



Effects of *Phoenix dactylifera* Tree Fruit Extract on Cadmium Induced Renal Damage in Adult Wistar Rats

*EHIMIGBAI, ROA; NWOSU, F

Department of Anatomy, University of Benin, Benin City, Edo State, Nigeria

*Corresponding Author Email: agbonluai.ehimigbai@uniben.edu

Other Authors Email: chinonsoyosuwu621@yahoo.com

ABSTRACT: The objective of the study is to investigate the ameliorative potential of date palm tree (*Phoenix dactylifera*) fruit on cadmium induced kidney damage in adult Wistar Rat using standard technique. Thirty (30) adult Wistar rats were divided into six groups of five rats per group. Group A (control); Group B (0.1ml/kg body weight of cadmium); Group C (200mg/kg body weight of *Phoenix dactylifera*); Group D (600mg/kg body weight of *Phoenix dactylifera*); Group E (0.1ml/kg body weight of cadmium and 200mg/kg body weight of *Phoenix dactylifera*); Group F (0.1ml/kg body weight of cadmium and 600mg/kg body weight of *Phoenix dactylifera*). Treatments were administered once daily for 30 days. After day 30, biochemical and histopathological studies were conducted to appraise oxidative stress and renal toxicity. Serum levels of creatinine, urea, catalase (CAT) and superoxide dismutase (SOD) were quantified. Animals treated alone with cadmium (Group B), showed significant ($P < 0.05$) increase in serum urea, serum creatinine and CAT, SOD levels statistically. Treatment of rats with *Phoenix dactylifera* alongside cadmium (Group E and F) showed significant ($P < 0.05$) improvement in renal function and restoration of biochemical parameters mentioned earlier. Histopathological findings confirm these conservations. Therefore, the administration of aqueous extract of *Phoenix dactylifera* has protective effect on cadmium-induced renal toxicity and oxidative stress in wistar rats which can be attributed to *Phoenix dactylifera* antioxidant activity.

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The liver is the target organ for cadmium during acute intoxication, while kidney becomes the target organ when chronic cadmium intoxication arises (Brzoska *et al.*, 2003; Casalino *et al.*, 2002). Cadmium is very toxic and is an essential pollutant in soil, water and food (Jarup *et al.*, 1998). It is mainly used in the industry for coating steel, glass and plastics (Tsalev and Zaparianov, 1993).

The chronic cadmium exposure in human appears to result in nephrotoxicity, pulmonary emphysema, liver dysfunction (Berghlund *et al.*, 2000; Goyer and Cheria, 1995; Rikans and Yamano, 2000; Shaikh *et al.*, 1999). Date palm tree (*Phoenix dactylifera* L.) is an important crop, which is cultivated in many countries extending from North Africa to the Middle East (Allaith, 2008). Dates palm are chemically composed of sugars (81–88%, mostly fructose, glucose, and

sucrose), dietary fiber (~ 5–8.5%) and a small amount of protein, ash, and high quantities of phenols (Elleuch *et al.*, 2008). It is also scientifically proved to possess immunomodulatory, vascular protective, and sex hormone modulator effects. (Chaira *et al.*; 2009, Rahmani *et al.*; 2014, Wittenborg *et al.*; 1998). *In vitro* antioxidant activity of the date fruit is demonstrated in many studies based on its phenolic compounds with potent free radical scavenging activity. (Vayalil, 2002, Pagliano *et al.*, 2004). The date palm fruit has been used in remedies for the treatment of infectious diseases and cancer (Puri *et al.*, 2007).

The objective of the study is to investigate the ameliorative potential of date palm tree (*Phoenix dactylifera*) fruit on cadmium induced kidney damage in adult Wistar rat using standard technique.

*Corresponding Author Email: agbonluai.ehimigbai@uniben.edu

MATERIALS AND METHODS

The fruits date palm (*Phoenix dactylifera*) was procured from the village market in Ikhin town in Owan East local Government Area of Edo state. The fruit, date palm (*Phoenix dactylifera*) was placed in an open place but away from direct sunshine for two (2) weeks, so that it will air dry. It was matched by mortar, pestle and macerated into a chromatographic jar separately for 24hrs with distilled water. Whatman paper was used to separate the filtrate from the residue. The filtrate was concentrated to a paste level using water bath at 100°C and was preserved in a sample bottle inside a refrigerator (-4°C) until needed.

Thirty (30) adult wistar rats weighing between 200-260g were used for this study. The rats were purchased and bred in the animal house of the Department of Anatomy, University of Benin, Benin City, Edo State. The rats were allowed to acclimatize for two weeks, they were fed with growers mash Topfeeds feed manufactured by Bendel Feed Flours Mill Ltd. Plc. The animals were exposed to natural room temperature and lighting conditions and were handled according to standard protocols for the use of laboratory animals (National Institute of Health Guide for care and Use of Laboratory Animals).

Experimental design: The rats were randomly selected and distributed evenly into six groups A, B, C, D, E, and F with five rats per group. Each group was kept in a separate cage.

Table 1: Showing the various groups of experimental animals and their dosage of date palm (*Phoenix dactylifera*) extract and cadmium.

GROUPS	DOSAGE
CONTROL	Normal diet and distilled water
B	0.1ml/kg of Cadmium only
C	200mg/kg of Date palm only (Imo et al 2018)(low dose)
D	600mg/kg of Date palm only (high dose)
E	0.1ml/kg of Cadmium + low dose of date palm 200mg/kg
F	0.1ml/kg of Cadmium + high dose of date palm 600mg/kg

Daily administration of date palm and cadmium were given through an orogastric tube for 30 days. At the end of the experimental period (at day 30) the animals were grossly observed for general characteristics. The rats in each group were re-weighed to determine their final weight using a top loader weighing balance, and it was observed that the food consumption of the control group increased significantly throughout the study period. Similarly, an increase in body weight was also observed in the control group. The food consumption of the experimental rats (group B) decreased during the treatment with cadmium. This

reduction was accompanied by a significant decrease in body weight. A midline incision was made through the anterior abdominal wall of the rats under mild anesthesia using chloroform. The kidney were excised, fixed in formalin in readiness for routine histological procedure and weighed using the high precision weighing balance. The tissues were dehydrated in ascending grades of alcohol (ethanol), cleared in xylene and embedded in paraffin wax. The deparaffinized sections were stained routinely with hematoxylin and eosin. The slides were then examined under light microscope for pathological lesions. Photomicrographs were taken at x100 and x400 magnifications using a photomicroscope (LEICA microscope DM, 350; with DIGITAL CAMERA).

Superoxide dismutase (SOD) activity was determined by the method of Nishikimi *et al.*, 1972

The activity of catalase (CAT) was assayed by the method of Aebi (1984), creatinine was determined according to Henry *et al.* (1974). Urea was determined according to Tietz (1995).

Data was reported as means \pm SEM. The statistical analysis was performed using the Graph-pad prism statistical software version 5.0. Unpaired Student t-test was used to compare the dependent variable against the independent variable. The level of significance was set at $P < 0.05$.

RESULTS AND DISCUSSION

The mean values of serum urea, creatinine, SOD and CAT concentration following the administration of cadmium and date palm extract on Wistar rats is presented in Table 1. Cadmium is one of the pollutants on the earth. Casalino *et al.* (2002) demonstrated that SOD activity is strongly inhibited by cadmium, probably by interacting with metal moieties of SOD (Cu, Zn, or Mn) and thus reducing its activity. It is indicated that cadmium-induced elevation in lipid peroxidation is not only due to the inhibition of the activity of the superoxide dismutase (SOD) but also due to the direct action of Cd²⁺ on the peroxidation reaction (Hussain *et al.*, 1987).

Their results is in accordance with our study where we discovered that cadmium causes significant decrease in the level of SOD and CAT as depicted in group B biochemical results when compared with control group A.

In another study, Al-Qarawi *et al* 2008 discovered that antioxidant components in the date (e.g. melatonin, vitamin E and ascorbic acid) were suggested to be the basis of the nephro protection.

Table 2: Showing the mean values of serum urea, creatinine, SOD and CAT concentration following the administration of cadmium and date palm extract on Wistar rats.

Parameters	Group A (Control)	Group B	Group C	Group D	Group E	Group F
Serum urea concentration (mg/dl)	27.60 ± 1.60	74.40 ± 0.54*	32.80 ± 0.36	33.20 ± 0.32	33.20 ± 0.36	38.40 ± 0.75*
Serum creatinine concentration (mg/dl)	0.40 ± 0.09	2.48 ± 0.16*	0.56 ± 0.08	0.60 ± 0.09	0.63 ± 0.06	1.04 ± 0.08*
SOD(unit/mg protein)	10.12 ± 1.43	88.65 ± 0.30	14.01 ± 0.79	11.89 ± 0.65	15. ± 51±0.04	18.21± 0.10
CAT(unit/mg protein)	24.42± 1.40	61.11± 0.61*	17.52± 0.75	14.20 ± 0.42	17.22± 0.05	19.41± 0.93

**P* < 0.05 indicates significant difference when other groups are compared with group A (control).

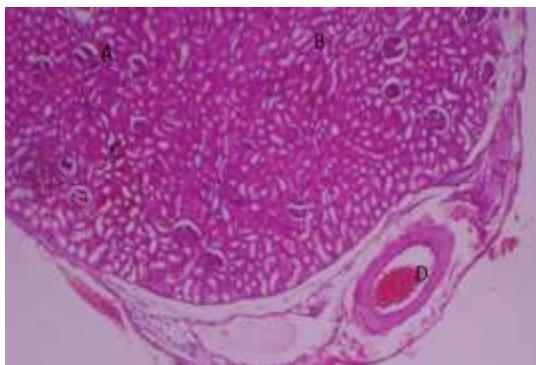


Fig.1 Control: Rat kidney composed of A, glomeruli, B, tubules, C, interstitial space and D, artery (H&E x 40)

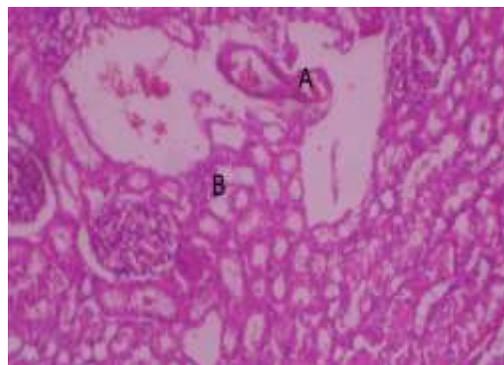


Fig. 4: Rat kidney given Cadmium only showing A, severe vascular stenosis and obstruction and B, focal tubular necrosis (H&E x 100)

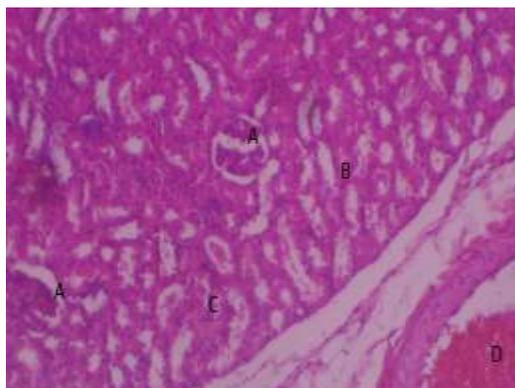


Fig. 2 Control: Rat kidney composed of A, glomeruli, B, tubules, C, interstitial space and D, artery (H&E x 100)

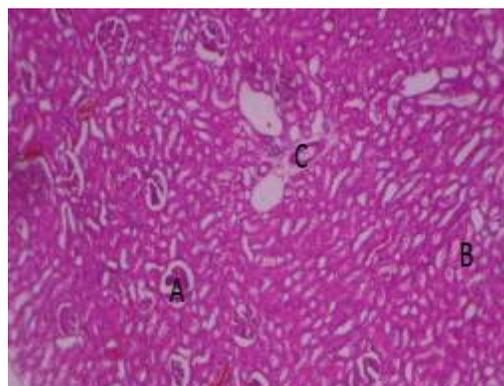


Fig. 5: Rat kidney given low dose Date palm showing A, glomeruli, B, tubules and C, normal vessel (H&E x 40)

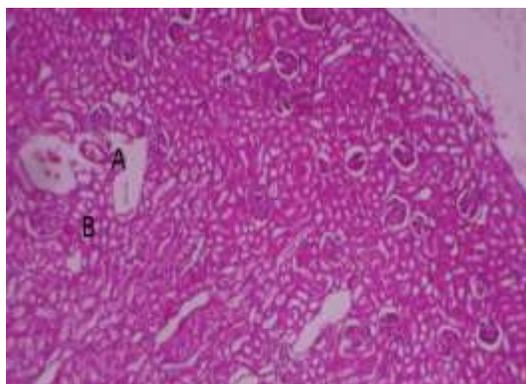


Fig. 3: Rat kidney given Cadmium only showing A, severe vascular stenosis and obstruction and B, focal tubular necrosis (H&E x 40)

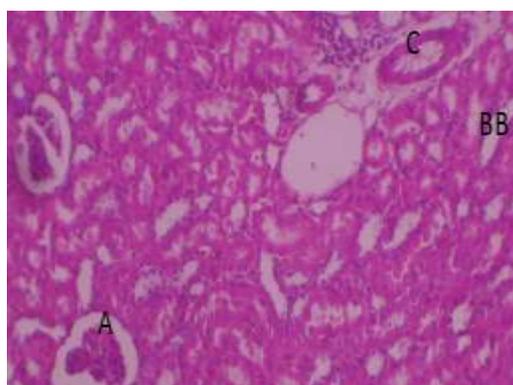


Fig.6: Rat kidney given low dose Date palm showing A, glomeruli B, tubules C, normal vessel (H&E x 100)

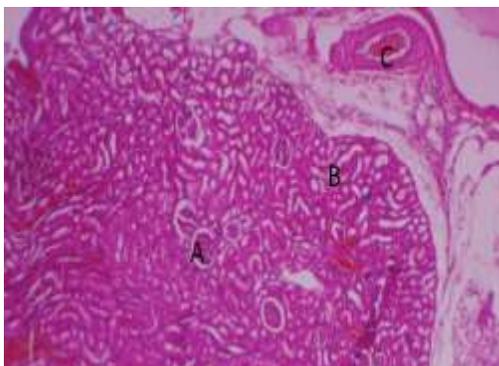


Fig. 7: Rat kidney given high dose Date palm showing A, glomeruli B, tubules and C, normal vessel (H&E x 40)

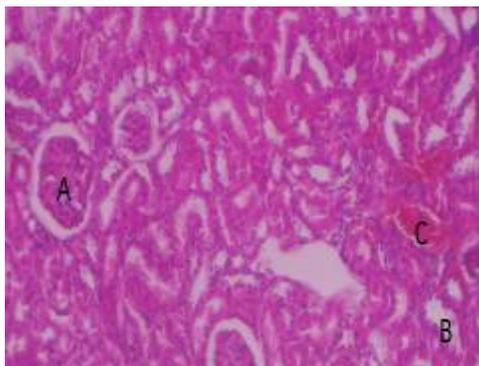


Fig. 8: Rat kidney given high dose Date palm showing A, glomeruli B, tubules and C, normal vessel (H&E x 100)

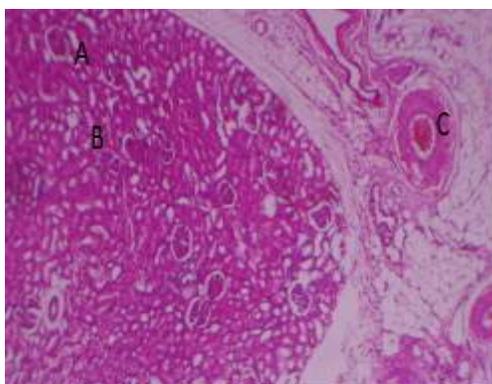


Fig. 9: Rat kidney given Cadmium plus low dose Date palm showing A, normal glomeruli, B, tubules and C, vascular architecture (H&E x 40)

Furthermore, Pujari *et al.*, 2011 evaluated the neuroprotective effect of *P. dactylifera* against bilateral common carotid artery occlusion, they discovered that rats pretreated with methanolic extract of *P. dactylifera* fruits at a dose of 30, 100 and 300 mg/kg for 15 consecutive days showed high level of recovery from all depletion induced by ischemia in GSH levels and SOD and CAT activities at a dose of 100 and 300 mg/kg, while no significant changes were recorded at the low dose 30 mg/kg (Pujari *et al.*, 2011). This observations support our biochemical

results in groups A, C, D, E and F where we discovered that there were significant elevation in serum value of SOD and CAT. Our result therefore revealed the antioxidant potential of *phoenix dactylifera* in ameliorating cadmium damaged effect in the renal tissue biochemically.

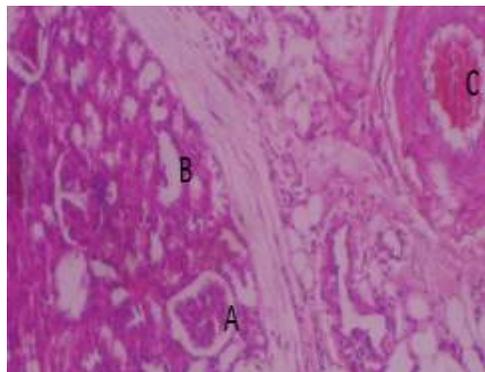


Fig. 10: Rat kidney given Cadmium plus low dose Date palm showing A, normal glomeruli, B, tubules and C, vascular architecture (H&E x 100)

Cadmium also affects the renal function when exposed to the environment (Templeton and Liu, 2010). The serum levels of creatinine and urea were significantly increased after cadmium administration (group B) when compared to control group, indicating the impairment in the kidney function. Similar observation was obtained by Ashraf *et al.*, 2007. They stated that impaired glomerular filtration in their cadmium study may occurs due to increases in serum urea and creatinine, thereby leading to renal toxicity.

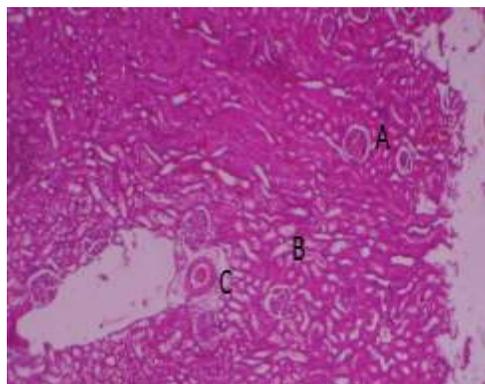


Fig.11: Rat kidney given Cadmium plus high dose Date Palm showing A, normal glomeruli, B, tubules and C, blood vessel (H&E x 40)

Also, serum level of creatinine and urea were significantly in the normal range in the groups that were given high dose of date palm only (group D), low dose of date palm only (group C), high dose of date palm plus cadmium (group E), low dose of date palm plus cadmium (group F) when compared to control group (group A).

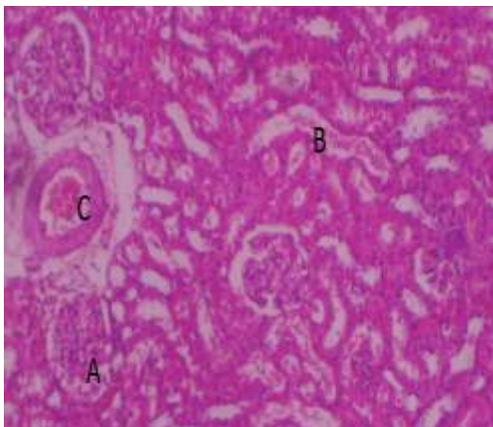


Fig.12: Rat kidney given Cadmium plus high dose Date Palm showing A, normal glomeruli, B, tubules and C, blood vessel (H&E x 100)

These results are in accordance with previous studies done by Marah, 2015 and El Arem *et al.*, 2014. Marah 2015 examined the effect of lead acetate exposure on serum concentration of creatinine and urea in rats. They concluded that date palm has the potential to counteract the toxic effect of lead acetate associated with improvement of renal histology and serum concentration of creatinine and urea. El Arem *et al.*, 2014 stated that date palm play key role to maintain normal level of blood urea and creatinine. Histologically, the photomicrograph of the experimental group (B) given cadmium only showed altered kidney architecture i.e. the renal corpuscles were highly affected (there was dilatation and swelling of the glomerular capillaries) accompanied with narrowing of the urinary spaces (focal tubular necrosis) and severe vascular stenosis when compared to the control group. The result is supported by previous work done by Jonah *et al.* They concluded that chronic accumulation of cadmium in blood may affect the kidney and causes renal injury. (Jonah and Bhattacharya, 1998; Oner *et al* 1996).

Furthermore, histological results in group A,C,D,E and F (figure 1,2,5,6,7,8,9,10,11, and 12) in our study, are in accordance with previous studies done by Saafi-Ben *et al.*, 2012. They investigated the antioxidant activity of date palm on dimethoate induced renal damage and they revealed that date palm extract and vitamin C significantly reduced lipid peroxidation, restored the antioxidant defense enzymes in the renal tissue, and improved the histopathology changes. They therefore concluded that date palm fruit may be helpful for the prevention of oxidative stress-induced renal toxicity. Also, Al -Qarawi *et al.*, 2008 investigated the effect of extract of the flesh of *Phoenix dactylifera* on gentamicin induced nephrotoxicity in rats. They noticed that the *Phoenix dactylifera* flesh were effective in reducing the

increases in plasma creatinine and urea concentrations that was induced by gentamicin and also ameliorating the proximal tubular damage of the kidney.

Conclusion: It can be concluded that *Phoenix dactylifera* fruit extract was able to ameliorate the structural damage caused by cadmium on the renal tissue of an adult Wistar rat.

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