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Original Research

Toxicological evaluation of leaf extract of *Terminalia chebula* extract on wistar rats biochemical parameters

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Abstract

Terminalia chebula is widely utilized in South Asia, ranging from India to Africa. It is frequently utilized in the treatment of many illnesses. The purpose of this study is to determine the toxicity of Terminalia chebula on the lungs, blood, and heart of wistar rats. The first group received distilled water (10 ml/kg), while the second, third, and fourth groups received Terminalia Chebula 200, 400, and 800 mg/kg, respectively. Animals were kept in conventional cages and provided oral access to extract, water, and food for 28 days before being weighed and slaughtered. Blood was drawn for hematological and chemopathological testing. The lungs and brain were also removed for histopathological examination. There was a substantial ($P<0.05$) drop in RBC, HGB, and MCV, but no change in neutrophils, basophils, eosinophils, or platelets. When compared to the control, Terminalia chebula induced a small but not statistically significant ($p<0.05$) increase in the size of the heart and lungs at all doses. When compared to the control, there was no significant ($p<0.05$) change in triglyceride or HDL levels, however there was a significant ($p<0.05$) decrease in LDL levels. At all doses, there were minor alterations in histological characteristics. The study's findings indicated that at normal doses, the plant may have no adverse compromise on several organs.

Keywords: Terminalia chebula, rat, blood, heart, lung.

Introduction

The apex of the heart is located to the left of the sternum (8 to 9 cm from the midsternal line) at the point where the fourth and fifth ribs meet the costal cartilages (Asuzu and Chineme 1990). Atherosclerosis is a disorder that causes plaque to build up in the arterial walls. This buildup constricts blood flow by narrowing the arteries (Emily, 2007). A blood clot can impede blood flow

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when it forms. This can lead to a heart attack or a stroke. The lungs are the most essential organs in the respiratory system, and they are divided into lobes. The right lung has three lobes as opposed to the left lung's two. The mediastinum is the space between the lungs (Tona et al., 1999).

Terminalia chebula tree can grow to be 50-80 feet tall10. It features a circular crown and branches that stretch out. The bark is dark brown in color and has some longitudinal fractures (Bass and Ockner 1996). T. chebula can be found in the Sub Himalayan tracks that run from Ravi eastward to West Bengal and Assam, up to 1500 m in the Himalayas. This tree grows naturally in the forests of Northern India, the central provinces, and (Benga Zhou et al., 2008; Duncan 1957). The tree is also found in Africa. The fruit has laxative, stomachic, tonic, alterative, and antispasmodic properties (Benga Zhou et al., 2008). It can help with ophthalmology, hemorrhoids, dental caries, bleeding gums, and ulcerated oral cavity. Its water-based paste has been shown to be anti-inflammatory, analgesic, and wound-purifying and healing. Its decoction is used as a gargle in cases of oral ulcers and sore throat. Its powder is an effective astringent dentifrice for loose gums, bleeding, and gum ulceration (Hietala 1987;Joseph et al., 2019). It works well as an appetite stimulant, digestive aid, liver stimulant, stomachic, gastrointestinal prokinetic agent, and moderate laxative14. T. chebula fruit powder has been used to treat chronic diarrhea. It is used to treat nervous weakness and irritation. It increases the reception power of the five senses (Jones 1999). The purpose of this study is to see how an ethanol extract of Terminalia chebula affects the lungs, blood, and heart of rats.

Materials and Method

Bingham University's Animal House provided male and female wister rats. They were fed ordinary animal pellets and given unlimited water. Bingham University's College of Health Sciences Animal Ethics Committee granted permission and approval for animal studies.

Plant collection

Terminalia chebula leaves were taken in their native habitat near Karu village in Nasarawa State, Nigeria. The plant was verified by the Department of Botany at Bingham University in Nasarawa State, Nigeria. The plant was granted a voucher number (BUO27).

Plant extraction:

For two weeks, the leaves were shadow dried. The dried plant material was then pulverized and reduced into little pieces. In 70% ethanol, the powdered material was macerated. Using a rotary evaporator, the liquid filtrates were concentrated and evaporated to dryness at 40 C in vacuum.

Animal study:

Twenty-four (24) rats of either sex (125-250g) were chosen and randomly assigned to four groups of six rats each. The rats in groups 2, 3, and 4 were given 200, 400, and 800 mg/kg of extract, respectively, while group 1 acted as the control and received normal saline (10ml/kg). The rats' weights were recorded at the start of the experiment and at weekly intervals. D0 denoted the initial day of dosage, while D29 denoted the day of sacrifice.

Haematological analysis:

On the 29th day of the study, the rats were sacrificed. A heart puncture was used to collect blood samples. One portion of the blood was collected into EDTA-containing sample bottles for hematological analysis such as hemoglobin concentration, white blood cell counts (WBC), differentials (neutrophils, eosinophils, basophils, lymphocytes, and monocytes), red blood cell

count (RBC), platelets, and hemoglobin (Hb) concentration using an automated haematology machine (Cell-Dyn, Abbott, USA).

Histopathology

Following blood collection, all animals were euthanized for extensive pathological exams of the major organs. All of the animals' lungs and heart organs were taken for histopathology. The organ weights were calculated. The relative organ weights were determined by dividing the individual weight of each organ by the rat's ultimate body weight. By subtracting the dry weight of each organ from the weight of each wet organ, the % water content was calculated. The selected organs were fixed in 10% neutral buffered formalin, trimmed, and tissue slices of 4-5 m thickness were stained with hematoxylin and eosin for histological examination according to standard techniques.

Biochemical analysis

Urea, albumin, total protein, total cholesterol (TC), high density lipoprotein (HDL) cholesterol, and triglycerides (TG) were all measured in serum samples.

Statistical analysis

The mean and standard error of the mean (SEM) were used to express the data. One-way Analysis of Variance (ANOVA) was used to statistically assess the data before Dunnett's post hoc test for multiple comparisons between the control and treated groups. P values less than 0.05 were regarded as significant.

Result

Effect of sub-acute oral administration of Terminalia chebula on hematological parameters in rats.

At a dose of 400 mg/kg, Terminalia chebula induced a substantial ($p<0.05$) decrease in the levels of red blood cells, hemoglobin, platelets, and so on, as well as a significant ($p<0.05$) increase in mean corpuscular hemoglobin concentration in rats. However, mean corpuscular hemoglobin concentration had no effect on basophiles, neutrophils, eosinophils, or lymphocytes ($p<0.05$). (Table 1).

Effect of sub-acute oral administration of Terminalia chebula on body weight of rats.

When compared to the control, Terminalia chebula caused a small but nonsignificant ($p<0.05$) increase in the size of the heart and lungs at all doses provided. (Table 2 and 3).

Histopathological Investigations of the effect of 28 days oral administration of Terminalia chebula on heart indices in Wistar rats.

There was no significant ($p<0.05$) change in the level of triglyceride and HDL when compared to the control, while was significant ($p<0.05$) reduction in the level of LDL (Table 4).

Table 1: Effect of 28 days oral administration of ethanol leaf extract of Terminalia chebula on hematological parameters in wistar rats.

Hematological parameters	Treatment (mg/kg) DW(10ml/kg)	200 mg/kg	400 mg/kg	800 mg/kg
WBC ($\times10^9$/L)	9.166±0.772	7.640±1.429	4.700±0.556*	8.230±1.088
RBC ($\times10^{12}$/L)	9.23±0.32	9.65±0.67	7.11±0.75*	7.81±0.22
HGB (g/dL)	15.56±0.56	15.45±0.88	12.33±0.76*	15.58±0.37
HCT (g/dL)	57.18±2.03	57.60±3.75	35.67±3.18*	54.40±1.82
MCV (fL)	66.45±0.93	64.40±1.14	57.77±0.31*	69.61±1.73
MCH (pg)	19.17±0.17	17.80±1.02	18.83±0.37	18.80±0.20
MCHC (g/dL)	29.17±0.17	27.40±1.12	32.50±0.62*	27.60±0.68
PLT ($\times10^9$/L)	620.83±52.81	567.00±96.41	252.00±50.38*	670.40±55.72
LYM (%)	86.83±4.06	85.00±4.18	82.83±5.89	86.40±3.14
NEUT ($\times10^9$/L)	11.83±3.68	11.83±3.58	14.40±5.20	13.20±3.11
EOSI ($\times10^9$/L)	1.53±0.34	1.40±0.76	1.90±0.22	1.40±0.43
BASO ($\times10^9$/L)	1.10±0.28	2.45±0.43	2.50±1.50	3.40±2.23

*significantly different from the distilled water (DW) control at $p<0.05$. DW = distilled water

(WBC = white blood cells, RBC = red blood cells, PLT = platelet, LYM = lymphocyte, NEUT = neutrophils, EOSI = eosinophils, BASO = basophils HGB = hemoglobin, HCT = hematocrit, MCV = mean corpuscular volume, MCH = mean corpuscular hemoglobin, MCHC = mean corpuscular hemoglobin concentration).

Table 2: Effect of *Terminalia chebula* on body weight (g) in rats.

Treatment (mg/kg)	Week 1	Week 2	Week 3	Week 4
DW (10ml/kg)	192.30±5.72	186.11±4.35	189.11±5.55	195.72±4.66
100 mg/kg	190.33±33.11	191.65±15.220	194.20±3.12	197.26±5.07
200 mg/kg	222.24±19.51	222.17±12.75	226.23±11.67	225.10±17.47
400 mg/kg	215.22±11.49	220.11±7.25	224.47±6.71	223.14±7.69

*Significantly different from the distilled water (DW) control at $p<0.05$. DW = distilled water

Table 3: effect of *Terminalia chebula* on relative organ to body weight ratio in rats.

Treatment(mg/kg)	Relative organ to Body weight Ratio% HEART	LUNGS
DW(10ml/kg)	0.47±0.06	0.95±0.179
TC 200	0.39±0.03	0.73±0.063
TC (400)	0.39±0.11	1.681±0.345*
TC (800)	0.48±0.04*	0.743±0.079

*Significantly different from the distilled water (DW) control at $p<0.05$. TC = Terminalia chebula , DW = distilled water

Table 4: Effect of *Terminalia chebula* on lipid profile in wistar rats.

	Treatment (mg/kg)			
Lipid profiles	DW(10 ml/kg)	40000%	20000%	80000%
CHOL (mmol/L)	45.30±8.41	45.80±3.86	44.43±3.43	45.32±5.23
HDL (mmol/L)	42.20±3.28	43.00±3.12	40.20±1.88	56.75±4.11*
LDL (mmol/L)	7.98±2.51	6.20±1.81*	6.11±4.65	5.50±2.18*
TRIG (mmol/L	55.40±2.18	55.40±3.12	59.60±11.12	58.00±4.12

*significantly different from the distilled water (DW) control at $p<0.05$.

(HDL = high density lipoprotein, LDL = low density lipoprotein, CHOL = total cholesterol, TRIG = triglycerides.

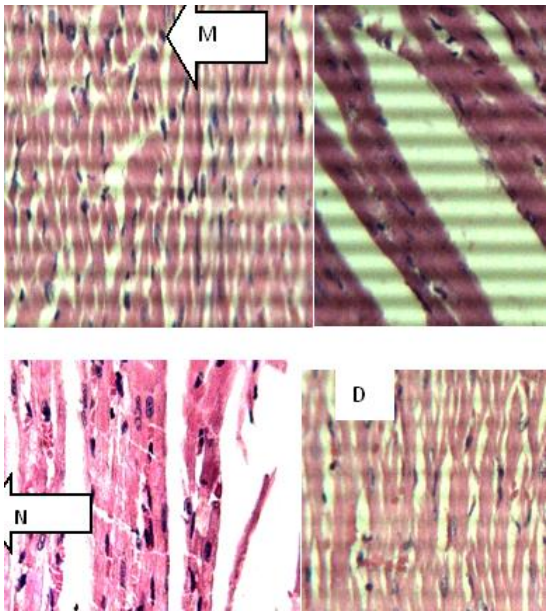

Figure 4: Histological sections of Kidneys of rats treated with Normal saline 10 ml/kg (1), *Terminalia chebula* 200 mg/kg (2), *Terminalia chebula* 200 mg/kg bw (3) and *Terminalia chebula* 400 mg/kg at magnification A (x100) and B(x400)) stained with H&E Technique.

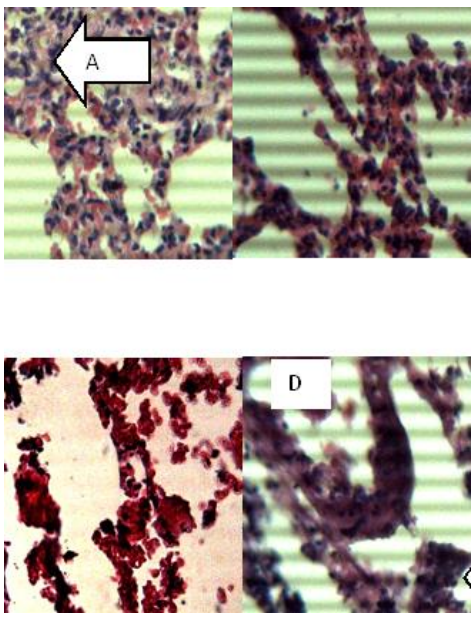

Figure 4: Histological sections of lungs of rats treated with Normal saline 10 ml/kg (1), *Terminalia chebula* 200 mg/kg (2), *Terminalia chebula* 200 mg/kg bw (3) and *Terminalia chebula* 400 mg/kg at magnification A (x100) and B(x400)) stained with H&E Technique.

Discussion

Hematological indicators are helpful indices for determining the toxicity of plant extracts in live systems (Joseph et al., 2019b). They can also be used to describe how a chemical compound/plant extract affects the blood. The current study found that Terminalia chebula ethanol leaf extract reduced the levels of red blood cells, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration, implying that it can significantly reduce the oxygen carrying capacity of the blood and thus cause anemia (Joseph et al., 2019b). Anemia is a disorder in which the blood lacks enough red blood cells to transport oxygen from the lungs to the rest of the body or lacks enough hemoglobin, the iron-rich protein that transports oxygen inside red blood cells and gives blood its red color (Krenzelok et al., 2003). Anemia comes in a variety of forms, with varying degrees of severity and duration19. Reduced packed cell volume (PCV) and red blood cell (RBC) levels were also found in rats given the extract. This suggests that Terminalia chebula could disrupt the osmoregulatory mechanism of blood cells and/or induce oxidative damage to the cell membrane. The extract has the potential to inhibit the haemopoietic system. The decline could possibly be attributed to blood cell lysis. Wazis et al. (2020) discovered a decrease in RBC, PCV, hemoglobin, and lymphocytes in rats fed Acalypha wilkesiana extracts. The primary roles of white blood cells and their variants are to combat infections, guard the body against invasion by foreign organisms via phagocytosis, and create or, at the very least, transport and disseminate antibodies in an immune response (Tona et al., 2019). The extract showed no influence on the parameters of white blood cells, implying that it has no effect on immune cells or the immune system.

The lungs are a pair of cone-shaped organs in the thoracic cavity separated from each other by the heart and other tissues in the mediastinum (Sathishkumar et al., 2014). The lungs are the foundational organs of the respiratory system, facilitating gas exchange from the environment into the bloodstream. The alveoli transfer oxygen into the capillary network, where it can enter the arterial system and eventually perfuse tissue. Asthma, pneumothorax or atelectasis, bronchitis, COPD, lung cancer, lung infection, pneumonia, and pulmonary edema are all examples of lung diseases (Pathan et al., 2013). Resonating haematological parameters with that of histology value it suggests that the plant may not cause cell apoptosis or tissue necrosis.

HDL, triglyceride, and cholesterol levels did not change considerably, but LDL values decreased significantly, indicating that it may have a lipid-profile improving tendency. Because it contributes to atherosclerosis, LDL cholesterol is usually recognized as harmful cholesterol (Zubairu et al., 2021). Excess cholesterol in the food, bile, or intestines causes hypercholesterolemia. Triglycerides are released into the bloodstream by the liver in the form of VLDL (Simeon et al., 2019). Triglycerides are released into the plasma by the intestines as chylomicrons. VLDL is transformed to LDL once it enters the plasma. LDL in the plasma then interacts with the LDL receptor on cells in various tissues Increased LDL is associated with an increased risk of cardiovascular disease (Simeon et al., 2019). Diabetes, hypertension, hypertriglyceridemia, and atherosclerosis are all prevalent symptoms. HDL functions as a scavenger, transporting LDL (bad) cholesterol from the

arteries to the liver, where it is broken down and expelled. HDL cholesterol, on the other hand, does not completely remove LDL cholesterol from the blood vessels. Only one-third to one-fourth of blood cholesterol is transported by HDL (Fungwe et al., 1993). Triglycerides are lipids that can be used to store excess energy. High triglyceride levels, whether alone or in combination with high LDL cholesterol or low HDL (good) cholesterol, have been linked to fatty buildups within artery walls, raising the risk of heart attack and stroke. The LDL receptor can be present in the liver as well as most other organs. It detects Apo B 100 and Apo E, facilitating LDL, chylomicron remnants, and IDL absorption by endocytosis. The lipoprotein particle is destroyed in lysosomes after internalization, and cholesterol is liberated. When cholesterol enters the cell, HMG CoA reductase activity rises, causing cholesterol to be synthesized and the expression of LDL receptors to be modulated. Plasma LDL levels are determined by LDL receptors on the liver (Knufman et al., 1987). When there are fewer receptors, the liver may take up less LDL from the blood, resulting in high plasma LDL levels. When there are more LDL receptors, the liver takes up more LDL from the blood, resulting in low plasma LDL levels (Knufman et al., 1987).

Phytochemical molecules such as tanins, phenols, triterpene saponins, terpenoids, flavonoids, and sterols were found in fresh and dried Terminalia chebula samples (Balaraman et al., 1993; Miller et al., 1991; Zubairu et al., 2021). The antioxidant properties of phytomolecules such as triterpene saponins, terpenoids, flavonoids, and sterols may have been responsible for the examined organ's less tissue damaging effect. Histology observation coincides with other parameters that the plant extract may be harmful at some levels while being harmless at others.

Conclusion:

According to the findings of the study, the plant has no adverse effects on the lungs, heart and haematological parameters. More research is needed to assess its tissue and organ protection activity..

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