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Research Article

Assessment of the Acute and Subacute Toxicity Profile of Diethylether Extract of *Jatropha Tanjorensis* leaf in Male Wistar Rats

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Abstract: The aim of study was to evaluate the acute and subacute toxicity of diethylether extract of *Jatropha tanjorensis* leaves in male Wistar rats. The acute toxicity study was conducted by placing Wistar albino rats into four groups of five rats each. These were sequentially dosed one at a time, using four graded doses of 1250, 2500, 3750 and 5000 mg/kg b.wt of the plant extract. Observations were made and recorded systematically daily for a seven days period for mortality, breathing and other behavioral changes after dose administration. For the sub-acute toxicity study, the animals were divided into ten groups of five rats each. Group 1 served as normal control and received distilled water for a 42 days period. Groups 2,3 and 4 received 167mg/kg b.wt of the plant extract for 14 days, 28 days and 42 days respectively. Groups 5, 6 and 7 received 250mg/kg b.wt of the plant extract for 14 days, 28 days and 42 days period respectively. Groups 8, 9 and 10 received 500mg/kg b.wt of the plant extract for 14, 28 and 42 days respectively. The animals were sacrificed at 14 days interval and the hematological and biochemical parameters were determined. There was a significant ($p \leq 0.05$) increase in RBC, Hb, HT, MCV and MCH and a decrease in WBC for 14, and 28 days treatment. There was significant increase in the levels of TP, ALB and a decrease in the levels of TBIL, ALP while ALT and AST remained unchanged. The serum markers of lipid profile, total–CHOL, LDL-CHOL, VLDL-CHOL and TG were significantly reduced and HDL-CHOL level was increased. The activities of the stress enzymes GPx, CAT and SOD were increased while the level of MDA was reduced. The K^+ level was unchanged, Na^+, Cl^- and HCO_3^- levels increased while urea and creatinine levels were decreased. *Jatropha tanjorensis* diethylether extract elicited non-toxic effect in the hematological and biochemical parameters. Thus, the extract can be considered safe for oral administration.

Keywords: acute toxicity, sub-acute toxicity, hematology, biochemical, *Jatropha tanjorensis*.

1. Introduction

Plants and plant-based treatments are used frequently to cure ailments throughout the world and are becoming more and more well-known as a result of their high efficacy. The majority of people still receive their care mostly through traditional medicine, especially in poorer nations (Elachouri et al., 2021). These plants are not only utilised

as medicines but also occasionally as vegetables and sauces in regional cuisines (Konyak et al., 2022; Asiwe et al., 2022a). As the frequency of chronic metabolic disorders rises, partly as a result of greater urbanisation and bad lifestyle choices, many people in industrialised countries are turning to plant-based diets and therapeutic options. *Jatropha tanjorensis* (Euphorbiaceae) is a well-known plant in Southern Nigeria that is used in ethnomedicine as well as a vegetable in different local cuisines. In some parts of Nigeria, the leaf is used as a heart tonic and a hypertension remedy (Ezeoguine *et al.,* 2021). It is also commonly used to treat diabetes, malaria, and anaemia (Chibuogwu *et al.,* 2021). Due to the high medicinal value of *Jatropha tanjorensis,* different names has been ascribed to this "wonder plant" by different local regions in Nigeria such as "hospital too far," in South-south, "catholic vegetable," in the North-central as well as "lyana lpaja" by the South-western Nigeria (Alawode *et al.,* 2021). There is mounting scientific evidence that suggest that this plant has medicinal properties such as its cardio protective functions (Sabbaghzadegan *et al.*, 2021; Alawode *et al.,* 2021), antibacterial and anti-anemic properties (Mariano *et al.*, 2022) as well as its protective effect against free radical-induced organ damage (Adebayo *et al.,* 2021).

Because of the numerous ailments that plants and plant-based medicines have been proved to effectively treat, they are widely accepted in society, profitable, and most importantly, widely accessible (Alabdallah and Hasan, 2021; Danziger and Bernstein, 2021). The possibility for toxicity linked to the intake of specific herbal products and vegetables, however, has been a source of concern (Khan et al., 2021). Certain components of medicinal plants, such as lactone glycosides, toxalbumines, and some alkaloids, such as quinoline, isoquinoline, lupine, senecio, and pyridine-piperidine alkaloids, are linked to harmful effects (Zhang et al., 2021). Instead of relying exclusively on claims of these medicinal plants' potency and safety in folkloric use, it is vital to determine the safety profile of these plants. With regard to *Jatropha tanjorensis* diethylether extract's acute and subacute toxicity effects, notably on biochemical markers, there is a knowledge gap that has to be filled.

2. Materials and Methods

Preparation of plant material

Fresh leaves of *Jatropha tanjorensis* were gathered from Ogbogoro in Port Harcourt, Rivers State, Nigeria, and were recognized by a taxonomist at the Herbarium unit, Department of Plant Science and Biotechnology, University of Port Harcourt, Rivers State, Nigeria. The leaf specimen was listed in their herbarium as UPH/P/343. 500g of the powdered leaves were extracted by maceration in 2.0 L of 96% diethylether for 48 hours after being air dried and ground into powder. To acquire the crude diethylether extract, (JTDE). This was followed by filtration, first using a mesh filter and then What man No. 1 filter paper. The filtrate was then concentrated using a rotary evaporator at 35°C.

Phytochemical Examination

Using Shaikh and Patil and Eruotor et al. Phytochemical screening approach, secondary metabolites in plant extract were identified (2022). The extract contained flavonoids, alkaloids, phenols, tannins, terpenoids, and steroids (Table 1).

Experimental animals

In the investigation, there were 70 male Wistar strain rats (8-10 weeks old and 180-220g average weight). They were given regular animal food and drink at will during their seven-day acclimatisation period in clean animal cages with good ventilation. The animal cages were kept clean each day of the trial. The animals were handled in compliance with the Institution's ethical standards (UPH-REC/2021/028), which strictly follow the Organization for Economic Cooperation and Development's (OECD) UPD/OECD 425 standard for the handling of laboratory animals.

Acute Oral Toxicity Test Procedure

The organization for Economic Cooperation and Development's up and down technique (UPD/OECD 425) as reported by Enegide et al (2013) was used to establish the LD_{50} value of diethylether extract of *Jatropha tanjorenis* leaf. This has been approved by the regulatory organization, Peta International Scientific Consortium Ltd (PISC, 2007). A total of twenty (20) male wistar rats were obtained and put into four groups, each with five rats. Four graduated doses of *Jatropha tanjorenis* diethylether extract (1250, 2500, 3750, and 5000 mg/kg body weight) were administered to each group's Wistar rats one at a time. The extract was administered to group one rats once at a dose of 1250 mg/kg body weight, and the rats were then watched for two days for indications of toxicity and mortality. After two days of observation, the original dose was doubled (to 2500mg/kg body weight) and given to the rats in group two because toxicity and mortality had not materialised. The extract's concentration was raised incrementally over a seven-day period until group 4 received 5000mg/kg of body weight. The Enegide et al. (2013) algorithm was used to determine the median lethal dose after toxicology and mortality data were collected.

$$LD50 = \frac{[M0-M1]}{2}$$

Where M_0 = Highest dose of test substance that caused mortality and M_1 = lowest dose of test substance that caused mortality.

Sub-acute Oral Toxicity Test Procedure

The animals were divided into ten (10) groups of five (5) animals each and tested for repeated dose oral toxicity according to OECD Guideline 407 (OECD, 2008). Group 1 served as the standard control and received distilled water for 42 days. For 14 days, 28 days, and 42 days, groups 2, 3, and 4 received 167mg/kg body weight of the plant extract respectively. For 14 days, 28 days and 42 days, groups 5, 6, and 7 received 250mg/kg body weight of the plant extract respectively. For 14 days, 28 days and 42 days, groups 8, 9, and 10 received 500 mg/kg body weight of the plant extract respectively.

Analysis of Haematological Parameters

Red blood cells (RBCs), white blood cells (WBCs), haemoglobin (Hb), and haematocrit (HCT) were among the haematological parameters examined from blood samples obtained in EDTA tubes. The examination was done using an automated haematology analyzer (SINNOWA, China). The mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) were calculated from RBC, HCT, and Hb using the techniques outlined by Asiweet al., (2022).

Assay of Biochemical Parameters

To measure biochemical factors such total bilirubin, albumin, transaminases (aspartate and alanine aminotransferases), alkaline phosphatase, cholesterol, and total protein in serum, Randox Commercial kits were utilised. Malondialdehyde, reduced glutathione concentration, glutathione peroxidase, superoxide dismutase, and catalase were all measured (Gutterdge and Wilkins, 1968; Sedlak and Lindsay, 1968; Rotrucket al., 1973; Maier et al., 2019; Beers and Sixer, 1952). Sodium (Na+), potassium (K+), and chloride were among the serum electrolytes that were measured using the techniques developed by Reitman and Frankel (1957) and Tietz (1970).

Statistical Evaluation

Using the statistical software for social sciences (SPSS) for Windows version 18.0, USA, the collected data was statistically analysed. One-way analysis of variance (ANOVA) was used for descriptive statistics, and Turkey Post hoc multiple comparisons were conducted with a confidence level of ($p \leq 0.05$). The average and standard error of the average are used to represent the data (SEM).

3. Results

Phytochemical Screening

Table 1 displays the findings of the phytochemical screening. The outcome indicates the presence of steroids, alkaloids, phenols, tannins, terpenoids, alkaloids, flavonoids, and saponins. With a concentration of 12.80 ± 2.4mg/100g, saponins were the most prevalent phytoconstituent, followed by flavonoids (9.78 ± 0.1mg/100g).

Effect of JTDE on Hematological Parameters of Experimental Animals

According to the data in Table 3, when administered at a dose of 500 mg/kg body weight, JTDE significantly ($p \leq 0.05$) increased RBC, Hb, HT, MCV, and MCH levels while significantly ($p \leq 0.05$) decreased WBC levels for 14, 28, and 42 days when compared to the normal control. JTDE 250mg/kg b.wt. provided for 14, 28, and 42 days resulted in substantial ($p \leq 0.05$) increases in RBC, Hb, HT, MCV, and MCH when compared to the normal control, as well as a contemporaneous drop in WBC level. In comparison to the normal control, there were no appreciable differences in the levels of HT when JTDE was given for 28, and 42 days, as well as RBC when JTDE was given for 14 days at 167 mg/kg b.wt.

Effect of JTDE on Serum Markers of Liver Function

The effects of JTDE at doses of 167 mg/kg, 250 mg/kg, and 500 mg/kg b.wt. for 14, 28, and 42 days are shown in Table 4. When compared to the normal control, there was a significant ($p \leq 0.05$) rise in the levels of TP and ALB for groups 2 through 9. Comparing the levels of TBIL and ALP to the normal control revealed a substantial ($p \leq 0.05$) decline in both. After receiving 500mg/kg b.wt of the extract, Groups 8, 9, and 10 displayed a substantial ($p \leq 0.05$) decline in ALT level in comparison to the normal control. when compared to the normal control, 167mg/kg b.wt (groups 3 and 4) and 250mg/kg b.wt (group 5) revealed no difference in the levels of ALT and AST.

Effect of JTDE on Serum Markers of Lipid Profile

At the extract concentrations at 167mg/kg, 250mg/kg, and 500mg/kg b.wt., the serum levels of Total-CHOL, LDL-CHOL, VLDL-CHOL, and TG considerably decreased ($p \leq 0.05$). In comparison to the control group, the treated groups' HDL-CHOL levels considerably ($p \leq 0.05$) rose (Table 5).

Effect of JTDE on Serum Markers of Oxidative Stress

CAT level was lowered for groups 2-10 when compared to the normal control (Table 6).

Effect of JTDE on Serum Markers of Kidney Function

when compared to the normal control, the levels of Na^+, Cl^- and HCO_3^- were significantly higher ($p \leq 0.05$) in the treated groups. For groups 2 (167 mg/kg, 14 days), group 3 (167 mg/kg, 28 days), and group 4 (167 mg/kg, 42 days), there were no appreciable increases in the levels of K+. The amounts of urea and creatinine significantly decreased ($p \leq 0.05$).

4. Discussion

The previously stated health benefits of the plant may be due to the high quantities of phytochemicals discovered during qualitative and quantitative screening of JTDE (Oladeleet al., 2020; Eruotoret al., 2022). According to Miceket et al. (2021), flavonoids have been proven to diminish the risk of coronary heart disease, whereas saponins have been demonstrated to have antioxidant and cholesterol-lowering properties (Ermoshinet al., 2021; Umorenet al., 2023). As an alternative medication, herbal remedies are becoming more and more in demand. To ensure their dependability and safety, it is crucial to identify their components and toxicological condition. Haematological and biochemical analyses, as well as behavioural observation results, are routinely used for this (Umorenet al., 2023). At the maximal oral dose of 5000mg/kg body weight of *Jatropha tanjorensis* leaf, there was no fatality in the acute toxicity trial. *Jatropha tanjorensis* may be regarded non-toxic and safe for ingestion, according to (Ajahet al., 2021), which is consistent with the results of other investigations (Uhuoet al., 2021; Harley et al., 2021). In particular at the higher doses of 250 mg/kg and 500 mg/kg, the haematological examination showed a considerable increase in RBC, Hb, HT, MCV, and MCH levels as well as a significant decrease in WBC levels. This exemplifies the haematopoietic effect of the herb. According to

research on the plant's anti-anemic qualities, it has the capacity to promote erythropoiesis (Shethet al., 2021), which is compatible with the results of our investigation. It's possible that the reduced WBC count reflects the plant extract's failure to elicit an immunological response.

Organ function markers and the impact of plant extracts or other compounds on critical organs are useful techniques for assessing the toxicity of such substances. The lipid profile indicators total-CHOL, LDL-CHOL, and VLDL-CHOL were decreased in the treated groups when compared to the untreated control group. The treated groups exhibited HDL-CHOL concentrations that were noticeably greater than those of the normal control group. This is significant because high levels of LDL-C and TG commonly put people at risk for developing cardiovascular diseases, whereas high levels of HDL-C can lessen the likelihood of developing cardiovascular diseases (Casulaet al., 2021). The plant's abundant flavonoid content, which may reduce bad cholesterol (LDL-C) while raising the level of good cholesterol (HDL-C) may help to explain this (HDL-C). This claim was made earlier by (Amssayef et al., 2021).

Both enzymatic and non-enzymatic defence mechanisms regulate the protective barrier against oxidative stress in cells. The plant may be able to defend against oxidative damage, as evidenced by the fact that MDA levels in the treated groups were lower than in the control group. This is supported by the elevated levels of the SOD, an enzyme that counteracts oxidative damage, in the groups that received various extract doses. This assertion is supported by research on the plant's capacity to reduce organ damage brought on by chemicals (Uchenduet al., 2020). This occurs as a result of the frequent involvement of these organs in the metabolism and excretion of xenobiotic chemicals. High levels of the enzymes are typically symptomatic of liver injury, and the liver enzyme assay is used to diagnose liver injuries (Chen et al., 2021; Eslamet al., 2021). All JTDE concentrations decreased the levels of AST, ALP, ALT, and TBIL when compared to the control. No signs of liver damage were found, which suggests that the extract is safe to eat. The elevated levels of TP and ALB may be a sign that the plant extract induced the liver's protein synthesis machinery to work more vigorously (Mu et al., 2020). Typically, blood urea nitrogen (BUN), serum creatinine concentration, and blood electrolyte balance are used to determine kidney function (Liu et al., 2020; Raoet al., 2021). The maximum dose of 500mg/kg raised the levels of Na+, Cl-, and HCO3- while keeping K+ constant. Lower urea concentrations were seen with all doses of the extract, and lower creatinine concentrations were seen with doses of 250 mg/kg and 500 mg/kg, suggesting that the kidneys weren't harmed.

5. Conclusion

When given up to 5000mg/kg body weight, the diethylether extract of the leaves of *Jatropha tanjorensis* demonstrated no mortality or harmful behavioural abnormalities in an acute toxicity trial. Moreover, repeated treatment for 14, 28, and 42 days at 250mg/kg, 500mg/kg, and 167mg/kg doses revealed no appreciable deleterious effects on haematological and biochemical indicators. In the phytochemical screening, substances such as tannins, flavonoids, saponins, alkaloids, phenols, terpenoids, and steroids were discovered, which may be the cause of the medicinal qualities. *Jatropha*

tanjorensis is therefore advised to be safe for use in both dietary supplements and ethnomedicine based on the findings of this study.

Abbreviations

Organization for Economic Cooperation and Development (OECD); World Health Organization(WHO); Diethylether Extract of *Jatropha tanjorensis*(JTDE); Ethylene diamine tetra acetic acid (EDTA); White Blood Cells(WBC); Red Blood Cells(RBC); Haemoglobin(Hb); Hematocrit(HT); Mean Corpuscular Volume(MCV); Mean Corpuscular Hemoglobin(MCH); Total Bilirubin(TBIL); Total Cholesterol(Total-CHOL); Albumin(ALB); Total Protein(TP) Alkaline phosphatase (ALP); High density lipoprotein cholesterol(HDL-C); Low density lipoprotein cholesterol (LDL-C); Very low density lipoprotein cholesterol(VLDL-C); Malondialdehyde(MDA); reduced glutathione(GSH); Glutathione peroxidase (GPx); Superoxide dismutase(SOD); Catalase(CAT); Sodium ion(Na^+); Potassium ion(K^+); Chloride ion (Cl^-); Bicarbonate ion (HCO_3^-), and Blood Urea Nitrogen(BUN).

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Authors' Contributions

The study was designed by CCM and CJI. The experimental technique, including photochemistry and animal handling as well as the statistical analysis of data, data interpretation, and manuscript writing were all done by OEE.

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Ethical consideration

The study was given the go-ahead by the University of Port Harcourt's Ethical Committee (UPH-REC/2021/028), which scrupulously adhered to national regulations for the care and use of animals as well as those set forth by the Organization for Economic Cooperation and Development (OECD).

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Table 1. Phytochemical Constituent of JTDE

Phytochemical	Concentration (mg/100 g)
Alkaloid	1.1±0.1
Anthraquinone	1.2±0.1
Flavonoid	9.78±0.1
Saponin	12.80±2.4
Steroid	0.46±0.12
Tannin	5.7±0.4
Terpenoid	6.7±1.6
Total	37.74±4.82

Table 2. Result of the LD50 of Diethylether extract of *Jatropha tanjorensis* (n=5).

Groups	Dose of Extract (mg/kg)	No of animals dead	Dose difference	Mean mortality
1	1250	0	1250	0
2	2500	0	1250	0
3	3750	0	1250	0
4	5000	0	1250	0

LD50 = 5000mg/kg

Table 3. Effect of JTDE on Hematological Parameters of Experimental Animals.

Treatment	RBC(×10^{12}/L)	Hb(mg/dl)	HT(%)	MCV (fl)	MCH(pg)	WBC(×10^{9}/L)
Normal control	5.66±0.09^{a}	14.34±0.09^{b}	46.60±0.51^{c}	91.20±0.58^{d}	24.60±0.51^{e}	9.60±0.40^{f}
167mg/kg 14 days	5.68±0.07	15.42±0.05^{b}	33.24±0.71^{c}	88.00±0.32^{d}	26.20±0.37^{e}	8.80±0.37^{f}
167 mg/kg 28 days	6.08±0.07^{a}	15.60±0.04^{b}	52.00±0.37	86.40±0.51^{d}	27.20±0.37	8.60±0.40^{f}
167 mg/kg 42 days	6.36±0.02^{a}	15.60±0.05^{b}	54.20±0.87	84.40±0.40^{d}	25.60±0.40^{e}	7.00±0.32^{f}
250 mg/kg 14 days	6.02±0.05^{a}	15.16±0.06^{b}	51.60±0.37	87.40±0.24^{d}	27.40±0.40^{e}	8.00±0.32^{f}
250 mg/kg 28 days	6.36±0.05^{a}	15.58±0.12^{b}	57.20±0.37^{c}	84.60±0.40^{d}	29.60±0.40^{e}	8.60±0.40^{f}
250 mg/kg 42 days	6.78±0.04^{a}	17.08±0.05^{b}	60.80±0.37^{c}	81.40±0.40^{d}	30.00±0.55^{e}	8.00±0.32^{f}
500 mg/kg 14 days	6.18±0.05^{a}	16.16±0.02^{b}	58.20±0.37^{c}	91.20±0.73	28.00±0.32^{e}	8.60±0.40^{f}
500 mg/kg 28 days	6.76±0.05^{a}	17.26±0.02^{b}	61.00±0.32^{c}	86.80±0.37^{d}	29.20±0.37^{e}	8.80±0.37^{f}
500 mg/kg 42 days	7.14±0.05^{a}	17.38±0.04^{b}	62.20±0.58^{c}	89.60±0.40^{d}	31.40±0.51^{e}	9.00±0.32^{f}

Values are reported as mean ± standard error of mean (M±SEM) (n =5). Values with similar superscript letters indicate significant differences (p≤ 0.05) down the column while those without or different superscripts show non-significant differences (p≥ 0.05) down the column when compared with the control group.

Table 4. Effect of JTDE on Serum Markers of Liver Function

Treatment	TP (g/L)	ALB (mmol/L)	TBIL (µmol/)L)	ALT (IU/L)	ALP (U/L)	AST (IU/L)
Normal control	64.60±0.51^{a}	39.40±0.40^{b}	7.66±0.07^{c}	13.46±0.39^{d}	125.80±4.84^{e}	16.80±0.20^{f}
167 mg/kg 14 days	66.40±0.75^{a}	46.60±0.51^{b}	5.34±0.02^{c}	15.80±0.37^{d}	144.80±1.88^{e}	18.00±0.32
167 mg/kg 28 days	71.60±0.60^{a}	44.60±0.75^{b}	5.06±0.02^{c}	13.40±0.40	136.00±1.14^{e}	17.60±0.40
167 mg/kg 42 days	71.80±0.37^{a}	50.20±0.37^{b}	4.32±0.04^{c}	13.60±0.24	135.20±0.58^{e}	16.40±0.75
250 mg/kg 14 days	74.80±0.58^{a}	48.80±0.37^{b}	4.26±0.14^{c}	12.40±0.93	118.60±0.75^{e}	18.00±0.32
250 mg/kg 28 days	76.60±0.51^{a}	49.60±0.60^{b}	4.16±0.06^{c}	9.00±0.55^{d}	115.00±0.84^{e}	13.40±1.44^{f}
250 mg/kg 42 days	78.60±0.51^{a}	54.20±2.85^{b}	4.02±0.04^{c}	11.40±0.24^{d}	117.00±0.84^{e}	13.00±0.32^{f}
500 mg/kg 14 days	80.20±0.37^{a}	50.60±1.83^{b}	3.04±0.24^{c}	10.40±0.51^{d}	111.40±0.67^{e}	15.00±0.32
500 mg/kg 28 days	83.40±0.68^{a}	49.60±0.93^{b}	3.06±0.06^{c}	9.40±0.40^{d}	106.00±1.14^{e}	13.60±0.68^{f}
500 mg/kg 42 days	84.60±0.60^{a}	61.60±0.51^{b}	2.96±0.02^{c}	8.40±0.24^{d}	110.40±1.50^{e}	13.80±0.58^{f}

Values are reported as mean ± standard error of mean (M±SEM) (n =5). Values with similar superscript letters indicate significant differences (p≤ 0.05) down the column while those without or different superscripts show non-significant differences (p≥ 0.05

Table 5. Effect of JTDE on Serum Markers of Lipid Profile

Treatment	Total-CHOL (mmol/L)	HDL-CHOL(mmol/L)	LDL-CHOL(mmol/L)	VLDL-CHOL(mmo/L)	TG(mmol/L)
Normal control	5.66±0.02^{a}	0.98±0.06^{b}	0.20±0.04^{c}	1.26±0.07^{d}	2.56±0.16^{e}
167mg/kg 14 days	3.72±0.37^{a}	0.87±0.03^{b}	0.12±0.00^{c}	0.95±0.01^{d}	2.08±0.00^{e}
167 mg/kg 28 days	3.96±0.02^{a}	1.09±0.07^{b}	0.12±0.00^{c}	0.94±0.01^{d}	1.46±0.01^{e}
167 mg/kg 42 days	3.68±0.06^{a}	1.03±0.06^{b}	0.12±0.00^{c}	0.89±0.01^{d}	1.21±0.00^{e}
250 mg/kg 14 days	3.88±0.06^{a}	1.05±0.02^{b}	0.11±0.00^{c}	0.94±0.01^{d}	1.23±0.00^{e}
250 mg/kg 28 days	4.04±0.02^{a}	1.07±0.02^{b}	0.10±0.01^{c}	0.86±0.01^{d}	1.19±0.00^{e}
250 mg/kg 42 days	3.76±0.02^{a}	1.07±0.03^{b}	0.12±0.00c	0.86±0.02^{d}	1.16±0.00^{e}
500 mg/kg 14 days	3.48±0.02^{a}	1.08±0.05^{b}	0.08±0.00^{c}	0.79±0.05^{d}	1.16±0.01^{e}
500 mg/kg 28 days	3.60±0.17^{a}	1.10±0.10^{b}	0.11±0.01^{c}	0.87±0.02^{d}	1.12±0.02^{e}
500 mg/kg 42 days	3.56±0.02^{a}	1.13±0.11^{b}	0.09±0.00^{c}	0.89±0.00^{d}	1.08±0.01^{e}

Values are reported as mean ± standard error of mean (M±SEM) (n =5). Values with similar superscript letters indicate significant differences ($p \leq 0.05$) down the column while those without or different superscripts show non-significant differences ($p \geq 0.05$) down the column when compared with the control group.

Table 6. Effect of JTDE on Serum Markers of Oxidative Stress

Treatment	MDA (nmol/L)	GSH (mmol/gHb)	GPx (ng/ml)	CAT (mU/L)	SOD (U/ml)
Normal control	24.42±1.11^{a}	72.57±0.63^{b}	4.76±0.02^{c}	114.51±1.43^{d}	35.18±0.85^{e}
167mg/kg 14 days	20.23±0.51^{a}	78.80±0.20^{b}	3.60±0.03^{c}	109.14±0.01^{d}	41.28±0.48^{e}
167 mg/kg 28 days	22.23±0.35^{a}	83.64±0.64^{b}	2.82±0.09^{c}	109.20±0.29^{d}	39.75±0.24^{e}
167 mg/kg 42 days	21.86±0.35^{a}	83.58±0.64^{b}	2.82±0.09^{c}	100.49±0.25^{d}	39.85±0.18^{e}
250 mg/kg 14 days	22.36±0.25^{a}	80.80±0.37^{b}	3.24±0.50^{c}	100.20±0.25^{d}	40.37±0.56^{e}
250 mg/kg 28 days	20.01±0.24^{a}	82.86±0.10^{b}	2.78±0.58^{c}	96.25±1.55^{d}	40.15±0.25^{e}
250 mg/kg 42 days	21.75±0.36^{a}	87.64±0.37^{b}	2.36±0.05^{c}	89.08±0.18^{d}	40.66±0.45^{e}
500 mg/kg 14 days	22.95±0.16^{a}	89.62±0.26^{b}	4.96±0.02	99.10±0.28^{d}	40.72±0.41^{e}
500 mg/kg 28 days	22.21±0.20^{a}	93.20±0.07^{b}	4.16±0.16^{c}	93.21±0.40^{d}	40.66±0.45^{e}
500 mg/kg 42 days	21.71±0.58^{a}	90.32±0.52^{b}	2.16±0.16^{c}	93.75±0.36^{d}	39.56±0.43^{e}

Values are reported as mean ± standard error of mean (M±SEM) (n =5). Values with similar superscript letters indicate significant differences ($p \leq 0.05$) down the column while those with different superscripts show non-significant differences ($p \geq 0.05$) down the column when compared with the control group.

Table 7. Effect of JTDE on Serum Markers of Kidney Function

Treatment	Na^+(mmol/L)	K^+(mmol/L)	Cl^-(mmol/L)	HCO_3^-(mmol/L)	Urea (mg/dl)	Creatinine (mmol/L)
Normal control	157.60±1.47[a]	6.32±0.04[b]	99.00±0.32[c]	21.60±0.81[d]	21.96±0.66[e]	0.74±0.01[f]
167mg/kg 14 days	164.20±0.37[a]	6.08±0.04	98.80±0.73	23.60±0.40	26.70±0.20[e]	0.70±0.00
167 mg/kg 28 days	163.40±0.93[a]	6.14±0.04	102.60±2.48	21.40±0.51	26.34±0.10[e]	0.71±0.00
167 mg/kg 42 days	156.80±1.69	6.16±0.35	88.80±0.66[c]	23.60±0.75[d]	23.66±0.50[e]	0.71±0.01
250 mg/kg 14 days	163.00±0.55[a]	6.70±0.07[b]	115.00±7.46[c]	23.20±0.58[d]	25.90±0.34[e]	0.69±0.00[f]
250 mg/kg 28 days	161.60±3.23[a]	6.78±0.05[b]	114.40±0.81[c]	27.60±0.51[d]	24.58±0.33[e]	0.70±0.00[f]
250 mg/kg 42 days	163.60±0.60[a]	6.68±0.05[b]	120.60±3.53[c]	26.80±0.49[d]	25.60±0.68[e]	0.71±0.00[f]
500 mg/kg 14 days	165.80±0.66[a]	6.84±0.07[b]	115.20±2.03[c]	28.20±0.37[d]	21.94±0.04[e]	0.69±0.00[f]
500 mg/kg 28 days	171.60±0.51[a]	6.90±0.04[b]	105.80±1.59	29.00±0.45[d]	22.38±0.13[e]	0.61±0.00[f]
500 mg/kg 42 days	172.60±0.68[a]	6.66±0.06	112.60±0.81[c]	30.00±0.32[d]	20.22±0.39[e]	0.61±0.00[f]

Values are reported as mean ± standard error of mean (M±SEM) (n =5). Values with similar superscript letters indicate significant differences ($p \leq 0.05$) down the column while those without or different superscripts show non-significant differences ($p \geq 0.05$) down the column when compared with the control group.