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Original Research Article

Evaluation of Acute and Subacute Toxicity of Aqueous Extract of *Picralima nitida* Seeds in Wistar Rats

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ABSTRACT

Picralima nitida (Stapf.) Durand and Hook, (fam. Apocynaceae) is a widely used medicinal plant in the traditional treatment of ailments such as malaria, diabetes, hypertension, and inflammation in West Africa. The study assessed the acute and subacute toxicity of aqueous extract of *Picralima nitida* (AEPN) seed in Wistar rats. In the acute phase, female Wistar rats weighing 170 ± 10 g were employed, and the treatment group received a single oral dose of 5,000 mg/kg body weight of AEPN, while the control group received distilled water only. Male and female healthy rats, divided into four groups each (n = 5) were used for the subacute toxicity study. Each of the groups in either gender was administered orally with 0, 250, 500 and 1000 mg/kg b.w. AEPN daily for 28 days. Observations focused on adverse effects, behavioral changes, mortality and morbidity, with satellite groups assessing recovery post-treatment. Rats were sacrificed on the 29th day and biochemical parameters, such as liver and kidney function markers were investigated. There were no significant changes in the body weights of rats, no mortality, as well as no observed behavioral and physical changes during the 14-day recovery period of the acute toxicity study. During the 28-day exposure, no significant changes were noted in the parameters such as liver and kidney function markers and hematological parameters, up to 1,000 mg/kg AEPN, compared to control. The LD_{50} of AEPN was greater than 5,000 mg/kg, indicating that doses up to 1,000 mg/kg may be considered safe for potential medicinal applications.

Keywords: Acute Toxicity, Diabetes, Hypertension, Subacute Toxicity, *Picralima nitida*

Introduction

Medicinal plants have been utilized globally as traditional remedies for treating a wide range of ailments, such as asthma, gastrointestinal issues, skin conditions, respiratory and urinary problems, as well as hepatic and cardiovascular diseases.[1] WHO estimates that about 80% of the developing world still relies on plants and plant products, and numerous documented species of these plants are indicated as promising sources for new drug development.[2] *Picralima nitida* is a member of the Apocynaceae family. The plant has achieved widely used in traditional West African medicine for its numerous medicinal uses.[3] All parts of the plant are used by traditional healers to treat conditions like fever, hypertension, jaundice, gastrointestinal problems, and malaria. The practitioners address a wide range of human health issues by using raw materials and extracts from various *P. nitida* components, which could be linked to the various secondary metabolites including alkaloids, triterpenes flavonoids, lycosides, polyphenols, akuammicine, saponins, and tannins that are inherent in the plant.[4]

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The plant is widely spread throughout the West-Central African region with different names.[5,6] *Picralima nitida* seeds are known for their high concentrations of essential elements like zinc, vitamin A and E, iron, and manganese as well as amino acids. Further research into the plant extracts has indicated possible biological activity, including antibacterial, hyperglycemia, larvicidal, and hypoproteinaemia characteristics.[7-9] The phytochemical screening of the crude extract of *P. nitida* conducted by Igboasoiyi [10] revealed the presence of alkaloids, tannins, saponins, glycosides, terpenes, anthraquinones, flavonoids. Moreover, numerous investigations have consistently shown that methanolic extracts contain higher phenol and flavonoid content than extracts made using other solvents.[11-13] Additionally, it has been discovered that the seeds are a good source of amino acids, vitamins A and E, and important minerals including zinc, iron, and manganese. The high-performance liquid chromatography (HPLC) analysis revealed the presence of compounds such as apigenin, caffeic acid, catechin, chlorogenic acid, ellagic acid, gallic acid, luteolin, p-coumaric acid, quercetin, and rutin. These may be responsible for the plant's traditional medicinal use.[14]

Studies by Akinwunmi and Amadi [15] and Okhuarobo et al. [16] demonstrated 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity of various parts of *P. nitida* seed extracts, indicating that the seed extracts may contain some hydrogen donor molecules that may aid the reduction of free radical production. All seed extracts, however, had less scavenging power than the ascorbic acid reference molecule. Although several plants have shown several medicinal properties, many remain unproven, and are either inadequately or not regulated. Also, their interactions with the current orthodox treatment can result in major side effects and complications that will necessitate further costs.[17-19] The primary issues that must be addressed to reduce unanticipated dangers in herbal medicine are efficacy, safety, and the use of traditional pharmaceuticals and herbs in combination.[19] It is crucial to evaluate the safety of herbal medicine to reduce unanticipated

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risks because the efficacy and safety of using herbal remedies continued to constitute major concerns. Moreover, increasing the use of medicinal herbs and its side effects would result in a global health problem that needs to be addressed. The aim of the study was, therefore, to assess the toxicity profile of aqueous extract of *P. nitida* (AEPN) seed.

Materials and Methods

Materials

Collection and identification of plants material

The seeds of *Picralima nitida* (Apocynaceae), known as "Abere" among the Yorubas, were sourced from a local market in Akure, Ondo State, Nigeria (latitude 7° 15' 0.00"N and longitude 5° 11' 42.00"E) according to GPS coordinate of Akure, Nigeria. Prior to use, the seeds were identified and authenticated in the Department of Plant Science and Biotechnology, Faculty of Sciences, Ekiti State University, Ado-Ekiti, Nigeria. The plant sample, with voucher number: UHAE 2023008, was deposited in the departmental herbarium.

Preparation of plant extract

Before extraction, the seeds were air-dried for two weeks, following which the epicarps were removed and further dried for three weeks. The dried seeds were pulverized using a laboratory electric blender. For extraction, 1000 g of the pulverized seeds were soaked in 3.5 L of distilled water in a 5 L plastic container and allowed to stand for 24 h before preliminary filtration with a muslin cloth, and further filtering using Whatman No. 1 filter paper. The filtrate was then concentrated using a rotary evaporator (BOSCH XDYQ-5/10). The concentrates were then placed in a crucible to remove any further trace of water. The concentrates were weighed, and the total yield was 12.6% before storing in a clean glass bottle at 4 °C until needed.

Experimental animals

Healthy rats (both sexes) of Wistar strain were procured from the animal house at Afe Babalola University, Ado-Ekiti, Nigeria. The rats were housed in cages within the Biochemistry department's animal facility at Afe Babalola University, Ado-Ekiti, Nigeria. The rats were acclimatized for 14 days with free access to clean water and pelletized food. The temperature was maintained at 23 ± 2 °C and a 12-hour light/dark cycle was followed. Approval (ABUADHREC/10/03/2022/183) was obtained from the ethics committee of Afe Babalola University Health Research Ethical Committee. The procedures used in this study adhered to the principles of the Declaration of Helsinki.

Methods

Acute oral toxicity study

The World Health Organization (2000) guideline for evaluating the acute toxicity of medicinal plants was followed, with minor modifications, in conducting the acute oral toxicity research. Adult female Wistar rats, weighing between 160 and 180 g each, were divided into two groups – a control group and a treatment group, each of which contained five animals. The treatment group was given a single oral dose of AEPN (5000 mg/kg body weight), whereas the control group was given distilled water. The animals' behavior, toxicity indicators, changes in body weight, and mortality were all meticulously assessed. Observations were made during the first four hours following the initial therapy, then once daily for 14 days.

Subacute oral toxicity studies

The subacute oral toxicity study followed the guidelines established by the Organization for Economic Cooperation and Development (OECD) with minor adjustments.[20] In this study, male and female rats were randomly divided into four groups, each consisting of five females and five males. Groups I and II served as control groups for females and males, respectively. Groups III and IV were females and males, and each received 250 mg/kg AEPN. Groups V and VI were females and males, and each were administered with 500 mg/kg AEPN. Groups VII and VIII were females and males, and received 1,000 mg/kg (AEPN). The selection of these doses was based on the findings from the acute toxicity study in rats, with the highest dose set at one-fifth of the maximum dose used in the acute toxicity study. All animals were treated daily for 28 days. They were closely monitored for any adverse effects, signs of toxicity, behavioral changes, mortality, and morbidity until the completion of the study. Additionally, four satellite groups consisting of two control groups and two groups receiving the highest dose of 1,000 mg/kg, were prepared to assess the potential continuous, delayed or reversible toxic effect of the extract during a 14-day recovery period. Body weights of the rats in all groups were recorded before the initiation of dosing, at weekly intervals during the treatment period, and finally, on the day of sacrifice. Daily food and water intake were also recorded for each group throughout the study.

Relative organ weights

After an overnight fast, all animals were sacrificed on the 29th and 42nd (for recovery) days by cervical dislocation. Organs, including the liver, kidneys, brain, heart, testes, ovaries, and spleen, were pulled out and weighed. The following formula was used to determine each animal's proportionate organ weight:

$$\text{Relative organ weight} = \frac{\text{absolute organ weight (g)} \times 100}{\text{body weight of rat sacrifice day (g)}}$$

Blood sample

Blood was drawn from the heart through cardiac puncture. One portion of the blood was collected in heparinized (plain) bottles for hematological analysis, while another portion was collected in heparinized bottles and centrifuged using a bench centrifuge (800D Desktop Electric Medical Lab Centrifuge, China) at 3000 x g for 10 min for other biochemical assays.

Hematology analysis

Heparinized blood was employed for hematological analysis, which included assessments of packed cell volume (PCV), white blood count (WBC), neutrophils (NP), lymphocytes (LC), monocytes (MC), eosinophils (EP), hemoglobin (HB), platelets (PL), and red blood cells (RBC). This was done by using an automated hematology analyzer (Symex-RX, 21, Japan) (Ref).

Biochemical analyses

Serum levels of urea, creatinine, glucose total protein, and albumin, and the activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST) were measured using standard assay kits (from Randox Laboratories (Crumlin, United Kingdom). Serum creatinine assay was performed in line with Jaffe's method, as described by Bartels et al. [21]; serum urea assay was done colorimetrically following Berthelot's reaction [22]; albumin level was assessed by the bromocresol Green (BCG) method as described by Doumas et al.[23], while the activities of AST and ALT were measured following the method described by Reitman and Frankel [24].

Statistical analysis

Data was statistical analyzed by one-way analysis of variance (ANOVA) using windows GraphPad prism 5 for Windows. Results were presented as mean ± standard deviation (SD). Where applicable, intergroup comparisons were performed using Tukey's test, and p values less than 0.05 were considered statistically significant.

Results and Discussion

According to the findings of the acute toxicity study, the lethal median dose (LD_{50}) is greater than 5,000 mg/kg, which falls into category 5 (unclassified) according to Globally Harmonized Classification System (GHS) for chemical substances and mixtures,[25] and this can be considered non-toxic.[26] Single exposure to AEPN showed no observable behavioral changes or negative reactions during the 14-day period. At 24 h, 7 days, and 14 days, no changes were noted in the weight between the treatment group and the control group. Additionally, no mortality, behavioral and signs of toxicity were noted during the period. This implies that a single oral exposure to AEPN at a dose of 5,000 mg/kg could be considered non-toxic, and it agrees and falls within the range of LD50 greater than 2,000 mg/kg in previous findings using different plant extracts.[27,28] It is crucial to remember that the acute toxicity study only offers preliminary data and acts as a starting point for additional toxicological research.

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To provide evidence for its safety in clinical applications, it was necessary to investigate the effects of repeated exposure of AEPN on both female and male rats. This was especially important, considering the potential accumulation of plant extracts when used to treat chronic diseases.[29] The sub-acute toxicity investigation of AEPN at doses of 250, 500, and 1,000 mg/kg did not result in any sign of toxicity or mortality. Several biochemical parameters were used to access the effects of a 28- day repeated exposure to AEPN on both female and male rats.

According to a study by Adewale et al. [30] measuring the body weight and relative organ weights of rats is a critical indicator for determining toxicity. Compared to the control group, the AEPN-treated rats showed a typical rise in body weight throughout the trial, which implies that the rats' growth was unaffected by the repeated administration of the AEPN. Also, no significant differences were noted in the relative organ weights of rats treated with AEPN in either the main study (28 days) or the satellite group (Tables 1a and b) compared with the control. Repeated intake of herbal remedies or plant extracts may cause compounds to build up in organs, perhaps resulting in toxicity. But given the negligible variations in body and relative organ weights noted in rats subjected to different doses of the plant extract, it may be concluded that the plant extract is not hazardous to humans.

According to Bariweni *et al.* [31] the liver and kidneys play crucial roles in the body's metabolism and expulsion of foreign chemicals, and abnormal elevations in hepatic enzymes like ALT and AST are a sign of liver injury.[32] Additionally, a drop in albumin and total protein levels indicates a deterioration in the liver's functional integrity. While AST is broadly distributed across several organs, including the kidney, heart, and skeletal muscles in addition to the liver, ALT is mostly located in the liver.[31] The effect of AEPN on serum levels of ALT and AST is presented in Fig. 1 and 2, respectively. No significant difference was noted in the levels of these parameters in both genders of rats administered with all doses of AEPN compared with the control. The effect of AEPN on serum levels of albumin and total protein exhibited non-significant difference in both parameters in both female and male rats at doses of 250, 500, and 1,000 mg/kg AEPN compared with the control, as presented in Fig. 3 and 4.
The fact that there were no significant differences in the level of these parameters in the experimental (AEPN administered) group in comparison with the control group showed that the plant extract had no negative effects on the body's important organs. This result confirms the negligible changes in the relative weights of these organs.

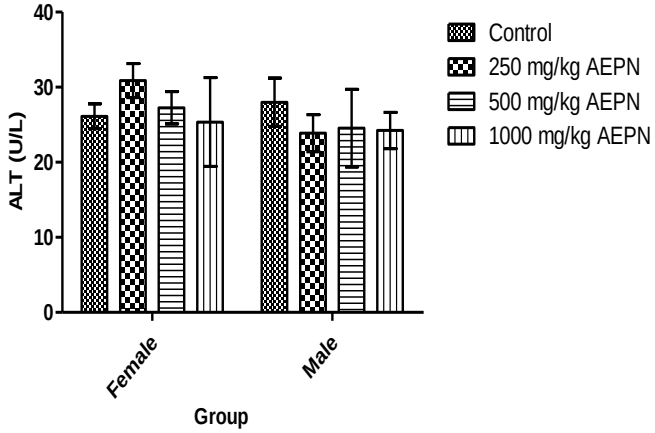

Figure 1: Effect of AEPN on serum alanine transferase in female and male rats
Values are presented as Mean ± SD (n = 5, females or males). AEPN: Aqueous extract of *Picralima nitida*

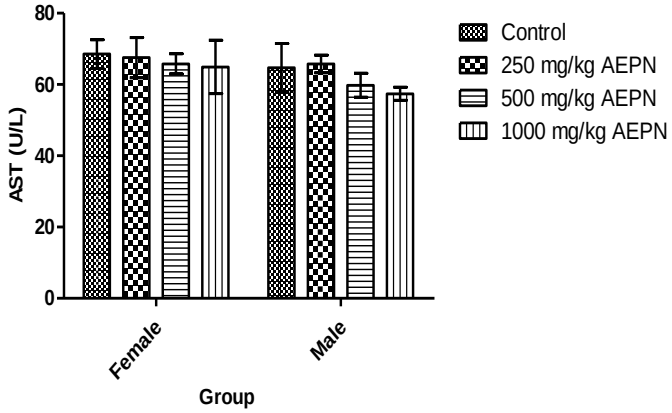

Figure 2: Effect of the extract on serum aspartate transferase in female and male rats
Values are presented as Mean ± SD (n = 5, females or males). AEPN: Aqueous extract of *Picralima nitida*

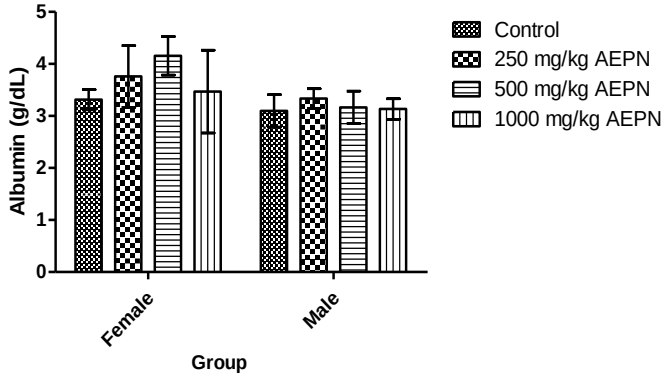

Figure 3: **Effect of the extract on serum albumin in female and male rats**
Values are presented as Mean ± SD (n = 5, females or males). AEPN: Aqueous extract of *Picralima nitida*

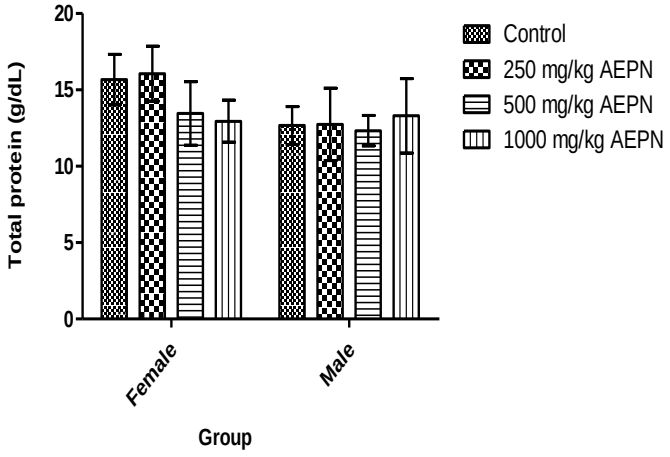

Figure 4: Effect of the extract on serum total protein level in female and male rats
Values are presented as Mean ± SD (n = 5, females or males). AEPN: Aqueous extract of *Picralima nitida*

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Table 1a: Relative organ weights of rats administered with AEPN in the subacute toxicity study

Female							
Treatment	**Liver**	**Kidney**	**Spleen**	**Heart**	**Lung**	**Ovaries**	**Brain**
Control	4.13 ± 0.50	0.77 ± 0.08	0.45 ± 0.14	0.42 ± 0.04	0.80 ± 0.14	0.04 ± 0.04	1.15 ± 0.23
250 mg/kg	3.78 ± 0.22	0.70 ± 0.04	0.10 ± 0.18	0.39 ± 0.02	0.90 ± 0.27	0.07 ± 0.03	1.01 ± 0.15
500 mg/kg	4.01 ± 0.44	0.76 ± 0.11	0.42 ± 0.13	0.34 ± 0.02	0.69 ± 0.11	0.07 ± 0.03	0.97 ± 0.05
1000 mg/kg	4.03 ± 0.58	0.71 ± 0.08	0.36 ± 0.08	0.40 ± 0.05	0.76 ± 0.07	0.10 ± 0.01	0.93 ± 012

Male							
Treatment	**Liver**	**Kidney**	**Spleen**	**Heart**	**Lung**	**Testes**	**Brain**
Control	3.95 ± 0.31	0.72 ± 0.05	0.38 ± 0.09	0.36 ± 0.03	0.68 ± 0.08	1.32 ± 0.06	0.75 ± 0.10
250 mg/kg	4.04 ± 0.18	0.71 ± 0.03	0.36 ± 0.10	0.35 ± 0.06	0.72 ± 0.07	1.33 ± 0.22	0.76 ± 0.05
500 mg/kg	3.64 ± 0.17	0.73 ± 0.05	0.35 ± 0.06	0.35 ±0.05	0.78 ± 0.03	0.65 ± 0.92	0.65 ± 0.02
1000 mg/kg	3.86 ± 0.31	0.75 ± 0.08	0.42 ± 0.08	0.25 ± 0.14	0.51 ± 0.34	2.01 ± 1.24	0.82 ± 0.08

Values are presented as Mean ± SD (n = 5, females or males). AEPN: Aqueous extract of *Picralima nitida*

Table 1b: Relative organ weights of rats administered with AEPN in the subacute toxicity study during the recovery period

Recovery period							
Female							
Treatment	**Liver**	**Kidney**	**Spleen**	**Heart**	**Lung**	**Ovaries**	**Brain**
Control	3.29 ± 0.46	0.63 ± 0.05	0.45 ± 0.10	0.31 ± 0.04	0.71 ± 0.06	0.08 ± 0.01	0.91 ± 0.02
1000 mg/kg	3.88 ± 0.58	0.73 ± 0.01	0.43 ± 0.16	0.40 ± 0.05	0.90 ± 0.16	0.11 ± 0.01	0.99 ± 0.27

Male							
Treatment	**Liver**	**Kidney**	**Spleen**	**Heart**	**Lung**	**Testes**	**Brain**
Control	3.39 ± 0.82	0.64 ± 0.07	0.37± 0.16	0.33 ± 0.09	0.64 ± 0.12	1.38 ± 0.28	0.65 ± 0.10
1000 mg/kg	4.30 ± 1.27	0.70 ± 0.03	0.46 ± 0.10	0.36 ± 0.01	0.69 ± 0.13	1.54 ± 0.16	0.91 ± 0.01

Values are presented as Mean ± SD (n = 2, females or males). AEPN: Aqueous extract of *Picralima nitida*

The levels of urea and creatinine in the serum were tested to evaluate the kidney's functional integrity. Although an increase in these indicators is normally a sign of kidney impairment, no such rise was seen in rats given any of the tested doses of plant extract in this study. Further, concentrations of electrolytes including potassium, sodium, chloride, and bicarbonate ions, which help to assess the functions of the kidney were determined in this study, as they play an important role in gaseous exchange and water balance. Any abnormal increase or reduction in the concentrations of these parameters could indicate kidney dysfunction.[33] The effects of serum levels of creatinine and urea and concentrations of electrolytes such as potassium, sodium, bicarbonate, and chloride ions are presented in Fig. 5 – 10. No significant difference was noted in the levels of this parameters in both female and male rats administered with all doses of AEPN compared with the control. Based on the results of these parameters, it can be suggested that there was no indication of kidney abnormalities.

The effect of AEPN on serum glucose level is presented in Fig. 11. There was no significant difference in the level of glucose in both genders at all doses of AEPN tested compared with the control. This suggested that there was neither hypoglycemia nor hyperglycemia associated with the consumption of AEPN.

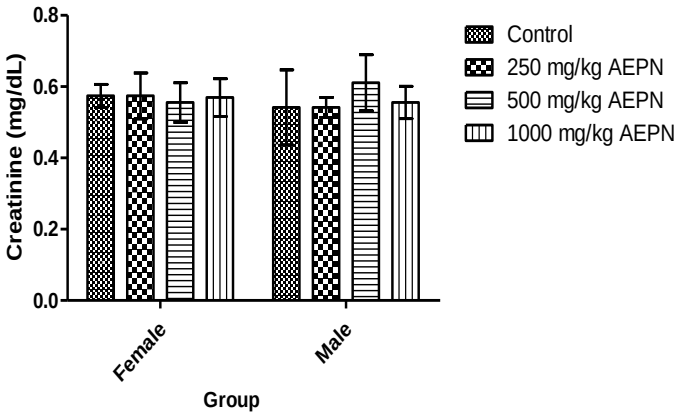

Figure 5: Effect of the extract on serum creatinine level in rats in female and male rats

Values are presented as Mean ± SD (n = 5, females or males). AEPN: Aqueous extract of *Picralima nitida*

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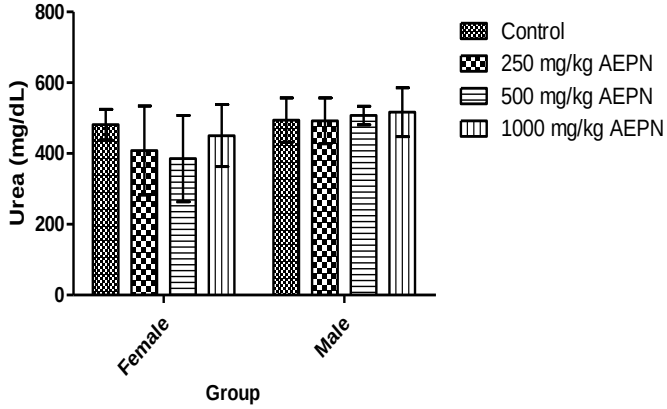

Figure 6: Effect of the extract on serum urea level in rats in female and male rats

Values are presented as Mean ± SD (n = 5, females or males). AEPN: Aqueous extract of *Picralima nitida*

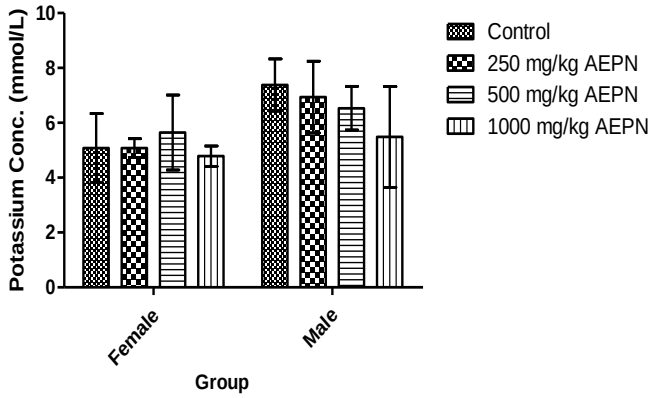

Figure 7: Effect of the extract on serum potassium concentration in female and male rats

Values are presented as Mean ± SD (n = 5, females or males). AEPN: Aqueous extract of *Picralima nitida*

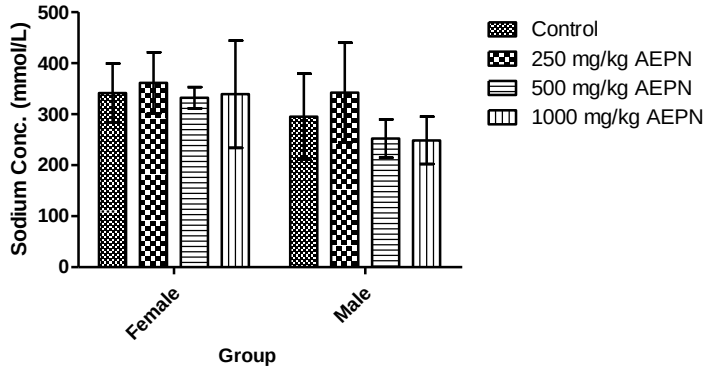

Figure 8: Effect of P. nitida on serum sodium concentration in female and male rats

Values are presented as Mean ± SD (n = 5, females or males). AEPN: Aqueous extract of *Picralima nitida*

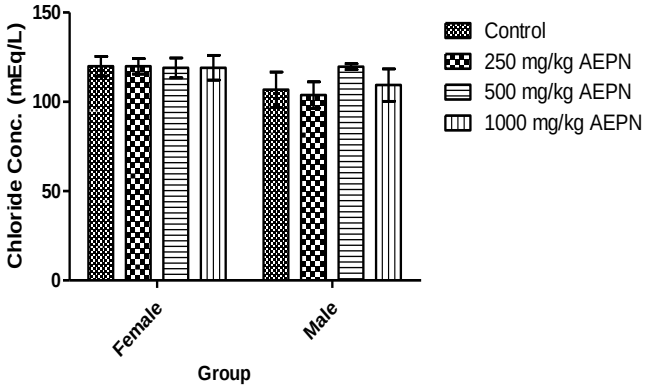

Figure 9: Effect of *P. nitida* on serum chloride concentration in female and male rats

Values are presented as Mean ± SD (n = 5, females or males). AEPN: Aqueous extract of *Picralima nitida*

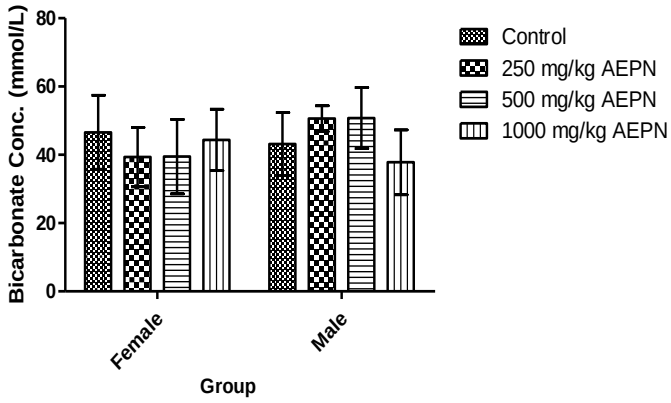

Figure 10: Effect of P. nitida on serum bicarbonate concentration in female and male rats

Values are presented as Mean ± SD (n = 5, females or males). AEPN: Aqueous extract of *Picralima nitida*

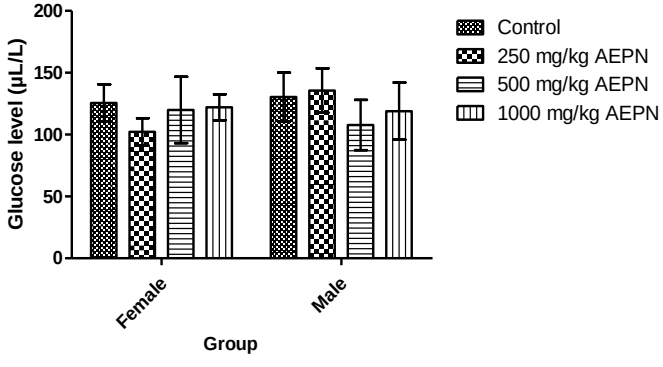

Figure 11: Effect of P. nitida on serum glucose level in female and male rats

Values are presented as Mean ± SD (n = 5, females or males). AEPN: Aqueous extract of *Picralima nitida*

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Hematological characteristics can be used to measure the impact of foreign compounds on the hematopoietic system because blood is essential for the movement of several nutrients and foreign chemicals throughout the body.[30] The effect of AEPN on hematological parameters is presented in tables 2a and b. No significant difference was noted in hematological parameters such as white blood cells, red blood cells, white blood counts (granulocytes, MID cells, and lymphocytes), platelets, hematocrits, and hemoglobin in rats administered with AEPN in both the main study (28-day) and the satellite group when compared to the control (Tables 2a and b). This means that the immune system and regular blood function are also unaffected.

Table 2a: Hematological parameters of rats administered with AEPN

Treatment	WBC (10^3 /ml)	LYM	MID	GRAN	RBC (10^6 /ml)	HGB	HCT	PLT
Female								
Control	7.97 ± 1.57	77.77 ± 5.14	16.6 ± 3.21	5.63 ± 2.02	7.18 ± 0.18	14.63 ± 0.55	40.27 ± 1.10	809.33 ±81.51
250 mg/ kg	12.23 ± 1.64	81.7 ± 4.67	13.45 ± 3.32	4.85 ± 1.34	7.86 ± 0.20	15.63 ± 0.72	42.37 ± 1.18	732.67 ±56.44
500 mg/ kg	20.77 ± 1.08	67.2 ± 16.83	18.3 ± 4.67	14.5 ± 2.16	7.58 ± 0.57	14.63 ± 1.68	40.43 ± 5.24	830.33 ±24.09
1000 mg/ kg	13.28 ± 8.45	79.80 ± 0.00	15.10 ±0.00	5.10 ± 0.00	8.00 ± 0.41	15.45 ± 0.73	42.40 ± 2.22	659.50 ± 14.42
Male								
Control	12.03 ± 2.76	82.1 ± 5.48	14.13 ± 4.07	4.28± 1.08	7.73 ± 0.08	15.73 ± 0.74	43.1 ± 2.45	856.00 ± 14.05
250 mg/ kg	11.5 ± 2.98	79.48 ± 2.54	14.35 ± 1.14	6.18 ± 1.69	7.76 ± 0.47	15.95 ± 0.17	43.25 ± 1.61	851.25 ± 16.74
500 mg/ kg	11.76 ± 0.37	80.79 ± 0.00	14.24 ± 0.00	5.23 ± 0.00	7.74 ± 0.02	15.84 ± 0.16	43.18 ± 0.11	853.63 ± 3.36
1000 mg/ kg	17.13 ± 6.30	80.37 ± 3.75	13.13 ± 2.48	6.50 ± 1.40	8.15 ± 0.63	16.15 ± 1.15	44.55 ± 3.89	586.60 ± 37.39

Values are presented as Mean ± SD (n = 5, females or males). AEPN: Aqueous extract of *Picralima nitida*

Table 2b: Hematological parameters of rats administered with AEPN during the recovery period

Recovery period								
Female								
Treatment	**WBC (10^3 /ml)**	**LYM**	**MID**	**GRAN**	**RBC (10^6 /ml)**	**HGB**	**HCT**	**PLT**
Control	13.40 ± 2.83	87.90 ± 7.14	7.15 ± 1.71	4.95 ± 2.06	6.92 ± 0.13	14.10 ± 0.71	36.80 ± 0.28	487.00 ± 82.02
1000 mg/ kg	9.75 ± 6.43	87.90 ± 2.14	7.15 ± 2.27	4.95 ± 1.63	7.12 ± 0.16	14.20 ± 0.42	38.00 ± 2.55	405.00 ± 16.97
Male								
Control	10.75 ± 4.74	78.10 ± 0.00	13.80 ± 0.00	8.10 ± 0.00	7.04 ± 0.66	15.50 ± 0.57	38.40 ± 1.56	490.00 ± 14.70
1000 mg/ kg	11.15 ± 3.75	77.40 ± 0.99	14.80 ± 1.41	7.80 ± 0.42	6.84 ± 0.98	13.55 ±2.33	35.50 ±8.20	722.50 ±13.40

Values are presented as Mean ± SD (n = 2, females or males). AEPN: Aqueous extract of *Picralima nitida*. White blood count (WBC), Lymphocytes (LC), mid -range absolute (MID), granulocytes (GRAND), Red blood cell (RBC). Hemoglobin (HGB), Hematocrits (HCT), Platelets (PL), Values are expressed as Mean ± SD, n = 5 (females or males)

Conclusion

These findings suggest that aqueous extract of *Picralima nitida* holds significant promise as a safe medicinal plant to be considered for use in medicinal applications. This was demonstrated by the oral LD_{50} which was greater than 5000 mg/kg. Repeated administration of the plant extract revealed no immediate, delayed, or continuous toxicity to both sexes of rats at all tested doses. Further research and clinical studies may provide valuable insights into the specific therapeutic benefits and mechanisms of its natural remedy against diseases.

Conflict of Interest

The Authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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