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Renal Effects of *Mandragora officinarum* Leaf Extracts on Wistar Albino Rats

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Abstract

This study demonstrates the renal features of wistar albino rats exposed to *Mandragora officinarum* leaf extract. Twenty-four (24) rats were randomly divided into 4 groups labelled A, B, C and D and kept in a well-ventilated room. Group A served as control and these rats were treated with distilled water. Rats in the groups B, C, and D were treated with 3 different doses of the sample (1.5, 3.5 and 5.0mL/KgBW) respectively. Samples were administered once daily for 14 and 28days consecutively. Animals were sacrificed 24 hours after the last treatment. Blood samples were collected into heparinized sample bottles for analysis. Serum urea and creatinine concentrations increased in a dose dependent manner at all durations of administration. This increase was significant for urea at the dose of 5.0ml/kgBW when administered for 14 days. This trend was present at all doses for 28 days of administration. Histology done showed normal kidney tissue architecture at all doses of 14days of administration. All doses in the 28 days group showed abnormalities of destroyed renal tubules, absent glomeruli and occluded bowman's capsular spaces. This study demonstrates that long-term use of this leaf extract increases the risk of subacute kidney abnormalities.

Keywords: Renal toxicity *Mandragora officinarum* leaf extract.

INTRODUCTION

From the story of Leah and Rachel in the Bible to the strong relationship between mandrakes and witchcraft in the medieval times, it can be seen that this plant is one with a long history. The word 'mandrake' refers to the roots of a group of plants found either in the Mediterranean region (genus Mandragora) or an English version (genus Bryonia) (Wyk 2018). The most popular being the genus Mandragora and belonging to the nightshade family Solanacea (Al-Ahmad 2020). The roots of these plants especially *Mandragora officinarum* resemble the human body and has a long history of association with medical and mystical properties even until this day (Yaniv 2014).

Mandrakes are perennial herbaceous plants with long thick branched roots and almost no stem. They possess leaves that are variable in size and either elliptical or ovoid in shape. All Mandragora species contain poisonous alkaloids especially tropane alkaloids (Monadi *et al.*, 2020). These are found in both the roots and leaves and give anticholinergic, hallucinogenic and hypnotic features (Oncel and Erdemir 2017). Some clinical demonstrations of these features are blurred vision, dilated pupils, dry mouth, headache, vomiting, blushing, hyperactivity, rapid heart rate and hallucinations, amongst others (Al-Ahmad 2020).

In past times, the juice from either the root or leaves were used as anesthesia for surgery, to induce vomiting, as a purgative, to promote conception and to treat melancholy, mania and convulsions (Oncel and Erdemir 2017). It was also externally applied to relieve rheumatic pain in affected persons (Yaniv 2014). Mandrakes are still being used by neopagan worshippers such as wicca, to treat constipation, asthma, hay fever and convulsions (Yaniv 2014).

The kidney is indispensable in the metabolism and excretion of most substances (Oforibika and Uzor 2020). Medicinal plants like mandrakes that is used by some African traditional medicine practitioners exposes the essential organs of patients to possible injury (Oforibika *et al*., 2017; Oforibika and Oforibika 2020; Simoben *et al*., 2020). For this reason, this paper focuses on the effects of mandrake leaf extract on the kidney function and histology of some albino wistar rats.

MATERIALS AND METHOD

Plant collection and identification

Mandragora officinarum leaves were purchased from a traditional medicine practitioner at Okujagu town in Port Harcourt Local Government Area of Rivers State. The plant specimen was confirmed by a Botanist and fellow researcher.

Sample Preparation

The leaves were weighed, washed with distilled water and allowed to air dry. A new mortar and pestle were used to pulverize it and the sample was extracted with distilled water for 24hours at 35.0•C. The extracts were filtered using a Muslim cloth and concentrated using a rotary evaporator (Buchi-Rotavapor -R110) at a low pressure.

Specimen (animal) used for the experiment

Twenty-four (24) wistar albino rats with weights between 140-194g purchased from animal house of the Department of Biochemistry, University of Port Harcourt, Choba Park. The animals were fed with rat pellets, water ad libitum. All animal experiments were in accordance with the guideline stipulated by the National Institute of Health for Care and use of laboratory animals (Pub. No. 85: 23 revised 1985).

Chemicals and reagents: All chemicals and reagents used in this study were obtained from Randox Laboratories UK.

Preparation of Drug solution for administration: 1.5ml/kg, 3.5ml/kg and 5.0ml/kg of the preparation was given to the rats each day after weighing depending on their respective groups.

Experimental Procedure

A total twenty-four (24) albino rats of weight range (124-160g/BW) were randomly divided into four groups labelled A, B, C and D where group A served as control and rats (n=3rats/dose) were treated with distilled water. Rats in groups B, C and D (n = 3 rats/dose) were orally treated with 3 different doses of the leaf extract 1.5ml/kgBW, 3.5ml/kgBW and 5.0ml/kgBW for 14 and 28 days respectively. Animals were sacrificed twenty-four (24) hours after last treatment.

Collection of blood and preparation of serum

The rats were withdrawn from the cages in each of the group twenty-four (24) hours after the last administration of the drugs for 14 and 28 days and placed in a desiccator containing cotton wool soaked in chloroform to anaesthetize the rats. The blood samples were obtained by cutting the jugular vein of the rat on the neck by means of surgical blade and put in anticoagulant sample bottles smeared with lithium-heparin. The blood samples were spun at 5000rpm using MSE Centrifuge to obtain plasma. The animal was dissected and only the kidney was collected for pathological studies.

Measurement of Urea

10ul of distilled water was dispensed into an empty test tube while another test tube contains the standard solution with the third test tubes for the samples. Then 100ul of reagent I solution was added into the three test tubes, mix immediately and incubate at 37^0C for 10 minutes. 250 ml of reagent two was then added to the three test tubes, mixed thoroughly and incubated in a water bath at 37°C for 10 minutes. Absorbances of the sample and standard were measured against the blank at 546nm using a spectrophotometer.
Urea concentration = A Sample x (0.467mg) standard concentration

Determination of creatinine

Equimolar solution of picric acid and sodium hydroxide were mixed to form the working reagent stable. To the labeled test tubes, 50ul of distilled water, standard and working reagent was dispensed into 3 different curvettes. Then mixed and put into the Rix Monza flow cell holder and this is incubated at 37^oC to maintain temperature in the water bath. The 1^{st} reading was taken after 10minutes and labeled A1 being the first standard. Absorbance of A2 was measured against the blank at 520nm using a spectrophotometer after 5 mins. Then $A_2 - A_1$ = amount of creatinine in the standard. The same procedure was also carried out for the sample solution.

Calculation: Optical density of sample x Standard concept specified.

Histological procedures and analysis

The kidney was cut on slabs about 0.5cm thick and fixed in 10% normal saline for a day after which they were transferred to 70% alcohol for dehydration. The tissues were passed through 90% alcohol and chloroform for different durations before they were transferred into two changes of molten paraffin wax for 20mins each in an oven at 57%. Several sections of the 5µm thick were obtained from a solid block of tissue and were stained with hematoxylin and eosin staining after which they were passed through a mixture of equal concentration of xylene and alcohols, following clearance of xylene, the tissues were oven dried. Photomicrographs were taken with a JVC colour video digital camera (JVC China) mounted on an Olympus light microscope (Olympus UK Ltd Essex, UK) to demonstrate cytoarchitecture of the kidney.

RESULT AND DISCUSSION

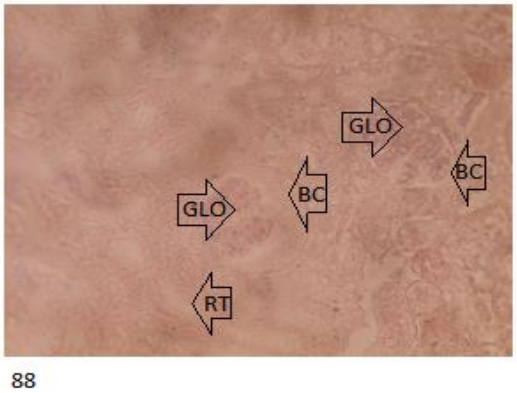
Table 1: Urea and Creatinine (mmol/l) results on 14 days of exposure

Extract volume (ml/kgBW)	Urea (mmol/l)	Creatinine (mmol/l)
Control (distilled water)	3.0±2.5	0.031±0.03
1.5	4.4	0.041
3.5	6.8	0.046
5.0	9.0	0.065

Table 2: Urea and Creatinine results on 28 days of exposure

Extract volume (ml/kgBW)	Urea (mmol/l)	Creatinine (mmol/l)
Control (distilled water)	3.0±2.5	0.031±0.03
1.5	10.2	0.066
3.5	10.9	0.082
5.0	14.2	0.093

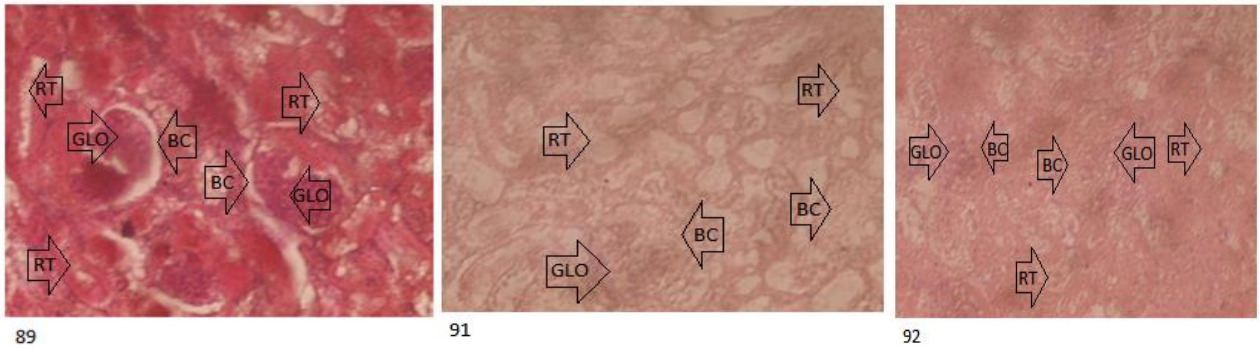
Histology



88

Figure 1: Control

Slide 88: photomicrograph of kidney tissue treated with distilled water showed normal tissue having glomeruli with tuffs made up of glomerular cells, mesangial matrix and glomerular capillaries. Glomeruli are surrounded by bowman's capsular spaces. Renal tubules are lined by simple epithelial cells (control).



89 91 92

Fig 2: Result for 14 days of administration

Slide 89: photomicrograph of kidney tissue treated with 1.5ml/kg showed histologically normal kidney tissue with normal glomeruli, renal tubules and patent bowman's capsular spaces.

Slide 91: photomicrograph of kidney tissue treated with 3.5ml/kg showed histologically normal kidney tissue with normal glomeruli, renal tubules and patent bowman's capsular spaces.

Slide 92: photomicrograph of kidney tissue treated with 5.0ml/kg showed histologically normal kidney tissue with normal glomeruli, renal tubules and patent bowman's capsular spaces.

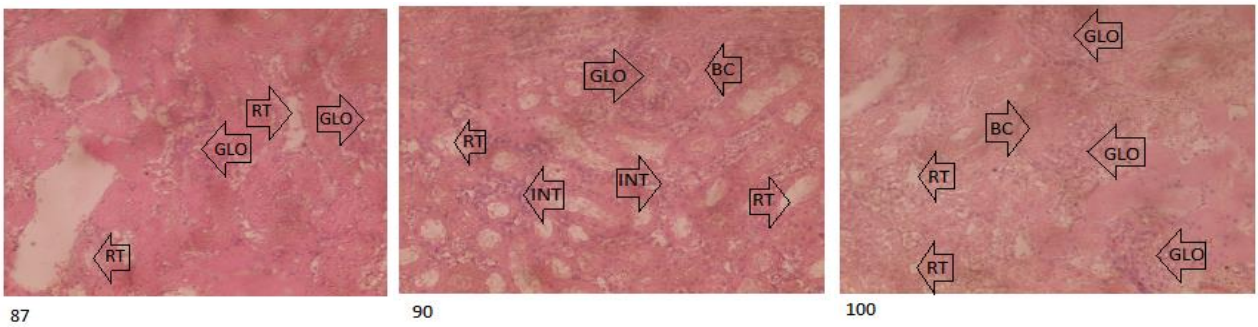


Fig 3: Result for 28 days of administration

Slide 87: photomicrograph of kidney tissue treated with 1.5ml/kg showed histologically distorted kidney tissue with glomerula tufts with no bowman's capsular spaces. Renal tubules are normal.

Slide 90: photomicrograph of kidney tissue treated with 3.0ml/kg showed histologically distorted kidney tissue with normal glomerula tufts and renal tubules. Interstitial tissue is infiltrated with inflammatory cells.

Slide 100: photomicrograph of kidney tissue treated with 5.0ml/kg showed histologically distorted kidney tissue with occluded bowman's capsular spaces.

Table 1 which represents 14 days of exposure, showed a progressive increase in both urea and creatinine with increasing concentrations of the samples given. In spite of this, this increase was not significant when compared to the control. The exception is the concentration of urea at 5.0ml/KgBW. This was significantly greater than control values.

Table 2 representing 28 days of administration showed a significant increase in all dosages for both urea and creatinine when compared to the control. This increase was more for urea than for creatinine.

Figure 2 showed normal histology of the kidney at all dosages of the leaf extract administered for 14 days. As shown in figure 3 at 28 days, there were changes in the histoarchitecture at all dosages. These changes were structural, seen as absent and/or occluded bowmans capsular spaces in slides 87 and 100 and also inflammatory, seen as inflammatory cells in slide 90.

The result above s hows evidence of kidney changes, both biochemical and histological. The changes seen were most significant at the highest dosages and periods of administration. This corresponds to the the study done by Alwirfi *et al*., 2021 and Tijani *et al.*, 2020. These were done on datura metel leaf extract, a plant in the same family as Mandrake officinarum. The results showed deleterious effects on the kidney and liver at all concentrations when used weekly. This is in line with this study where daily use of Mandrake officinarum leaf extract for prolonged durations showed greater adverse effects. This shows that longer periods of using large unregulated amounts of some of these medicinal plants have a real risk of causing kidney injury (Oforibika and Uzor 2020). This may initially be reversible but will inevitably progress to being irreversible as more of the structural components of the kidney are lost. This points to a problem noted with traditional medicine prescriptions and the use of medicinal plants (Moyo *et al*., 2015; Oguntibeju 2018). Patients are usually advised to use these prescriptions with unknown compositions for months to years on end (Oforibika and Oforibika 2020). As there is no way to monitor organ function without presenting to the hospitals patients are exposed to long periods with no effective monitoring.

CONCLUSION

Indiscriminate use of medicinal plants should not be condoned by regulatory bodies. The pharmaceutical industry and the traditional medicine industries should work hand in hand in researching to find out safe and effective prescriptions of these important plants.

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