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Hepatic Impact of *Mandragora officinarum* Leaf Extract on Wistar Albino Rats

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Abstract

This study evaluates the hepatic effects of *Mandragora officinarum* leaf extract on wistar albino rats. A total of twenty-four (24) rats were randomly divided into 4 groups labeled A, B, C and D and kept in a well-ventilated room. Group A served as control and these rats were fed distilled water. Rats in groups B, C, and D were given three (3) different doses of the leaf extract (1.5, 3.5 and 5.0 mL/KgBW) respectively. They were administered once daily for 14 and 28 days consecutively. Animals were sacrificed 24 hours after the last treatment. Blood samples were collected into heparinized sample bottles for analysis. Aspartate aminotransferase, Alanine aminotransferase and histology results were normal when the leaf extract was given for 14 days. Alkaline phosphatase significantly decreased within the same time interval. Alkaline phosphatase increased in a dose-dependent manner for 28 days. All other liver enzymes were within normal limits. Histopathological changes were seen in all doses when *Mandragora officinarum* leaf extract was used for 28 days. These changes also worsened with increasing doses. This suggests that the use of *mandragora officinarum* leaf extract for long periods at a time can cause hepatic damage.

Keywords

Mandragora officinarum, Hepatic, Leaf Extract

1. Introduction

Mandrake is one of the most important plants that have existed on earth, its usefulness cannot be over-emphasized as it has been applied in traditional and modern medicines. The cultural, ornamental and economic nature of mandrake is notable hence referred to as "the wonder plant". The word "mandrake" comes from Middle English, "mandrage" which refers to its roots that resemble the

human body and "drake" refers to "dragon" which alludes to its supposed mystical powers. Mandrakes are the root of a perennial herb found in the South of the Mediterranean, e.g. Croatia and Slovenia [1]. Mandrakes belong to the family Solana cea or the nightshades. The most common specie is *Mandragora officinarum*. The plant has a large taproot, almost no stem with simple leaves and five lobed flowers [2]. The fruits are yellow aromatic, poisonous and also called Devil's apples. All parts of mandrakes are poisonous but especially the leaves and the roots. Other common names are witch's drink, testes of the demon, and man's plant, amongst others [3].

Mandrakes have a long history of superstition. It was made into an amulet for good fortune and increased fertility, a hallucinogen, a narcotic, an anaesthetic, the juice from the root relieves rheumatic pains, treat convulsions, warts and mania [4] [5]. Some clinical features of excessive mandrake use include dizziness, asphyxiation, hallucinations, vomiting, and diarrhea [11]. Modern pagan religions such as the Wicca, Odinism, and African traditional religions use mandrake plants in rituals and treatments prescribed to patients [6] [7]. The liver is the biochemical powerhouse of the human body. It is the primary organ of detoxification and elimination of ingested substances [8] [9]. Mandrakes are medicinal plants used by African traditional medicine practitioners in their prescriptions [10]. There is not enough knowledge on its effects on organ functioning, as is the case with most medicinal plants [11] [12] [13]. This led the interest in this study on the biochemical and histological effects of mandrake leaf extract on the liver of wistar albino rats.

2. 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 24 hours 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) albino rats were purchased from animal house of the Department of Biochemistry, University of Port Harcourt, Choba Park. The animals were fed with rat pellets, water and libitum.

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

Preparation of drug solution for administration: 1.5 ml/kg, 3.5 ml/kg and 5.0 ml/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 (120 - 160 g/BW) were randomly divided into four groups labelled A, B, C and D where group A served as control and rats (n = 3 rats/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 1.5 ml/kgBW, 3.5 ml/kgBW and 5.0 ml/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 5000 rpm using MSE Centrifuge to obtain plasma. The animal was dissected and only the liver was collected for pathological studies.

Measurement of AST and ALT: The activities of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) was analysed according to the method specified by Reitman and Frankel (1957).

Measurement of ALP: Plasma alkaline phosphatise activity was measured by the method of Rec (1972).

Histological procedures and analysis: The liver was cut on slabs about 0.5 cm 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 20 mins each in an oven at 57%. Several sections of the 5 μm 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 liver.

3. Result and Discussion

Histology

Slide 72—photomicrograph of normal liver tissue treated with distilled water showed a sinusoid, central vein and hepatocytes arranged in cords and radiating away from the central vein (control).

Slide 73—photomicrograph of normal liver tissue treated with 1.5 ml/KgBW showed a sinusoid, central vein and hepatocytes arranged in cords and radiating away from the central vein.

Slide 76—photomicrograph of normal liver tissue treated with 3.5 ml/KgBW

showed a sinusoid, central vein and hepatocytes arranged in cords and radiating away from the central vein

Slide 77—photomicrograph of normal liver tissue treated with 5.0 ml/KgBW showed a sinusoid, central vein and hepatocytes arranged in cords and radiating away from the central vein

Slide 74—photomicrograph of histologically distorted liver tissue treated with 1.5 ml/KgBW showed dilated sinusoids containing congestion, congested central vein and normal hepatocytes.

Slide 75—photomicrograph of histologically distorted liver tissue treated with 3.5 ml/KgBW showed dilated sinusoids, congested central vein and normal hepatocytes.

Slide 86—photomicrograph of markedly distorted liver tissue treated with 5.0 ml/KgBW showed hepatocytes at different stages of steatosis and patent portal vein.

Table 1 represented 14 days of administering the leaf extract showed ALT and AST within normal limits as compared to the control. ALP was reduced at all dosages when compared to control. A general trend of increasing liver enzymes with increasing dosage was noted.

Table 2 showed liver enzymes that showed no significant changes when compared to the control.

Figure 1 served as the control which showed no change in liver histoarchitecture at all dosages when the mandrake leaf extract was administered.

Figure 2 showed no change in liver histoarchitecture at all dosages when the mandrake leaf extract was administered for 14 days. Figure 3 showed that increasing the duration to 28 days caused varying degree of abnormalities of liver structure. This was worse at 5.0 ml/kgBW which showed marked distortion and presence of steatosis. Wistar albino rats given 1.5 ml/kgBW and 3.5 ml/kgBW of the leaf extract showed dilated sinusoids and congested central veins.

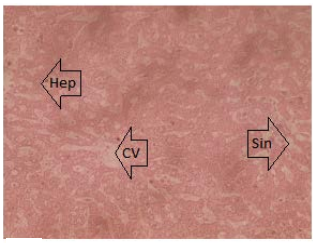
Aspartate aminotransferase and Alanine aminotransferase were within normal limits at both 14 days and 28 days of administration of the mandrake leaf extract. This is in contrast to Alkaline phosphatase which reduced during 14 days of extract administration but was significantly elevated for 28 days of administration. There was also a general trend of elevated results as dosage increased, even if not significant.

Table 1. Liver enzymes (U/l) results on 14 days of exposure.

Extract volume (ml/kgBW)	Aspartate Aminotransferase (AST U/l))	Alanine Aminotransferase (ALT U/l))	Alkaline Phosphatase (ALP U/l))
Control (distilled water)	100 ± 10	25 ± 8	50 ± 10
1.5	76	18	17
3.5	103	32	20
5.0	111	41	21

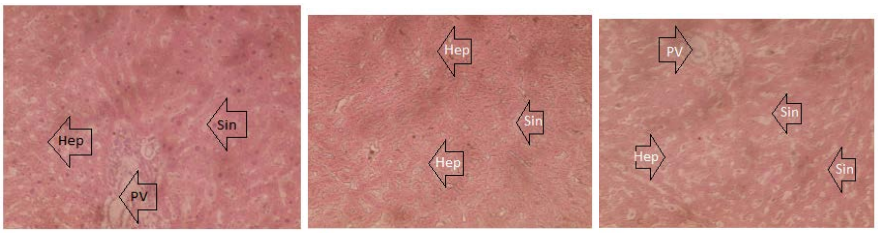
Table 2. Liver enzymes (U/l) results on 28 days of exposure.

Extract volume (ml/kgBW)	Aspartate Aminotransferase (AST U/l))	Alanine Aminotransferase (ALT U/l))	Alkaline Phosphatase (ALP U/l))
Control (distilled water)	100 ± 10	25 ± 8	50 ± 10
1.5	104	32	59
3.5	106	35	73
5.0	115	38	77



72

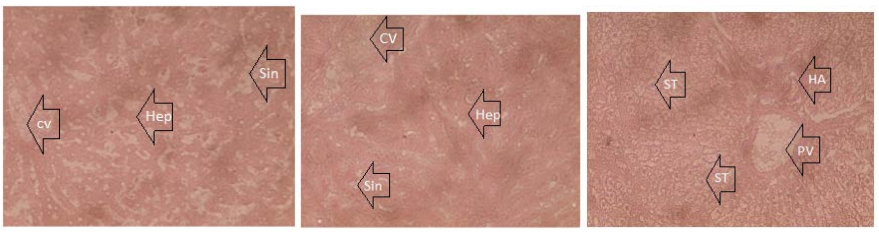
Figure 1. Control.



73 76 77

x2

Figure 2. Result for 14 days of administration.



74 75 86

x2

Figure 3. Result for 28 days of administration.

Histology results showed that even if the liver biochemical markers of inflammation were normal, structural abnormalities have already set in in the liver. This was more obvious as the extracts were used for longer periods, irrespective of the dosage.

Aspartate aminotransferase and Alanine aminotransferase are biochemical tests used to monitor for hepatocyte injury while Alkaline phosphatase tends to suggest injury to the biliary tract. Short term results showed features of Alkaline

phosphatase reductions. This caused the researchers to suspect the presence of micronutrient deficiencies developing with the use of this plant. Important micronutrients for Alkaline phosphatase activity include Zinc and Magnesium. On the other hand, Alkaline phosphatase increased in the long term which suggests biliary injury. This suggests that prolonged use may lead to cholestasis developing. This is in contrast to the study done by [13] on *Datura metel*, a member of the Solanacea family and also rich in tropane alkaloids as *Mandragora officinarum*. There were no changes in liver enzymes even with background histology changes.

This research shows that in the long-term, mandrake leaf has deleterious histological effects that are visible on the liver. This is in line with the result of [13] and Tijani *et al.* 2021 on a fellow member of the Solanacea fanily. Their studies showed increased liver pathologies on histology with increasing dosage and duration of use. Most clients of traditional medicine practitioners use these prescriptions made of medicinal plants for very long periods without review or monitoring of normal organ functioning [14] [15]. All these will be best avoided if the medical and dental council of Nigeria better regulates these traditional medicine practitioners. Also, these practitioners should partner with pharmaceutical companies to produce safe forms and durations for the use of their medications.

4. Conclusion

Medicinal plants can be dangerous with indiscriminate use. These plants should be safely processed to avoid subacute organ damage. However, the research has also shown that in the long-term, mandrake leaf has deleterious histological effects that are visible on the liver, therefore, there is the need for proper regulations and monitoring of the relevant practitioners or agencies by the regulators for best standards, practices and administrations.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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