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ACUTE TOXICITY EFFECT OF THE AQUEOUS EXTRACT OF *Terminalia avicennioides* ON WHITE ALBINO RATS.

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ABSTRACT

Lorke's method was used to study the acute toxicity effect of aqueous extracts from the stem bark of *Terminalia avicennioides* (ATA) on white albino rats. The study involved intraperitoneal administration of different doses of the extract to groups of male rats. Signs accompanying toxicity and possible death of animals were monitored for two weeks to ascertain the median lethal dose (LD_{50}) of the extract. At the end of the two week study, all the animals in all the dose groups were sacrificed and the mean internal organ-body weight ratios (OBR) were determined and compared with values from those of the control group. The LD_{50} was found to be > 5000 mg/Kg body weight. There was no significant weight decrease (P>0.05) among dose groups up to 1000 mg/Kg body weight. Liver congestion was observed with 100 mg/kg body weight dose group. The OBR mean values for Kidney, liver and heart were not significantly (P>0.05) different from that of the control group. The safety usage of extracts from this plant in traditional medicine vis-à-vis phytochemical consideration is discussed.

***Key words**:* Acute toxicity, *Terminalia avicennioides*, Albino Rats, Traditional medicine.

INTRODUCTION

An estimated 4000 million inhabitants of the world, that is about 80% of world's population, are thought to rely chiefly on traditional medicine, which is largely of plant origin, for their primary health care needs (Norman, *et al.,* 1985). However, it is widely believed that this valuable medicinal resources in plants are largely untapped because of inadequate scientific technical and commercial infrastructures in developing countries (Olayiwola, 1993).

In recent years, there is a growing interest in herbal therapy. Data on scientific screening of plant extracts, whether crude or purified, appears to be accumulating gradually but steadily. Literatures on antidiarrhoeal, antimalarial and antitrypanosomal activities of plants-based products support this claim (Abdullahi *et al.,* 2001; John *et al.,* 2001; Nok 2002; Atawodi *et al*., 2003). The major contributory factors to this growing interest include: rising costs of orthodox medications, low therapeutic index of synthetic compounds and the growing incidence of drug resistance (Onyeyilli & Egwu, 1995; Seed, 2000) among the pathogens especially in developing countries with very weak economic indices. It is thought that the use of plant-derived active principles will offer people access to safe and effective products for the prevention and treatment of diseases through self-medication.

One major and overriding criterion in the selection of herbal medicines for use in health services is safety. Plants extracts should not only be efficacious but safe for consumption. Therefore, closely associated with screening of plants extracts for their activities against microorganism or disease conditions is the need to know their toxic potentials.

Terminalia avicennioides (Guill and Perr) is a tropical herb common in North central vegetation of Nigeria. It is locally called *Baushe* (Hausa dialect). The plant is known to be active against trypanosomes (Bulus *et al*., 2008) and against conditions like diarrhoea (Abdullahi *et al.,* 2001). The aim of this work is to evaluate the toxic potential of this plant with the view to endorse or refute the safety usage of its aqueous extract in traditional medicine.

MATERIALS AND METHODS

Plant Collection: The plant, *Terminalia avicennioides,* (Guill and Perr) was obtained from Tashan Fulani village in Zaria Local Government of Kaduna State. The plant's identity was confirmed at the Herbarium of the Department of Biological Sciences, Ahmadu Bello University, Zaria, Nigeria with a voucher number 901452.

Preparation of Aqueous Extract of *T. avicennioides*: Fresh stem samples were cut into small pieces and then dried under shade for a week. Exactly 200 g of the dried sample was ground and boiled in 1 litre of distilled water contained in a conical flask for one hour. The extract was thereafter filtered hot first with muslin cloth and then with filter paper. The filtrate was concentrated in a water bath with its temperature set at 50 ^{o}C for 2 days. The concentrated extract was finally exposed to air to complete drying. The dried extract was stored in a refrigerator at 4 ^{o}C until required.

Experimental animals: Eighteen white male albino rats (Wistar stock) were obtained from the Department of Pharmacology and Clinical Pharmacy, Ahmadu Bello University, Zaria, Nigeria. The animals were fed on diet specially prepared from chick Grower's mash (Pfizer Company, Nigeria) and were given water *ad libitum* throughout the study period. Animals' weights ranged from 100 g to 200 g just before the commencement of the experiment.

Experimental design for Acute toxicity Study: The acute toxicity study was conducted in accordance with Lorke's method (Lork, 1983). The study was conducted in two phases using a total of sixteen male rats. In the first phase, nine rats were divided into 3 groups of 3 rats each. Groups 1, 2 and 3 animals were given 10, 100 and 1000 mg/kg body weight (b.w.) of the extract, respectively, to possibly establish the range of doses producing any toxic effect. Each rat was given a single dose after at least 5 days of adaptation. In addition, a fourth group of three rats was set up as control group and animals in the group were not given the extract.

In the second phase, further specific doses (1600, 2900 and 5000 mg/kg b.w.) of the extract were administered to three rats (one rat per dose) to further determine the correct LD_{50} value. The extract was dissolved in Phosphate buffered saline (PBS) solution and given via intraperitoneal route. All animals were observed frequently on the day of treatment and surviving animals were monitored daily for 2 weeks for signs of acute toxicity. Recovery and weight gain were seen as indications of having survived the acute toxicity. At the end of 14 days, all surviving rats were sacrificed and then autopsied at the Department of Veterinary Pathology A.B.U., Zaria, and the internal organs examined macroscopically for pathological changes compared to the control group. The weights of these organs were also taken and the mean organ-body weight ratios calculated and compared with those of the control group.

Statistical Analysis: The statistical analyses were carried out using statistical package for social sciences (SPSS- computer

package). Percentage organ-body weight ratios and rats' body weights were expressed as mean ± SD. Values in all groups were compared using the analysis of variance (ANOVA). For all analyses the level of statistical significance was fixed at $p<0.05$ (Murray, 1992).

RESULTS

The acute lethal study of ATA on rats (Table 1) shows that no animal died within 24 hours after treatment with the extract and the LD_{50} was greater than 5000 mg/kg b.w. Again, no death was recorded among all the dose groups throughout the two weeks experimental period. Observation: The LD_{50} > 500 mg / kg b.w. Furthermore, a dose-dependent weight loss occurred but the weight variations noticed among the extract-treated groups (Table 2) were not found to be significant ($p>0.05$) when compared with the control group. Table 3 gives the gross pathological features of some internal organs. Liver congested was seen in all rats treated with the extracts. This observation appears to be in harmony with the increased OBR values given in Table 4, though the values were not statistically significant ($p>0.05$).

TABLE 1. ACUTE LETHAL EFFECT OF AQUEOUS STEM EXTRACT OF *Terminalia avicennioides* ADMINISTERED INTRAPERITONEALLY (I.P) TO WHITE ALBINO RATS.

Experiment	Dose (mg/kg bw)	No Dead rats after 24hrs	Treated rats after 24 hrs
Phase-1*	10	0/3	0/3*
	100	0/3	0/3
	1,000	0/3	0/3
Control	0	0/3	0/3
Phase 2	1,600	0/1	0/1
	2,900	0/1	0/1
	5,000	0/1	0/1

(*Experiment was conducted in two phases; each dose group of phase-1 made up of 3 rats while those in phase 2 have 1 rat per group)

TABLE 2. EFFECT OF INTRAPERITONEAL ADMINISTRATION OF AQUEOUS EXTRACT OF *T. avicennioides* ON THE BODY WEIGHTS OF RATS DURING ACUTE TOXICITY EXPERIMENT.

Experiment	Dose (mg/kg b.w.)	Weight gain (g) (x ± SD)
Phase-1	10	43.84 ± 6.06b
	100	37.32 ± 9.65b
	1000	32.73 ±4.79b
Control	0	40.75 ±14.25b
Phase-2	1600	13.48
	2900	5.9
	5000	4.9

* Test of significance was done in rows. Same superscripts indicate no significant difference ($p > 0.05$).
Weight values in phase-2 (were $n<3$) were not compared due to absence of measure of variability.

TABLE 3. POST MORTEM RESULT FOR ACUTE TOXICITY OF AQUEOUS STEM EXTRACT OF *Terminalia avicennioides* ADMINISTERED INTRAPERITONEALLY (I.P) TO WHITE ALBINO RATS

Organ	Gross pathology observed			
	Dose (mg/kg b.w.)			
	0	10	100	1000
Liver	None	Congestion	Congestion	Congestion
Lungs	None	None	None	None
Kidneys	None	None	None	None
Heart	None	None	None	None
Spleen	None	None	None	None

TABLE 4. EFFECT OF INTRAPERITONEAL (I.P) TREATMENT WITH AQUEOUS EXTRACT OF *Terminalia avicennioides* ON PERCENT ORGAN-BODY WEIGHT RATIOS OF RATS AFTER THE ACUTE TOXICITY STUDY.

Organ	(%) Organ-body weight ratio						
	Dose (mg/kg b.w.)						
	10	100	1000	1600*	2900	5000	Control
Kidney	0.3600^{a} ±0.0265	0.3867^{a} ±0.0702	0.4300^{a} ±0.0000	0.3700	0.2900	0.31	0.3520^{a} ±0.0536
Liver	3.5667^{b} ±0.4726	3.5670^{b} ±0.6110	3.7000^{b} ±0.3536	4.900	3.4000	4.8	3.0400^{b} ±0.3362
Lungs	0.5100^{c} ±0.0721	0.7670^{d} ±0.0814	0.8100^{d} ±0.4240	0.5800	0.6000	0.86	0.7000^{d} ±0.1229
Spleen	0.4333^{c} ± 0.1007	0.7700^{d} ± 0.2476	0.3850^{c} ± 0.0636	0.3700	0.2700	0.39	0.3060^{c} ± 0.1036
Heart	0.3130^{e} ±0.0150	0.2870^{e} ±0.0150	0.29500^{e} ±0.0070	0.3800	0.3500	Dead	0.3040^{e} ±0.0321

*Test of significance was done in rows. Values (mean ± standard deviation) in the same row with different superscripts differ significantly ($p < 0.05$). Dose groups with single rat per group ($n<3$) were not compared due to absence of measure of variability.

DISCUSSION

The acute lethal effect of ATA on rats (Table 1) shows that no animal died within 24 hours after treatment with extract. The major signs of toxicity noticed within 24 Hours included difficulty in breathing, loss of appetite and general weakness. These signs were not seen in 10 mg/kg b.w. dose group but progressed and became increasingly pronounced as the dose increased towards 5000 mg/kg b.w. The LD_{50}, being greater than 5000 mg/kg b.w., is thought to be safe as suggested by Lork (1983). Again, the absence of death among rats in all the dose groups throughout the two weeks of the experimental seems to support this claim. Furthermore, the dose-dependent weight loss observed, were not found to be statistically significant ($p>0.05$) when compared with the control group (Table 2).

Liver congestion appeared to be the major gross pathology accompanying treatment of rats with aqueous extract of *T. avicennioides* (Table 3). This observation is in harmony with the increased OBR values given in Table 4, though the values were not statistically significant ($p>0.05$). When compared with aqueous extract of *Terminalia mollis* (Bulus, *et al.,* 2007), extracts from *Terminalia avicennioides* appears safer for usage in traditional medicine. It is possible that this variation is due to the quantitative variation of saponin in these plants as the toxic potential of *Terminalia mollis* was attributed to saponin in it (Bulus, *et al.,* 2007). Saponins are known to have deleterious haemolyzing effect on circulating erythrocytes (Igweh & Onabanjo, 1989; Sofowora, 1993) and their presence in aqueous extract of *Annona senegalensis* accounted for its low therapeutic index found against *T. brucei brucei* infection in mice (Igweh & Onabanjo, 1989). Again, liver congestion could be attributed, in part, to its role in biotransformation of xenobiotics. It is not clear why the administration of 100 mg/kg b.w., and not higher doses, increased the size of the spleen significantly.

Survey by Atawodi *et al.,* (2003) has shown that *Terminalia avicennioides* is one of the herbs commonly used to treat local diseases in Northern Nigeria. However, there are few scientific literatures to support this (Abdullahi, *et al.,* 2001; Bulus *et al*., 2006). To what extent ingestion of extracts from this plant will be toxic is yet to be ascertained.

From the results of this study, it is hypothesized that extracts of TA is safe for usage in traditional medicine. Higher doses should, however, be avoided and users should not rule out completely the possibility of chronic toxicity developing with the continual usage of aqueous extract of *T. avicennioides*. It is now left for the therapeutic dosage to be determined for clinical applications.

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