PROGRESS IN MEDICAL SCIENCES, 2018
VOL 2, NO. 1, PAGE 1 – 8
DOI: doi.org/10.47363/PMS/2018(2)116

ORIGINAL ARTICLE

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A sub-acute toxicity study to assess the effects of methanol extract of date palm fruit on kidney functions in adult Wistar rats

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ABSTRACT

Background: *Phoenix dactilifera* (PD) has been used as a medicinal remedy for swollen limbs, aching legs, cough, sneezing, and acceleration of hair growth. Although studies have suggested the beneficial aspects of this agent to human health, it is not yet clear of the dosage that may become detrimental.

Methods: Twenty adult albino rats divided into four groups of five rats each were used in this experiment. Methanol extract of PD was orally administered at doses of 4, 8, and 16 mg/kg to groups 2, 3, and 4, respectively, while group 1 (control) received distilled water. After 8 hours, blood was collected from the animals for the assessment of packed cell volume, serum urea, creatinine, glucose, potassium, chloride, and sodium. The data generated were expressed as the mean ± standard error of mean. The means were compared with Student's *t*-test and analysis of variance with a *p*-value of 0.05 considered statistically significant.

Results: In all parameters analyzed, kidney function was improved only at doses of 4 and 8 mg/kg, which was attributed to the antioxidant and free radical scavenging properties of PD. A higher dose of 16 mg/kg significantly increased the K^+ (36.0 ± 4.5/22.6 ± 2.3 mEq/l) and serum urea (32.0 ± 3.8 mg/dl/25.2 ± 1.4 mg/dl) concentrations when compared with the control but other parameters measured were unchanged. These revealed that high doses of PD might impair normal renal functions.

Conclusions: It was, therefore, concluded that methanol extract of PD fruit improved kidney functions at doses of 4 and 8 mg/kg and that at 16 mg/kg, PD might be deleterious to the kidney by impairing urea and potassium excretion.

ARTICLE HISTORY

Received October 23, 2018
Accepted December 20, 2018
Published December 28, 2018

KEYWORDS

Phoenix dactilifera (PD); urea; creatinine; electrolytes; glucose; packed cell volume (PCV)

Introduction

Date palm [*Phoenix dactilifera* (PD)] is a plant in the genus *Phoenix* and belongs to the family Arecaceae cultivated for its edible sweet fruit. Morton [1] and Al-Alawi et al. [2] explained that although the origin of the plant is unknown because of long cultivation, it probably could have its origin from lands around the Persian Gulf. Date palm fruit or its juices were reported to be used in ancient Egypt in many medicinal remedies, such as treating swollen limbs and aching legs, cough, sneezing, acceleration of hair growth, and the likes [1–3]. In more contemporary times, the pharmacological properties of this plant have been investigated and reported to have anti-ulcer activities [3]. Another report by Arshad et al. [4] also stated that it had anticancer activities, while the anti-diarrheal activity was demonstrated by Abdulla and Al-Taher [5]. More recently, Salim [6] observed that date palm pollen has the ability to counteract the toxic effects of lead acetate with improved renal histological features, as well as a serum concentration of urea and creatinine. Saafi-Ben et al. [7] reported that date palm fruit extract significantly reduced lipid peroxidation and restored antioxidant defense enzymes in the kidney and improved the histopathology changes in the kidney of rats, in which oxidative stress and nephrotoxicity were induced by dimethoate. Although studies have suggested the beneficial aspects of date palm to human health and that of the kidneys, it is not yet clear of the

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dosage that may become detrimental to health and its possible effects on the kidney in health. Therefore, assessing the wellness of the kidneys involves carrying out renal function tests which include assessment of serum concentrations of some ions which are useful in assessing kidney functions as explained by Traynor et al. [8]. Packed cell volume (PCV) is carried out mainly to measure the percentage of red blood cells (RBCs) in the blood. It could be influenced by the same factors that can affect the kidneys' production of erythropoietin, which is a measure factor for erythropoiesis (formation of RBC). This experiment was, therefore, carried out to investigate the effects of PD on kidney functions of adult Wistar rats with the view of establishing its possible physiological effects on the kidney and clarifying the dosage at which it may be harmful to renal health.

Materials and Methods

Collection and preparation of plant material

The fruits were bought from the local market in Benin City and authenticated by the Forest Research Institute of Nigeria, Ibadan, where a herbarium specimen FHI 108336 was deposited. The fruits were oven-dried at 50°C and grounded into the powdered form using an electric blender. About 2 kg of the fruit was macerated with 4.5 l methanol for 72 hours at room temperature with occasional shaking and stirring. It was then filtered and the filtrate concentrated to dryness using rotary evaporator at 40°C.

Experimental animals

Twenty adult albino Wistar rats weighing between 150 and 240 g were obtained from the animal facility of the Department of Anatomy, University of Benin. The animals were housed within the facility and fed with standard rat pellet, they were allowed to acclimatize for 14 days before the commencement of the experiments. The rats were randomly placed into four groups of five animals each. Group 1 (control) was administered distilled water, groups 2, 3, and 4 received PD at doses of 4, 8, and 16 mg/kg, respectively, with the aid of an orogastric cannula and were kept in separate cages for 8 hours and thereafter sacrificed with inhalational anesthesia using chloroform. The blood was collected through cardiac puncture with the aid of a needle and 5 ml syringe and placed in properly labeled heparinized and Ethylenediamine tetraacetic acid (EDTA) bottles. A portion of the collected blood samples was analyzed for PCV, while the remaining was centrifuged to separate serum for the investi-

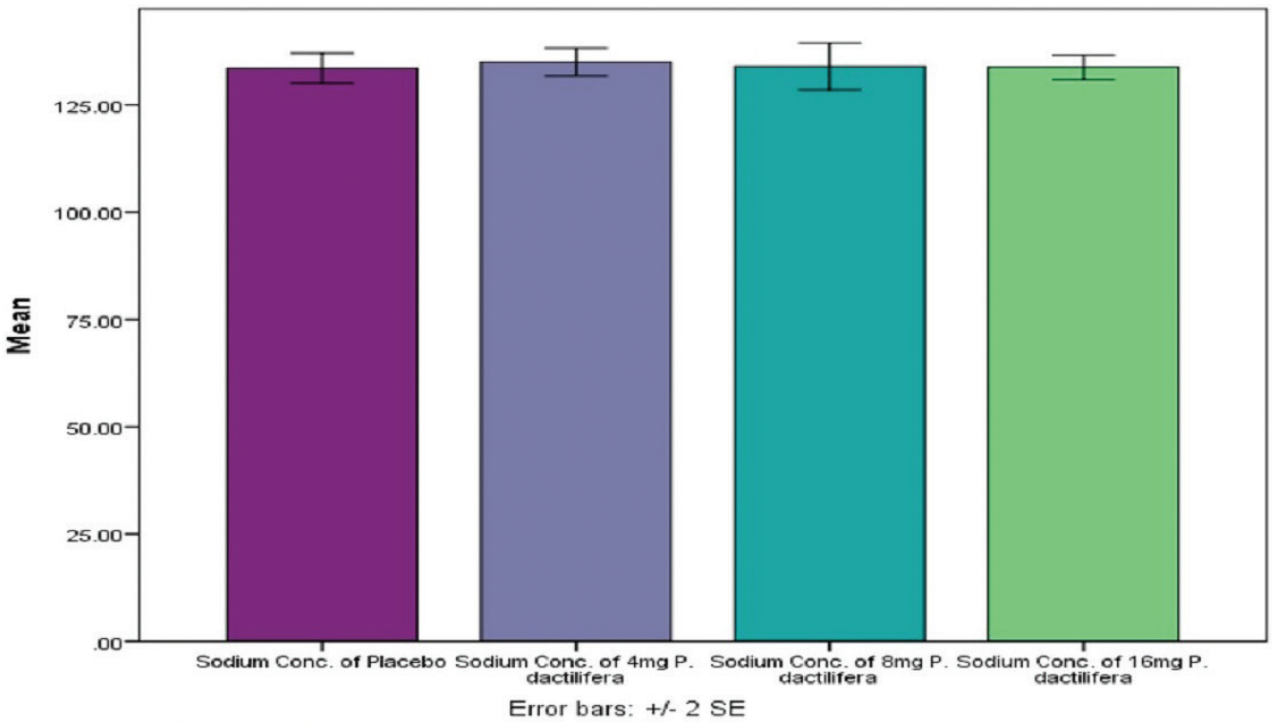

Figure 1. A graph showing the mean values of sodium ion.

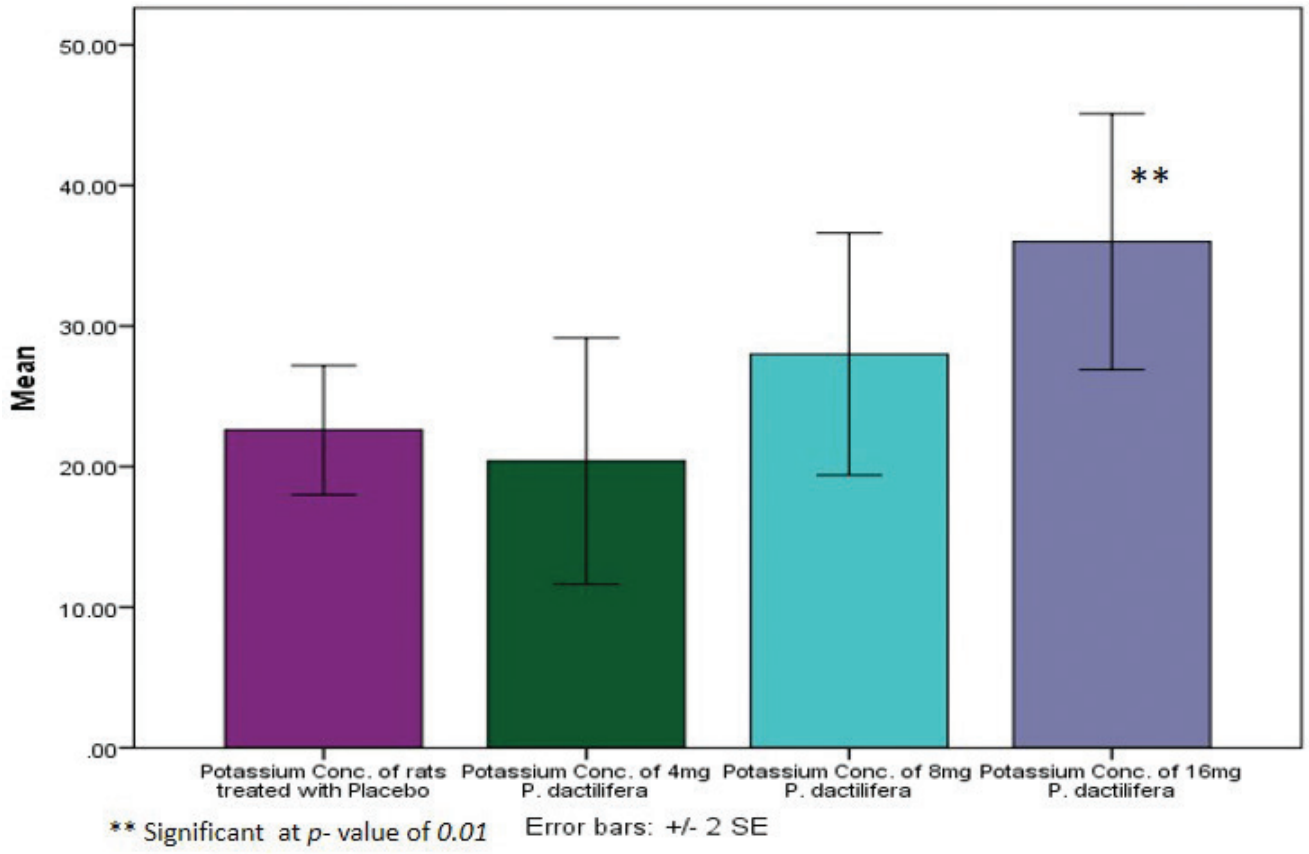

Figure 2. A graph showing the mean values of potassium ion.

gation of serum concentration of sodium, chloride, potassium, creatinine, urea, and glucose.

Statistical analysis

The data were analyzed with the use of IBM SPSS for Windows version 21. The data generated were expressed as the mean ± standard error of mean and were represented in bar charts and error bars. The means were compared with Student's *t*-test and analysis of variance with a *p*-value of 0.05 and 0.01 considered statistically significant.

Ethical clearance

Approval for this study was obtained from the Research Ethics Committee of the Faculty of Medicine, University of Benin, Nigeria and was carried out in strict adherence with the Institutional and National guidelines for the care and use of animals for research.

Results

The result of this study is presented in Figures 1–6, respectively. There was no significant difference in the serum sodium and chloride ion concentration of the group (Figs. 1 and 3) but the potassium concentration in the group treated with 16 mg/kg was significantly higher than that of the control at a *p*-value of 0.01 (Fig. 2).

The serum creatinine of group treated with 4 mg/kg of the extract was significantly lower than that of the control (Fig. 4). Urea concentration in groups treated with 4 and 8 mg/kg was also significantly lower than the control, while that of the group treated with 16 mg/kg was significantly higher than the control (Fig. 5).

The result also shows a significant reduction in blood glucose levels in the treated groups 3 and 4 (Fig. 7), while the PCV of groups treated with 4 and 8 mg/kg was significantly higher than the control (Fig. 6).

Discussion

In the present study, there was a significant increase in serum potassium in group 4 (Fig. 2), which could have resulted from the high potassium content of this plant. Al-Shahib and Marshall [9] earlier reported that potassium was as high as 0.9% in fruit flesh of PD. This may have influenced the increase in potassium

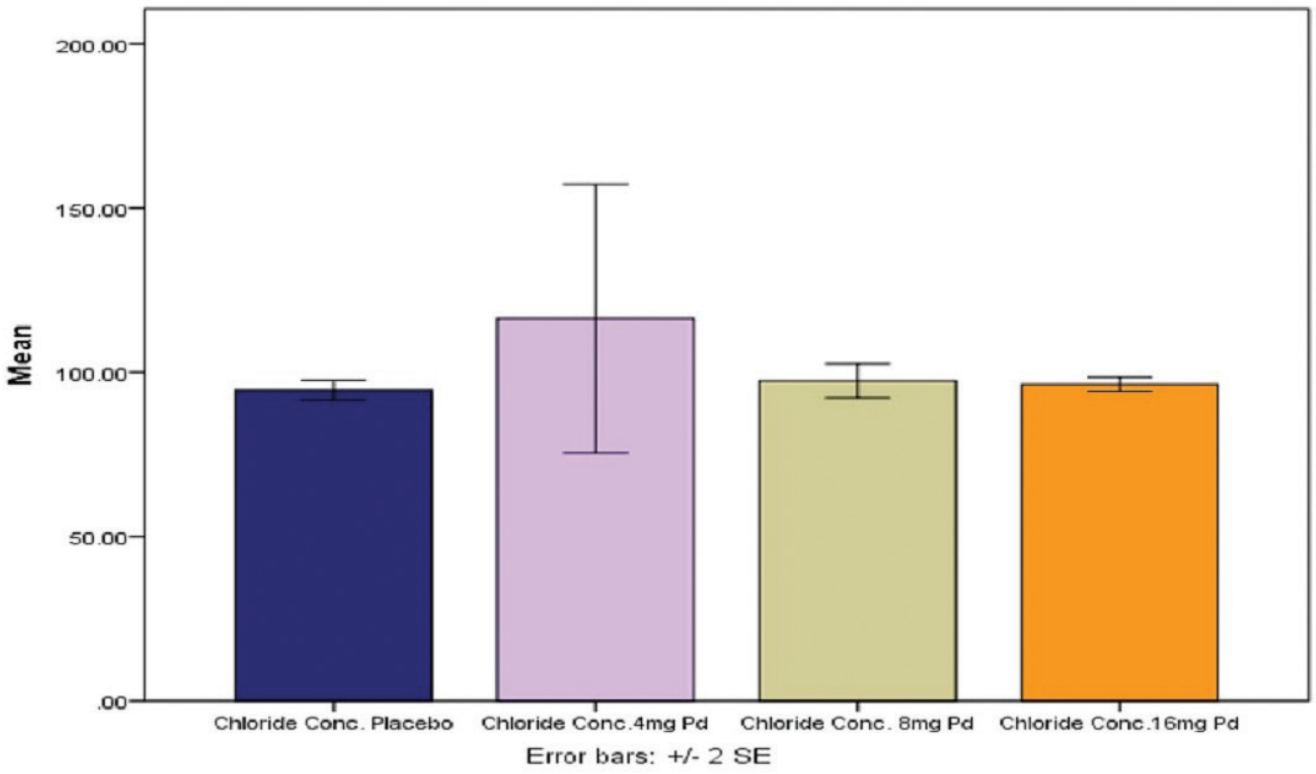

Figure 3. A graph showing the mean values of chloride ion.

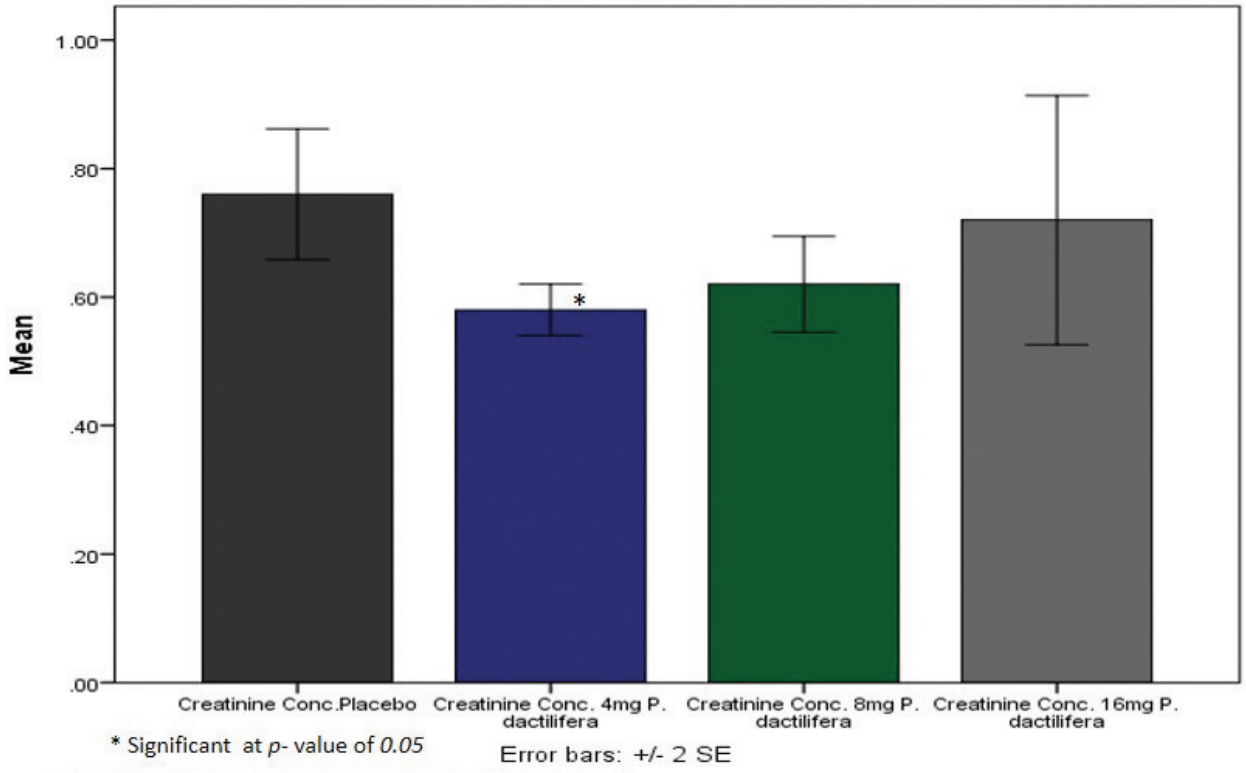

Figure 4. A graph showing the mean values of Creatinine.

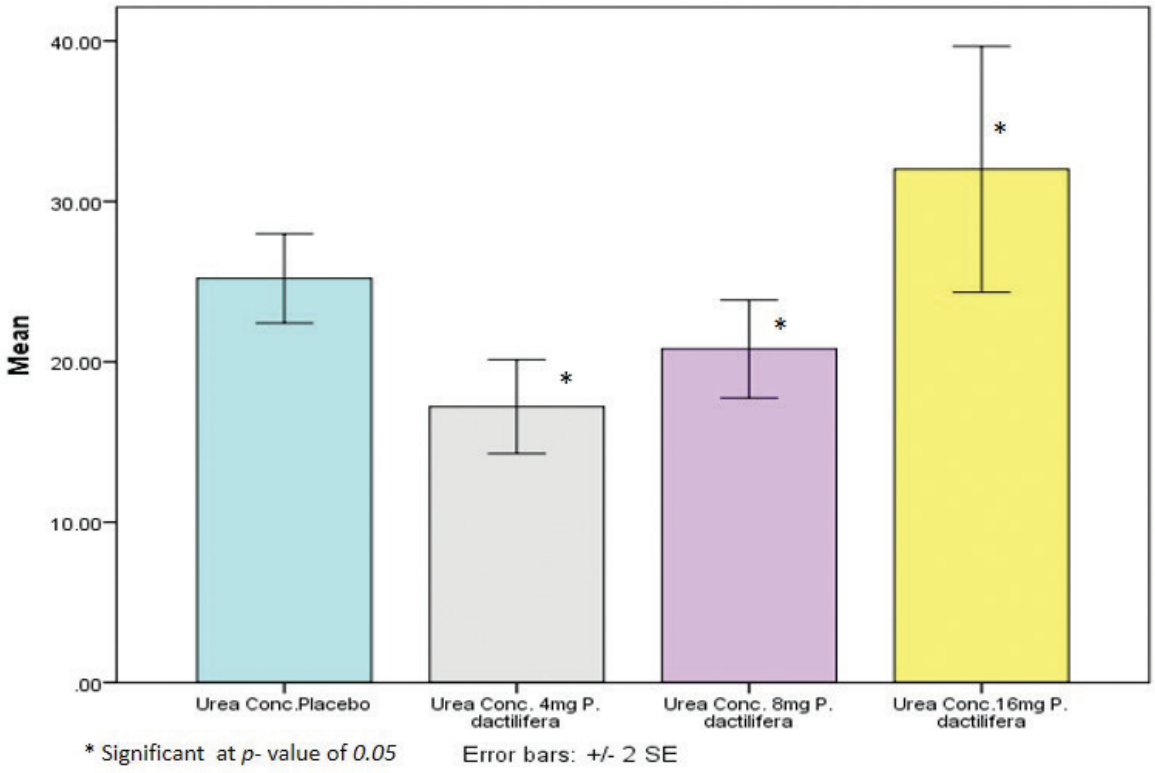

Figure 5. A graph showing the mean values of Urea.

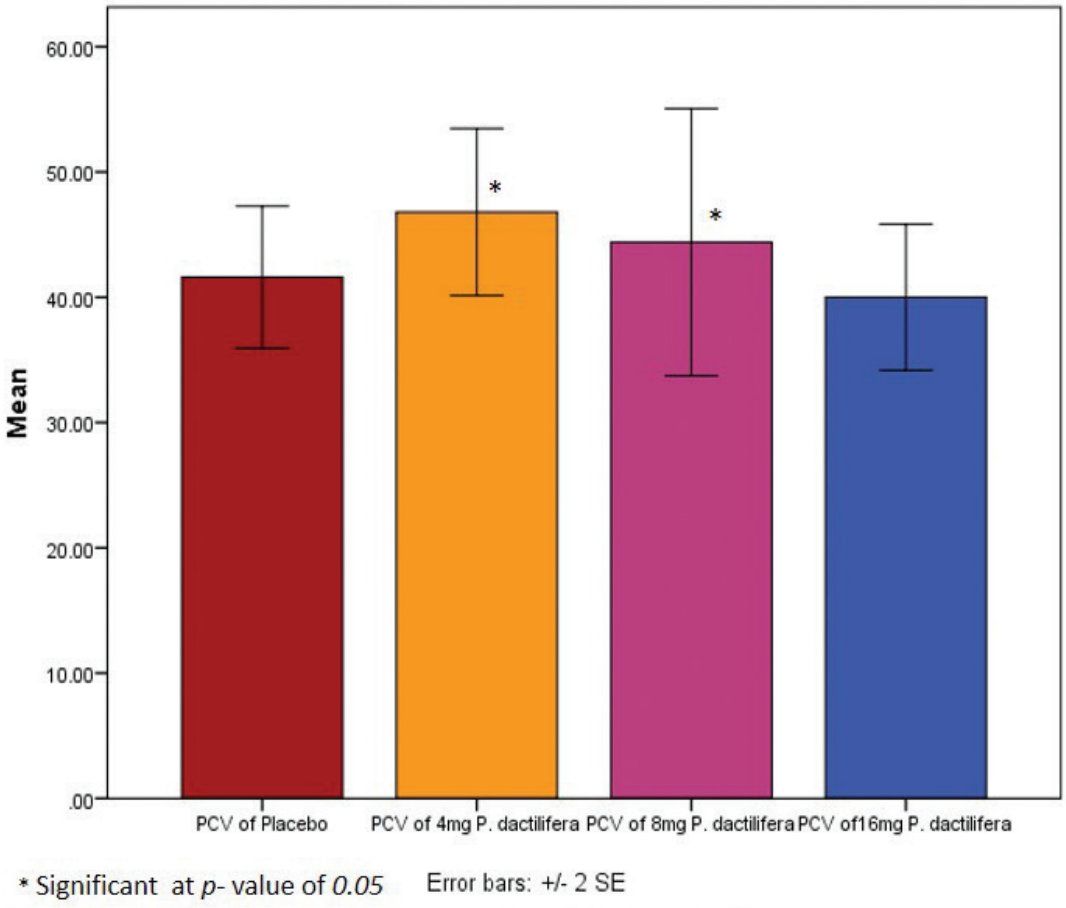

Figure 6. A graph showing the mean values of PCV (packed cell volume).

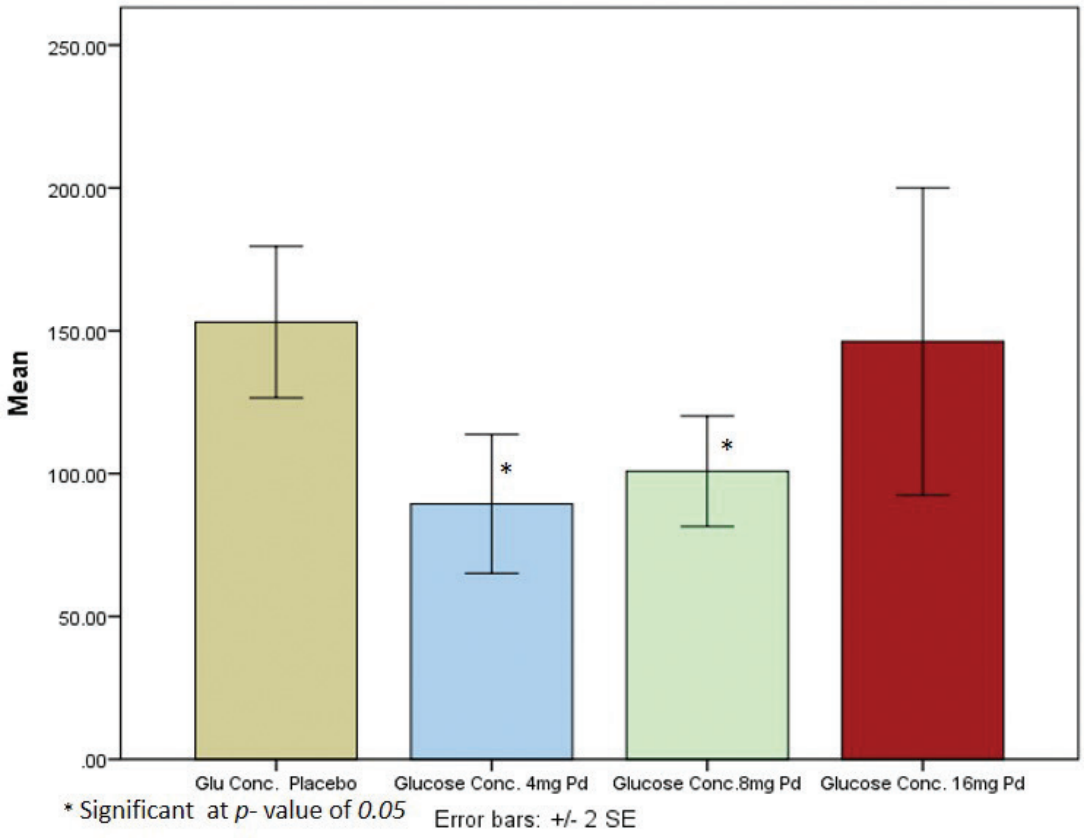

Figure 7. A graph showing the mean values of glucose.

observed in our study, as shown in Figure 2. The rats treated with 4 mg/kg PD showed a significant reduction in their serum creatinine when compared with the control. Traynor et al. [8] described serum creatinine to be an important indicator of renal health, and that it is a measure of the by-product of muscle metabolism, normally excreted unchanged by the kidneys. Since serum creatinine is a useful pointer to the assessment of kidney function [8], its reduction observed in this study (Fig. 4) suggests that this extract increased the creatinine clearance capacity of the kidney; which is an indication that the extract has the potential of enhancing the role of the kidneys in the excretion of creatinine. Again, there was a significant reduction in serum urea concentration in the experimental group (Fig. 5). This is an indication that when the extract is given at a dosage not higher than 8 mg/kg, it could improve renal capacity to excrete urea in order to keep serum urea concentration within the normal level. This report is in line with that of Abdelaziz et al. [10] who noticed a similar reduction in urea concentration from the administration of the extract. It is noteworthy that an elevated serum glucose concentration may suggest kidney failure as usually noticed in diabetic nephropathy, but this study revealed a significant reduction in serum glucose concentration at a dosage not higher than 8 mg/kg (Fig. 7), thereby demonstrating the hypoglycemic properties of this plant. The possible mechanism for hypoglycemic properties of the extract is by stimulating and enhancing the activities of insulin thereby leading to proper utilization of glucose by the tissue of the body. Other mechanisms are by activating and promoting peripheral utilization of glucose and by promoting promotes the rapid conversion of glucose into glycogen (glycogenesis). This hypoglycemic property of the plant was also observed in an earlier study by Abdelaziz et al. [10]; Abdelaziz and Ali [11] which reported that PD seeds at a dose of 1 g/kg/day ameliorated the complications of diabetes mellitus by lowering blood glucose, urea, creatinine, alanine aminotransferase (ALT), and aspartate aminotransferase (AST). Furthermore, there was a significant upsurge in PCV of rats treated with 8 mg/kg of the extract when compared with the control (Fig. 6). This was earlier observed by Onuh et al. [12] in their study in which aqueous and methanolic extract of PD significantly increased RBC, hemoglobin (Hb), PCV, reticulocytes, and platelet count. This upsurge in PCV, therefore, suggests that the extract increased

erythropoietin secretion from the interstitial fibroblasts of the kidney.

It can, therefore, be inferred that PD at a dose of 4 mg/kg improved kidney function in healthy rats, and at a dose of 8 mg/kg, it significantly reduced serum concentration of urea and glucose and significantly increased PCV when compared with that of control. When treated with 16 mg/kg of PD, there was no significant difference in the serum concentration of creatinine, glucose, and PCV but there was a significant increase in urea concentration. The results from this study revealed that high doses of PD does not improve kidney function and might even impair the normal functions of the kidneys. This is line with the report of Iteire et al. [13] that revealed mild vessel congestion in the liver of rats treated with a high dose of the extract. The observed improved kidney function in rats is attributed to the antioxidant and free radical scavenging properties of PD, which was previously observed in the liver of rats by Al Qarawi et al. [14] and Mohamed et al. [15,16] It was as also observed by Salim [6] that PD has the ability to counteract the toxic effect of lead acetate associated with improved renal histology and serum concentration of urea and creatinine and as observed by Saafi-Ben et al. [7,17], date palm fruit extract significantly reduced lipid peroxidation and restored antioxidant defense enzymes and improved histopathologic changes in kidneys of rats.

Conclusions

It is, therefore, concluded from this study that methanol extract of PD fruit improved kidney function at doses of 4 and 8 mg/kg. We suggest that 4 mg/kg of PD should be the optimum dosage for improved kidney function. At 16 mg/kg, it might be deleterious to kidney function.

Funding

This research was self-funded.

Recommendations

We recommend that biochemical parameters should also be assessed to buttress the physiological findings of this study as this may go a long way in ascertaining the medicinal importance of this plant.

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