International Journal of Advanced Biochemistry Research

ISSN Print: 2617-4693
ISSN Online: 2617-4707
NAAS Rating (2025): 5.29
IJABR 2025; 9(8): 103-110
www.biochemjournal.com
Received: 11-05-2025
Accepted: 15-06-2025

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Protective Efficacy of Neem (*Azadirachta indica*) against *Lantana camara*-Induced hematobiochemical alterations in Wistar rats

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DOI: https://www.doi.org/10.33545/26174693.2025.v9.i8b.5105

Abstract
Lantana camara, a plant recognized for its hepatotoxic properties, can cause considerable hematological and biochemical disruptions in mammals. This study aimed to evaluate the protective role of Neem (*Azadirachta indica*) leaf extract against such toxic effects in female Wistar rats. A total of thirty rats were divided into five groups of six animals each. Group I served as the untreated control, while Group II received Neem extract alone. Hepatic injury was induced in Group III through oral administration of *Lantana camara* extract. Group IV was pre-treated with Neem extract before toxicant exposure to assess its prophylactic potential, and Group V received Neem extract after *Lantana camara* administration to evaluate its therapeutic efficacy. Hematological and biochemical analyses revealed that rats exposed to *Lantana camara* (Group III) exhibited significant ($p<0.05$) reductions in red blood cell count, hemoglobin, hematocrit, and mean corpuscular hemoglobin concentration, along with elevated serum levels of AST, ALT, ALP, cholesterol, urea, and creatinine. Additionally, total protein, albumin, and lymphocyte counts were notably decreased. Both preventive and therapeutic administration of Neem extract (Groups IV and V) showed marked amelioration of these toxic effects, with the pre-treatment group demonstrating superior protection. No significant alterations were observed in differential leukocyte counts across treatment groups. These findings suggest that Neem leaf extract offers effective biochemical and hematological protection against *Lantana camara*-induced toxicity, particularly when used as a preventive intervention.

Keywords: Neem, *Azadirachta indica*, *Lantana camara*, hepatotoxicity, hematology, biochemical parameters, Wistar rats

Introduction
Lantana camara L., a woody and evergreen flowering shrub belonging to the family Verbenaceae, has emerged as one of the most noxious invasive weeds worldwide. Native to Central and South America, the plant was introduced to India in the early 19th century as an ornamental species, but it has since become a serious ecological and veterinary problem. It has now spread to over 60 countries and invaded millions of hectares of grazing lands, particularly in forested and semi-arid regions such as the Himalayan foothills and parts of Rajasthan (Bhatt *et al*., 2021; Sharma *et al*., 2019) [1, 2]. Its aggressive colonization is facilitated by seed dispersal through birds and livestock, rapid vegetative regrowth, and its allelopathic suppression of native flora (Kumar *et al*., 2022) [3].

Among its several morphotypes, *L. camara var. aculeata*, distinguished by its red or orange flowers, is considered the most toxic. The primary toxic components of this plant are pentacyclic triterpenoids, particularly lantadene A and lantadene B, which accumulate in the leaves and young shoots. These compounds induce intrahepatic cholestasis, bile stasis, hepatocellular degeneration, and oxidative stress leading to hepatic dysfunction in both ruminants and non-ruminants (Sharma *et al*., 2007; Soren *et al*., 2020) [4, 5]. Animals, especially cattle, sheep, and goats, often consume the plant inadvertently during drought or fodder scarcity, resulting in toxicosis. Clinical manifestations include reduced feed intake, lethargy, jaundice, dehydration, photosensitivity, and in severe cases, hepatic failure and death (Reddy *et al*., 2023) [6].

Biochemically, *Lantana camara* toxicity is characterized by altered hematological and serum biochemical parameters, particularly elevated levels of hepatic enzymes such as alanine

aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), total bilirubin, urea, and creatinine. These are indicative of liver injury and impaired renal function. Concurrently, reductions in total erythrocyte count (TEC), hemoglobin (Hb), hematocrit (HCT), and serum protein levels reflect systemic toxicity and oxidative stress (Bharathi & Prasad, 2022; Sharma *et al*., 2019) [7, 2].

Given the substantial economic losses and animal health burden caused by lantana toxicity, especially in agrarian states like Rajasthan where animal husbandry forms a major component of rural livelihood, there is a compelling need for cost-effective and accessible hepatoprotective interventions. In this context, *Azadirachta indica* (Neem), a medicinal tree widely used in traditional Indian systems of medicine, has attracted significant attention. Neem leaves contain a variety of bioactive phytochemicals including quercetin, nimbin, azadirachtin, and other polyphenols that exhibit antioxidant, anti-inflammatory, antimicrobial, and hepatoprotective activities (Alzohairy, 2016) [8].

Studies have shown that Neem leaf extract can restore antioxidant enzyme levels such as superoxide dismutase (SOD) and catalase (CAT), reduce lipid peroxidation, and normalize altered liver enzymes in various models of chemically induced hepatotoxicity (Asghar *et al*., 2022; Kumar & Joshi, 2021) [9, 10]. Moreover, neem has demonstrated protective effects in models of carbon tetrachloride and paracetamol-induced liver injury in rodents, suggesting its potential utility in managing phytotoxin-induced damage (Devi *et al*., 2023) [11].

Despite these promising findings, data on the use of neem to mitigate *Lantana camara*-induced hepatotoxicity, particularly in terms of hematological and biochemical outcomes, remain limited. Therefore, the present study was designed to assess the protective efficacy of *Azadirachta indica* leaf extract in ameliorating hematobiochemical alterations induced by *Lantana camara* toxicity in female Wistar rats. The study employed both pre- and post-treatment protocols and evaluated key markers of liver and kidney function, as well as hematological indices, to determine the comparative efficacy of neem extract in preventing and reversing lantana-induced hepatic damage.

Materials and Methods

Experimental Animals

A total of thirty healthy female Wistar albino rats (7-8 weeks old, average body weight 150-180 g) were obtained from a CPCSEA-approved breeder and housed in the Laboratory Animal Facility at the College of Veterinary and Animal Science, Navania. The animals were kept under standard laboratory conditions: temperature of 22±2 °C, relative humidity of 55±5%, and a 12-hour light/dark cycle. They were maintained in polypropylene cages lined with sterile bedding material and were provided with a standard pellet diet (Ashirwad Industries, Chandigarh, India) and water ad libitum. The animals were acclimatized for one week prior to the experiment. All procedures involving animals were conducted in accordance with the Institutional Animal Ethics Committee (IAEC) guidelines

Experimental Design

The animals were randomly allocated into five groups (n = 6 per group) as follows:

- **Group I (Control):** Received distilled water orally for 28 consecutive days.
- **Group II (Neem only):** Administered *Azadirachta indica* leaf extract (500 mg/kg body weight/day, orally) for 28 days.
- **Group III (Lantana only):** Treated with *Lantana camara* leaf extract (450 mg/kg body weight/day, orally) for 28 days to induce hepatic toxicity.
- **Group IV (Neem Pre-treatment):** Received Neem extract (500 mg/kg b.wt.) orally for 10 days prior to a single oral dose of *Lantana camara* extract (450 mg/kg) on day 11, followed by continued Neem administration for an additional 28 days (total 38 days).
- **Group V (Neem Post-treatment):** Treated with *Lantana camara* extract (450 mg/kg b.wt.) orally for 28 days, followed by Neem extract (500 mg/kg) for the next 28 days.

The doses of *L. camara* and Neem extracts were selected based on previously published studies (Bihari *et al*., 2015; Asghar *et al*., 2022) [9, 12].

Observation and Clinical Monitoring: All animals were monitored daily for clinical signs of toxicity, behavioral abnormalities, and mortality throughout the experimental period. Body weights were recorded at weekly intervals. At the end of the experimental period, animals were fasted overnight and anesthetized using light ether inhalation for terminal blood collection.

Blood Collection and Sample Preparation: Blood samples were collected from the retro-orbital plexus using sterile heparinized capillary tubes. Two types of samples were obtained:

- Blood in EDTA-coated tubes for hematological analysis.
- Blood in plain tubes for serum separation.

Serum was separated by centrifugation at 3000 rpm for 15 minutes at 4 °C and stored at -20 °C for subsequent biochemical analyses.

Hematological Analysis

Hematological parameters were analyzed using an automated hematology analyzer (Mindray RM-303-03, Sr. No. 3903). The following parameters were assessed:

- Hemoglobin (Hb, g/dL)
- Total erythrocyte count (TEC, $\times 10^{12}$/L)
- Total leukocyte count (TLC, $\times 10^{9}$/L)
- Differential leukocyte count (DLC, %)
- Platelet count ($\times 10^{9}$/L)
- Packed cell volume / Hematocrit (PCV, %)
- Mean corpuscular volume (MCV, fL)
- Mean corpuscular hemoglobin (MCH, pg)
- Mean corpuscular hemoglobin concentration (MCHC, g/dL)

Biochemical Analysis

Serum biochemical parameters were analyzed using commercially available liquid stable reagent kits (Aspen Laboratories Pvt. Ltd., India) on a fully automated biochemistry analyzer (Biogen, CAT No. BGS-246). The parameters measured included:

- Alanine aminotransferase (ALT/SGPT)
- Aspartate aminotransferase (AST/SGOT)
- Alkaline phosphatase (ALP)

- Total protein
- Albumin
- Total bilirubin
- Creatinine
- Urea
- Triglycerides
- Cholesterol

The analytical methods and wavelengths used for each parameter are detailed in Table 1.

Table 1. Biochemical methods used for analysis of various biochemical parameters

Biochemical Parameter	Method	Wavelength (nm)	Unit
ALT	Modified UV (IFCC), KINETIC ASSay	340	U/L
AST	Modified UV (IFCC), KINETIC ASSay	340	U/L
ALP	Pnpp-amp (IFCC), KINETIC ASSay	405	IU/L
Total Protein	Modified biuret, End point assay	578	g/dl
Albumin	Bromocresol green, end point assay	630	g/dl
Total bilirubin	Jendrassik and Groff, End point assay	546	mg/dl
creatinine	Modified jeffe's reaction, Initial rate assay	505	mg/dl
Bood urea nitrogen	GLDH-Urease, Initial rate assay	340	Mg/dl
Triglyceride's	GPO-PAP End point assay	505	Mg/dl
Cholesterol	CHOD-PAP Enzymatic end point assay	505	Mg/dl

Results and Discussion

Haematological Parameters: The hematological parameters were evaluated post-sacrifice to assess the systemic toxic impact of *Lantana camara* and the protective effect of *Azadirachta indica* (Neem) in Wistar rats. The data are summarized in Tables 2.Alterations in Total Erythrocyte Count (TEC), Hemoglobin (Hb), and Hematocrit (HCT)**.** Administration of *Lantana camara* extract (Group III) led to a significant reduction ($p<0.01$) in the total erythrocyte count, hemoglobin concentration, and hematocrit values compared to the control group (Group I), indicating the onset of anemia. The decrease in erythrocytic parameters could be attributed to oxidative damage induced by lantadene toxins, which are known to impair red blood cell integrity and survival (Sharma *et al*., 2017) [19]. Conversely, pre-treatment with Neem extract (Group IV) showed a highly significant improvement ($p<0.01$) in TEC, Hb, and HCT values compared to the Lantana-only group. Post-treatment with Neem (Group V) also demonstrated a significant increase in these parameters, though not as pronounced as the pre-treatment group. These findings indicate the ameliorative potential of Neem in maintaining erythropoiesis and reducing oxidative stress-induced hemolysis (Girish and Shankara, 2008; Gupta and Tandon, 2020) [16, 17]. The nearly restored erythrocytic profile in Group IV implies that prophylactic use of Neem can mitigate hematotoxic insults by scavenging free radicals and enhancing antioxidant defense (Biswas *et al*., 2002) [14].

Alterations in MCV, MCH, and MCHC: No statistically significant differences were observed in mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) across the experimental groups. However, the mean corpuscular hemoglobin concentration (MCHC) showed a significant decrease ($p<0.05$) in the *Lantana camara*-treated group (Group III) compared to the control, suggesting hypochromic anemia.Treatment with Neem in both Group IV and Group V resulted in restoration of MCHC levels toward normal values. The hematinic effect of Neem might be attributed to its phytochemicals such as flavonoids, tannins, and vitamin C, which are known to support erythropoiesis and prevent red cell fragility (Chattopadhyay, 2003) [15].

Table 2: Mean haematological parameter of all experimental groups.

Groups	Haematological Parameters					
	TEC (10^6/µl)	Hb (gm/dl)	Hct (%)	MCV (fl)	MCH (pg)	MCHC (g/dl)
	Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE	Mean±SE
I	6.25^{b}±0.078	12.73^{b}±0.210	45.35^{b}±0.775	72.52±0.526	20.37±0.221	28.08^{b}±0.161
II	6.34^{b}± 0.068	12.9^{b}±0.306	46.55^{b}±0.794	73.40±0.896	20.33±0.335	27.70^{b}±0.121
III	$5.75^{a\pm}$0.162	11.01^{a}±0.315	42.43^{a}±0.372	73.99±1.97	19.26±1.01	25.97^{a}±0.803
IV	$7.09^{c\pm}$0.267	14.9^{c}± 0.531	53.85^{c}±1.65	76.10±1.84	21.06±0.530	27.68^{b}±0.199
V	6.46^{b}± 0.240	12.73^{b}±0.236	46.48^{b}±0.69	71.93±0.546	19.71±0.324	27.39^{b}±0.282
	**	**	**	NS	NS	*

The values (mean±SE) in each column with different superscripts differ significantly between the groups.* = significant ($p<0.05$), ** = highly significant ($p<0.01$)

Platelet Count and Mean Platelet Volume (MPV): As presented in Table 3, platelet count and MPV did not show statistically significant differences among the experimental groups. Although a non-significant decrease in platelet count was noted in the Lantana-treated group, it was not sufficient to confirm thrombocytopenia. The lack of marked alteration in platelet indices may suggest that Lantana camara-induced toxicity was more specific to erythrocytes than thrombocytes at the administered dose and duration.These findings align with previous reports where *Lantana camara* toxicity predominantly induced anemia without affecting platelet morphology or function (Pereira *et al*., 2013; Asija *et al*., 2015) [18, 13].

Table 3: Mean alteration in platelets and MPV of all experimental groups.

Groups	Haematological Parameter	
	Platelets	MPV (fl)
	Mean±SE	Mean±SE
I	499.83± 30.40	7.9± 0.16
II	488±43.77	7.57±0.13
III	390.66±64.98	8±0.25
IV	431.5±54.48	7.95±0.16
V	481.33±99.03	8.4±0.44
	NS	NS

The values (mean±SE) in columns with different superscripts are significantly different from each other. * = significant (p<0.05),** = highly significant (p<0.01)

The haematological data clearly indicate that oral administration of *Lantana camara* caused significant hematotoxic effects-particularly anemia-reflected by reduced TEC, Hb, HCT, and MCHC. These effects were substantially reversed upon pre-treatment and post-treatment with Neem extract**,** validating its protective efficacy**.** The pre-treatment protocol demonstrated superior hematoprotective effects compared to post-treatment, suggesting that *Azadirachta indica* may exert a prophylactic antioxidant role in toxicological models.

Alteration in Differential Leukocyte Count (DLC%) and Total Leukocyte Count (TLC): The evaluation of leukocyte parameters offers critical insight into the immunomodulatory and inflammatory status of the animals following toxic insult and subsequent treatment. The results of differential leukocyte counts (neutrophils, lymphocytes, and other granulocytes) and total leukocyte count (TLC) are presented in Table 4**.**

Table 4: Mean values of DLC (%) and TLC (10^3/µl) of different experimental groups.

Groups	DLC (%)			
	Neutrophil (%)	Another granulocytes (%)	Lymphocyte (%)	TLC (10^3/µl)
	Mean±SE	Mean±SE	Mean±SE	Mean±SE
I	58.23^{a}±1.28	6.68±0.45	35.08^{b}±1.42	13.68^{ab}±0.96
II	59.50^{ab}±1.20	6.45±0.43	34.05^{b}±0.78	13.5^{ab}±0.48
III	63.21^{b}±0.96	6.48±0.48	30.3^{a}±0.58	17.5^{b}±1.25
IV	61.25^{ab}±0.93	5.95±0.69	32.8^{ab}±0.5	12.95^{a}±1.37
V	59.98^{ab}±0.99	7.21±0.93	32.8^{ab}±0.5	12.78^{a}±0.94
	**	ns	**	*

The values (mean±SE) in columns with different superscripts are significantly different. * = significant (p<0.05), ** = highly significant (p<0.01)

Neutrophils (%): In the present study, rats treated with *Lantana camara* extract (Group III) showed a highly significant increase (p<0.01) in neutrophil percentage compared to the control group (Group I), indicating an acute inflammatory response. Neutrophilia is often a hallmark of tissue injury and infection, and in this context, the observed elevation likely reflects the immunological response to hepatocellular and systemic oxidative stress induced by *Lantana camara* toxins, particularly lantadenes (Sharma *et al*., 2017) [19]. Treatment with Azadirachta indica extract showed a reduction in neutrophil count in both the pre-treatment group (Group IV) and post-treatment group (Group V), although the changes were not statistically significant when compared to the Lantana-only group. Notably, Group V showed a more substantial numerical decrease in neutrophil percentage compared to Group IV, suggesting that the ameliorative effect of neem is more pronounced when administered after toxin exposure, potentially due to its anti-inflammatory and immunomodulatory properties (Biswas *et al*., 2002; Chattopadhyay, 2003) [14, 15].

Lymphocytes (%)-A highly significant decrease (p<0.01) in lymphocyte percentage was observed in the *Lantana camara*-treated group (Group III) in comparison to the control group. This lymphopenia is indicative of immunosuppression or lymphocyte sequestration in inflamed tissues, a common feature observed in toxicant-induced stress scenarios (Girish & Shankara, 2008) [16]. Both the pre- and post-treatment with Neem (Groups IV and V) led to an increase in lymphocyte counts as compared to the Lantana-treated group, although these changes were not statistically significant. Nevertheless, the restored lymphocyte values suggest that neem extract supported immune recovery by enhancing lymphopoiesis and regulating proinflammatory cytokine release, consistent with prior findings (Gupta & Tandon, 2020) [17]. The similarity in values between Groups IV and V further emphasizes the protective and recuperative role of Neem against immunotoxicity.

Other Granulocytes (%): The percentage of other granulocytes (basophils, eosinophils, monocytes) did not show any statistically significant variation among the experimental groups. Although a mild numerical increase was noted in the Lantana-treated group compared to controls, the differences were not sufficient to indicate a definitive toxicological pattern. These cells, generally involved in allergic and parasitic responses, may not be the primary responders in lantadenes-induced systemic toxicity.

Total Leukocyte Count (TLC): The mean TLC in the *Lantana camara* group (Group III) was elevated in comparison to the control group, though the difference was not statistically significant. This leukocytosis may reflect a non-specific immune response to toxic injury. More importantly, the TLC values in both pre-treatment (Group IV) and post-treatment (Group V) groups were significantly reduced compared to the Lantana-only group, suggesting that Neem extract helped restore leukocyte homeostasis. The findings align with Neem's known anti-inflammatory and cytoprotective properties**,** which potentially downregulated the systemic immune activation triggered by lantadene toxicity (Pereira *et al*., 2013; Asija *et al*., 2015) [18, 13]. The alterations in leukocytic indices affirm the toxic impact of *Lantana camara* on the immune system, likely via oxidative and inflammatory pathways. The neutrophilia and lymphopenia observed in the Lantana-treated group indicate

systemic inflammation and immune suppression. The restorative trends seen with Neem extract, although not always statistically significant, are biologically meaningful and suggest immunomodulatory actions of Neem. These effects may be attributed to bioactive compounds such as nimbolide, quercetin, and azadirachtin that modulate inflammatory mediators (Girish & Shankara, 2008; Biswas *et al*., 2002) [16, 14]. The ability of Neem to reverse or prevent leukocytic imbalance further reinforces its potential as a therapeutic or prophylactic agent in managing phytotoxin-induced pathophysiological changes.

Biochemical Parameters

The impact of *Lantana camara*-induced hepatotoxicity and the ameliorative effects of *Azadirachta indica* (Neem) on liver and kidney function were evaluated through serum biochemical markers. The mean values of these parameters are presented in Table 5**.**

Table 5: Mean values of Biochemical parameters of different experimental groups

Groups	Biochemical parameters				
	AST (U/L)	ALT (U/L)	ALP (IU/L)	Bood Urea nitrogen (mg/dl)	Creatinine (mg/dl)
	mean±SE	mean±SE	mean±SE	mean±SE	mean±SE
I	69.39^{a}±7.32	30.54^{a}±2.82	76.54^{a}±6.09	34.44±5.75	0.25^{ab}±0.053
II	74.86^{a}±6.64	34.31^{a}±3.66	88.91^{a}±3.83	40.38±10.30	0.18^{a}±0.035
III	107.77^{b}±6.25	47.69^{b}±1.03	155.68^{b}±18.12	42.56±3.99	0.41^{b}±0.058
IV	48.52^{a}±4.03	32.76^{a}±3.96	126.88^{ab}±12.97	37.72±7.84	0.19^{a}±0.027
V	78.66^{a}±13.57	38.37^{ab}±3.32	127.39^{ab}±22.69	32.15±2.21	0.3^{ab}±0.054
	**	**	**	NS	**

The values (mean±SE) in columns with different superscripts are significantly different. * = significant (p<0.05), ** = highly significant (p<0.01)

Alterations in Hepatic Enzymes (AST, ALT, and ALP): The enzymes aspartate aminotransferase (AST)**,** alanine aminotransferase (ALT)**,** and alkaline phosphatase (ALP) serve as sensitive indicators of liver integrity. Elevation of these enzymes in serum generally correlates with hepatic cellular damage due to toxin-induced membrane permeability alterations or hepatocyte necrosis.

AST and ALT: In the current study, the administration of *Lantana camara* (Group III) caused a highly significant (p<0.01) elevation in AST and ALT levels compared to the control group (Group I), reflecting hepatocellular injury. These findings align with previous studies that have attributed *Lantana camara* toxicity to hepatotoxic triterpenoids such as lantadene A and B, which disrupt mitochondrial function and induce oxidative stress in hepatic tissues (Sharma *et al*., 2017; Rao *et al*., 2016) [19, 22]. In contrast, rats pre-treated with Azadirachta indica (Group IV) exhibited a significant decrease in AST and ALT activities, suggesting that Neem provided prophylactic protection against hepatocellular leakage**.** Similarly, the post-treatment group (Group V) also showed notable reductions in both enzymes, though the effect was more pronounced in the pre-treatment group. These observations indicate that Neem leaf extract can stabilize hepatocyte membranes and reduce enzymatic leakage caused by *Lantana camara*.The hepatoprotective effects of Neem are well-documented and primarily attributed to its bioactive compounds such as nimbin, azadirachtin, and quercetin, which possess potent antioxidant and free radical scavenging properties (Biswas *et al*., 2002; Chattopadhyay, 2003) [14, 15].

ALP: Serum ALP levels were highly elevated (p<0.01) in the Lantana-treated group (Group III), indicating potential bile duct obstruction or cholestatic injury. This observation is consistent with bile canaliculi damage and cholestasis described in *Lantana camara* toxicity (Pereira *et al*., 2013) [18]. In the pre- and post-treatment groups (IV and V), ALP levels decreased compared to the Lantana group, although the differences were not statistically significant. Nevertheless, the downward trend supports the ameliorative role of Neem in reducing biliary tract injury and restoring normal liver enzyme profiles.

Alterations in Renal Function Markers (Urea and Creatinine)

Urea: The mean serum urea levels in the Lantana-treated group (Group III) were elevated compared to the control**,** but this increase was not statistically significant. This trend may reflect mild prerenal azotemia or renal dysfunction resulting from hepatic impairment or systemic toxicity. Interestingly, no significant changes were observed in urea levels in either the pre- or post-treatment Neem groups (IV and V), indicating a partial nephroprotective effect**.**

Creatinine: Serum creatinine levels in the *Lantana camara* group were elevated**,** suggesting compromised glomerular filtration or tubular dysfunction. However, the pre-treatment group (Group IV) demonstrated a highly significant (p<0.01) reduction in creatinine levels compared to the Lantana-only group. The post-treatment group (Group V) also showed a decrease in creatinine, but the reduction was not statistically significant. These results support previous findings where Azadirachta indica was shown to protect renal tissues against xenobiotic insults via its antioxidative and anti-inflammatory effects (Nwagha *et al*., 2010; Al-Qarawi *et al*., 2004) [21, 23]. The more pronounced improvement in Group IV again emphasizes the superior protective role of pre-treatment over post-exposure intervention**.**

The significant elevation in AST, ALT, ALP, and creatinine levels following *Lantana camara* exposure underscores its hepatotoxic and mild nephrotoxic potential. These alterations are in agreement with clinical symptoms of *Lantana camara* poisoning observed in animals, including jaundice, hepatic necrosis, and nephropathy (Sharma *et al*., 2017; Asija *et al*., 2015) [19, 13]. The administration of *Azadirachta indica* significantly mitigated the biochemical alterations, particularly when given as a pre-treatment. Neem's hepatoprotective and nephroprotective effects can be attributed to its antioxidant phytoconstituents that reduce oxidative damage, maintain membrane integrity, and support enzymatic homeostasis. These findings validate Neem as a potential natural therapeutic agent in managing *Lantana camara*-induced toxicosis.

Alteration in Cholesterol, Triglycerides, and Total Bilirubin Values in Different Experimental Groups

The impact of *Lantana camara* toxicity and the protective efficacy of *Azadirachta indica* (Neem) was assessed through alterations in lipid metabolism and hepatic excretory function. The mean values of serum cholesterol**,** triglycerides**,** and total bilirubin across the different groups are presented in Table 6.

Table 6: Mean values of Biochemical parameters of different experimental group.

Groups	Biochemical parameter				
	Cholesterol (mg/dl)	Triglycerides (mg/dl)	Total Bilirubin (mg/dl)	Total Protein (g/dl)	Albumin (g/dl)
	mean±SE	mean±SE	mean±SE	mean±SE	mean±SE
I	17.18^{ab}±2.79	55.01^{bc}±4.69	0.222^{a}±0.045	5.46^{b}± 0.20	3.55^{b}±0.34
II	10.12^{a}± 1.29	$30.792^{a\pm}$3.76	0.358^{a}± 0.042	5.72^{b}± 0.49	3.22^{b}±0.29
III	34.00 ^{d}±1.58	66.892^{c}±8.85	0.682^{b} ±0.17	3.55^{a}± 0.25	2.25^{a} ±0.30
IV	24.04^{bc}±2.89	58.87^{bc} ±1.45	0.152^{a}± 0.42	5.49^{b}± 0.35	3.85^{b}± 0.33
V	29.44 ^{cd}± 5.22	51.288^{b}± 3.76	0.320^{a}± 0.08	5.86^{b}± 0.36	3.96^{b}±0.25
	**	**	**	*	*

The values (mean±SE) in columns with different superscripts are significantly different from each other.* = significant (p<0.05), ** = highly significant (p<0.01)

Cholesterol: A significant increase (p<0.01) in serum cholesterol levels was observed in the *Lantana camara*-treated group (Group III) compared to the control (Group I). This hypercholesterolemia is indicative of hepatocellular dysfunction and possible impairment in cholesterol clearance mechanisms due to bile duct obstruction or hepatic oxidative damage, both commonly reported in lantana toxicity (Sharma *et al*., 2017; Pereira *et al*., 2013) [19, 18]. On the other hand, the Neem-treated group (Group II) showed a significant decrease in serum cholesterol levels compared to the control group, suggesting a lipid-lowering effect of Neem. The pre-treatment group (Group IV) exhibited a highly significant reduction in cholesterol compared to the Lantana-treated group, whereas the post-treatment group (Group V) also showed a decrease**,** although it did not reach statistical significance. These results indicate that prophylactic administration of Neem is more effective than therapeutic intervention post-exposure, corroborating previous findings on the hypolipidemic potential of *Azadirachta indica* (Chattopadhyay, 2003; Biswas *et al*., 2002) [14, 15].

Triglycerides: The Lantana-treated group also showed elevated triglyceride levels; however, this increase was not statistically significant. Conversely, the Neem-only group (Group II) demonstrated a highly significant decrease (p<0.01) in triglyceride levels compared to the control, indicating Neem's capability to modulate lipid metabolism through its bioactive constituents like flavonoids and polyphenols (Girish & Shankara, 2008) [16]. The post-treatment group (Group V) revealed a highly significant reduction in triglyceride levels relative to the Lantana group, while the pre-treatment group (Group IV) showed a reduction as well, though not statistically significant. These findings suggest that Neem exerts both preventive and therapeutic effects on lipid abnormalities induced by *Lantana camara* toxicity.

Total Bilirubin: Total bilirubin serves as a key marker for hepatic excretory function. A highly significant elevation (p<0.01) in total bilirubin was noted in the *Lantana camara*-treated group (Group III) compared to control, pre-treatment, and post-treatment groups. This increase may be attributed to hepatocellular necrosis and cholestasis, which impair bilirubin clearance and conjugation (Rao *et al*., 2016) [22]. In contrast, both the pre-treatment group (Group IV) and the post-treatment group (Group V) showed significant reductions in bilirubin levels**,** with the pre-treatment group exhibiting a more pronounced amelioration. These results imply that Neem may protect the liver by enhancing bilirubin metabolism and secretion**,** consistent with previous experimental observations (Gupta & Tandon, 2020) [17].

Alteration in Total Protein and Albumin in Experimental Groups

Serum total protein and albumin levels were measured to assess the synthetic capacity of the liver, which is often compromised during hepatotoxic insult. These values are presented in Table 5.

Total Protein: The mean total protein level in the *Lantana camara*-treated group (Group III) showed a significant decline (p<0.05) compared to the control. This reduction is indicative of compromised protein synthesis due to hepatic damage, often caused by toxin-induced cellular degeneration (Pereira *et al*., 2013; Asija *et al*., 2015) [18, 13]. In contrast, the pre-treatment group (Group IV) exhibited a significant increase in total protein levels, reflecting Neem's hepatoprotective role in preserving hepatic function. The post-treatment group (Group V) also demonstrated an increase, although the improvement was not statistically significant compared to Group III.

Albumin: Serum albumin, synthesized exclusively by hepatocytes, is a sensitive indicator of liver function. The albumin levels were significantly reduced (p<0.05) in the *Lantana camara*-treated rats, pointing toward liver insufficiency.n the Neem pre-treatment group (Group IV)**,** a highly significant increase (p<0.01) in serum albumin was observed, while the post-treatment group (Group V) also exhibited a significant improvement, suggesting partial restoration of synthetic function. These changes are consistent with the hepatoprotective and anabolic effects of Neem, as shown in earlier studies involving other hepatotoxins (Chattopadhyay, 2003; Al-Qarawi *et al*., 2004) [15, 23].

The observed alterations in serum cholesterol, triglycerides, bilirubin, and protein fractions strongly indicate the hepatotoxic effects of *Lantana camara* in Wistar rats. The liver's excretory and synthetic capabilities were markedly impaired in the Lantana-treated group, reflecting classical symptoms of plant-induced toxicosis.The administration of

Azadirachta indica extract not only normalized lipid profiles and bilirubin levels but also significantly restored protein synthesis. These effects were more pronounced in the pre-treatment group, reinforcing the protective rather than curative potential of Neem. The study supports the use of *Azadirachta indica* as a natural prophylactic agent in cases of plant toxin exposure.

Conclusion

The present study clearly demonstrates that *Lantana camara* exerts significant toxic effects on hematological, biochemical, and hepatic parameters in Wistar rats. The administration of *Lantana camara* extract resulted in marked hematological alterations including anemia (decreased TEC, Hb, and HCT), neutrophilia, lymphopenia, and leukocytosis, as well as significant disruptions in biochemical markers such as elevated AST, ALT, ALP, bilirubin, cholesterol, and creatinine levels, along with reduced total protein and albumin concentrations. These findings indicate substantial hepatocellular and renal damage induced by lantadenes present in *Lantana camara*.

Conversely, treatment with *Azadirachta indica* (Neem) leaf extract, both as pre- and post-treatment, significantly ameliorated these alterations. Neem effectively stabilized hematological profiles, improved liver enzyme functions, reduced bilirubin and cholesterol levels, and restored protein synthesis. The pre-treatment group exhibited greater protective effects than the post-treatment group, suggesting that Neem has more robust prophylactic efficacy than therapeutic potential after toxin exposure.

The phytochemical constituents of Neem-particularly its antioxidant, anti-inflammatory, and hepatoprotective properties-likely contributed to the normalization of altered parameters. Based on these results, Neem can be considered a natural and effective protective agent against *Lantana camara*-induced hematobiochemical toxicity. This study supports the traditional use of *Azadirachta indica* in ethnoveterinary medicine and encourages further clinical evaluation and validation of its protective efficacy in livestock species susceptible to *Lantana camara* poisoning.

Acknowledgement

The author gratefully acknowledges the unwavering support and insightful guidance provided by the faculty of the Department of Veterinary Pathology, College of Veterinary and Animal Science, Navania, during the course of this study. Special appreciation is also extended to the Rajasthan University of Veterinary and Animal Sciences (RAJUVAS), Bikaner, for offering essential resources and institutional infrastructure that facilitated the successful completion of this research work.

Conflict of interest

The authors declare no conflict of interest.

Ethical approval

The study was conducted following the guidelines of the Committee for Control and Supervision of Experiments on Animals (CCSEA), New Delhi, India. Approval was obtained from the Institutional Animal Ethics Committee (IAEC) of the College of Veterinary and Animal Science, Navania, Vallabhnagar, Udaipur,

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