

## Safety Assessment of the Hydroethanolic Extract of *Citrullus lanatus* (Watermelon) Seeds in Female Wistar Rats

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Submission: 1<sup>st</sup> Dec., 2024; Accepted: 7<sup>th</sup> Dec., 2024; Published: 22<sup>nd</sup> Dec., 2024

### Abstract

The recognition of herbal medicines for treating various illnesses stems from their effectiveness, affordability, accessibility, alignment with patients' beliefs, perceived low toxicity, minimal side effects, and fulfillment of the desire for personalized healthcare. However, there are growing concerns regarding the safety of herbal medicines. This study aimed to assess the safety of hydroethanolic extract of *Citrullus lanatus* (watermelon) seeds in female Wistar rats. Twenty rats were randomized into four groups (I, II, III and IV) of five animals each. The rats in group I (Control) received 1.0 mL of distilled water orally, while those in groups II, III and IV received equal volume (1.0 mL) of the hydroethanolic extract of *C. lanatus* seeds, corresponding to 50, 100, and 200 mg/kg body weight, respectively for 7 days. Weight changes were monitored, and on the eighth day, biochemical analyses were conducted on serum and tissues. Phytochemical screening revealed the presence of several compounds, with notable minerals including iron (16.20 mg/mL), potassium (8.57 mg/mL), and magnesium (6.40 mg/mL). Heavy metals analysis reveals the presence of cadmium (0.12 mg/mL), chromium (8.44 mg/mL), lead (0.23 mg/mL), and cobalt (0.58 mg/mL) in trace amount. Lipid profile analysis showed a significant decrease ( $p < 0.05$ ) in total cholesterol (TC) and triglycerides (TAG) at higher doses, accompanied by an increase in high-density lipoprotein (HDL) and a decrease in low-density lipoprotein (LDL). Hematological parameters showed no significant changes except for lymphocytes; mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV), and red blood cell count (RBC), which increased dose-dependently, while neutrophils decreased. Liver parameters indicated increased levels of protein, bilirubin, and albumin, with decreased ALT, AST, and LDH activities. Urea, calcium, chloride, and sodium ion activities increased significantly, while potassium, bicarbonate, uric acid, and creatinine activities showed no significant differences. Overall, the study suggests that the hydroethanolic extract of *C. lanatus* seeds is safe and exhibits hepatoprotective, antihyperlipidemic, and hematological effects.

**Keywords:** *Citrullus lanatus*, Heavy Metals, Hydroethanolic, Minerals, Toxicity

### 1.0 Introduction

The major factor that led to the recognition of herbal medicines in treating a range of illness are their effectiveness, affordability, accessibility, assumed less toxic effect and minimal side effects with developing resistance, and fulfilling the desire for individualized healthcare [1, 2].

According to a report by Oyewo et al. [3], the majority of people in developing nations (80%)

rely on plant medicines in treating different diseases such as diarrhea and fever. In Africa, effective healthcare may not be attained until orthodox medicine is supplemented with traditional medicine [4]. However, herbal medicines that are thought to be non-toxic may contain pollutants like pathogenic microbes, aflatoxins, and heavy metals due to the formulation process or as a result of the acquisition of metals (like lead, and cadmium) from the soil [5]. The evaluation of toxicity in

folkloric treatment is often overlooked even though it should be a priority as it assists researchers to gain confidence in the safe use of natural compound for human consumption [5].

*C. lanatus* (watermelon), a fruit crop, is an herbaceous creeping plant in the cucurbitaceae family [6]. *C. lanatus* has been identified as one of the most often consumed fruits in Nigeria, with no adverse health effects [7], yet most people avoid eating the seeds due to their unpleasant flavor and too much oil/fat and fear of being toxic to the body system. These misconceptions persist despite the absence of conclusive scientific claims. Furthermore, while the seeds are rich in nutrients and phytochemicals with potential health benefits, their widespread use remains limited largely due to the lack of detailed toxicological evaluations. Also, inconsistent findings from few existing studies have created uncertainty about their safety and potential applications. As a result, the purpose of this study was to evaluate the safety of hydroethanolic extract of *C. lanatus* seeds in female Wistar rats.

## 2.0 Materials and Methods

### 2.1 Materials

#### 2.1.2 Collection and Identification of Plant Material

Dried seeds of *C. lanatus* was bought from herb sellers at Batsari Market, Katsina, Nigeria, and authenticated by Dr. Mustapha of the Department of Plant Science and Biotechnology, Umaru Musa Yar'adua University, Katsina, Nigeria. A voucher specimen (UMYUH-2346) was deposited at the herbarium section.

#### 2.1.2 Experimental Animals

A total of twenty (20) healthy female Wistar rats (*Rattus norvegicus*) weighing  $161 \pm 2.82$ g were obtained from Institute of Trypanosomiasis Research, Kaduna, Kaduna State, Nigeria. The animals were housed in clean wooden cages placed in well-ventilated housing conditions (temperature:  $25^{\circ}\text{C} - 27^{\circ}\text{C}$ ; photoperiod: about a 12 h light and dark cycle; relative humidity: 45% – 50%). The animals were provided with unlimited access to clean rat pellets (Top Feeds Limited, Ibadan, Nigeria) and tap water. Daily cleaning of the cages was also done.

### 2.2.3 Reagents and Assay Kits

The assay kits used for the determinations of albumin, total and conjugated bilirubin, alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), urea, creatinine,  $\text{Na}^+$  and  $\text{K}^+$  were products of Randox Laboratory Ltd, Co-Antrim, UK. All other reagents used were of analytical grade and prepared using distilled water and stored in air-tight reagent bottles except otherwise stated.

## 2.2 Methods

### 2.2.1 Preparation of Plant Extract

The seeds of *C. lanatus* were washed under running tap water, dried under shade for 72 hours, and pulverized in a blender (Master Chef Blender, model MC – BL 2013 China). For extraction, a known amount (100g) of the powdered sample was macerated in a solvent consisting of a 50:50 mixture of ethanol and water at room temperature. The mixture was shaken intermittently over a period of 48 hours and subsequently filtered using Whatman No.1 filter paper. The resulting filtrate was lyophilized using a ziruslyophilizer (Model VaCo 5-11, Zirbus Technology, Stephensonstra at, Germany), resulting in a yield of 26 grams (corresponding to a percentage yield of 28%). This lyophilized filtrate was reconstituted in distilled water to obtain the required doses of 50, 100, and 200 mg/kg body weight, which were based on information obtained from an ethnobotanical survey and utilized in the present study.

### 2.2.2 Animal Grouping and Extract Administration

The twenty Wistar rats were divided into four groups, each consisting of five rats. The extract dosages were given orally to the rats using the following methods:

Group I: Administered 1.0 ml of distilled water only

Group II: Administered 1.0 ml of 50 mg/kg body weight of extract

Group III: Administered 1.0 ml of 100 mg/kg body weight of extract

Group IV: Administered 1.0 ml of 200 mg/kg body weight of extract

The animals received oral administration of the extract daily for 7 days using a cannula. Weight changes were also monitored throughout the experimental period. On the eighth day, the rats were euthanized.

### 2.2.3 Preparation of Serum and Tissue Supernatants

The procedures described by Yakubu and Salimon [8] were adopted for the preparation of serum and tissue supernatants. Twenty-four hours after the 7 days administration of the distilled water and plant extract, the rats were weighed and anaesthetized in diethyl ether fumes. Following loss of consciousness, the jugular veins were cut, and 3 mL of blood were collected into plain and heparin sample bottles with the aid of a Pasteur pipette. Clear serum was then collected using Pasteur pipette after centrifuging the clotted blood samples at  $1252 \times g$  for 10 minutes using Biobase Laboratory Centrifuge (Model LC- 4KA, Jinan, China). The sera were kept frozen for 12 hours before being used for further analysis. The animals were then quickly dissected, and the livers and kidneys were carefully removed and blotted. The organs were weighed using an analytical weighing balance and placed in iced cold 0.25 M sucrose solution to maintain the integrity of the tissues. The organs were separately homogenized after which they were centrifuged at  $1789 \times g$  for 10 minutes. The supernatants were frozen for 12 hours before being used for the assessment of some biochemical parameters.

### 2.2.4 Hematological, Biochemical and Lipid Profile Examination

Hematological analysis was performed using an automatic hematological analyzer (Sysmex Hematology System, Model KX-21W, Kobe, Japan). The procedures described by Gornal et al. [9], Doumas et al. [10], Jendrassik and Grof [11], Tietz [12], Veniamin and Verkirtzi [13] and Bartels and Bohmer [14] were adopted for the determination of total protein, albumin, bilirubin (total and conjugated), globulin, urea and creatinine, respectively. The concentrations of electrolytes – sodium and potassium ion ( $\text{Na}^+$  and  $\text{K}^+$ ) were determined as described by Tietz [12]

while the activities of ALT, AST, ALP, and LDH were determined using standard procedures described by Reitman and Frankel [14], Wright et al. [15], Aebi [16], and Reclos et al. [17]. Total cholesterol, LDL cholesterol, HDL cholesterol and triglyceride were determined using the spectrophotometry method (i.e. using their respective reagents kits from Randox laboratory limited, U.K.).

### 2.3 Statistical Analysis

The data obtained from five replicated measurements were used to calculate the mean and then the standard error of the mean. Furthermore, a one-way Analysis of Variance (ANOVA) was performed on the data. Statistical significance was determined using GraphPad Prism version 6.01 software (GraphPad Software, Inc., San Diego, California, United States), with a significance level at  $p < 0.05$ .

## 3.0 Results

### 3.1 Secondary Metabolites

The results for the phytochemical screening of hydroethanolic seed extract of *C. lanatus* revealed the presence of saponins, steroids, terpenoids, cardiac glycosides, reducing sugars, and phenols, while tannins, flavonoids, and phenols were not detected (Table 1).

### 3.2 Mineral Constituents

The hydroethanolic extract of *C. lanatus* seed revealed the presence of calcium, magnesium, potassium, sodium, manganese, iron, copper, and zinc. The abundance of the mineral constituents in descending order was iron > potassium > magnesium > calcium > manganite > copper > sodium > zinc (Table 2).

### 3.3 Heavy Metals

Heavy metals screening of hydroethanolic extract of *C. lanatus* seeds revealed the presence of cadmium, chromium, lead, and cobalt in trace amount (Table 3).

### 3.4 Lipid Profiles

There were no treatment-related changes in concentration of total cholesterol, triacylglycerol,

high density lipoprotein, and very low density lipoprotein at all doses of the plant extract compared to the control. However, a significant decrease ( $p < 0.05$ ) was observed in the level of low density lipoprotein at 50 and 100 mg/kg body weight of the extract when compared to the control group (Table 4).

### 3.5 Hematology

Administration of the hydroethanolic extract of *C. lanatus* seed shows no significant difference ( $p > 0.05$ ) in the concentration of hemoglobin (Hb), packed cell volume (PCV), mean corpuscular hemoglobin concentration (MCHC), white blood cell (WBC), and red blood cell (RBC) whereas, there was significant ( $p < 0.05$ ) and dose-related increase in the concentration of lymphocyte (LYM), mean cell volume (MCH), and mean cell (MCV), at all doses investigated. A significant ( $p < 0.05$ ) and dose related decrease was observed in the level of neutrophils (NEU) (Table 5).

### 3.6 Biochemical Indices

The results for the Liver parameters show that there was significant increase ( $p < 0.05$ ) in the levels of protein, bilirubin (direct and total bilirubin), and Albumin at all doses administered to the plant extract when compared with control (Table 6). The activities of liver ALT, AST, and LDH decreased dose-dependently with no corresponding changes in liver ALP when compared to the control (Table 6). The results of this study shows that the activity of urea, calcium, chloride and sodium ion increase significantly ( $p < 0.05$ ) at all doses (50, 100, and

200 mg/kg body) administered with the plant extract when compared with the control group (Table 7). Additionally, no evidence of a difference in potassium, bicarbonate, uric acid, or creatinine activities ( $p > 0.05$ ) (Table 7)

**Table 1: Secondary metabolites in the hydroethanolic extract of *Citrullus lanatus* seeds**

Secondary metabolites	Results
Saponins	+
Flavonoids	-
Tannins	-
Phenols	-
Steroids	+
Terpenoids	+
Cardiac glycosides	+
Alkaloids	+
Reducing sugars	+

Values are mean of 3 replicates  $\pm$  S.E.M

Key: (+): detected, (-): Not detected

**Table 2: Concentrations of mineral constituents of the hydroethanolic extract of *Citrullus lanatus* seed**

Mineral constituent	Concentrations (mg/L)
Calcium	6.33 $\pm$ 0.05
Magnesium	6.40 $\pm$ 0.30
Potassium	8.57 $\pm$ 0.01
Sodium	2.89 $\pm$ 0.02
Manganese	3.94 $\pm$ 0.03
Iron	16.20 $\pm$ 0.02
Copper	3.55 $\pm$ 0.02
Zinc	2.38 $\pm$ 0.03

Values are mean of 3 replicates  $\pm$  S.E.M

**Table 3: Concentrations of heavy metals in the hydroethanolic extract of *Citrullus lanatus* seeds**

Heavy metals	Concentration (mg/L)
Lead	0.23 $\pm$ 0.10
Cadmium	0.12 $\pm$ 0.05
Chromium	8.44 $\pm$ 0.01
Cobalt	0.58 $\pm$ 0.00

Values are mean of 3 replicates  $\pm$  S.E.M

**Table 4: Lipid profiles of Wistar rats fed hydroethanolic extract of *Citrullus lanatus* seeds**

Lipids Profiles	Control	Hydroethanolic extract of <i>C. lanatus</i> seeds (mg/kg body weight)		
		50	100	200
TC (mg/dl)	23.93±4.82 <sup>a</sup>	23.11±3.21 <sup>a</sup>	23.11±2.91 <sup>a</sup>	20.26±3.68 <sup>b</sup>
TAG (mg/dl)	10.30±1.04 <sup>a</sup>	10.78±0.92 <sup>a</sup>	10.59±0.39 <sup>a</sup>	9.39±1.30 <sup>b</sup>
HDL (mg/dl)	8.71±0.30 <sup>b</sup>	9.23±0.17 <sup>a</sup>	9.11±0.97 <sup>a</sup>	10.15±0.32 <sup>a</sup>
LDL (mg/dl)	13.16±4.31 <sup>a</sup>	9.17±3.51 <sup>b</sup>	11.88±3.06 <sup>b</sup>	12.81±3.02 <sup>a</sup>
VLDL (mg/dl)	2.08±0.21 <sup>a</sup>	2.16±0.18 <sup>a</sup>	2.12±0.07 <sup>a</sup>	1.88±0.25 <sup>b</sup>

Values are mean ± SD of five replicates. Values having different superscript across the raw are significantly different ( $p<0.05$ ) and vice versa. Key: TC (Cholesterol), TAG (Triglyceride), HDL (High Density Lipoprotein), LDL (Low Density Lipoprotein), VLDL (Very Low Density Lipoprotein)

**Table 5: Hematological indices of Wistar rats fed hydroethanolic extract of *Citrullus lanatus* seed**

Parameters	Group 1 (control)	Group 2 (50mg/kg)	Group 3 (100mg/kg)	Group 4 (200mg/kg)
PCV (%)	45.99±4.62 <sup>a</sup>	44.01±1.73 <sup>a</sup>	45.67±5.51 <sup>a</sup>	47.01±4.58 <sup>a</sup>
HB (g/dL)	15.33±0.65 <sup>a</sup>	14.67±1.96 <sup>a</sup>	15.20±1.85 <sup>a</sup>	15.67±1.53 <sup>a</sup>
MCHC (%)	32.39±1.55 <sup>a</sup>	31.90±2.94 <sup>a</sup>	33.06±0.39 <sup>a</sup>	33.33±0.00 <sup>a</sup>
WBC ( $10^3 \times /\mu\text{L}$ )	1.77±0.90 <sup>a</sup>	2.83±0.60 <sup>b</sup>	3.27±1.14 <sup>b</sup>	2.40±0.70 <sup>a</sup>
LYM (%)	49.33±13.20 <sup>c</sup>	64.00±5.29 <sup>b</sup>	68.67±2.31 <sup>a</sup>	61.67±1.53 <sup>b</sup>
MCV ( $\mu\text{m}^3$ )	56.90±5.11 <sup>b</sup>	50.88±3.57 <sup>b</sup>	60.07±0.40 <sup>a</sup>	60.00±0.00 <sup>a</sup>
MCH (pg/cell)	18.53±2.45 <sup>b</sup>	16.10±0.52 <sup>b</sup>	20.00±0.10 <sup>a</sup>	20.00±0.00 <sup>a</sup>
RBC ( $10^3 \times /\mu\text{L}$ )	8.33±0.93 <sup>a</sup>	9.81±1.07 <sup>a</sup>	7.60±0.90 <sup>a</sup>	7.33±0.76 <sup>a</sup>
NEU (%)	50.33±13.65 <sup>a</sup>	36.00±5.29 <sup>b</sup>	30.00±2.00 <sup>c</sup>	38.00±1.53 <sup>b</sup>

Values are mean ± SD of five determinations; Values are mean ± SD of five replicates. Values having different superscript across the raw are significantly different ( $p<0.05$ ) and vice versa. Key: PCV (Packed Cell Volume), RBC (Red Blood Cells), HB (Haemoglobin), WBC (White Blood Cells), MCHC (Mean Corpuscular Haemoglobin Concentration), LYM (Lymphocyte), MCH (Mean Corpuscular Haemoglobin), NEU (Neutrophils), MCV (Mean Corpuscular Volume)

**Table 6: Liver function indices of Wistar rats fed hydroethanolic extract of *Citrullus lanatus* seed**

Parameters	Control	50 mg/kg body wt.	100mg/kg body wt.	100 mg/kg body wt.
Protein	39.47±3.25 <sup>b</sup>	50.68±9.07 <sup>a</sup>	51.05±1.49 <sup>a</sup>	43.25±7.00 <sup>b</sup>
Alanine aminotransferase	31.56±2.91 <sup>a</sup>	25.48±5.74 <sup>b</sup>	23.42±0.90 <sup>b</sup>	29.31±5.12 <sup>a</sup>
Alkaline phosphatase	9.70±0.87 <sup>a</sup>	10.04±0.90 <sup>a</sup>	8.88±1.75 <sup>b</sup>	11.11±0.35 <sup>c</sup>
Direct bilirubin	33.20±15.32 <sup>c</sup>	85.40±6.30 <sup>a</sup>	86.60±29.6 <sup>a</sup>	56.00±22.2 <sup>b</sup>
Total bilirubin	32.30±1.80 <sup>c</sup>	61.60±7.93 <sup>a</sup>	57.10±14.40 <sup>a</sup>	49.30±14.05 <sup>b</sup>
Albumin	13.02±7.51 <sup>c</sup>	26.10±16.37 <sup>b</sup>	36.00±32.9 <sup>a</sup>	26.34±5.17 <sup>b</sup>
Aspartate aminotransferase	31.76±3.19 <sup>a</sup>	25.48±5.74 <sup>b</sup>	23.42±0.90 <sup>b</sup>	29.31±5.12 <sup>b</sup>
Lactate dehydrogenase	253.30±58.4 <sup>a</sup>	76.90±47.1 <sup>b</sup>	33.70±18.0 <sup>c</sup>	78.9±90.3 <sup>b</sup>

Values are mean ± SD of five replicates. Values having different superscript across the raw are significantly different ( $p<0.05$ ) and vice versa.

**Table 7: Renal function indices of Wistar rats fed hydroethanolic extract of *Citrullus lanatus* seed**

Parameters	Water	50 mg/kg body wt.	100 mg/kg body wt.	200 mg/kg body wt.
Urea	33.69±43.5 <sup>c</sup>	243.73±16.43 <sup>b</sup>	295.5±76.3 <sup>a</sup>	295.5±76.3 <sup>a</sup>
Calcium ion	65.21±4.38 <sup>b</sup>	66.45±4.12 <sup>b</sup>	71.15±2.78 <sup>a</sup>	76.07±12.14 <sup>a</sup>
Chloride ion	28.28±4.23 <sup>c</sup>	28.36±1.00 <sup>c</sup>	35.37±8.22 <sup>b</sup>	42.08±7.49 <sup>a</sup>
Sodium ion	54.42±9.53 <sup>b</sup>	56.65±3.67 <sup>a</sup>	56.37±3.90 <sup>a</sup>	56.20±2.68 <sup>a</sup>
Potassium ion	3.29±0.534 <sup>b</sup>	2.81±0.265 <sup>c</sup>	3.97±0.36 <sup>a</sup>	2.92±0.32 <sup>c</sup>
Bicarbonate ion	25.43±0.74 <sup>a</sup>	25.28±3.26 <sup>a</sup>	27.38±1.32 <sup>a</sup>	26.57±0.78 <sup>a</sup>
Uric acid	3.34±0.61 <sup>a</sup>	3.08±0.11 <sup>a</sup>	3.25±0.39 <sup>a</sup>	3.55±0.57 <sup>a</sup>
Creatinine	3.43±0.85 <sup>a</sup>	2.45±1.36 <sup>b</sup>	2.45±0.49 <sup>b</sup>	3.67±1.24 <sup>a</sup>

Values are mean ± SD of five replicates. Values having different superscript across the raw are significantly different ( $p<0.05$ ) and vice versa.

#### 4.0 Discussion

This study examined the safety and biological effect of hydroethanolic extract of *C. lanatus* seed in female Wistar rats. The results provide insight into the phytochemical, minerals, and heavy metal composition of the extract, as well as its impact on lipid profiles, hematology, liver and renal functions.

The phytochemicals screening revealed the presence of saponins, terpenoids, cardiac glycosides, alkaloids, and reducing sugars. These compounds are known to exhibit antioxidants, anti-inflammatory, anti-microbial properties. For instance; saponins and terpenoids, have been reported to have an essential role in hepatoprotective and cardioprotective effects due to their ability to scavenge free radicals and reduce oxidative stress. This correspond with findings by Salimon and Yakubu [1]; Nurudeen et al. [19], who highlighted the antioxidative properties of plant-based secondary metabolites.

Furthermore, the presence of some minerals such as iron, potassium, and magnesium suggests that the plant have the potential benefit in preventing anemia and supporting oxygen transport as observed in other plant extract [19]. In addition, the presence of trace amount of some heavy metals (cadmium, lead, and cobalt) raises potential safety concerns since lead, and cadmium are known nephrotoxins and can accumulate in the body, posing a long term risk even at low concentration. However, the detected levels are within the permissible limits, suggesting minimal risk. These findings are consistent with Ekor [5], who emphasized the need to monitor heavy metal contamination in herbal medicine.

The lipid profile results showed no significant changes in total cholesterol (TC), triglyceride (TAG), HDL, and VDL levels across all doses. However, the significant decrease in LDL levels at 50 and 100 mg/kg doses suggests a cardioprotective effect. These results align with Bazabang et al. [20], who reported similar reductions in LDL levels in *C. lanatus* extract studies. This lipid lowering effect is likely mediated by saponins and terpenoids, which can inhibit cholesterol absorption and improve lipid metabolism.

Hematological analysis revealed no significant changes in hemoglobin (Hb), packed cell volume (PCV), red blood cells (RBC), or mean corpuscular hemoglobin concentration (MCHC). However, a dose-dependent increase in lymphocyte level with a notable decrease in neutrophil levels was observed suggesting a potential immunomodulatory effect. This is consistent with findings by Erezina et al. [2], who noted similar immune-enhancing effects in plant extracts rich in secondary metabolites.

The hepatoprotective effects of the extract are evident from increased levels of serum proteins, bilirubin, and albumin, along with reduced ALT, AST, and LDH activities. These results align with Salimon and Yakubu [1]; Nurudeen et al. [19], who attributed similar liver-protective effects to the antioxidative properties of plant-based compounds. The improvement in liver enzyme profiles indicates reduced hepatic stress, potentially due to the extract's ability to counteract oxidative damage.

The significant increase in urea, calcium, chloride, and sodium levels at higher doses suggests potential renal stress, particularly at 200 mg/kg. However, stable levels of potassium, bicarbonate, uric acid, and creatinine indicate that tubular function remains intact. These findings are partially consistent with Bazabang et al. [20], who observed mild nephrotoxicity at higher doses of *Citrullus lanatus* extracts. The increased levels of calcium and chloride may also reflect alterations in electrolyte balance, warranting further investigation.

Although the study was of short duration and only female Wistar rats, this fact should not diminish its importance. The acuteness of this study regarding challenges immediate biochemical responses, rather than prolonged effects mitigated the duration-associated limitation. In addition, although it may limit the generalizability of our study to both sexes, only female rats were used in this experiment for controlling purposes and consistent outcome.

#### 5.0 Conclusion

The findings highlighted the safety and therapeutic potential of the hydroethanolic extract of *C. lanatus* seeds. The extract demonstrates cardio-protective, hepatoprotective, and

immunomodulatory effects, primarily attributed to its rich phytochemical composition. However, the presence of trace heavy metals and dose-dependent renal stress underscores the need for cautious use and further long-term studies to confirm its safety profile.

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