of 35.72 ± 1.55, 82.46 ± 3.37, 122.37 ± 4.76, and 0.45 ± 0.04, respectively. Rats in the low dose (G3) showed reduced ALT (64.48 ± 2.71) and AST (122.42 ± 2.73), while the high-dose group (G4) demonstrated significant change, with ALT and AST de-

creasing to 45.14 ± 2.36 and 92.18 ± 3.96, respectively. Similarly, ALP and total bilirubin decreased to 137.63 ± 5.41 and 0.58 ± 0.04 in G4, which represented considerable protection against high-fat diet-induced hepatic dysfunction. These findings demonstrated significantly improved all hepatic biomarkers with the *Clitoria ternatea* flower nanoparticles.

Table 2: Effect of *Clitoria ternatea* Flower Nanoparticles on Liver Function Biomarker[cite: 2].

Parameter	G1	G2	G3	G4	p-value
ALT (U/L)	35.72 ± 1.55 ^c	92.63 ± 3.54 ^a	64.48 ± 2.71 ^b	45.14 ± 2.36 ^c	0.004[cite: 2]
AST (U/L)	82.46 ± 3.37 ^c	172.65 ± 5.72 ^a	122.42 ± 2.73 ^b	92.18 ± 3.96 ^c	0.005[cite: 2]
ALP (U/L)	122.37 ± 4.76 ^c	227.34 ± 6.81 ^a	172.52 ± 4.74 ^b	137.63 ± 5.41 ^c	0.006[cite: 2]
Total Bilirubin (mg/dL)	0.45 ± 0.04 ^c	1.27 ± 0.08 ^a	0.81 ± 0.05 ^b	0.58 ± 0.04 ^c	0.005[cite: 2]

Data = mean ± SEM (n = 15). Different superscripts (^{a,b,c}) differ significantly at p < 0.05[cite: 2].

This study demonstrated significant changes in the antioxidant status of the rats in the groups (Table 3). High-fat diet showed a significant increase in lipid peroxidation with the higher MDA concentration, which improved from 2.17 ± 0.12 nmol/mL in the normal control group to 6.82 ± 0.17 nmol/mL in the hyperlipidemic group. In contrast, the SOD, CAT, and GPx were considerably reduced in G2, reaching 5.11 ± 0.21, 32.74 ± 1.54, and 42.63 ± 2.06, respectively. This study of *Clitoria ternatea* flower nanoparticles ef-

ficiently restored the oxidant-antioxidant balance. G3 group significantly decreased MDA levels while increasing the activities of SOD, CAT, and GPx. The high-dose group (G4), showed MDA declined to 2.87 ± 0.16 nmol/mL, with the recovery of SOD (11.07 ± 0.32 U/mL), CAT (59.22 ± 1.17 U/mL), and GPx (71.23 ± 2.77 U/mL). These findings indicate the alleviation of oxidative stress and reinforce the endogenous antioxidant defense system.

Table 3: Effect of *Clitoria ternatea* Flower Nanoparticles on Oxidative Stress Biomarkers[cite: 3].

Parameter	G1	G2	G3	G4	p-value
Malondialdehyde (nmol/mL)	2.17 ± 0.12 ^c	6.82 ± 0.17 ^a	4.43 ± 0.21 ^b	2.87 ± 0.16 ^c	0.004[cite: 3]
SOD (U/mL)	12.42 ± 0.38 ^a	5.11 ± 0.21 ^c	8.63 ± 0.47 ^b	11.07 ± 0.32 ^a	0.005[cite: 3]
CAT (U/mL)	62.72 ± 2.26 ^a	32.74 ± 1.54 ^c	48.46 ± 2.03 ^b	59.22 ± 1.17 ^a	0.005[cite: 3]
GPx (U/mL)	75.94 ± 2.14 ^a	42.63 ± 2.06 ^c	61.28 ± 2.41 ^b	71.23 ± 2.77 ^a	0.006[cite: 3]

Data = mean ± SEM (n = 15). Different superscripts (^{a,b,c}) differ significantly at p < 0.05[cite: 3].

Rats in the G2 group demonstrated a marked inflammatory response with significant increases in serum TNF-α, IL-6, IL-1β, and CRP levels as compared to the control group. Specifically, TNF-α improved from 17.43 ± 0.84 in G1 to 46.23 ± 1.72 in G2, while IL-6 and IL-1β rose from 13.74 ± 0.63 and 7.87 ± 0.41 to 39.42 ± 1.54 and 27.46 ± 1.23, respectively. Similarly, CRP concentration increased from 0.81 ± 0.05 mg/L in the control group to 3.91 ± 0.18 mg/L

in hyperlipidemic rats. The G3 group presented reductions in TNF-α (31.62 ± 1.46), IL-6 (24.18 ± 1.11), IL-1β (18.76 ± 0.82), and CRP (3.26 ± 0.12) compared with G2. G4 group indicated a better anti-inflammatory outcome because of lower levels of IL-6, TNF-α, IL-1β, and CRP, at 21.61 ± 1.12, 17.41 ± 0.85, 12.53 ± 0.66, and 1.19 ± 0.08, respectively. These results indicated significant changes in the inflammatory biomarkers in the groups (Table 4).

Table 4: Effect of *Clitoria ternatea* Flower Nanoparticles on Systemic Inflammatory Biomarkers[cite: 4].

Parameter	G1	G2	G3	G4	p-value
TNF-α (pg/mL)	17.43 ± 0.84 ^c	46.23 ± 1.72 ^a	31.62 ± 1.46 ^b	21.61 ± 1.12 ^c	0.005[cite: 4]
IL-6 (pg/mL)	13.74 ± 0.63 ^c	39.42 ± 1.54 ^a	24.18 ± 1.11 ^b	17.41 ± 0.85 ^c	0.006[cite: 4]
IL-1β (pg/mL)	7.87 ± 0.41 ^c	27.46 ± 1.23 ^a	18.76 ± 0.82 ^b	12.53 ± 0.66 ^c	0.005[cite: 4]
CRP (mg/L)	0.81 ± 0.05 ^c	3.91 ± 0.18 ^a	3.26 ± 0.12 ^b	1.19 ± 0.08 ^c	0.005[cite: 4]

4. DISCUSSION

This study examines the *C. ternatea* flower nanoparticles and observed enhanced liver role, oxidative stress, and inflammatory biomarkers in rats. This study reported higher total cholesterol, triglycerides, low-density lipoprotein/VLDL, and less HDL in Hyperlipidemic animals and restored these alterations with *Clitoria ternatea* nanoparticles. Similarly, Dewanjee et al. (2020) conducted an experimental study on *C. ternatea* and reported reduced serum cholesterol in rats and triglycerides while improving HDL concentrations due to the action of anthocyanins and flavonoids. Sasmana et al. (2024)

demonstrated that phytochemicals in *C. ternatea* can suppress hepatic cholesterol synthesis and reduce fat accretion in tissues. Omodanisi et al. (2017) reported that *Moringa olifera* supplementation can reduce oxidative damage and improve dyslipidemia in animals. Similarly, Ahmed (2024) and Kresnapati et al. (2025) studied the butterfly pea petal extract and observed reduced hepatic lipid and enhanced lipid digestion in mice. Similar findings were also observed by Ochoa et al. (2026), who observed significant decreases in TC, TG, LDL-C, and VLDL-C, along with increased HDL-C by the supplementation of *Saussurea costus* extract in hyperlipidemic rats.

This study also observed increased serum ALT, AST, ALP, and

total bilirubin levels, which are consistent with excessive hepatic lipid accumulation, disrupting membrane integrity; however, with the *C. ternatea* nanoparticles, the ALT, AST, ALP, and total bilirubin were reduced, indicating the hepatoprotective effect. Similar findings were also documented by Al-Salmi *et al.* (2019), who recorded a reduction in liver enzymes with green tea supplementation as a nanoparticle in rats. Nithianantham *et al.* (2013) also observed alterations in liver enzymes with *C. ternatea* and demonstrated improved antioxidant status and reduced hepatic injury. Comparable outcomes were reported by Mobasher *et al.* (2023), who reported significantly reduced levels of liver enzymes in diabetic rats with the application of *C. ternatea*. Similarly, Damodaran *et al.* (2020) reported the safe effect of *C. ternatea* against oxidative damage and preserving liver function.

The present study showed higher MDA levels with reduced activities of SOD, CAT, and GPx with the *Clitoria ternatea* flower nanoparticles; this alteration was reversed by reducing MDA levels and restoring the antioxidant enzymes. Comparable outcomes were stated by Balderas *et al.* (2022), who reported better antioxidant activities and less damage with the use of *Clitoria ternatea* in high-fat diet-fed animals. Similarly, Rasool *et al.* (2014) demonstrated that *Glycyrrhiza glabra* nanoparticles improved SOD and CAT and observed decreasing lipid peroxidation in rats. Mobasher *et al.* (2023) also found that anthocyanin-rich extracts can strengthen the antioxidant defenses and effectively scavenge reactive oxygen species. Koushan *et al.* (2022) studied *Illicium verum* nanoparticles and observed normal hepatic function and improved antioxidant status by reducing MDA levels.

Significantly elevated serum TNF- α , IL-6, IL-1 β , and CRP concentrations were observed in the high-fat diet rats in this study, and *Clitoria ternatea* nanoparticles reduced the levels of all inflammatory biomarkers. Similarly, Memarzai *et al.* (2021) observed the reduction in IL-1 β and CRP with curry leaves in diabetic rats and recorded improvements in oxidative stress and liver function. Nair *et al.* (2015) reported suppressed production of cytokines owing to high anthocyanin and flavonoid content in *Clitoria ternatea*, while Maneesai *et al.* (2021) demonstrated that butterfly pea extract reduced the levels of all inflammatory biomarkers, which was attributed to inhibit oxidative stress and regulate inflammatory signaling pathways. Widowati *et al.* (2024) documented reduced inflammatory biomarkers and a comprehensive effect against hyperlipidemia-induced metabolic injury with *C. ternatea*.

CONCLUSION

This study concluded that *Clitoria ternatea* flower nanoparticles efficiently ameliorate dyslipidemia, protect liver function, restore antioxidant defenses, and suppress systemic inflammation in rats. Nanoparticles provide enhanced stability and bioavailability of anthocyanins. The *Clitoria ternatea* flower nanoparticles exert anti-hyperlipidemic, hepatoprotective, and antioxidant effects. It is regarded as a promising nanotherapeutic strategy for managing hyperlipidemia and related metabolic complications in rats. This limitation of this study was No non-nanoparticle group was included for comparison

Acknowledgements:

The authors sincerely acknowledge the Department of Zoology, Lahore College for Women University, Lahore, for supporting the research trial.

Author Contributions:

A.K.: conducting and writing the manuscript; M.N. and B.Z.: Data analysis, Validation, Review

Conflict of Interest:

No conflicts of interest for publication of this manuscript.

Funding:

No Funding

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