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Original Article

Phytochemistry and haematological markers in cadmium-induced toxicity mitigated by date palm (*Phoenix dactylifera* L.) fruit extract in rabbit bucks

OPEN ACCESS

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ABSTRACT

This study investigated the phytochemical composition of *Phoenix dactylifera* L. fruit, the effect of cadmium (Cd) on haematological parameters, and the potential of the methanolic extract of *Phoenix dactylifera* (MEPD) fruit to mitigate Cd-induced toxicity. Forty-five rabbit bucks (24–28 weeks old, 1.41–1.43 kg) were randomized into five groups: control, 3 mg $CdCl_2$/kg feed, Cd + 300 mg MEPD, Cd + 600 mg MEPD, and Cd + 900 mg MEPD. Cd was administered for 7 days, followed by MEPD treatment every 72 hours for 28 days. The result of phytochemical analysis showed the absence of tannins, phlobatannins, and starch, with a moderate presence of sterols and protein-xanthoproteins. Saponins, terpenoids, cardiac glycosides, alkaloids, phenols, and flavonoids were abundant. Haematological findings revealed no significant differences ($P > 0.05$) in the Cd-only group compared to the control. MEPD treatment produced a non-significant, dose-dependent increase in packed cell volume, haemoglobin, and red blood cell counts. Significant differences ($P < 0.05$) were found in mean corpuscular volume and mean corpuscular haemoglobin concentration, though all values remained within the normal range. Platelet counts, significantly ($P < 0.05$) reduced by Cd (204.30 $\times 10^3/\mu l$), improved significantly with MEPD treatment. This study highlights the phytochemical richness of *Phoenix dactylifera* and its potential to alleviate Cd-induced haematological toxicity.

K E Y W O R D S : *Blood, Date fruit, Heavy metal, Phytotherapy*

INTRODUCTION

The escalating environmental pollution presents a significant global concern attributed mainly to the use of harmful chemical substances. Among these, heavy metals, notably implicated in adverse effects even at low concentrations, are of particular concern (Edo *et al*., 2024. While these metals exist naturally in ecosystems in varying amounts, human activities contribute significantly to their introduction, posing ecological risks due to their toxicity, persistence, and ability to traverse food chains (Briffa *et al*., 2020). This contamination, affecting land and water, poses health risks not only to livestock and wildlife but also to various organisms like fish, birds, and humans.

Cadmium (Cd), a prominent heavy metal, has profound implications for public health, being linked to liver enzyme alterations, kidney damage, and long-term impacts on the reproductive, renal, hepatic, and endocrine

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systems (Fahim *et al*., 2012; Orisakwe, 2014). In the face of this escalating environmental concern, particularly the adverse impacts of heavy metals like Cd, there is a growing interest in exploring natural remedies which is believed to be a holistic therapy (Karim *et al*., 2015) when compared to its synthetic counterpart. *Phoenix dactylifera*, commonly known as the date palm, is a tropical tree known for its rich phytochemicals (Al-Daihan & Bhat, 2012). These inherent bioactive compounds in various parts of the Date palm tree have been reviewed to possess diverse beneficial properties (Al-Okbi, 2022). It was suggested that these properties conferred by Date palm's phytochemicals could potentially serve as an effective therapy against physiological dysfunctions induced by Cd exposure (Zouari *et al*., 2016; El-Said *et al*., 2023).

With this perspective, the investigation into the phytochemical screening and haematological parameters becomes imperative in understanding the potential protective effects of the methanolic extract of *Phoenix dactylifera* fruit against cadmium-induced toxicity. The intricate interplay between the phytochemical components and haematological markers holds the key to unravelling the potential therapeutic benefits of Date palm against the toxic effects induced by cadmium. Therefore, this study aims to assess the phytochemical composition of the methanolic extract of *Phoenix dactylifera* fruit and evaluate its effect on haematological parameters in rabbit bucks subjected to cadmium exposure.

MATERIALS AND METHODS

Location of study

The experiment was carried out at the Rabbitry Unit of the Teaching and Research Farm in the Department of Animal Science, University of Benin, Benin City, Nigeria. Benin City is located on latitude 6°20′17.34″ N and longitude 5°37′32.70″ E.

Source of *Phoenix dactylifera* fruits

Dates from the *Phoenix dactylifera* plant were obtained from the Nigerian Institute for Oil Palm Research (NIFOR) in Benin City, Edo State, Nigeria. The acquired fruits were authenticated by a botanist in Department of Plant Biology and Biotechnology, Faculty of Life Sciences, University of Benin, Benin City. The fruits were split, air-dried, finely ground using an electric blender and subsequently stored in an airtight container.

Preparation of fruit extracts

A quantity of 0.5 kg of finely ground *Phoenix dactylifera* fruits was measured and the extraction process was conducted using 99 % methanol in a Soxhlet apparatus. The resulting extract was concentrated with the aid of a rotary vacuum evaporator and freeze dried using a lyophilizer (Wang and Weller, 2006). The freeze-dried extract was then stored in a sealed bottle.

Qualitative phytochemical screening

Qualitative analysis of phytochemicals was conducted on the obtained crude extract, following the established procedures outlined by Harborne (2013). The constituents of interest included tannins, saponins, alkaloids, phenols, flavonoids, sterols, phlobatannins, protein-xathoprotein, cardiac glycosides, terpenoids, and starch.

Acute toxicity evaluation

Acute toxicity of methanolic extract of *Phoenix dactylifera* (MEPD) fruit was studied using the method outlined by Lorke (1983). Twenty-five (20) matured albino rats of both sexes with body weight range of 25 to 30 g were randomized into five groups of four rats per group. Each group received a single dose of NBL extract at 0, 500, 1000, 2000 and 3000 mg/kg body weight, respectively, through oral routes, while the control group received normal saline at 10 ml/kg body weight. The rats were closely observed for signs of toxicity for 72 hours.

Experimental materials and management

A total of forty-five (45) composite rabbit bucks aged 24 - 28 weeks and weighing between 1.41-1.43 kg was used for this study. The rabbits were kept in separate cages under intensive management. A period of two weeks was set aside for quarantine during which the rabbits received Ivomec® injections to control haemoparasites, as well as internal and external parasites. Throughout the study, the rabbits had unrestricted access to both water and commercial grower diet comprising 15 % crude protein and energy content of 2650 kcal/kg.

Experimental design

The treatment protocols consisted of 5 groups: group 1 (control), group 2 (3 mg of $CdCl_2$/kg feed/day for 7 days), group 3 ($CdCl_2$/kg feed/day for 7 days + 300 mg/kg body weight of MEPD fruits for 28 days), group 4 ($CdCl_2$/kg feed/day for 7 days + 600 mg/kg body weight of MEPD fruits for 28 days) and group 5 ($CdCl_2$/kg feed/day for 7 days + 900 mg/kg body weight of MEPD fruits for 28 days). Each treatment group was replicated three times with three bucks constituting a replicate in a completely randomized design.

Data collection and evaluation

Blood collection: At the end of 35 days research period, 2.5 ml of blood sample was aspirated from each rabbit buck through the ear vein using needle and syringe at 0600 to 0900 hours. The aspirated blood was emptied into

sample bottles containing ethylene diamine tetra acetic acid (EDTA) for haematological analysis

Estimation of haematological parameters: Haematological parameters including haemoglobin (Hb) concentration, red blood cell (RBC) count, packed cell volume (PCV), white blood cell (WBC) count, lymphocyte, eosinophils, monocytes, basophils, neutrophils and platelet counts were measured in the whole blood using the automated multi-parameter blood analyser SYSMEX KX21. 50 µl of blood samples was introduced into the equipment and it automatically employed the differences in characteristics possessed by each of the blood components to distinguish and estimate the haematological parameters.

Statistical analysis

The data obtained in this study was subjected to statistical analysis of variance (ANOVA) procedure of GenStat 12th edition at significance level of 5 %. Significant means were separated using Duncan Multiple Range Test (DMRT).

RESULTS AND DISCUSSIONS

The result of qualitative phytochemical screening in this study is summarized in Table 1. The result shows that saponin, terpenoids, cardiac-glycosides, alkaloids, phenols and flavonoids were highly present in MEPD fruit. The presence of sterols was moderately detected while tannins, phlobatannins and starch were absent.

Table 1: Phytochemical screening of the methanolic extract of *Phoenix dactylifera* fruit

Phyto-constituents	*Phoenix dactylifera* L.
Tannins	_
Saponins	+ +
Terpenoids	+ +
Sterols	+
Phlobatannins	_
Protein-xathoprotein	+
Cardiac-glycosides	+ +
Alkaloids	+ +
Phenols	+ +
Flavonoids	+ +
Starch	_

++ highly present; + moderately present; - absent.

In the result of haematological study shown in Table 2, there were no significant (P > 0.05) differences between the control and the Cd-only treated group for all the measured parameters.

Table 2: Haematological profile of cadmium exposed rabbits administered *Phoenix dactylifera* extract

Parameters	Control	Cd	Cd + 300 MEPD	Cd + 600 MEPD	Cd + 900 MEPD	SEM
PCV (%)	30.00	30.00	32.67	33.67	35.67	3.53
Hb (g/dl)	8.77	9.10	9.90	10.63	10.83	1.23
RBC ($\times10^6$/µl)	4.19	4.12	5.11	5.12	5.20	0.62
MCV (fl)	72.23^{a}	65.77^{ab}	64.00^{b}	65.83^{ab}	68.73^{ab}	2.25
MCH (pg)	20.63	20.17	19.40	20.77	20.83	0.84
MCHC (g/dl)	29.27^{b}	30.70^{ab}	30.30^{ab}	31.50^{a}	30.30^{ab}	0.51
WBC ($\times10^3$/µl)	5.13	3.33	5.87	5.13	5.93	0.93
Neutrophils (%)	30.67	35.67	32.00	40.33	44.00	5.76
Lymphocytes (%)	67.00	60.67	64.33	56.00	52.33	5.82
Eosinophils (%)	1.67	2.00	2.00	2.00	2.00	0.39
Monocytes (%)	0.67	1.67	1.67	1.33	1.33	0.80
Basophils (%)	0.00	0.00	0.00	0.33	0.33	0.21
Platelets ($\times10^3$/µl)	279.70^{ab}	204.30^{b}	361.30^{a}	344.00^{ab}	315.30^{ab}	44.10

^{a,b} Means bearing different letters of superscript within the same row differ significantly (P < 0.05), PCV- Packed cell volume; Hb- Haemoglobin; RBC- Red blood cell; MCV- Mean corpuscular volume; MCH- Mean corpuscular haemoglobin; MCHC- mean corpuscular haemoglobin concentration; WBC- White blood cell

The administration of MEPD significantly affected (P < 0.05) MCV, MCHC and platelets counts. The MCV value for 300 mg/kg group was significantly (P < 0.05) lower than the control group but similar (P > 0.05) to Cd-only, 600 mg/kg and 900 mg/kg groups. Also, the 600 mg/kg group was significantly (P < 0.05) higher than the control group but similar to Cd-only, 300 mg/kg and 900 mg/kg treated groups. Although the mean values for PCV, Hb, RBC and WBC counts were not significantly different, these indices presented higher numerical differences in the extract treated groups when compared to both the control and Cd-only treated rabbit bucks. PCV, Hb, RBC, MCV, MCH and neutrophils had a dose dependent effect which progressively increased as the levels of extract administration increases. Only the 600 mg/kg and 900

mg/kg treated groups recorded a mean value for basophils which was 0.33 % apiece for both treatment groups.

The assessment of the methanolic extract from *Phoenix dactylifera* fruit revealed the presence of various phytochemical compounds, including tannins, saponins, terpenoids, sterols, phlobatannins, protein-xathoprotein, cardiac glycosides, alkaloids, phenols, flavonoids, and starch. Notably, alkaloids, phenols, flavonoids, saponins, and tannins are important secondary metabolites and have significant role in the medicinal properties of herbs. Previous study on the entire *P. dactylifera* plant by Vyawahare *et al*. (2008), indicated the presence of carbohydrates, alkaloids, steroids, flavonoids, vitamins, and tannins. Moreover, investigations into the phytochemical composition of date fruit pulp revealed the abundance of phenolics, sterols, carotenoids, anthocyanins, procyanidins, and flavonoids (Al-Daihan & Bhat, 2012). Additionally, Nadeem *et al*. (2011) identified oxalate, phytate, and tannin in *P. dactylifera* fruit extract.

Discrepancies observed in the presence of these constituents in *P. dactylifera* across different studies may be attributed to variations in date fruit variety, processing methods, fruit-picking stage, geographical location, and soil conditions. Comparative analyses involving fresh and dried dates have indicated a significant rise in phenolic content during the drying process, likely due to tannin degradation and the maturation of degradative enzymes at elevated temperatures (Al-Farsi *et al*., 2005). Consequently, the drying process may lead to a reduction in tannin concentration, potentially explaining its absence in the present study.

The assessment of acute oral toxicity in this study revealed that the MEPD fruit caused neither mortality nor observable health concerns in the test rats, even when given at the highest dose of 3000 mg/kg over the 72-hour monitoring period. The rats exhibited typical behaviour, retained their regular feeding patterns, and showed no variation in the consistency of their droppings compared to the control group.

Cd has been reported to induce the formation of metallotioneins and reactive oxygen species (ROS) in the blood, leading to oxidative damage in erythrocytes and various tissues (Kanter *et al*., 2005). In this study, rabbits that were fed cadmium chloride did not exhibit any significant differences ($P > 0.05$) in the mean values of erythrocyte counts, haemoglobin (Hb), and packed cell volume (PCV). Moreover, these values aligned with the normal range of 3.48-6.0 $\times 10^6/mm^3$ (Chineke *et al*., 2006; Amata, 2010), 8.9-15.5 g/dl (Poljičak-Milas *et al*., 2009) and 33-50 % (Fudge, 2000) reported for erythrocyte, Hb and PCV respectively.

Previous research by Hounkpatin *et al*. (2013) on Wistar rats exposed to chronic doses of cadmium chloride at 0.25 and 2.5 mg/kg, given orally for 28 days did not show any significant differences ($P > 0.05$) in various haematological indices. In contrast, other studies by Dallak (2009) and Onwuka *et al*. (2010) indicated decreased values in erythrocyte counts, Hb, and haematocrit as well as a decreased MCV, MCH and MCHC, suggesting microcytic and hypochromic anaemia in rats orally administered $CdCl_2$.

In this study, administration of MEPD resulted in a dose-dependent non-significant increase ($P > 0.05$) in PCV, Hb, and RBC. This finding is consistent with the observations of Onuh *et al*. (2012), who found increased levels of RBC, Hb, PCV, reticulocytes, and platelet count in Wistar rats treated with extracts of *Phoenix dactylifera* in a dose-dependent manner. Similarly, Wahab *et al*. (2010) reported improved haematological indices in rats with lead acetate-induced haematotoxicity after being administered the ethanolic extract of *Phoenix dactylifera* fruit. This outcome may be related to the phytochemical composition of MEPD, which could have stimulated haematopoietic activity and enhanced bone marrow function.

Erythrocyte indices play a crucial role in the initial categorization of anaemia and serve as an indicator of the bone marrow's ability to generate red blood cells (Brugnara and Mohandas, 2013). The result of erythrocyte indices in this study indicated significant variations ($P < 0.05$) among the treatment means for mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC). Despite these significant differences, the mean values fell within the normal range of 58.0-79.6 fl and 27-34 g/dl as reported by Poljičak-Milas *et al*. (2009) and Fudge (2000) for MCV and MCHC, respectively. Therefore, the observed differences in MCV and MCHC may not have presented any clinical concerns for the rabbits in the study.

While the Cd-only treated group showed the lowest mean value for white blood cell (WBC) count among all treatment groups, the total and differential WBC counts did not show significant differences ($P > 0.05$) among the treatment means and were within the established range of 3-12 $\times 10^3/\mu l$, 30-70 %, 30-70 %, 0-3 %, and 0-1 % for WBC, neutrophils, lymphocytes, monocytes, and basophils, respectively, as reported by Hein and Hartmann (2003). Similarly, Wahab *et al*. (2010) did not observe significant differences in WBC values and its differentials when administering the ethanolic extract of *Phoenix dactylifera* fruits to rats with lead-induced haematotoxicity.

In this study, although cadmium treatment significantly ($P < 0.05$) reduced platelet counts, the administration of MEPD significantly ($P < 0.05$) increased mean platelet counts in the groups treated with the extract. This supports the conclusions of Ramadhas *et al*. (2014), suggesting that *Phoenix dactylifera* extract may be effective in correcting bleeding disorders associated with thrombocytopenia.

CONCLUSION AND RECOMMENDATION

In conclusion, the study indicates that the methanolic extract from *Phoenix dactylifera* fruit contains various phytochemicals and may have a protective effect on haematological parameters in rabbits exposed to cadmium chloride, potentially due to its haemopoietic activity. It is recommended that *Phoenix dactylifera* fruit extract, particularly at doses of 600 mg/kg and 900 mg/kg, be further investigated for its potential to mitigate cadmium-induced haematotoxicity and enhance haematopoietic function.

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Authors Contribution

Research Design: AAA; Data analysis/interpretation: AAA; Data Collection: OA; Literature Search: OME; Writing/proofreading: AAA & OME. All authors read and approved the final manuscript.

Ethical Committee Approval

This experiment was approved and conducted according to the provisions of the Ethical Committee on the use of animals for biomedical research at the University of Benin, Benin City, Nigeria (Approval No: PG/AGR1312015).

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