RESEARCH PAPER

Pharmacological and Molecular Evaluation of *Ricinus communis* Extract Targeting MDR Bacteria: A Toxicological and Histopathological Study in Mice

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Abstract:

Objective: This study aimed to evaluate the antimicrobial activity, predicted molecular interactions and metabolic properties, and in vivo toxicity of methanolic and aqueous *Ricinus communis* leaf and seed extracts, with particular emphasis on their effects on hematological, biochemical, and histopathological parameters.

Methods: The antimicrobial activity of methanolic and aqueous extracts of *R. communis* leaves and seeds was evaluated against Gram-positive and Gram-negative bacteria and *Candida albicans* using the agar well diffusion method. In silico analyses were conducted to predict organ-specific toxicities, Tox21 assay activity, molecular initiating events (MIEs), and potential interactions with cytochrome P450 enzymes. For the in vivo assessment, BALB/c mice were administered intraperitoneal doses of the extracts ranging from 10 to 150 mg/kg daily for 7 days. Hematological and biochemical analyses were performed, and the liver, kidneys, and spleen were examined histopathologically.

Results: Methanolic leaf extracts demonstrated significant antimicrobial activity, producing inhibition zones of up to 33 mm against *Candida albicans*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. In contrast, the aqueous extracts and seed extracts showed no appreciable antimicrobial activity. In silico toxicity predictions indicated potential hepatotoxic, neurotoxic, and immunotoxic effects, with predicted activity involving pathways related to aromatase and estrogen receptor signaling. Molecular initiating event analysis suggested possible interactions with acetylcholinesterase and hormone-related receptors. Predicted cytochrome P450 interactions indicated potential effects on CYP2C9 and CYP3A4, suggesting possible metabolic implications. Histopathological examination revealed dose-dependent tissue injury, characterized by inflammatory infiltration, vascular hemorrhage, and structural disintegration, with more severe alterations observed at higher doses. Repeated daily administration also resulted in cumulative hepatic, renal, and splenic changes.

Conclusion: Methanolic *Ricinus communis* leaf extract demonstrated considerable antimicrobial potential, particularly against *C. albicans*, *P. aeruginosa*, and *S. aureus*. However, its significant dose-dependent systemic toxicity highlights the need for careful dose determination and comprehensive toxicological evaluation. These findings support the therapeutic potential of *R. communis* while emphasizing that further safety investigations are essential before potential clinical application.

Keywords: *Ricinus communis*, antimicrobial activity, Multidrug-resistant bacteria, Histopathology, In vivo toxicity.

How to cite this article: Aloriby MA, Hasen YMA, Garalla HM, Almabruk AMA, Shaafi E, Bleiblo FA, Bobtina N, Alsaity JO, Al-Orfi A, Elshaibani A, Al-Qatrani R, Alglaly SA, Al-Shwehidi AS, Alshalmani S, Aldrsy S, Mikael AS, Alkadike JS, Abd Elatif AN, Elgadari AA, Faraj Saad RH, Ibrahim AM, ALhayin AM. Pharmacological and Molecular Evaluation of Ricinus communis Extract Targeting MDR Bacteria: A

Toxicological and Histopathological Study in Mice. Int J Drug Deliv Technol. 2026;16(71s): 1542-1561. DOI: 10.25258/ijddt.16.71s.181

1. Introduction:

Antimicrobial resistance (AMR) has emerged as a major global health threat, causing an estimated 1.14 million deaths directly attributable to drug-resistant bacterial infections in 2021. Historically, cultures worldwide have relied on medicinal plants as key components of healthcare systems. In recent decades, interest in herbal medicine has surged due to rising microbial resistance to conventional antibiotics and the increasing incidence of adverse reactions associated with synthetic drugs [1]

Among these plants, *Ricinus communis* Linn., or the castor oil plant, has garnered significant attention. Classified within the Euphorbiaceae family, *R. communis* thrives in tropical and temperate regions at altitudes ranging from 400 to 4,500 meters above sea level. This perennial plant can reach up to 10 meters in height, with thick hollow stems, distinctive green or reddish leaves, and thorny seed capsules [2]

Despite the effectiveness of antimicrobial agents over the past century, their utility is now threatened by multidrug-resistant pathogens. This global challenge has intensified scientific interest in plant-derived alternatives [3]. *R. communis* exemplifies this trend, as nearly all its parts, including the leaves, roots, stem, flowers, seeds, and aerial sections, have been used medicinally.

This study was also inspired by a personal observation. A poultice made from *R. communis* leaves was used on the researcher's mother to treat a skin abscess. Within days, inflammation and swelling resolved, suggesting the plant's antimicrobial and anti-inflammatory potential and prompting formal scientific evaluation.

Extensive literature documents the broad pharmacological activities of *R. communis*, including antibacterial, antifungal, anti-HIV, antidiabetic, hepatoprotective, and anticancer properties [4]. Traditional uses in Tunisia, Egypt, and India include treating warts, boils, abscesses, various skin conditions, and digestive disorders [5.6]. Leaves are commonly used in poultices for inflammation, while roots and seeds are used as purgatives or anti-parasitics.

Phytochemical studies have identified bioactive components such as flavonoids, tannins, sterols, terpenes, alkaloids, ricinine, and ricinoleic acid, which are likely responsible for the plant's therapeutic effects. Antimicrobial activity has been confirmed in methanolic and ethanolic leaf extracts against pathogens including *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans* [2, 4,6].

In Libya, antimicrobial resistance poses a serious public health threat. Surveillance data are limited, but reports indicate high resistance rates, such as 54 to 68 percent methicillin-resistant *Staphylococcus aureus* prevalence and rising multidrug resistance among Gram-negative pathogens [7]. Widespread self-medication and over-the-counter availability of antibiotics exacerbate this issue. The World Health Organization has recognized Libya's vulnerability to antimicrobial resistance due to weak regulatory systems and supports the development of national action plans to address this problem (World Health Organization, 2019). Given the urgent need for novel antimicrobial agents in Libya and globally, and supported by traditional use and personal experience, this study aims to scientifically evaluate the antibacterial and antifungal efficacy of *Ricinus communis* leaf extracts using both hot and cold extraction techniques.

2. Materials and Methods

2.1. Preparation of Plant Extraction

The current scientific work involved the use of *Ricinus communis* (RC). Leaves and seeds of the plant were collected in February 2025 during the early morning from a castor tree approximately 15 years old, located in the Buhdima area of Benghazi. The collected materials were rinsed with tap water and then air-dried in a shaded, well-ventilated area at room temperature for six days. Once dried, the plant materials were ground into a fine powder using a household food blender. Next, 20 grams of the powdered *Ricinus communis* were soaked separately in 200 milliliters of different solvents (methanol and distilled water) in sterile containers. These mixtures were left at room temperature for 24 hours, after which they were filtered through multiple layers of gauze. To further eliminate coarse particles, the filtrates were passed through 180-millimeter filter paper. The resulting extracts were concentrated using a rotary evaporator under reduced pressure: methanolic extracts were processed at 45 °C, while the aqueous extract was heated at 100 °C. Each concentration process lasted for 20 minutes. Afterward, the methanolic extracts were left uncovered at room temperature for 24 hours, while the aqueous extract underwent further concentration using a Soxhlet apparatus to produce a stock solution. This process yielded 4 grams of extract, corresponding to an approximate extraction ratio of 1:5 for *Ricinus communis*. Subsequently, 10 milliliters of a 1% dimethyl sulfoxide (DMSO) solution were added to each extract, and the resulting mixtures were stored in dark containers at room temperature. Filter paper discs were prepared by punching standard-sized circles and were used to evaluate antimicrobial activity via the well diffusion method. These discs were saturated with seven different *Ricinus communis* extracts, placed in Petri

dishes, and covered with nylon. They were kept at room temperature for 12 hours to assess their antimicrobial effects against bacteria.

2.2. Selection and Preparation of Microbial Strains

2.2.1. Culture Maintenance

2.2.1.1. Bacterial Culture

Representative strains of Gram-positive and Gram-negative bacteria were identified using the VITEK 2 COMPACT (bioMérieux). Reference strains with known susceptibility profiles were also used to ensure the reliability of the results. This study involved bacterial species representing both Gram-positive and Gram-negative classifications.

Mueller-Hinton agar (HiMedia) was used as the culture medium for all bacteria. The bacteria were spread on MH agar plates using a cotton swab, and the well diffusion method was used for the initial screening.

2.2.2. Inoculum Standardization

Bacterial suspensions were standardized to a 0.5 McFarland turbidity standard, which corresponds to a defined bacterial concentration, ensuring consistency in microbiological testing. A colony was collected using a sterile inoculating loop and transferred into a conical glass tube containing 10 mL of distilled water.

2.2.3. Fungal Culture

Candida albicans was isolated from the sputum of a 35-year-old male using Sabouraud Dextrose Agar (SDA), a selective medium for fungi. The culture was incubated at 37 °C to promote optimal fungal growth.

2.3. Antimicrobial Assay Setup and Control

2.3.1. Control Measure

Distilled water and methanol were used as negative controls to validate the accuracy and reliability of the experimental procedures.

2.4. In Vivo Efficacy

2.4.1. Animal Model

Twenty healthy male BALB/c mice were procured from the Animal House Department at the University of Benghazi. The mice were approximately 1–2 months old, with an average body weight ranging between 25 and 30 grams. Throughout the experiment, they were housed in a controlled environment maintained at 24–25 °C with a 12-hour light/dark cycle. During both the acclimatization and experimental periods, the mice had unrestricted access to a standard commercial diet and tap water. The mice were randomized into six groups (n = 5) for administration of the leaf extracts. Subsequently, intraperitoneal doses were given: 25 mg/kg of RC for Group I, 50 mg/kg for Group II, 100 mg/kg for Group III, 150 mg/kg for Group IV, or 100 mg/kg of distilled water for Group V (control). Group VI (daily) was injected daily with gradually increasing doses of RC. Mice were fasted for seven days, with free access to water during the 24 hours prior to sacrifice.

2.4.2 Histotechnique and Sample Collection

Mice were anesthetized by diethyl ether inhalation 24 h after the injection of olive leaf extracts. These animals were then euthanized, and liver (hepatectomy), kidney (nephrectomy) and Spleenectomy tissues were extracted in aseptic conditions. Each tissue sample was placed in 10% neutral-buffered formalin for 24 h to preserve the structure. After fixation for the first time, standard histological preparations were performed as described by Suvarna *et al*. (2020). Briefly, samples remained in 10% formalin to stabilize tissue architecture, and tissues were sequentially exposed to increasing ethanol concentrations (50%, 70%, 90%, and 100%) to remove residual water. Dehydrated samples were immersed in xylene for ∼2 h to replace ethanol and increase tissue transparency. Tissues were infiltrated with molten paraffin wax, providing mechanical support and enabling thin sectioning, and transferred to metallic molds, which were then rapidly cooled (−4◦C) to solidify the wax block, thereby fixing the tissue orientation. Blocks were trimmed into 3 µm sections with a rotary microtome for sectioning. Ribbon sections were floated on a39- 40◦C water bath and subsequently mounted onto microscope slides pre-treated with an adhesive or 50% ethanol to facilitate adherence. The slides were then dried before staining 0.50% ethanol or adhesive is needed to perform well, and the slides were dried before staining.[18]

2.4.3 Hematoxylin and eosin staining

The staining procedure was conducted according to the method described by Fischer *et al.* (2008), with minor modifications. For deparaffinization and rehydration, the slides were placed in xylene for about 2 min, then in descending concentrations of ethanol (96%, 90%, 70%) to rehydrate the tissue sections. Slides were then immersed in hematoxylin solution for 4 min, rinsed under running water, briefly dipped in acid alcohol (one dip) for differentiation, and thoroughly rewashed. These sections were transferred to eosin for 2 min, then lightly rinsed in water to remove excess stain and dehydrated for mounting. The slides were finally immersed in xylene to clear residual ethanol and mounted with DPX (Distyrene plasticizer xylene). A coverslip was gently lowered to seal the tissue sections.[19]

2.4.4 Histopathological Assay

Prepared slides were examined under an Olympus BX41 light microscope. Images were captured digitally with an Olympus DP2-BSW system.

Pathological assessments focused on identifying inflammatory lesions, necrosis, and other cellular or architectural alterations relevant to R.C extract treatment effects.

2.4.5 Hematological and Biochemical Analysis

Blood samples were drawn via puncture using a 30-gauge needle. A portion of the blood was collected into EDTA tubes for complete blood count (CBC) analysis using a SYSMEX XN330 (Diamond Diagnostics, USA) hematology analyzer, determining red blood cells (RBCs), white blood cells (WBCs), hemoglobin, and platelets. The remaining blood sample was placed into plain tubes centrifuged at 4,000 rpm, and the resulting serum was evaluated for liver and kidney function using a Cobas Integra 400 plus platform (Roche Diagnostics, Germany). Parameters such as alanine transaminase (ALT), aspartate transaminase (AST), creatinine, and urea were measured to assess organ function (Arantes-Rodrigues et al., 2011; Clewell et al., 2015).[20,21]

2.4.6 Bioinformatic and Toxicoinformatic Analysis

In silico toxicity profiling was performed using bioinformatic and toxicoinformatic prediction tools to evaluate the potential organ-specific toxicity and toxicological endpoints associated with *Ricinus communis* leaf and seed extracts. Predicted organ toxicities, including hepatic, renal, cardiac, and other systemic toxicities, were assessed together with toxicity endpoints such as carcinogenicity, mutagenicity, cytotoxicity, and other relevant adverse biological effects. Tox21 nuclear receptor pathway analysis was conducted to investigate the potential activity of the extracts against key nuclear receptor-related pathways, including aryl hydrocarbon receptor (AhR), androgen receptor (AR), estrogen receptor (ER), androgen receptor ligand-binding domain (AR-LBD), estrogen receptor ligand-binding domain (ER-LBD), peroxisome proliferator-activated receptor gamma (PPARγ), and aromatase. Tox21 stress-response pathway analysis was performed to assess potential effects on major cellular stress-response mechanisms, including the nuclear factor erythroid 2–related factor 2/antioxidant response element (Nrf2/ARE) pathway, heat shock response (HSE), mitochondrial membrane potential (MMP), tumor protein p53, and ATAD5-associated DNA damage response pathways. Molecular initiating event (MIE) analysis was performed to predict potential interactions between extract constituents and key molecular targets associated with toxicity and pharmacological activity. The evaluated targets included thyroid hormone receptors α and β (THRα and THRβ), γ-aminobutyric acid receptors (GABAR), N-methyl-D-aspartate receptors (NMDAR), α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptors (AMPAR), acetylcholinesterase (AChE), ryanodine receptors (RYR), constitutive androstane receptor (CAR), pregnane X receptor (PXR), voltage-gated sodium channels (VGSC), transthyretin (TTR), and the sodium/iodide symporter (NIS).

Potential metabolic interactions were evaluated by predicting the effects of the extracts on major cytochrome P450 (CYP450) enzymes involved in xenobiotic metabolism. The analyzed enzymes included CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4. The resulting bioinformatic predictions were used to identify potential toxicological mechanisms, molecular targets, and metabolic interactions associated with *R. communis* extracts and to complement the in vivo hematological, biochemical, and histopathological findings.

2.5 Ethical Approval:

The study protocol was reviewed and approved by the Scientific Committee of the Faculty of Biomedical Sciences, University of Benghazi. All animal procedures were conducted in accordance with the institutional guidelines for the care and use of laboratory animals and complied with international standards for animal welfare.

2.6 Statistical analysis

All data were processed using Microsoft Excel 2023 and are expressed as means ± standard deviation (SD). Statistical significance across multiple experimental groups was assessed via one-way analysis of variance (ANOVA) with repeated measures, utilizing SPSS software (SPSS, Inc., Chicago, IL). Additionally, a t-test was conducted to determine differences between two independent group means. Furthermore, two-way ANOVA was employed to simultaneously evaluate the influence and interactions of two independent factors, providing a more comprehensive understanding of their combined effects on the results. Differences with p-values below 0.05 (p less than 0.05) were considered statistically significant.

3. Results

3.1 Antimicrobial Activity of Ricinus communis:

Table 1. Zone of inhibition (in mm) of Ricinus communis leaf extracts used to evaluate antimicrobial activity via the well diffusion.

Sample	CD100%	CD200%	CM100%	CM200%	HD100%	HD200%	HM10%	HM200%

S.aureus	6 mm	19 mm	25 mm	30 mm	6 mm	6 mm	29 mm	6 mm
K.pneumonia	6 mm	25 mm	6 mm	6 mm	6 mm	6 mm	30 mm	6 mm
E.coli	6 mm	30 mm	16 mm	6 mm	6 mm	6 mm	6 mm	6 mm

Table 2. Zone of inhibition (in mm) of Ricinus communis seed extracts used to evaluate antimicrobial activity via the well diffusion.

Ricinus communis.S	CD 100 %	CD 200 %	CM 100 %	CM 200 %	HD 100 %	HD 200 %	HM 100 %	HM 200 %
S.aureus	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm
K.pneumonia	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm
E.coli	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm
P.argingosa	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm
C.albicans	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm	6 mm

Results represent the diameter of the inhibition zones produced by various concentrations and extraction methods: CD = Cold Distilled, CM = Cold Methanol, HD = Hot Distilled, HM = Hot Methanol, at 100% and 200% concentrations. A zone of 6 mm indicates no antimicrobial activity beyond the disc diameter (Table-2).

Table 3: By Bacterial Strian

Strain	Mean (mm)	SD	Skewness	Kurtosis
S. aureus	10.28	7.032	1.900	2.756
K. pneumoniae	11.72	7.932	1.477	0.987

P.argingosa	6 mm	6 mm	15 mm	20 mm	27 mm	6 mm	6 mm	33 mm
C.albicans	6 mm	6 mm	28 mm	6 mm	27 mm	6 mm	6 mm	32 mm

Results represent the diameter of the inhibition zones produced by various concentrations and extraction methods: CD = Cold Distilled, CM = Cold Methanol, HD = Hot Distilled, HM = Hot Methanol, at 100% and 200% concentrations. A zone of 6 mm indicates no antimicrobial activity beyond the disc diameter (Table-1).

E. coli	10.21	6.457	1.717	1.702
Pseudomonas	9.60	6.949	2.361	4.671
C. albicans	10.23	7.537	2.502	5.330

Table 4; By Extract Type

Extract Type	Mean (mm)	SD	Skewness	Kurtosis
Leaf	12.74	9.999	0.968	-0.829
Seed	8.57	2.372	0.081	-1.383

3.2 Toxicity of Ricinus communis

Table 5. Predicted organ and endpoint-specific toxicity of Ricinus communis extract as determined by in silico analysis

Classification	Target	Prediction	Probability
Organ toxicity	Hepatotoxicity	Active	0.69
Organ toxicity	Neurotoxicity	Active	0.87
Organ toxicity	Nephrotoxicity	Inactive	0.90
Organ toxicity	Respiratory toxicity	Active	0.98
Organ toxicity	Cardiotoxicity	Inactive	0.77
Toxicity end points	Carcinogenicity	Inactive	0.62
Toxicity end points	Immunotoxicity	Active	0.96
Toxicity end points	Mutagenicity	Inactive	0.97
Toxicity end points	Cytotoxicity	Inactive	0.93

Toxicity end points	BBB-barrier	Inactive	1.00
Toxicity end points	Ecotoxicity	Active	0.73
Toxicity end points	Clinical toxicity	Inactive	0.56
Toxicity end points	Nutritional toxicity	Inactive	0.74

The table summarizes the predicted activity (active/inactive) and associated probabilities for various toxicity parameters, including organ toxicity and general toxicity endpoints targets, their respective classifications, . (Table-3).

3.3 Tox21 Screening of Ricinus communis

Table 6. Predicted interactions of Ricinus communis extract with Tox21 nuclear receptor signalling and stress response pathways.

Classification	Target	Prediction	Probability
Tox21-Nuclear receptor signalling pathways	Aryl hydrocarbon Receptor (AhR)	Inactive	0.97
Tox21-Nuclear receptor signalling pathways	Androgen Receptor (AR)	Inactive	0.99
Tox21-Nuclear receptor signalling pathways	Androgen Receptor Ligand Binding Domain (AR-LBD)	Inactive	0.99
Tox21-Nuclear receptor signalling pathways	Aromatase	**Active**	1.0
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Alpha (ER)	**Active**	0.99
Tox21-Nuclear receptor signalling pathways	Estrogen Receptor Ligand Binding Domain (ER-LBD)	**Active**	0.1
Tox21-Nuclear receptor signalling pathways	Peroxisome Proliferator Activated Receptor Gamma (PPAR-Gamma)	Inactive	0.99
Tox21-Stress response pathways	Nuclear factor (erythroid-derived 2)-like 2/ antioxidant responsive element (nrf2/ARE)	Inactive	0.88
Tox21-Stress response pathways	Heat shock factor response element (HSE)	Inactive	0.88
Tox21-Stress response pathways	Mitochondrial Membrane Potential (MMP)	Inactive	0.70
Tox21-Stress response pathways	Phosphoprotein (Tumor Suppressor) p53	Inactive	0.96
Tox21-Stress response pathways	ATPase family AAA domain-containing protein 5 (ATAD5)	Inactive	0.99

The table lists

3.4 Ricinus communis extract interacts with various Molecular Initiating Events (MIEs):

Table 7. Predicted activity of Ricinus communis extract on molecular initiating events (MIEs) relevant to toxicity pathways.

Classification	Target	Prediction	robability
Molecular Initiating Events	Thyroid hormone receptor alpha (THRα)	Inactive	0.90

Molecular Initiating Events	Thyroid hormone receptor beta (THRβ)	Inactive	0.78
Molecular Initiating Events	Transtyretrin (TTR)	Inactive	0.97
Molecular Initiating Events	Ryanodine receptor (RYR)	Inactive	0.98
Molecular Initiating Events	GABA receptor (GABAR)	Inactive	0.96
Molecular Initiating Events	Glutamate N-methyl-D-aspartate receptor (NMDAR)	Inactive	0.92
Molecular Initiating Events	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate receptor (AMPAR)	Inactive	0.97
Molecular Initiating Events	Kainate receptor (KAR)	Inactive	0.99
Molecular Initiating Events	Acetylcholinesterase AChE)	**Active**	0.69
Molecular Initiating Events	Constitutive androstane receptor (CAR)	Inactive	0.98
Molecular Initiating Events	Pregnane X receptor (PXR)	Inactive	0.92
Molecular Initiating Events	NADH-quinone oxidoreductase (NADHOX)	Inactive	0.97
Molecular Initiating Events	Voltage gated sodium channel (VGSC)	Inactive	0.95
Molecular Initiating Events	Na+/I-symporter (NIS)	Inactive	0.98

The table lists target proteins/receptors, their classifications, predicted activity as active or inactive, and associated probabilities indicating the likelihood of interaction.

3.5 Metabolic Activity of Ricinus communis:

Table 8. Predicted interactions of Ricinus communis extract with cytochrome P450 enzymes involved in drug metabolism.

Classification	Target	Prediction	Probability
Metabolism	Cytochrome CYP1A2	Inactive	0.76
Metabolism	Cytochrome CYP2C19	Inactive	0.87
Metabolism	Cytochrome CYP2C9	**Active**	0.56
Metabolism	Cytochrome CYP2D6	Inactive	0.63
Metabolism	Cytochrome CYP3A4	**Active**	0.71
Metabolism	Cytochrome CYP2E1	Inactive	0.98

The table shows the probability, predicted activity (active/inactive), target enzyme, and classification related to metabolic processes.

3.6 Effect of different doses of Ricinus communis a histopathological study:

3.6.1. The histopathology feature of Liver

The liver control sample demonstrates a healthy histological profile with normal hepatic structure and cellular organization. Key observations include well-arranged hepatocytes, clear and intact sinusoids with Kupffer cells, and preserved portal tracts without any pathological changes like inflammation, fibrosis, or cholestasis. No abnormalities such as steatosis, necrosis, or regenerative alterations are seen, indicating a baseline of normal liver function and integrity (Figure-1).

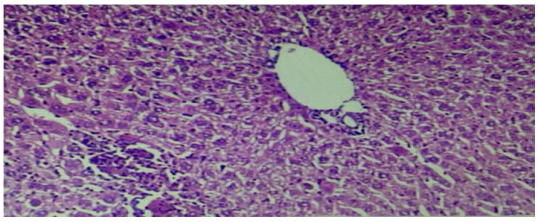


Figure-1. Histological section of a liver from mice which was intraperitoneal injection (control) section stained with H & E X40.

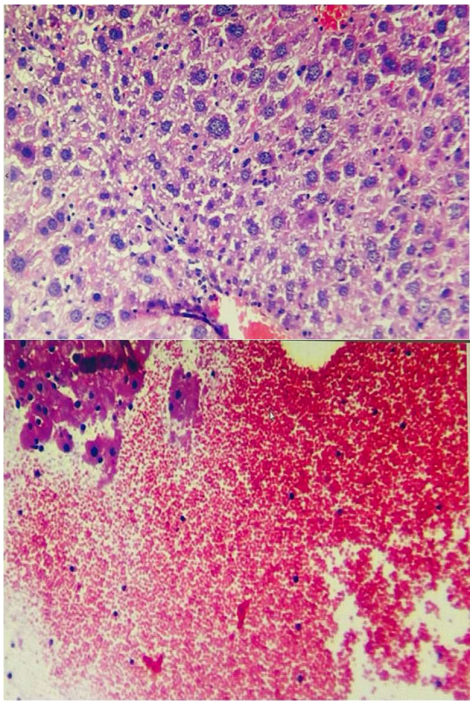


Figure-2: Histological section of a liver from mice which was intraperitoneal injection 10mg /Kg of R.C section stained with H & E X40.

Histological examination of liver sections from mice treated with 10 mg of *Ricinus communis* leaf extract revealed generally preserved hepatic architecture. Hepatocytes were arranged in normal radial cords around central veins, with no evidence of cellular degeneration or necrosis. However, mild infiltration of inflammatory cells was observed, primarily in the portal and periportal areas, indicating a localized immune response to the extract. Additionally, vascular hemorrhage was evident, characterized by the presence of extravasated red blood cells within the hepatic sinusoids and adjacent parenchyma. No signs of fatty change, fibrosis, or bile duct proliferation were detected, suggesting that the overall structural and functional integrity of the liver tissue remained intact (Figure-3).

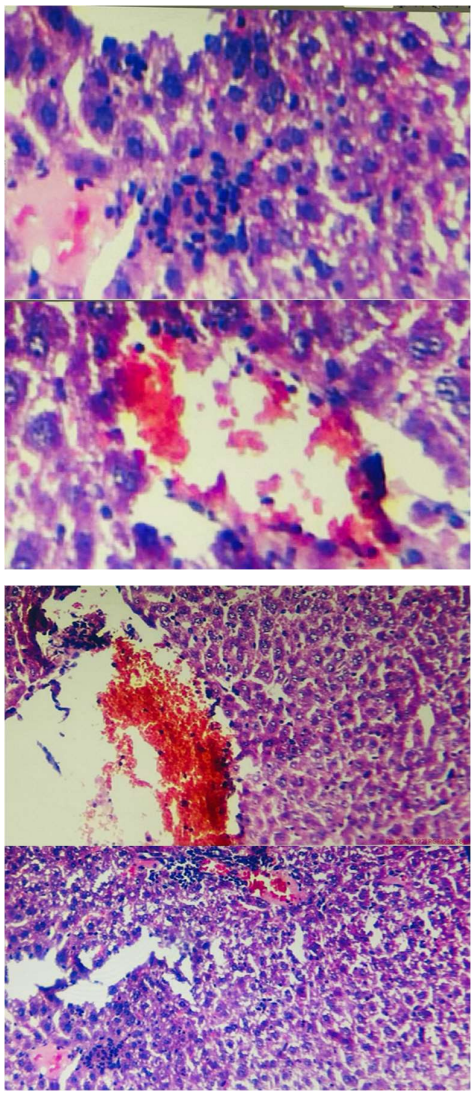


Figure-3. Histological section of a liver from mice which was intraperitoneal injection 25mg /Kg of R.C section stained with H & E X40.

Histological analysis of liver sections from mice administered 25 mg of *Ricinus communis* leaf extract demonstrated notable but localized pathological changes. The hepatic lobular architecture was largely preserved with no gross distortion; however, areas of hepatocellular necrosis were evident, particularly in the centrilobular regions. These necrotic foci were often accompanied by moderate infiltration of inflammatory cells, mainly lymphocytes and mononuclear cells, distributed around necrotic zones and within some portal areas. Moreover, multifocal haemorrhagic areas were observed, characterized by extravasation of red blood cells within hepatic sinusoids and parenchymal tissue (Figure-3).

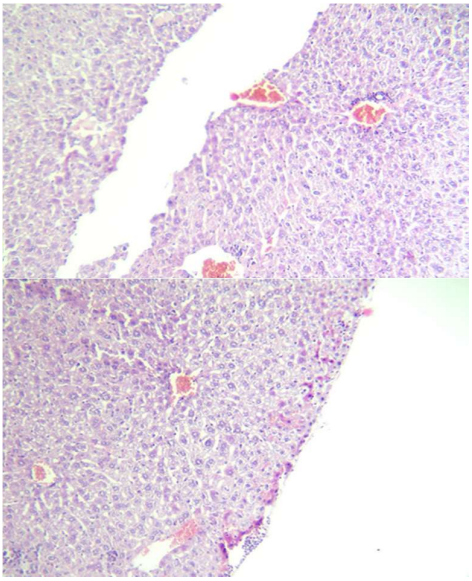


Figure4: Histological section of a liver from mice which was intraperitoneal injection 50mg /Kg of R.C section stained with H & E X40.

Liver sections from mice treated with 50 mg of *Ricinus communis* leaf extract exhibited minimal histopathological alterations. The overall hepatic architecture remained intact, with normal lobular organization and preserved hepatocyte morphology. Mild vascular changes were observed in the form of scattered hemorrhagic areas, indicated by focal extravasation of red blood cells within hepatic sinusoids. Additionally, a few inflammatory cells—predominantly mononuclear—were noted in limited periportal regions. These findings suggest a subtle tissue response to the extract, with no significant hepatocellular damage.

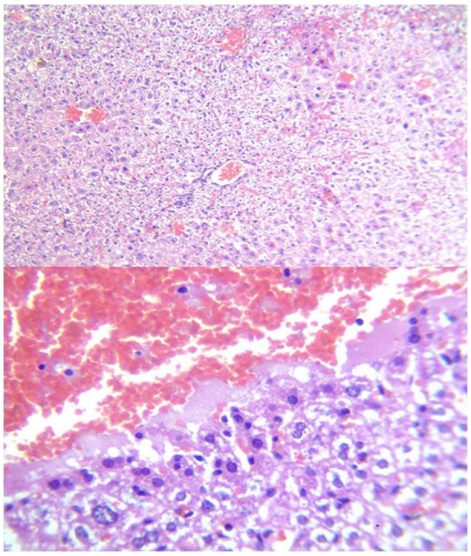


Figure 5: Histological section of a liver from mice which was intraperitoneal injection 100mg /Kg of R.C section stained with H & E X40.

Liver sections from mice treated with 100 mg of *Ricinus communis* leaf extract exhibited minimal histopathological alterations. The overall hepatic architecture remained intact, with normal lobular organization and preserved hepatocyte morphology. Mild vascular changes were observed in the form of scattered hemorrhagic areas, indicated by focal extravasation of red blood cells within hepatic sinusoids. Additionally, a few inflammatory cells—predominantly mononuclear—were noted in limited periportal regions. These findings suggest a subtle tissue response to the extract.

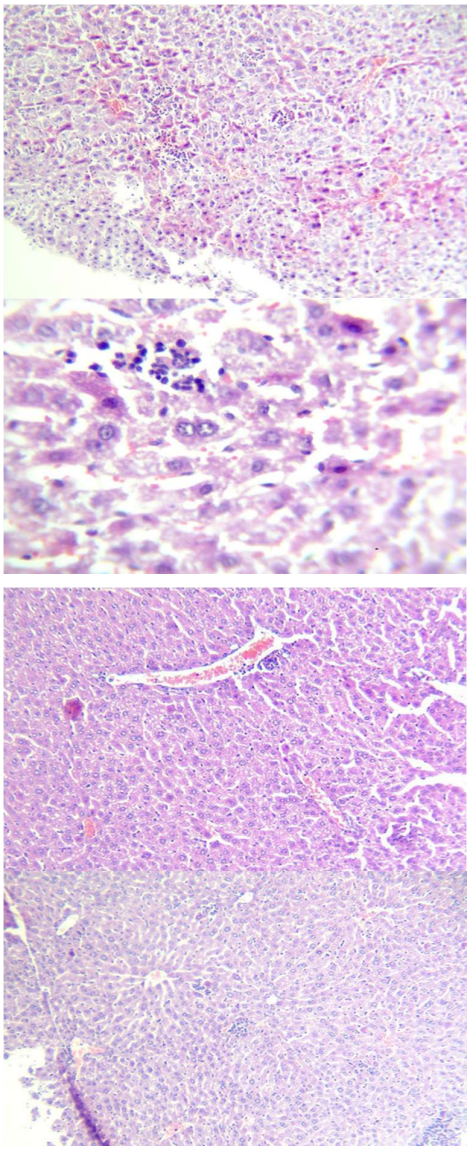


Figure6: Histological section of a liver from mice which was intraperitoneal injection 150mg /Kg of R.C section stained with H & E X40.

Histopathological examination of liver tissues from mice treated with 150 mg of *Ricinus communis* leaf extract revealed more pronounced alterations compared to lower doses. While the general lobular

structure was still recognizable, there was evident separation between hepatic tissue components, particularly between hepatocyte plates and sinusoidal spaces, suggestive of intercellular edema or early disintegration of hepatic cords. Furthermore, a marked increase in inflammatory cell infiltration was observed, predominantly around portal triads and extending into the parenchyma. Despite these changes, no widespread necrosis or fibrosis was noted, though the tissue response at this dose suggests the onset of more significant hepatotoxic effects.

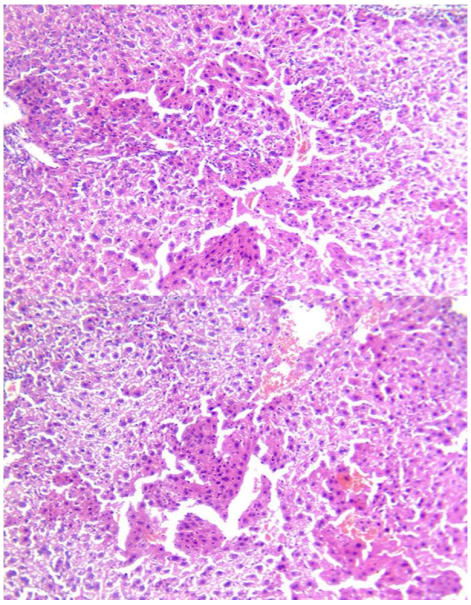


Figure 7: Histological section of a liver from mice which was intraperitoneal injection daily of R.C section stained with H & E X40.

Liver sections from mice subjected to daily intraperitoneal injections of *Ricinus communis* leaf extract exhibited notable histopathological changes. Prominent cytoplasmic vacuolation was observed in hepatocytes, indicating potential early degenerative changes or intracellular accumulation of fluid or lipids. The interseptal spaces appeared widened, reflecting possible interstitial edema or loss of tissue cohesion. Inflammatory cell infiltration was evident, particularly in periportal and parenchymal areas, composed mainly of mononuclear cells. Additionally, focal hemorrhages were present, characterized by the extravasation of red blood cells within hepatic sinusoids and surrounding parenchyma. These findings collectively suggest a cumulative hepatic response to repeated dosing, involving both inflammatory and degenerative processes.

3.6.2. The histopathology feature of Kidney

The kidney tissue shows preserved architecture with normal glomeruli, tubules, interstitium, and blood vessels. The glomeruli are of normal size and cellularity, with intact capillary loops. Renal tubules display well-maintained epithelial lining without signs of atrophy or degeneration. The interstitium is unremarkable, with no evidence of inflammation or fibrosis. Blood vessels appear normal, with no thickening or vascular pathology (Figure-8).

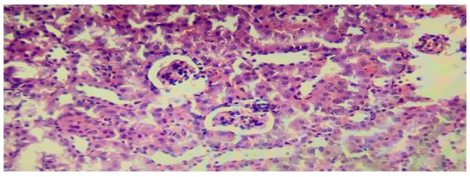


Figure-8. Histological section of a kidney from mice which was intraperitoneal injection (control) section stained with H & E X40

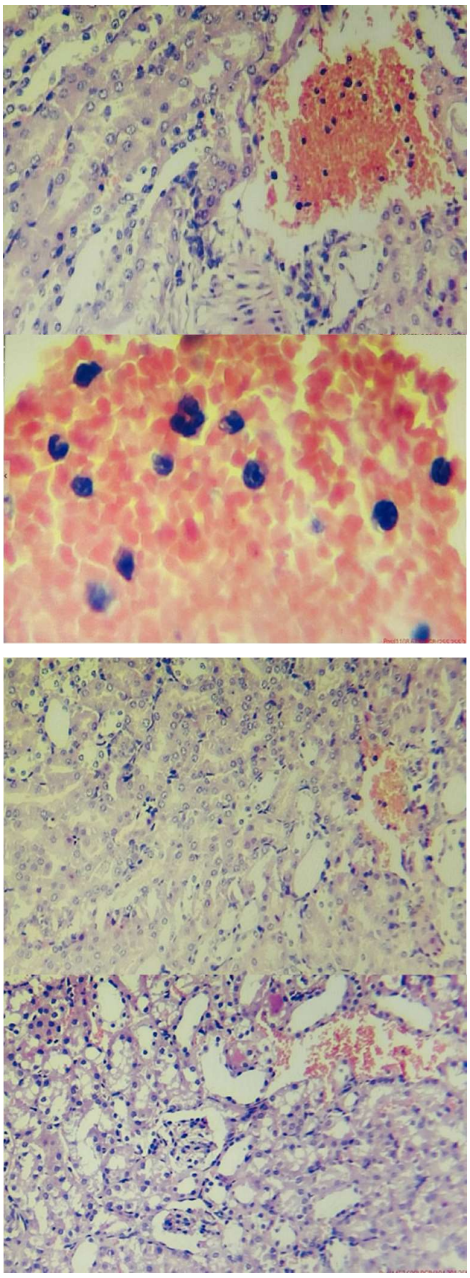
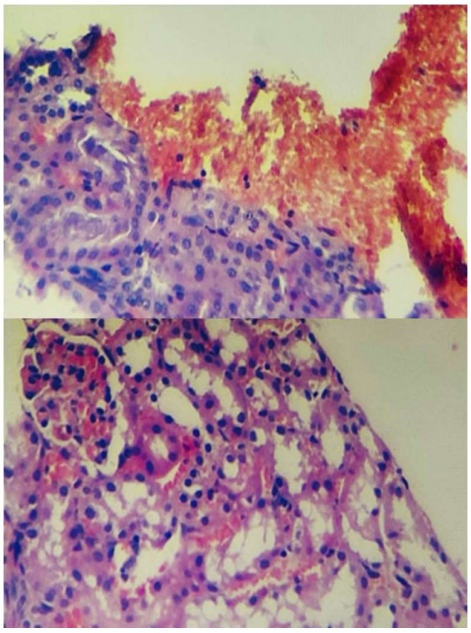


Figure-9. Histological section of a kidney from mice which was intraperitoneal injection 10mg /Kg of R.C section stained with H & E X40.

Histological examination of kidney sections from mice treated with 10 mg of *Ricinus communis* leaf extract revealed generally preserved renal architecture with intact glomeruli and tubules. However, mild infiltration of inflammatory cells was observed within the interstitial tissue, predominantly mononuclear cells, indicating a localized inflammatory response. Additionally, evidence of vascular hemorrhage was present, characterized by extravasation of red blood cells in peritubular capillaries and interstitial spaces. There were no signs of tubular necrosis, fibrosis, or significant structural damage. These findings suggest that low-dose exposure induces mild inflammatory and vascular changes without severe impairment of renal tissue (Figure-9).



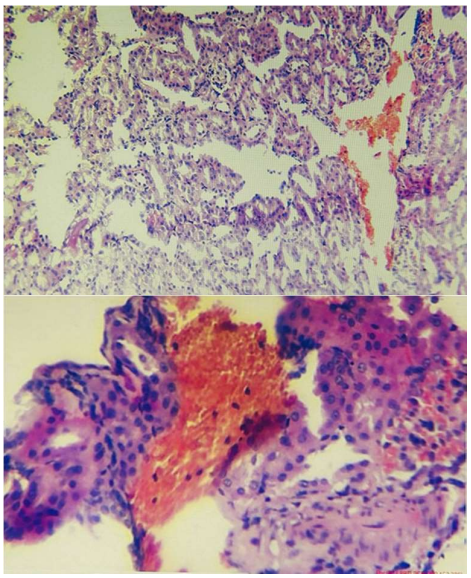
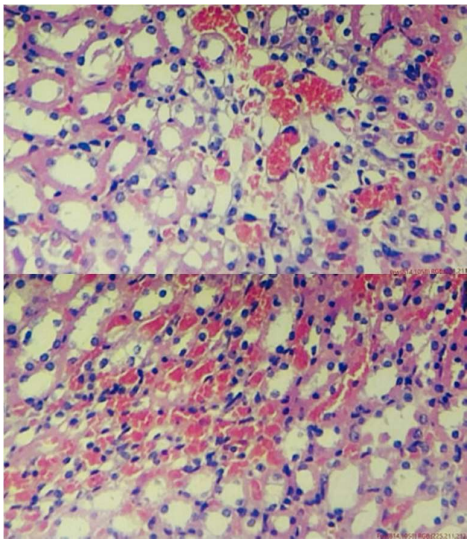


Figure-10. Histological section of a kidney from mice which was intraperitoneal injection 25mg /Kg of R.C section stained with H & E X40.

Histological analysis of kidney tissue from mice treated with 25 mg of *Ricinus communis* leaf extract revealed largely preserved renal architecture. The glomeruli and tubular structures appeared intact without significant morphological alterations. A few inflammatory cells, predominantly mononuclear, were observed scattered within the interstitial space, indicating a mild inflammatory response. Notably, focal hemorrhagic areas were detected in the renal cortex, characterized by the presence of extravasated red blood cells. These findings suggest that a 25 mg dose induces mild inflammatory and vascular effects localized primarily in the cortical region without extensive renal injury (Figure-10)



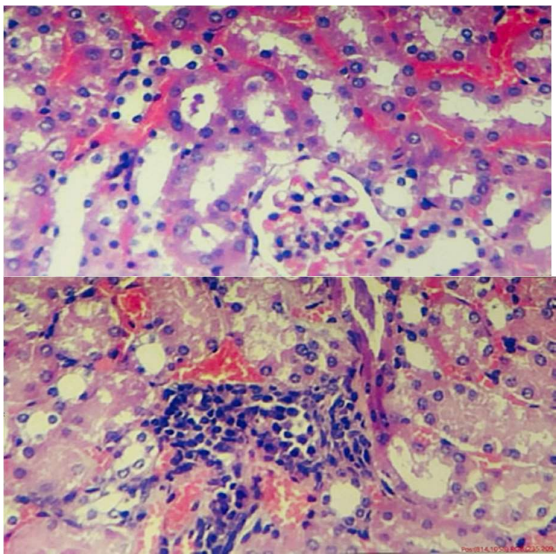


Figure11: Histological section of a kidney from mice which was intraperitoneal injection 50mg /Kg of R.C section stained with H & E X40.

Kidney sections from mice administered 50 mg of *Ricinus communis* leaf extract demonstrated more prominent histopathological changes compared to the 25 mg dose. While the overall renal architecture, including glomeruli and tubules, remained mostly intact, there was a marked increase in vascular hemorrhage, predominantly within the cortical region. Extravasation of red blood cells was more extensive, indicating increased vascular fragility or damage. Inflammatory cell infiltration was present but remained mild to moderate and scattered within the interstitial tissue. These findings indicate a dose-dependent exacerbation of hemorrhagic events in renal tissue, with relatively mild inflammatory involvement at this concentration.

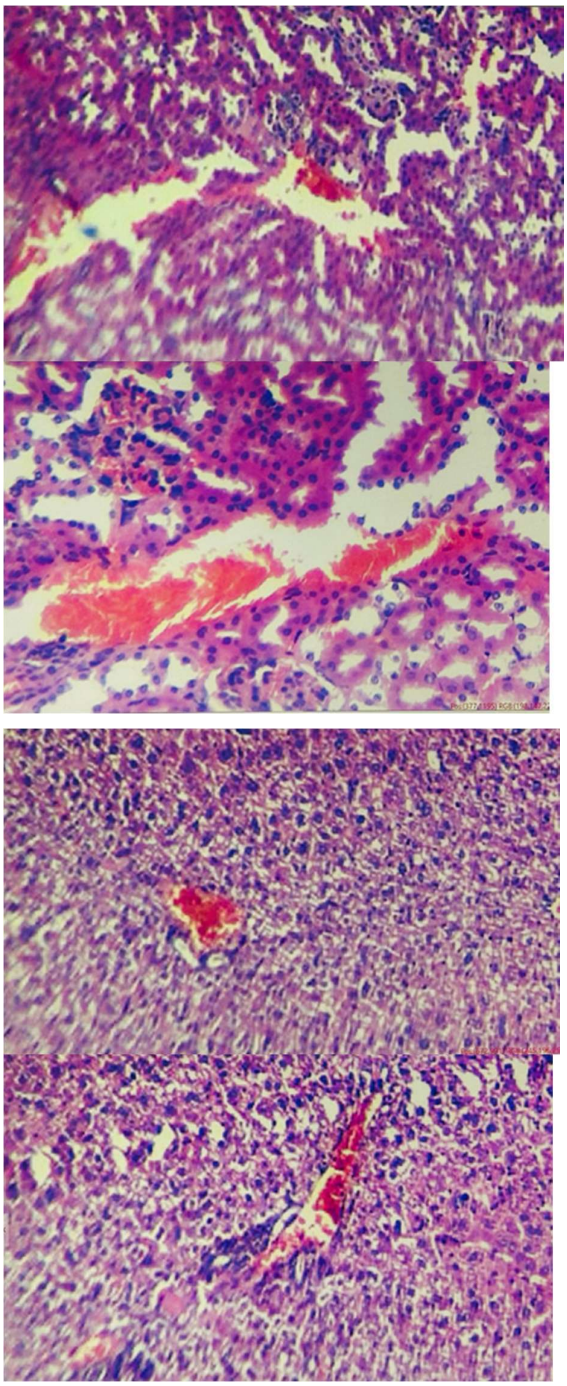


Figure12: Histological section of a kidney from mice which was intraperitoneal injection 100mg /Kg of R.C section stained with H & E X40.

Histological examination of kidney sections from mice treated with 100 mg of Ricinus communis leaf extract revealed severe vascular damage characterized by critical hemorrhage. Extensive extravasation of red blood cells was observed throughout the renal cortex and medulla, indicating widespread disruption of blood vessels. The renal architecture showed signs of localized tissue

disruption associated with hemorrhagic foci. Inflammatory cell infiltration was variable but generally moderate, predominantly consisting of mononuclear cells. No extensive tubular necrosis or fibrosis was noted; however, the severity of hemorrhage suggests significant acute vascular injury at this dose. These findings highlight the potential nephrotoxic effects of high-dose castor leaf extract.

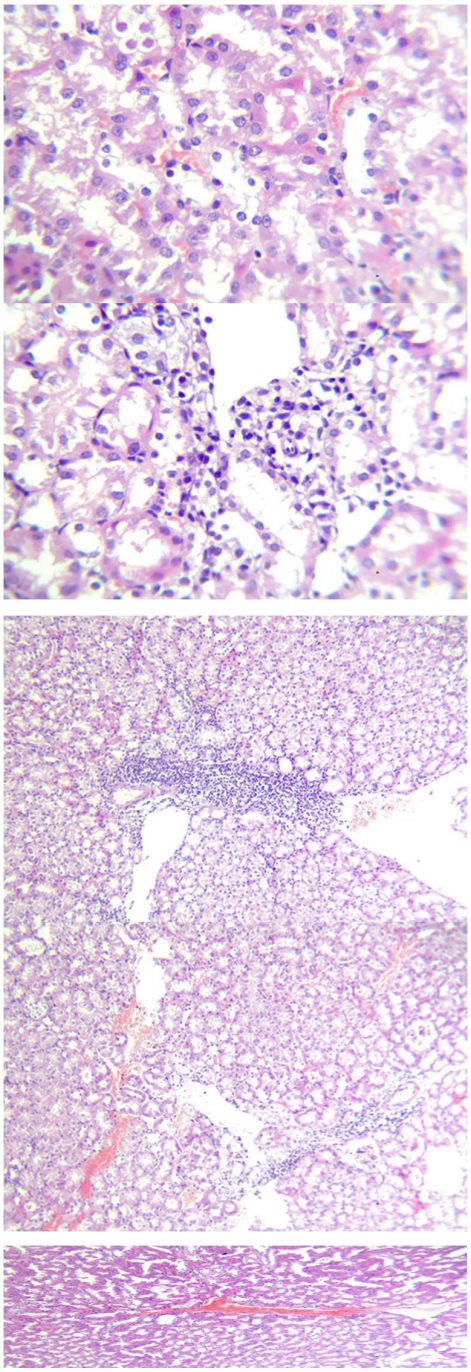


Figure13: Histological section of a kidney from mice which was intraperitoneal injection 150mg /Kg of R.C section stained with H & E X40.

Histological analysis of kidney sections from mice treated with 150 mg of *Ricinus communis* leaf extract revealed marked pathological changes indicative of nephrotoxicity. There was evident cellular degeneration affecting tubular epithelial cells, characterized by cytoplasmic vacuolation, swelling, and loss of cellular integrity. The interstitial tissue exhibited moderate to severe inflammatory cell infiltration, predominantly mononuclear leukocytes, suggesting active interstitial inflammation. These changes were accompanied by disruption of normal renal architecture, confirming the nephrotoxic potential of high-dose castor leaf extract. No significant fibrosis was detected at this stage, but the extent of cellular injury highlights the risk of progressive renal damage with increasing dosage.

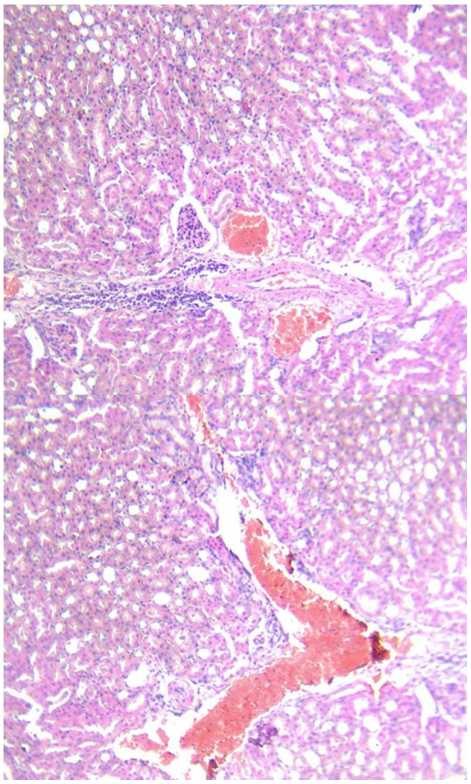


Figure14: Histological section of a kidney from mice which was intraperitoneal injection daily of R.C section stained with H & E X40.

Histopathological evaluation of kidney tissue from mice subjected to daily injections of *Ricinus communis* leaf extract revealed noticeable structural alterations. Vascular hemorrhage was evident, particularly in the cortical region, as indicated by widespread extravasation of red blood cells within glomerular capillaries and interstitial spaces. Additionally, prominent widening of intercellular spaces between tubular epithelial cells was observed, suggesting early signs of edema and loss of cellular cohesion. While the overall renal architecture remained recognizable, these changes

reflect cumulative vascular and parenchymal stress induced by repeated exposure to the extract. No marked necrosis or fibrosis was detected, but the findings support the onset of chronic nephrotoxic effects with continuous dosing.

3.6.3. The histopathology feature of Spleen.

The histopathological examination of the spleen shows normal architecture and cellular composition. There are no signs of inflammation, necrosis, fibrosis, or neoplastic changes. These findings are consistent with a healthy control mouse spleen (Figure-7).

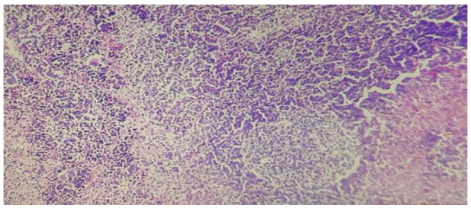
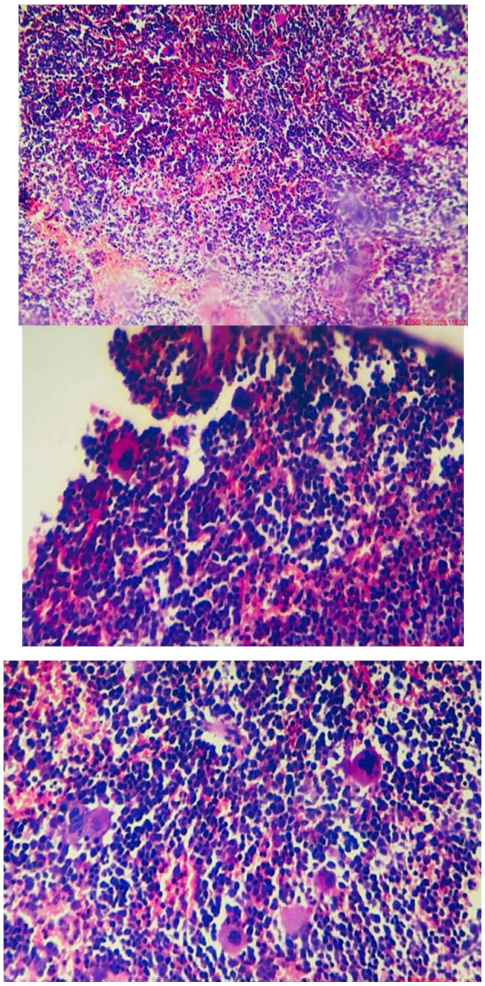


Figure-15. Histological section of a spleen from mice which was intraperitoneal injection (control) section stained with H & E X40.



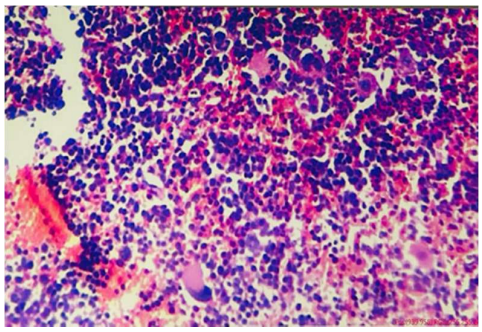


Figure-16. Histological section of a spleen from mice which was intraperitoneal injection 10mg /Kg of R.C section stained with H & E X40.

Histological evaluation of spleen sections from mice treated with 10 mg of *Ricinus communis* leaf extract revealed largely preserved splenic architecture. The white pulp and red pulp regions were identifiable and structurally intact. However, mild nuclear enlargement was noted in some splenic cells, particularly lymphocytes and macrophages within the white pulp, suggestive of mild cellular activation or early reactive changes. Additionally, small areas of focal hemorrhage were observed in the red pulp, with extravasated red blood cells present between splenic cords and sinusoids. These findings indicate that low-dose exposure to R.C leaf extract induces minimal splenic alterations, primarily involving mild vascular and reactive cellular changes without significant tissue disruption (Figure-16).

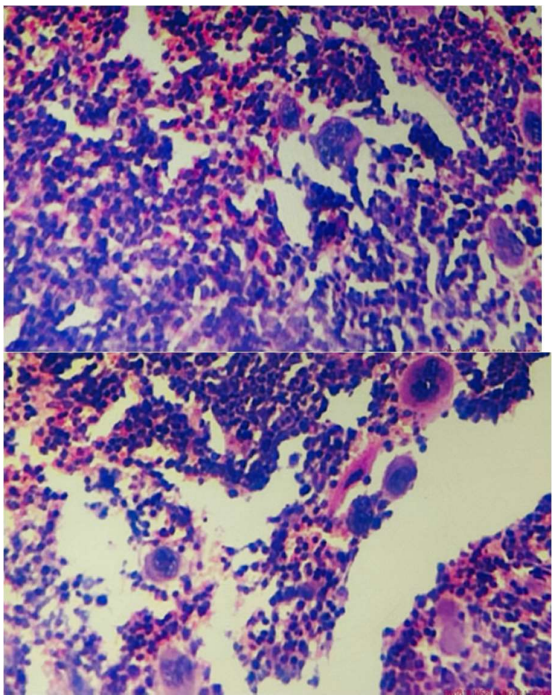


Figure17: Histological section of a spleen from mice which was intraperitoneal injection 25mg /Kg of R.C section stained with H & E X40.

Histopathological examination of spleen tissue from mice treated with 25 mg of *Ricinus communis leaf* extract revealed noticeable nuclear alterations. The overall splenic architecture, including white and red pulp zones, remained intact. However, a marked nuclear enlargement was observed in various splenic cells, particularly in lymphocytes and reticuloendothelial elements of the white pulp. This nuclear enlargement may reflect increased metabolic or proliferative activity in response to the extract. These findings suggest that a 25 mg dose elicits a moderate reactive cellular response in the spleen, possibly as part of a mild immune or stress-related activation (Figure-17).

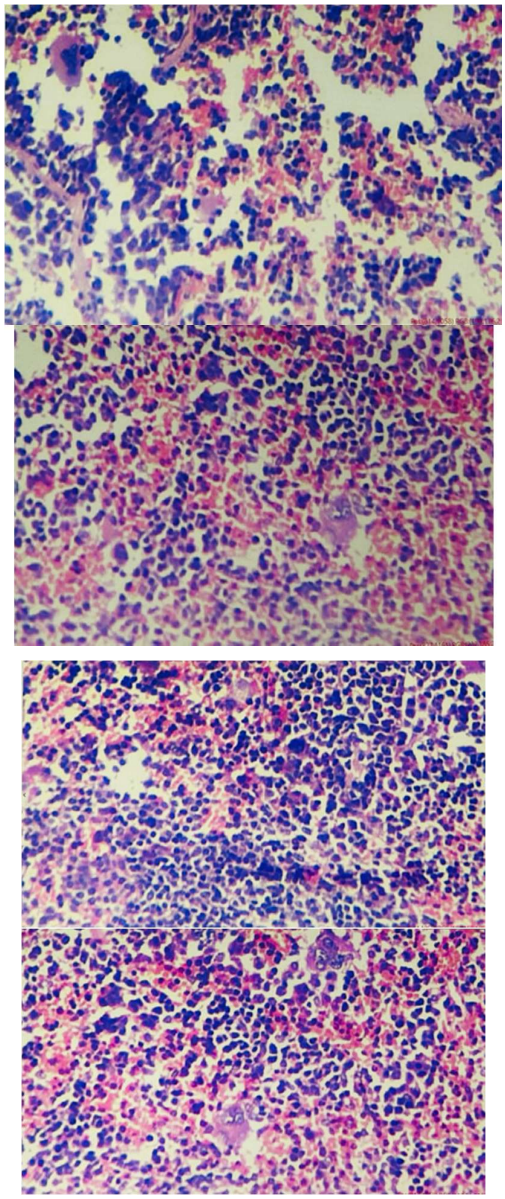


Figure18: Histological section of a spleen from mice which was intraperitoneal injection 50mg /Kg of R.C section stained with H & E X40.

Histological analysis of spleen sections from mice treated with 50 mg of *Ricinus communis* leaf extract demonstrated mild to moderate histopathological changes. The splenic architecture, including white and red pulp regions, remained preserved. However, nuclear enlargement was more prominent compared to lower doses, particularly among lymphocytes and macrophages in the white pulp, suggesting an ongoing or enhanced immune activation. In addition, small foci of hemorrhage were identified in the red pulp, with red blood cells scattered among the splenic cords and sinusoids. These findings indicate a dose-dependent increase in cellular and vascular responses, with mild splenic activation and localized hemorrhagic changes at this concentration (Figure-18).

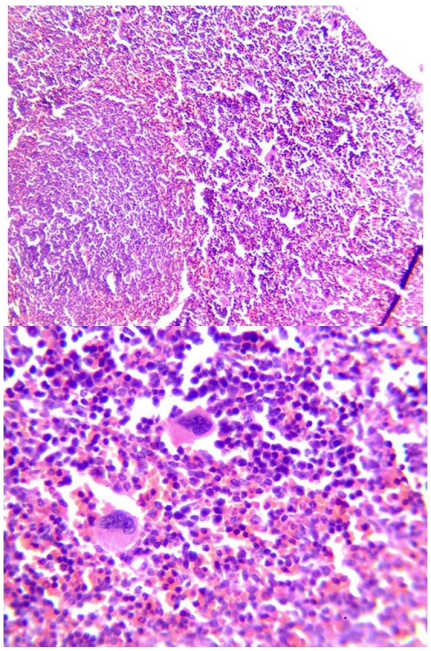


Figure19: Histological section of a spleen from mice which was intraperitoneal injection 100mg /Kg of R.C section stained with H & E X40.

Histopathological examination of spleen tissue from mice administered 100 mg of *Ricinus communis* leaf extract revealed marked nuclear enlargement across various splenic cell populations. The white pulp exhibited prominent activation with enlarged nuclei in lymphocytes and reticuloendothelial cells, indicating heightened cellular proliferation or metabolic activity. Despite these changes, the overall splenic architecture, including red and white pulp zones, remained preserved without evidence of necrosis or extensive hemorrhage. These observations suggest a dose-dependent enhancement of splenic cellular activation at 100 mg, reflecting an intensified immune or stress response to the extract.

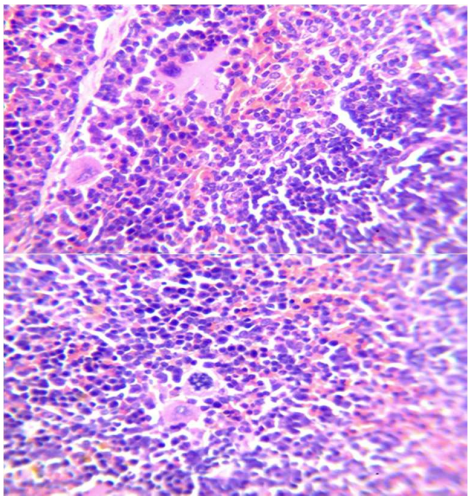


Figure20: Histological section of a spleen from mice which was intraperitoneal injection 150mg /Kg of R.C section stained with H & E X40.

Histological examination of spleen tissue from mice treated with 150 mg of *Ricinus communis* leaf extract revealed significant pathological alterations. There was evident tissue damage characterized by fragmentation and disruption of the normal splenic architecture. Marked hemorrhagic areas were observed throughout the red pulp, with extensive extravasation of red blood cells. The nuclear enlargement noted at lower doses was accompanied by signs of cellular degeneration and loss of structural integrity. These findings indicate severe splenic injury at this high dose, reflecting pronounced vascular and cellular toxicity induced by R.C leaf extract.

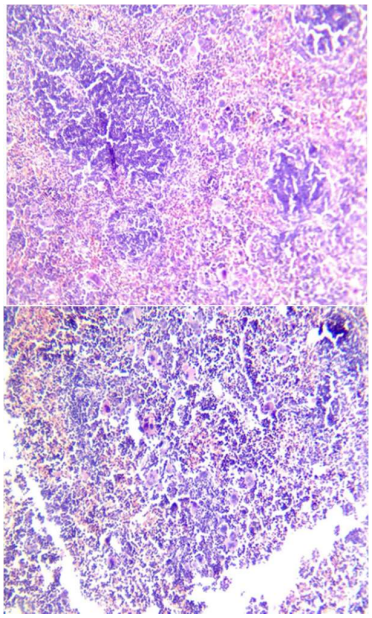


Figure21: Histological section of a spleen from mice which was intraperitoneal injection daily of R.C section stained with H & E X40.

Histopathological analysis of spleen tissue from mice subjected to daily injections of *Ricinus communis* leaf extract revealed notable but mild pathological changes. Focal areas of hemorrhage were evident, characterized by extravasation of red blood cells within the splenic red pulp. Scattered inflammatory cells, predominantly mononuclear leukocytes, were present in the interstitial spaces, indicating a mild immune response. Additionally, subtle cellular and architectural changes were observed, including mild nuclear enlargement and slight disruption of the normal splenic framework. These findings suggest that daily exposure to castor leaf extract induces mild vascular and inflammatory responses in the spleen without extensive tissue damage.

3.7 Biochemical Parameters by Concentration

Table 17: Liver Fanction Test and Renal Function Test

Parameter	10 Mean± S.d	25 Mean± S.d	50 Mean± S.d	100 Mean± S.d	150 Mean± S.d	Control Mean± S.d	Total Mean± S.d
Urea	1.70 ± 0.10	3.17 ± 0.31	1.53 ± 0.25	7.00 ± 1.00	1.40 ± 0.30	29.87 ± 0.35	7.44 ± 10.52
	(1.6–1.8)	(2.9–3.5)	(1.3–1.8)	(6–8)	(1.1–1.7)	(29.5–30.2)	(1.1–30.2)
B.U.N	0.79 ± 0.06	1.46 ± 0.07	0.71 ± 0.10	3.26 ± 0.27	0.56 ± 0.06	13.55 ± 0.27	3.39 ± 4.77
	(0.72–0.84)	(1.40–1.52)	(0.61–0.81)	(2.99–3.53)	(0.51–0.62)	(13.26–13.79)	(0.51–13.79)
Creatinine	0.37 ± 0.15	0.60 ± 0.10	0.73 ± 0.15	0.57 ± 0.15	0.20 ± 0.10	0.13 ± 0.06	0.43 ± 0.25
	(0.2–0.5)	(0.5–0.7)	(0.6–0.9)	(0.4–0.7)	(0.1–0.3)	(0.1–0.2)	(0.1–0.9)
ALT	0.50 ± 0.10	0.70 ± 0.60	5.47 ± 0.70	3.00 ± 1.00	0.47 ± 0.15	34.23 ± 0.64	7.39 ± 12.50

Parameter	10 Mean± S.d	25 Mean± S.d	50 Mean± S.d	100 Mean± S.d	150 Mean± S.d	Control Mean± S.d	Total Mean± S.d
	(0.4–0.6)	(0.1–1.3)	(4.8–6.2)	(2–4)	(0.3–0.6)	(33.5–34.7)	(0.1–34.7)
AST	18.93 ± 0.25	15.80 ± 0.36	31.97 ± 0.50	25.93 ± 0.25	30.33 ± 1.53	17.77 ± 0.35	23.46 ± 6.50
	(18.7–19.2)	(15.5–16.2)	(31.5–32.5)	(25.7–26.2)	(29–32)	(17.4–18.1)	(15.5–32.5)
Alk.pho	0.70 ± 0.10	1.20 ± 0.27	1.57 ± 0.21	1.77 ± 0.15	2.33 ± 0.58	1.23 ± 0.06	1.47 ± 0.58
	(0.6–0.8)	(0.9–1.4)	(1.4–1.8)	(1.6–1.9)	(2–3)	(1.2–1.3)	(0.6–3.0)
Total.Bil	0.07 ± 0.06	0.20 ± 0.10	0.07 ± 0.06	0.03 ± 0.06	0.13 ± 0.15	0.13 ± 0.06	0.11 ± 0.09
	(0.0–0.1)	(0.1–0.3)	(0.0–0.1)	(0.0–0.1)	(0.0–0.3)	(0.1–0.2)	(0.0–0.3)
Bil.Direct	0.07 ± 0.06	0.07 ± 0.06	0.13 ± 0.06	0.37 ± 0.55	0.07 ± 0.06	0.07 ± 0.06	0.13 ± 0.22
	(0.0–0.1)	(0.0–0.1)	(0.1–0.2)	(0.0–1.0)	(0.0–0.1)	(0.0–0.1)	(0.0–1.0)
Bil.IND	0.07 ± 0.06	0.07 ± 0.06	0.07 ± 0.06	0.10 ± 0.00	0.13 ± 0.06	0.13 ± 0.06	0.09 ± 0.05
	(0.0–0.1)	(0.0–0.1)	(0.0–0.1)	(0.1–0.1)	(0.1–0.2)	(0.1–0.2)	(0.0–0.2)

Urea: Range: 1.1–30.2, Mean = 7.44 ± 10.52. 150 had the lowest mean (1.40), whereas the control group had the highest (29.87).
Mean: 3.39 ± 4.77 (range: 0.51–13.79) is the B.U.N. The mean for the control group was 13.55, which was noticeably greater than the other concentrations.
Creatinine: Range: 0–1, Mean = 0.43 ± 0.25. There was little difference across the groups, however the Control group's mean was the lowest (0.13).
ALT: Range: 0–34.7; Mean = 7.39 ± 12.50. The lowest values (~0.5) were found in groups 10 and 150, while the control group peaked at 34.23.
AST: Range: 15.8–32.5; Mean = 23.46 ± 6.50. The means of 50 and 150 were higher (~31) than those of Control (17.77).
Total, Direct, and Indirect bilirubin all had low averages (<0.2) and little variation, with the exception of Bil.Direct, which was 100 (0.37 ± 0.55).
The control group continuously displayed extreme values (such as the highest urea/B.U.N/ALT and the lowest creatinine), which may have biological or experimental importance.

3.8 Hematological Parameters Across Concentration Gradients

This dataset uses duplicate measurements to systematically analyze 16 hematological parameters across six experimental concentrations (150, 100, 50, 25, 10, and Control). The information records the components of the complete blood count (CBC), which include:

Table 21: Measurements across 16 hematological parameters. Below is a summary of the mean ± standard deviation for each variable:

Variable	Mean ± SD	Range	Skewness	Kurtosis
WBC	6.67 ± 1.76	3.21–9.20	-0.665	-0.559
Neutrophil	27.63 ± 8.21	15.90–36.80	-0.148	-1.919
Eosinophil	0.49 ± 0.28	0.00–0.91	-0.095	-1.201
Basophil	20.14 ± 10.14	5.40–38.70	0.606	-0.106
Lymphocyt	55.64 ± 18.33	34.40–88.90	0.785	-0.498
Monocyte	9.76 ± 2.12	4.90–11.90	-1.570	1.319
RBC	9.84 ± 1.72	7.10–12.30	0.080	-1.087
HGB	14.21 ± 2.18	10.50–17.10	-0.259	-0.952
HTC	50.59 ± 7.56	36.30–59.10	-0.866	-0.104

MCV	51.93 ± 3.55	47.40 – 57.80	0.291	-0.780
MCH	14.79 ± 0.59	13.50 – 15.70	-0.260	-0.106
MCHC	27.52 ± 1.54	25.20 – 30.20	0.273	-0.813
Platelets	639.78 ± 142.50	410.00– 811.00	-0.524	-1.327
PDW	10.30 ± 2.07	6.00– 12.90	-0.538	-0.598
MPV	8.12 ± 1.49	6.10– 11.00	0.549	-0.565
PCT	0.60 ± 0.13	0.39– 0.78	-0.506	-1.177

4. Discussion

The Ricinus communis is the most active plants that suggestion a resolution to several kinds of diseases anti-inflammatory, ulcer and anthelmintic, it has numerous benefits for both health and beauty, due to the chemical constituents of Ricinus communis like flavonoids, alkaloids and steroids. Ricinus communis can be a suitable drug for many diseases such as cancer.

This study aimed to investigate both the antimicrobial activity and histopathological effects of Ricinus communis leaf and seed extracts using aqueous and methanolic solvents. The study provided valuable insight into the dual nature of R. communis as a potential therapeutic agent and a possible source of organ toxicity.

The antimicrobial assessment revealed that methanolic leaf extracts exhibited potent inhibitory effects against several pathogens. At 200% concentration, inhibition zones reached 33 mm against Candida albicans and approximately 30 mm against Pseudomonas aeruginosa, Staphylococcus aureus, and Klebsiella pneumoniae. These results align with prior studies demonstrating the strong antimicrobial capacity of methanol-based R. communis extracts (Gassim, 2021)[8]. In contrast, the aqueous extracts—including cold leaf and seed preparations—showed no activity, with inhibition zones matching the negative control (6 mm). This supports the idea that active phytochemicals in R. communis may be poorly extracted in water or degrade in aqueous environments (Naz, 2013)[9].

Methanolic extracts demonstrated significant antimicrobial activity even against highly resistant bacteria such as Pseudomonas aeruginosa and Escherichia coli. This suggests that specific bioactive compounds within the extracts might disrupt microbial membrane integrity or interfere with key metabolic pathways, leading to bacterial inhibition and death (Gharibi, 2021) [10] . Such findings are supported by various studies showing that methanol-based plant extracts exert antibacterial effects by altering cell membranes and critical enzymatic processes in pathogens, including multidrug-resistant strains (Jalali, 2020) [11]. The data support the traditional use of castor in ethnomedicine, and further reinforce its broad-spectrum potential, especially when properly extracted.

In parallel, the histopathological component of the study revealed a dose-dependent toxicity profile in liver and kidney tissues of treated mice. At lower doses (10 mg), tissue damage was minimal, involving mild inflammatory infiltration and vascular congestion. As the dose increased (25–150 mg), hepatic sections exhibited focal necrosis, cytoplasmic vacuolation, and disorganization of hepatic cords. Renal sections also showed progressive damage, including interstitial inflammation, cortical hemorrhage, and cellular degeneration. Daily administration of the extract further intensified these changes, suggesting a cumulative toxic effect.

These findings are consistent with previous research indicating that phytochemicals in R. communis may induce oxidative stress and inflammatory responses in vital organs (Rasool et al., 2022)[12]. The absence of fibrosis or full necrosis at this stage may suggest early-stage toxicity; however, the pattern of degeneration raises concerns regarding long-term safety with repeated or high-dose use.

The in-silico toxicity predictions in Table 3 revealed high probabilities of hepatotoxicity, neurotoxicity, immunotoxicity, and respiratory toxicity. These findings align with previous studies, such as Mboyazi et al. (2020)[13], who reported similar Tox21-based predictions for Ricinus communis phytocompounds. Ricin and related constituents are known to trigger inflammatory responses and cellular disruption even at low doses (Vhutshilo Nemudzivhadi & Masoko, 2014) [14]. While nephrotoxicity and carcinogenicity were predicted as inactive, the predicted hepatotoxic and immunotoxic effects are supported by animal studies showing elevated liver enzymes after extract exposure (Naveen et al., 2016)[15]. These results validate the predictive model and highlight the histopathological results which together show a systematic risk.

The predicted activation of aromatase and estrogen receptor alpha (ERα) by Ricinus communis extract (Table 4) suggests modulation of estrogenic

pathways. Similar effects have been observed with plant phytochemicals acting as selective estrogen receptor modulators (SERMs) that influence hormonal activity without triggering stress responses (Xue et al., 2020). The inactivity predicted for stress-related pathways such as Nrf2/ARE and p53 aligns with reports showing minimal oxidative or DNA damage from such extracts. Additionally, R. communis phytochemicals have been shown to affect reproductive hormones in animal models, supporting a hormonal mode of action with limited cellular stress (Jehan, 2015; Sandhyakumary, 2003). These findings help explain the dual therapeutic and toxic effects observed.

The predicted molecular initiating events (MIEs) of Ricinus communis extract indicate mostly inactive interactions with key receptors involved in neurotoxicity, hormone regulation, and metabolism, except for moderate predicted activity against acetylcholinesterase (AChE). This suggests potential effects on cholinergic signaling that could contribute to neurotoxicity. These findings align with experimental studies showing selective antimicrobial and cytotoxic activities of R. communis extracts without broad receptor engagement (Kebede & Shibeshi, 2022; Suurbaar et al., 2017) [2, 3]. Moreover, animal studies indicate possible hepatotoxicity at high doses but do not report widespread neuroreceptor disruption (Naveen et al., 2016) [15]. Overall, the data point to AChE as a key target related to R. communis toxicity, warranting further experimental validation.

The predicted interactions of Ricinus communis extract with cytochrome P450 enzymes, particularly the activation of CYP2C9 and CYP3A4 (Table 6), align with findings from prior studies highlighting the importance of these enzymes in herb–drug interactions. CYP3A4 is a major enzyme involved in the metabolism of many drugs and is commonly modulated by herbal compounds, potentially altering drug bioavailability and toxicity (Carlemi Calitz et al., 2015)[16]. Similarly, CYP2C9 plays a key role in drug metabolism, and inhibition or activation by plant constituents can lead to significant pharmacokinetic changes (Paine, 2020)[17]. An in silico and experimental study specifically on Ricinus communis reported potential inhibition of CYP3A4, supporting the possibility of herb–drug interactions . These data underscore the need for caution when using R. communis extracts concurrently with medications metabolized by these cytochrome enzymes and the importance of further experimental validation. This study highlights the promising antimicrobial activity of methanolic leaf extracts of R. communis, while simultaneously identifying potential hepatic and renal toxicity associated with prolonged or high-dose exposure. Future research should focus on isolating and characterizing the specific active compounds, elucidating their mechanisms of action, and determining safe dosage ranges through in vivo studies. These steps are essential before clinical application or pharmaceutical development of R. communis-based therapies.[16]

5. Conclusion

It is clear that Ricinus communis leaf extracts, particularly the methanolic extract, possess broad-spectrum antimicrobial activity against various bacterial and fungal pathogens, confirming their potential as effective natural treatments for infections. However, histopathological analyses revealed dose-dependent toxic effects, especially in liver and kidney tissues, highlighting potential health risks associated with excessive or prolonged use. This toxicity necessitates careful consideration and caution as well as a deeper understanding of the medicinal capabilities of Ricinus communis that can be harnessed to develop effective and safe natural therapies for public health.

6-Recommendation

- Isolate and identify the active chemical compounds in castor extracts.

- Investigate the cellular and molecular mechanisms of these compounds.

- Evaluate safe dosage ranges through comprehensive toxicological studies in multiple biological models.

- Study possible drug interactions to ensure safe clinical use.

- Develop extract formulations that minimize toxicity while enhancing therapeutic efficacy.

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