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Research Article

Evaluation of the Subchronic Toxicity of Seed Extract of *Datura Metel* Linn in Rats: A Psychoactive Substance

T. G. Okereke[1*], M. A. Dickson, E. C. Egwim[2], H. A. Muhammad[2], O. M. Onyeonoro[2]

[1]Department of Biochemistry, Ibrahim Badamasi Babangida University, Nigeria; [2]Department of Biochemistry, Federal University of Technology, Nigeria; 3Department of Biochemistry, Centre for the Right to Health, Nigeria

ABSTRACT

The seed and leaf of Datura metel known to contain the psychoactive substance atropine and scopolamine, also contain hyoscyamine which is classified as deliriants or anti-cholinergics used as hallucinogens. Most parts of the plant have been used over the years for both medicinal and psychoactive purposes. This study was aimed at evaluating the sub-chronic toxicity of the seed extract of Datura metel on selected liver and kidney parameters and Packed Cell Volume (PCV). Twenty rats were used for the subchronic study and were grouped into 5 groups of 4 rats each. Control group was administered 0.5 ml of normal saline while the other groups were orally administered 300, 1600, 2900 and 5000 mg/kg body weight of extract for 28 days. There was significant ($p<0.05$) reduction in PCV in all test groups when compared to the control group. The groups administered 1600, 2900, 5000 mg/kg bodyweight showed significant ($p<0.05$) increase in sodium, chloride and potassium. There was significant ($p<0.05$) increase in serum total and conjugated bilirubin, and aspartate aminotransferase in groups administered 300 and 1600 mg/kg bodyweight while the groups administered 2900 and 5000 mg/kg bodyweight showed significant ($p<0.05$) reduction. The findings from this study have demonstrated that seed extract of *D. metel* might be deleterious to the red blood cells and may affect liver and kidney function.

Keywords: Psychoactive substance; Hyoscyamine; Datura metel Linn; *D. stramonium*; Electrolytes

INTRODUCTION

Datura metel Linn is an annual shrub, grows erect with branches and glabrous herb sharing the sympodial growth of solanaceae attaining the height of 60 cm-100 cm [1]. Lamina is dentate, pointed petiole and asymmetric base [2] both the calyx and corolla are tubular and trumpet shaped about 26 cm long [3]. Fruits are capsules, round (1.25 inches in diameter), dehiscent and covered with blunt prickles or warts, usually pale green. The seeds have the highest alkaloid content compared to the flowers, stem, immature fruits and leaves [4]. The fruits and seeds have several uses; the spiny fruit is used to card cotton. Youths in some parts of Plateau State, Nigeria, who use it to perform rigorous work, have claimed that the water extract of the seeds alleviate pain. Seeds along with other substances are used as a remedy for the symptoms of madness based on homeopathic principle, and extract of seeds is said to be useful in eye diseases [4]. The seeds also constitute the potential source for hyoscine [4].

In Ayurvedic medicine, *D. Stramonium* which is another specie of Datura is described as a useful remedy for various human ailments including ulcers, wounds, inflammation, rheumatism, gout, sciatica, bruises and swellings, fever, asthma and bronchitis, toothache, etc. In the Hindu religion, the seed of *D. Stramonium* is believed to be associated with the God Shiva, which promotes misuse of the plant on religious occasions, such as Shivaratri and Swasthani Puja. The plant *Datura metel* Linn originated from India, but has been naturalized and become cosmopolitan in tropical Africa. In Nigeria, it occurs as a weed but sometimes cultivated.

The leaves and fruits are widely used in herbal medicine as anesthetic, antispasmodic, bronchodilator and as hallucinogenic [5]. *D. metel* is known as an anticholinergic, meaning it reduces spasms by blocking the transmission of nerve impulses [6]. Nigerians widely use its leaves in phytomedicine to cure diseases such as asthma, cough and convulsion [7]. All other parts of this plant such as leaves, seeds, roots and fruits are used worldwide for different purposes in medicine [2,8]. Many cases of unintent-

Correspondence to:TG Okereke, Department of Biochemistry, Ibrahim Badamasi Babangida University, Nigeria, E-Mail: tokereke3@gmail.com

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tional poisoning by *D. Stramonium* species have been reported when taken accidentally, or as decoction prepared from herbal prescription [9,10]. General symptoms of *D. Stramonium* poisoning include delirium, agitation and seizures, mydriasis, blurred vision, photophobia, dry mouth and mucous membranes, extreme thirst, tachycardia, nausea and vomiting, decreased bowel sounds, difficulty swallowing and speaking, hyperthermia, hypertension, loss of consciousness and coma [11]. Bouzidi A has reported that ingestion of *D. Stramonium* seed at concentrations of 0.5% or more in the diet produced adverse physiological changes in rats [12,13]. He reviewed the acute, subacute and chronic toxicity studies of alkaloids from the seeds of *D. Stramonium* 13]. According to Bouzidi A , single acute toxicity of 100 mg/kg *D. Stramonium* includes decreases in the weight of the liver, spleen and brain, and significant increases in the levels of red blood cells (RBC), hematocrit (HCT), hemoglobin (HGB), and white blood cells (WBC). Similarly, RBC, HGB, HCT and platelet levels were increased in 4 week subacute toxicity studies. However, the 120 day chronic toxicity study of *D. Stramonium* alkaloids showed decreased levels of RBC, HCT, HBG and WBC, with a significant increase in liver enzymes. Fatal dosages of *D. Stramonium* toxins occured with amounts exceeding 10 mg for adults, and 4 mg for children. The amount needed to poison an adult is about 20 seeds, and the estimated LD in an adult is >10 mg atropine or >2 to 4 mg scopolamine [14].

Although numerous studies have been conducted on abused drugs, most focus on the problems of addiction (dependence) and their neurotoxicities. He opined that commonly abused substances, including LSD, opiates (diacetylmorphine, morphine, opium and codeine), datura, cocaine, cannabis, betel quid and khat, are discussed for their potential genotoxicity/carcinogenicity [15]. The use of *Datura metel* as a psychoactive substance has been reported with little that is known about its toxicity especially against the gene. UNODC in 2010 reported increases in the abuse of *Datura metel* as a psychoactive substance. The plant substance has reportedly caused various health challenges including total or partial loss of sanity, coma and even death [4]. Young people resort to use of psychoactive substances to combat psychological issues such as depression, anxiety, fear of failure etc. However, some of these psychoactive substances have profound negative health effects. This study was aimed at evaluating the sub-chronic toxicity of the seed extract of *Datura metel* on selected liver and kidney parameters and Packed Cell Volume (PCV).

MATERIALS AND METHODS

Plant source

Datura metel pods were harvested from the plant which was located at Dutsen Alhaji, FCT, Abuja. The leave, pod, and stem of the plant sample was identified and authenticated at Nigerian Institute of Pharmaceutical Research and Development (NIPRD), Idu, Abuja with identification/voucher number NIPRD/H/6747. The samples were transported to a laboratory and kept at room temperature for cleaning, drying and extracting.

Animal model

Healthy albino rats of average weights between 150 g-180 g were purchased from small animal holding unit, Federal University of Technology, Minna, Niger State Nigeria. The rats were kept in clean plastic cages and maintained under standard laboratory conditions in the Biochemistry Laboratory, Federal University of Technology Minna to acclamatize for two weeks. They were allowed to feed on rat pellets and water ad-libitum.

Reagent and chemicals

Serum Aspartate transaminase (AST), Alanine transminase (ALT) and Total protein were evaluated using Randox Kit, (Randox Laboratories, USA), Total and Conjugated Bilirubin, Creatinine, Potassium, Chloride Agappa Test Kits (Agappe Diagnostics – Switzerland), while that of Sodium was done usings kits (Nums Diagnostics, Nigeria). Distilled water was used for all the washings, cleaning and preparation of solutions.

Sample preparation and extraction

The seeds were completely dried at room temperature and pulverized into coarse powder. The aqueous extract of the seed was prepared by soaking 100 g of pulverized seed of *D. metel* in 1000 ml distilled water (100 mg/ml) and stored at room temperature over a period of 48 hours. The soaked sample was then passed through rotary evaporator (Yamato, Rotary Evaporator, and Model-RE 801) for evapouration to dryness; a percentage yield of 39.43% was obtained after extraction and evaporation to dryness at 40°C. The weight of the residue was obtained. 1 g of the residue is dissolved in 10 ml of distilled water (100 mg/ml) and administered orally.

Acute toxicity study

The acute toxicity study was carried out using Lorke's method [16]. This involves a two-phase study. Phase 1: This phase requires nine animals. The nine animals were divided into three groups of three animals each. Animals in their respective groups were orally administered (10, 100 and 1000) mg/kg body weight of *D. metel* aqueous extract. The animals were placed under observation for 24 hours to monitor their clinical symptoms and mortality. Lack of mortality necessitated the second phase of the experiment. Phase 2: This phase involves three groups of 3 rats each that were orally administered (1600, 2900 and 5000) mg/kg bodyweight of the seed extract respectively. The animals were further observed for 24 hours for clinical symptoms and mortality.

Subchronic toxicity study

The subchronic study was carried out for twenty-eight days with twenty rats divided into five groups (A-E) of four animals each. Group A: (control) were administered 0.5 ml of normal saline. Group B: administered 300 mg/kg bodyweight of extract. Group C: administered 600 mg/kg bodyweight of extract. Group D: administered 3200 mg/kg bodyweight of extract. Group E: administered 5000 mg/kg bodyweight of body weight. The extract was orally administered to the rats for twenty-eight days after which the study was terminated. The rats were weighed prior for the

commencement of biochemical analysis.

Biochemical analysis

Haematological parameters: The PCV of rats were checked at three days intervals and before euthanizing using automated table top centrifuge for 5 minutes at 10,000 rpm.

Other biomakers: The experimental animals were fasted overnight their weights were measured. The rats were then euthanized through carotoid puncture and blood samples collected into both heparinized and non-heparinized laboratory tubes. The serum of the blood samples collected were separated using automated table top centrifuge for 5 minutes at 10,000 rpm. Serum Aspartate transaminase (AST), Alanine transminase (ALT) and Total protein were evaluated using Randox Kit, (Randox Laboratories, USA), Total and Conjugated Bilirubin, Creatinine, Potassium, Chloride Agappa Test Kits (Agappe Diagnostics Switzerland), while that of Sodium was done usings kits (Nums Diagnostics, Nigeria).

Statistical analysis

Results are presented as mean ± Standard deviation of mean (SD). Within groups comparisons were performed by the analysis of variance using ANOVA test (using SPSS 17.0 for windows Computer Software Package). Significant differences between groups were compared by Duncan's new Multiple Range test; a probability level of less than 5% ($P<0.05$) was considered significant.

RESULTS

There was no death recorded after the acute toxicity study. Rats administered 300 mg/kg bodyweight had highest bodyweight loss (-12.97 g) (Table 1).

There was reduction in PCV across all groups which are significant at ($p<0.05$) when compared to the control group. For ease of evaluation, the effect of *D. metel* on PCV was calculated using the initial PCV and the final PCV (Table 2).

For the renal function study, biochemical parameters such as urea, creatinine, sodium, potassium and chloride were evaluated using serum as presented in Table 3. The groups administered 300 and 5000 mg/kg showed significant increase ($p<0.05$) in serum urea concentration when compared the control group. There was no significant difference in serum creatinine concentration across all the groups when compared to the control. There was a dose dependent increase in serum concentration of sodium, potassium and chloride as groups administered 1600, 2900 and 5000 mg/kg showed significant increase ($p<0.05$) when compared the control group. For liver function study presented in Table 4, biochemical parameters such as Total and Conjugated bilirubin, Total protein, Aspartate and Alanine transaminases were evaluated. For serum concentration of Total and Conjugated bilirubin and Total protein, there was significant difference across all the groups when compared to control group. There was a significant increase ($p<0.05$) aspartate aminotransferase in groups administered 300 and 1600 mg/kg bodyweight while the groups administered 2900 and 5000 mg/kg bodyweight showed reduction (Tables 3 and 4).

Table 1: Effect of *D. metel* seed extract on weight of albino rat.

Groups (mg/kg)	Initial Weight (g)	Final Weight (g)	Weight (Diff.) (g)
Control	176.7 ± 3.36	182.44 ± 10.21	5.74 ± 13.61 b
300 mg	178.0 ± 2.9	165.03 + 6.23	-12.97 ± 9.86 a
1600 mg	170.3 ± 6.14	177.23 ± 2.05	6.99 ± 4.19 b
2900 mg	177.7 ± 3.72	186.12 ± 76.37	9.42 ± 79.99 b
5000 mg	174.2 ± 8.52	178.74 ± 69.42	4.54 ± 74.013 b

Table 2: Effect of *D. metel* seed extract on Mean PCV of albino rats.

Groups (mg/kg)	Initial PCV	Final PCV	% Change
Control	65.20 ± 13.04	67.20 ± 13.04	2.08 b
300 mg	68.80 ± 10.78	50.30 ± 10.78	26.89 a
1600 mg	60.50 ± 14.99	46.25 ± 14.99	23.55 a
2900 mg	70.80 ± 21.18	37.05 ± 21.18	47.67 c
5000 mg	72.33 ± 9.13	38.58 ± 9.13	60.83 c

Table 3: Effect of D. metel seed extract on serum Urea, Creatinine, Sodium, Potassium and Chloride concentration of albino rat.

Groups (mg/kg)	Total Bil. (mg/dL)	Conjugated Bil. (mg/dL)	Total protein (g/dL)	Aspartate transaminase (U/L)
Control (Normal saline)	1.20 ± 0.37 b	1.1 ± 1.15 b	5.0 ± 1.21 b	24.25 ± 3.38 b
300 mg	2.80 ± 0.71 c	1.7 ± 0.41 c	5.5 ± 1.14 b	34.25 ± 6.99 c
1600 mg	2.23 ± 0.81 c	1.4 ± 0.90 c	3.8 ± 1.83 a	31.88 ± 5.62 c
2900 mg	0.97 ± 0.23 a, b	0.6 ± 0.53 a	3.3 ± 0.61 a	23.67 ± 1.04 b
5000 mg	0.67 ± 0.64 a,	0.4 ± 0.53 a	3.4 ± 0.72 a	5.57 ± 2.64 a

Table 4: Effect of D. metel seed extract on serum Total and Conjugate bilirubin, Total protein, and Aspartate transaminase concentration of albino rat.

Groups (mg/kg)	Total Bil. (mg/dL)	Conjugated Bil. (mg/dL)	Total protein (g/dL)	Aspartate transaminase (U/L)	0.4 ± 0.53 a
Control (Normal saline)	1.20 ± 0.37 b	1.1 ± 1.15 b	5.0 ± 1.21 b	24.25 ± 3.38 b	0.4 ± 0.53 a
300 mg	2.80 ± 0.71 c	1.7 ± 0.41 c	5.5 ± 1.14 b	34.25 ± 6.99 c	0.4 ± 0.53 a
1600 mg	2.23 ± 0.81 c	1.4 ± 0.90 c	3.8 ± 1.83 a	31.88 ± 5.62 c	0.4 ± 0.53 a
2900 mg	0.97 ± 0.23 a, b	0.6 ± 0.53 a	3.3 ± 0.61 a	23.67 ± 1.04 b	0.4 ± 0.53 a
5000 mg	0.67 ± 0.64 a,	0.4 ± 0.53 a	3.4 ± 0.72 a	5.57 ± 2.64 a	0.4 ± 0.53 a

Table 5: Effect of *D. metel* seed extract on serum Alanine transaminase concentration of albino rat.

Groups (mg/kg)	Alanine transaminase (U/L)
Control (Normal saline)	19.75 ± 2.50 b
300 mg	26.63 ± 4.39 b
1600 mg	27.63 ± 2.93 b
2900 mg	22.80 ± 1.80 b
5000 mg	4.68 ± 2.47 a

DISCUSSION

Pyrazole carbohydrazidecompound as corrosion inhibitors for AA 8088 in a 1 M H2SO4 solution were investigated. For 1-(4-Methoxy-phenyl)-3-(5-phenyl-1,3,4-oxadiazol-2-yl) propan-1-one, their inhibition efficiency increased with increases in inhibitor concentration and they belonged to mixed-type inhibitors predominantly retarding the cathodic reaction. The inhibiting efficiencies determined by potentiodynamic polarization testing, and EIS measurements are all in good agreement. The surface morphologies images were good proof for the reduction of dissolution of AA 8088ascribed to the formation of protective Pyrazole carbohydrazidefilm on the metal surface.

CONCLUSION

The results of this study showed that *D. metel* may impair the functionality of the kidney and liver. The study also suggests that *D. metel* aqueous seed extract may have deleterious effect in the red blood cells. Abusing the substance extract of the seed of *D. metel* to achieve its psychoactive property may be harmful to the liver and kidney. Further studies however are needed to confirm the findings of this research and unravel the mechanism of action of *D. metel*, its impact on other organs, especially its impact on the integrity of the DNA. Though available literatures point that *D. metel* has ethnomedicinal properties.

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