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HISTOLOGICAL AND BIOCHEMICAL EFFECT OF GRADED DOSES OF *PHOENIX DACTYLIFERA* ON THE LIVER OF MALE WISTAR RATS

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ABSTRACT

Various parts of *Phoenix dactylifera* (Date palm) are used in traditional medicine to treat various disorders such as fever, abdominal troubles, etc. This study evaluated the histological and biochemical effects of graded doses of ethanolic extract of *Phoenix dactylifera* on the liver of adult male wistar rats. Dried fruit were pulverized, and the ethanolic extract obtained after soaking in ethanol for 48hrs. Twenty adult male wistar rats weighing between (188.00±4.89) were used for the study. They were distributed into four groups (A, B, C & D) of five animals each. Group A served as the control, groups B, C & D served as the treated groups and were orally administered 100 mg/kg, 200 mg/kg and 300 mg/kg of the extract for fourteen days. At the end of the experiment, the animals were sacrificed, blood samples collected and liver harvested for examination. There was significant increase in body weights of the rats at the end of the experiment. Significant increase was observed in serum AST level of the treated groups when compared with the control. Histological findings revealed cytoarchitectural changes in the treated groups. In conclusion, this study indicated that high doses of the *P. dactylifera* could result in hepatic damage.

KEYWORDS: *Phoenix dactylifera;* liver enzymes; liver.

INTRODUCTION

Phoenix dactylifera L. (date palm) is known to be one of the oldest cultivated trees in the world.[1] It is a monocotyledonous woody perennial belonging to the *Arecaceae family*, which comprises 3000 species and 200 genera.[2] Date fruits are a significant component of the diet in the majority of the Arab countries with low cost. Dates are of religious value to Muslims and they usually break their long day fasting with dates in the month of Ramadan.[3-5] Food and Agriculture Organization (FAO) reported Saudi Arabia as the second producer of dates in the world.[6] *Phoenix dactylifera* consist of three essential parts: flesh which constitutes between 85% to 90% of the fruit weight[7], seed or pit which constitutes about 6 to 12% of the total weight of the mature fruit and skin which is a thin layer surrounding the fruit to protect the fleshy part.[2,8,9]

Disorders of the liver have raised a great concern in public health with high endemicity in developing countries.[10,11] Hepatotoxic chemicals damage liver cells by inducing lipid peroxidation and other oxidative damages.[11,12] Liver plays an essential role in transforming and clearing metabolites and xenobiotics, and is susceptible to the toxicity from these agents.[13] This study evaluates the histological and biochemical effect of the liver following administration of graded doses of ethanolic extract of *phoenix dactylifera* in adult male wistar rats.

MATERIALS AND METHODS

Experimental Animals

Twenty (20) male Wistar rats weighing between 180-200 g were procured from the animal's house of the Department of Anatomy, Nnamdi Azikiwe University Anambra State, Nigeria. Ethical clearance was obtained from the ethical committee of the college for animal care and use, Nnamdi Azikiwe University which is in compliance with the National regulation for animal research. They animals were kept in wire gauze cages under normal temperature and fed with guinea feed and water *ad libitum*. They were allowed to acclimatize for a period of two weeks before administration.

Preparation of the fruit extract

Fresh fruits of *P. dactilfera* were purchased from a local market and were identified at the herbarium unit of Botany Department, Nnamdi Azikiwe University. The fruits were washed with water to remove dirt, cut into pieces and dried under room temperature. The dried fruits were grounded using manual blender into coarse powder. 400 g of the coarse powder was macerated in

four (4) litres of ethanol for 72 hours and then filtered using a clean white cloth. The filtrate was concentrated using a rotary evaporator which was further dried using a laboratory oven into a gel-like form.

Acute Toxicity Test (LD_{50})

Acute toxicity test described by Lorke[14] was carried out on fruits of *P. dactilfera*. A total of thirteen rats were used. Three groups of three rats each were used in the first phase and were administered 10 mg/kg, 100 mg/kg and 1000 mg/kg of ethanolic extract of the fruit of *P. dactilfera* orally. The rats were observed for mortality for 24 hours. After 24 hours no mortality was recorded and the second phase commenced. Four groups of one rat each were administered with 1200 mg/kg, 1600 mg/kg, 2900 mg/kg and 5000 mg/kg of ethanolic extract of the fruit of *P. dactilfera* respectively. The animals were observed for 24 hours for mortality. LD_{50} was calculated using the formula:

$$LD_{50} = \sqrt{(a \times b)}$$

Where, a = Highest dose that gave no mortality

b = Lowest dose that produced mortality

Study design

The twenty rats were randomly divided into four (4) groups of five rats each designated as groups A, B, C and D. The administration was given as follows;

GROUP A served as the control and received 2 ml/kg body weight of distilled water

GROUP B received 100 mg/kg body weight of ethanolic extract of the fruit of *P. dactilfera*.

GROUP C received 300 mg/kg body weight of ethanolic extract of the fruit of *P. dactilfera*.

GROUP D received 600 mg/kg body weight of ethanolic extract of the fruit of *P. dactilfera*.

The administration was given orally, once daily between the hours of 10 am and 12 pm for a period of 30 days. The animals were weighed on the 31st day, sacrificed by cervical dislocation and dissected. Incision was made in the abdominal and thoracic cavity to expose its contents. Blood samples were collected via cardiac puncture using sterile syringes and put in tubes without anticoagulant. The blood samples were then centrifuged at 3,000rpm for 10minutes using bench top centrifuge (MSE, Minor, England). Analysis on blood serum Alanine Transaminase (ALT), Aspartate Transaminase (AST), and Alanine Phosphatase (ALP) level were determined using the methods of Reitman and Frankel [15]. The livers of the rats were harvested and fixed in 10% formal saline for histological examination.

Statistical Analysis

Data was analyzed with one way Analysis of Variance (ANOVA) and students't-test, with values expressed as Mean ± SEM (Standard Error of Mean). This was achieved with the use of Statistical Package for Social Sciences (SPSS) software (V20, USA). The results were considered statistically significant at $P<0.05$ level of significance.

RESULT

LD_{50} of ethanolic extract of *P. dactilfera* fruit

There was no record of mortality during the acute toxicity test up till 5000mg/kg. No signs of toxicity like restlessness or seizures were observed.

Table 1: Phases of the acute toxicity level test of *P. dactilfera.*

	Dosage mg/kg body weight	Mortality
Phase I		
Group 1	10	0/3
Group 2	100	0/3
Group 3	1000	0/3
Phase II		
Group 1	1200	0/1
Group 2	1600	0/1
Group 3	2900	0/1
Group 4	5000	0/1

Body Weight

The result in Table 2 shows a significant increase ($P<0.05$) in the body weight in groups B and C when compared to the control. However, there was no significant difference ($P>0.05$) in the body weight of group D animals.

Table 2: Effect of ethanolic extract of fruit of *P. dactilfera* on body weight.

		MEAN	±SEM	P-VALUE	T-VALUE
Group A	Initial	100.00	±0.00		
	Final	182.50	±2.50	0.000*	-33.000
Group B	Initial	200.00	±0.00		
	Final	250.00	±4.08	0.001*	-12.247
Group C	Initial	137.50	±12.50		
	Final	242.50	±11.08	0.011*	-5.681
Group D	Initial	250.00	±0.00		
	Final	265.00	±6.45	0.103	-2.324

*$P<0.05$, **$P<0.001$

Levels of AST, ALT and ALP

Table 3 below shows a significant increase ($P<0.05$) in AST level in all treated groups when compared to control. However, there was no significant difference ($P>0.05$) in ALT and ALP levels in the treated groups when compared to the control.

Table 3: Effect of ethanolic extract of fruit of *P. dactilfera* on liver enzymes.

		Mean	±sem	P-value	F-value
Aspartate Transaminase (U/L)	Group A (Control)	48.66	±0.33		
	Group B (100 mg/kg of *P. dactilfera* fruit)	77.33	±0.33	0.000*	324.102
	Group C (300 mg/kg of *P. dactilfera* fruit)	71.67	±1.67	0.000*	
	Group D (600 mg/kg of *P. dactilfera* fruit)	92.00	±1.00	0.000*	
Alanine Transaminase (U/L)	Group A (Control)	29.00	±0.33		
	Group B (100 mg/kg of *P. dactilfera* fruit)	28.67	±0.00	0.580	0.611
	Group C (300 mg/kg of *P. dactilfera* fruit)	29.33	±0.66	0.282	
	Group D (600 mg/kg of *P. dactilfera* fruit)	29.08	±0.33	1.000	
Alkaline Phosphatase (U/L)	Group A (Control)	150.67	±1.37		
	Group B (100 mg/kg of *P. dactilfera* fruit)	152.66	±2.00	0.506	1.106
	Group C (300 mg/kg of *P. dactilfera* fruit)	151.67	±0.67	1.000	
	Group D (600 mg/kg of *P. dactilfera* fruit)	153.67	±0.33	0.156	

*P<0.05, **P<0.001

Histopathological Findings

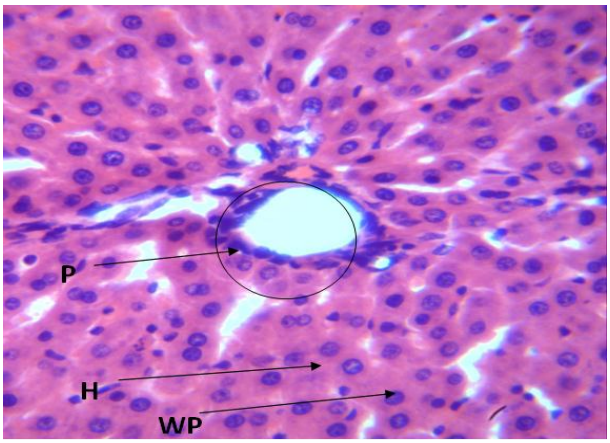

Plate A: Photomicrograph of the liver section of control showing normal hepatic architecture with well perfused cytoplasm (WPC) hepatocyte (H) and portal triad (PT).

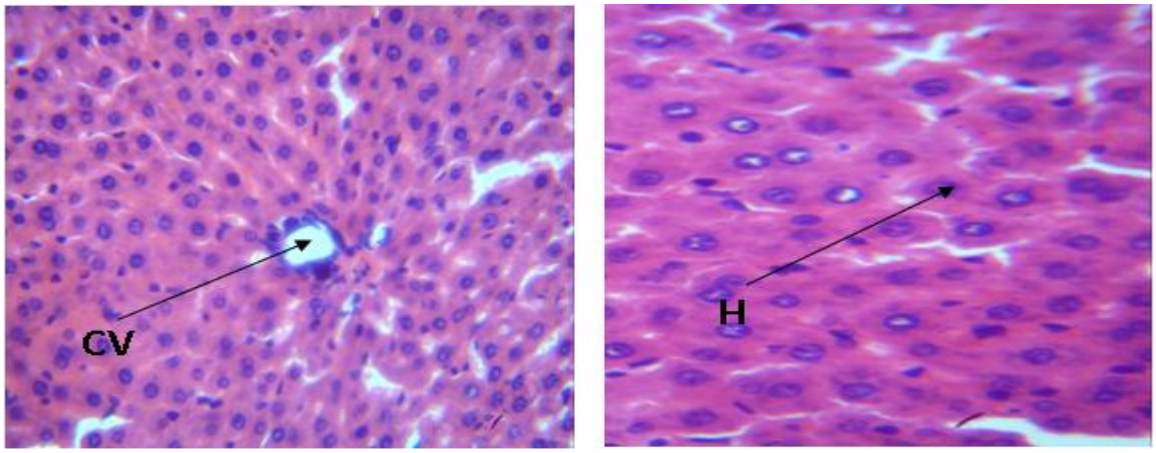

Plate B: Photomicrograph of the liver section of group B showing normal hepatic architecture with well perfused cytoplasm (WPC) hepatocyte (H) and central vein(CV).

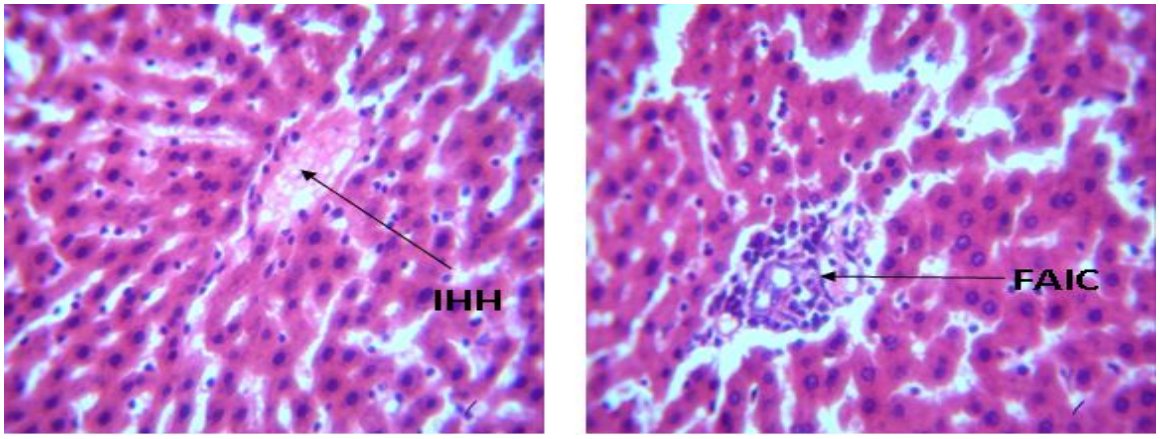

Plate C: Photomicrograph of the liver section of group C showing well perfused hepatic tissue with intra hepatic hemorrhage (IHH) and focal aggregate of inflammatory cell (FAIC).

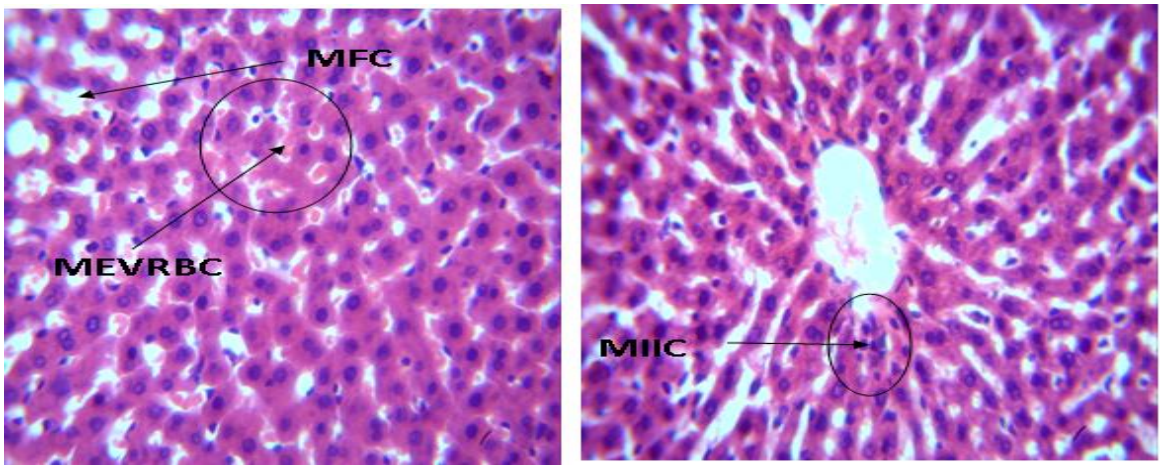

Plate D: Photomicrograph of the liver of group D showing well perfused hepatic tissue with moderate extra vasation of red blood cell (MEVRBC), Mild infiltration of inflammatory cell (MIIC) and mild fatty change (MFC).

DISCUSSION

Changes in body weight have been used as an indicator of adverse effect of drugs and chemicals.[16] The results from the body weights of the treated groups suggests that ethanolic extract of *P. dactylifera* fruits had no effect on the normal growth of the Wistar rats.[17] The extract was well tolerated by the animals when administered orally, no signs of toxicity like restlessness or seizures were observed during treatment. The absence of death in the groups of rats treated with the extract, even at 900 mg/kg body weight suggests that the extract is practically non-toxic acutely and is safe in when consumed.[18,19]

Histological analysis of the liver revealed changes in the liver architecture after the extract was administered at a higher dose. This corroborates the results of the activities of the enzyme AST which was significantly increased in the treated groups when compared to the control. An elevated level of the enzymes indicates damage to the liver tissues and cells where the enzymes are found.

CONCLUSION

Findings from this research indicate that high doses of the *P. dactylifera* could result in hepatic damage. It is recommended that the extract of *P. dactylifera* should be taken moderately and at lower doses.

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