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Effect of Date Palm Pollen (DPP) on the Histology, Heamatology, Renal and Hepatic Biomarkers in Female Albino Rats

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ABSTRACT

Introduction: date palm pollen (DPP) is used for applications ranging from diet supplements to fertility boosters. In this study, its effect on the biochemistry and histology of female albino rats.

Methods: forty rats weighing 130-170g were grouped into 4 groups of 10 rats each and group I was control while groups II-IV were administered 78 $mgkg^{-1}$, 156 $mgkg^{-1}$ and 312 $mgkg^{-1}$ doses of DPP for 28 days. On day 28, five rats were kept separate as group V and treatment discontinued for 14 days. After this, rats were sacrificed and body weight, heamatological indices, hepatic and renal enzyme markers, serum electrolytes and histology of organs were determined.

Result: DPP caused no significant change in organ weight, few changes were observed in histology of the organs. It caused no significant changes in MCHC, MCV, RBC, haemoglobin, platelet and decreased WBC count. DPP also significantly ($p<0.001$) increased serum albumin, cholesterol and LDL levels, decreased TP, triglyceride and HDL concentration. DPP also significantly ($p<0.001$) increased the serum levels of the liver enzymes ALT and ALP but had no effect on AST. DPP increased serum pottasium, urea and chlorine but had no significant effect on sodium and creatinine levels.

Conclusion: DPP was found to have deleterious effects at higher concentrations and when administration was discontinued, observed effects were reversed.

Glossary: DPP – Date palm pollen, LDL – Low density lipoprotein, HDL – High density lipoprotein, RBC – red blood cell, WBC – White blood cell, MCHC – Mean coposcular heamoglobin concentration, MCV – Mean corpuscular volume, AST - Aspartate aminotransferase, ALT - Alanine aminotransferase, ALP – Alkaline Phosphatase, TP- Total protein.

Keywords: Date Palm Pollen; Biomarkers; Renal; Hepatic; Organ weight; *Phoenix dactylifera*.

Introduction

Date Palm also known as *Phoenix dactylifera* has many economic and medicinal values. Various parts of this plant such as the seed, leaves, trunk, pollen grains, roots and fruits provide remedy to a lot of ailment and they are widely used in traditional medicine for the treatment of various disorders. Date palm pollen (DPP) which is the male reproductive dust of palm flowers, has long been used as a dietary supplement for treatment of several disorders by both genders. DPP is known to contain a variety of compounds including amino acids, fatty acids, flavonoids, saponins, and sterols[1,2,3].

Numerous studies carried out on DPP have shown its antioxidant, hepatoprotective, nephroprotective, neuroprotective, anti-inflammatory and gonads stimulating effects[4]. Date fruit extracts have been shown to ameliorate liver damage, suppress swellings and tumors, inhibit growth of *Streptococcus pyogenes* and improve sperm parameters[1,3]. In females, it is reported to improve lactation and icrease oogenesis and also reduce labour pain[6,7,8].

Whether DPP administration influences hematological, hepatic and/or renal functions and histoachitecture in female albino rats remains to be determined as many of the information available is related to studies carried out to determine these parameters in male albino rats. Thus, this study undertakes to evaluate the effect of DPP extract on body weight, heamatological indices, hepatic and renal enzyme markers, serum electrolytes and histology of some organs in female albino rats.

Material and Methods

A total of forty (40) healthy and young nulliparous female albino adult Wistar rats weighing 120- 170g aged ten weeks were used for this research study, the rats were randomly divided into four groups of ten rats each. The administration of the extract in all groups is decribed below.

Animal Grouping and Dosage

Group I which was the control group were administered distilled water equivalent in volume to the

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highest dosage administered to the experimental rats. Groups II, III and IV served as the experimental groups and were administered 78 $mgkg^{-1}$, 156 $mgkg^{-1}$ and 312 $mgkg^{-1}$ doses of aqueous suspension of DPP. Dose levels were selected based on the LD_{50} of greater than 5000 $mgkg^{-1}$ body weight, obtained from acute toxicity study previously conducted on DPP. The dose levels were calculated as ¼, $^1/_8$ and $^1/_{16}$ of 25% of LD_{50} which was determined to be greater than 5000 $mgkg^{-1}$ for highest, medium and lowest dose respectively[9]. reported that the highest repeated dose of any Experimental study should not exceed 25-30 % of LD_{50}. Group V consisted of rats that from group IV who did not receive further treatment from day 28 till day 48 when they were sacrificed.

Ethical Consideration

The study was approved by the Postgraduate Board of Studies, University of Maiduguri, and conducted conferring to the National Institute of Health Guide for the Care and Use of Laboratory Animals and ARRIVE Guidelines.

Experimental Protocol

The body weight of each rat was taken at the beginning of the experiment, this was repeated weekly and the volume of drug administered was adjusted to correspond to increase or decrease in body weight of each rat. The suspension of DPP was administered daily via the orogastric route for twenty eight consecutive days in all the groups. The rats in groups IV were then divided into two groups of 5 rats each on the twenty ninth day and the first five rats in group IV were sacrificed on the 28th day. To the remaining 5 rats, only equal doses of distilled water was administered to the rats in this group (PRG /group V) for 14 days. The rats in this group were sacrificed on the 42th day and same analyses carried out as with the rats sacrificed on the 28th day. This was to determine any changes in serum biochemical and histological structure in the organs in this group compared to the other groups.

Animal Sacrifice

On the twenty ninth day, the rats were euthanized by administering 0.1 $mgkg^{1}$ ketamine hydrochloride anaesthesia via the left thigh as an intra-muscular injection. Each rat was laid on its dorsal surface in a supine position and a thoraco- abdominal section was made to expose the internal organs.

Organ Harvest and Weighing

The liver, spleen, kidney and brain of all the animals were harvested, trimmed of any adherent connective tissue and wet weight measured to determine if there was any effect on the weight of the organs.

Serum Biochemical Markers and Haematological Analysis

Blood was quickly aspired into a syringe via cardiac puncture and hematological indices such as haemoglobin (Hb) concentration, packed cell volume (PCV), red blood cells count (RBCs), mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC), white blood cell (WBC) count, and platelet count were obtained from the blood drawn. The blood sample was also analyzed for biochemical determination of serum levels of alkaline phosphatase (ALP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), triglyceride, urea and creatinine. Haematological estimation of some electrolytes, total proteins, albumin, and cholesterol were determined. The analyses mentioned above were carried out according to standard techniques as described by studies carried out by[10, 11, 12, 13, 14].

Histopathological Analysis

The liver, brain, spleen and kidney tissue samples were fixed in 10% formaldehyde for 24 h and processed by routine tissue processing techniques to obtain microscopic sections 5µm thick. Following the processes of fixation and dehydration, the processed tissues were then embedded in paraffin blocks and sectioned to 5 µm thickness using a rotary microtome (Leica Biosystems, Nussloch GmbH). Sections were then mounted on glass slides, rehydrated and stained with Heamatoxylin and Eosin (H&E) according to routine procedures and then observed under the microscope to determine histopathological changes.

Statistical Analysis

The data was analysed by GraphPad Prism software version 8. Data was analysed by using Analysis Of Variance (ANOVA) followed by a multicomparison test to compare the groups with the control group. The p-value <0.05 was considered as statistically significant.

Results

Effects of 28 Days Administration of Aqueous Suspension of DPP Grains on Organ Weight

Administration of the suspension of DPP for 28 days did not cause any significant ($p> 0.05$) change in the weight of the spleen, brain, kidney and liver tissues in female rats in the same group. There was also no significant ($p> 0.05$) change in weight in the organs of rats in each experimental group when compared to the weight of organs in the control group as can be observed in Table 1. The organs of rats in group V also did not show significant difference in weight when compared to the control group indicating that withdrawal of aqueous extract of DPP did not have an effect on organ weight (Table 1).

Effects of the Aqueous Suspension of DPP Grains on Haematological Indices

The effects of administration of doses of aqueous suspension of DPP on haematological parameters in female rats are shown in Table 2. There was no significant ($p > 0.05$) effect on mean corpuscular haemoglobin concentration (MCHC), mean corpuscular volume (MCV), red blood cell (RBC), platelet count (PLT) and haemoglobin. There was a significant ($p < 0.05$) decrease noted in packed cell volume (PCV) concentration in groups III and IV when compared to the control group. The PCV level again increased in group V after withdrawal of DPP indicating that there was a reversal in its effect on the packed cell volume. A decrease was observed in serum level of white blood cell (WBC) in all the experimental groups when compared to the control group but this decrease was reversed in group V (Table 2).

Effects of Administration of the Aqueous Suspension of DPP Grains on Total Albumin, Protein, Lipid Profiles and Liver Enzymes in Female rats

The effects of administration of graded doses of aqueous suspension of DPP on total albumin is shown in Fig. 1. The results showed a decrease in serum albumin

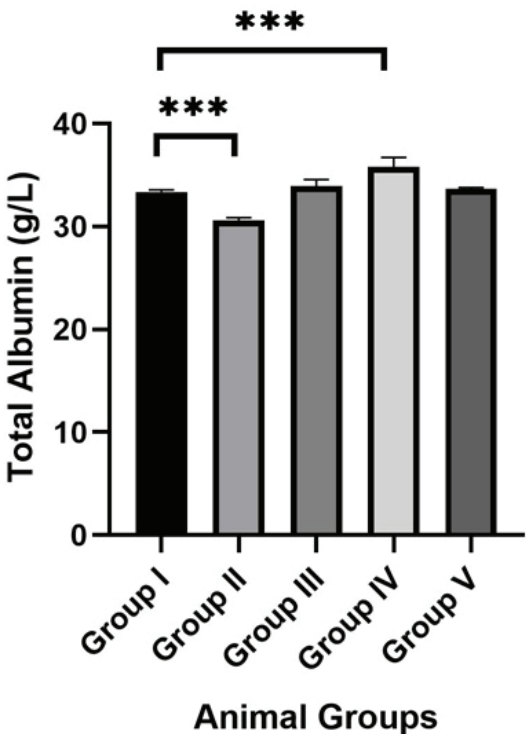

Figure 21. Showing the serum total albumin level in all groups. (***- p<0.001, ** - p<0.01, * - p<0.05).

Table 1. Showing the effect of DPP on the organ weights of animals in Groups I - V.

	Groups				
Weight (g)	**GP I (0mg/kg DPP)**	**GP II (78mg/kg DPP)**	**GP III (156mg/kg DPP)**	**GP IV (312mg/kg DPP)**	**GP V (PRG)**
Spleen	0.56 ± 0.02	0.59 ± 0.05	0.55 ± 0.02	0.56 ± 0.03	1.74 ± 0.11
Brain	1.50 ± 0.10	1.640 ± 0.07	1.60 ± 0.03	1.84 ± 0.02	5.70 ± 0.20
Liver	5.76 ± 0.11	5.76 ± 0.08	5.32 ± 0.26	0.71 ± 0.01	5.40 ± 0.20
Left Kidney	0.70 ± 0.01	0.69 ± 0.01	0.69 ± 0.01	0.72 ± 0.03	0.71 ±0.01
Right Kidney	0.71± 0.01	0.70 ± 0.01	0.70 ± 0.01	0.72 ± 0.03	0.72 ± 0.02

Results are presented as mean ± SEM. Significance relative to the control group PRG = Post Recovery Group V: Sacrificed 14 days after the last administration of the suspension. g= gram, mg/kg= milligram per kilogram body weight of suspension of DPP, 0 (control) = group 1, 78 (treatment) = group II, 156 (treatment) = group III, 312 (treatment) = group IV.

Table 2. showing the Effects of 28 Days Administration of Aqueous Suspension of DPP on the Haematological Indices in Female Rats in all Groups.

Parameter (Unit)	Doses Administered (mg/kg)				
	GP I (0mg/kg)	**GP II (78mg/kg)**	**GP III (156mg/kg)**	**GP IV (312mg/kg)**	**GP V (PGR)**
WBC × 10^9/l	5.28 ± 0.50	4.18 ± 0.51 *	4.32 ± 0.51 *	4.80 ± 0.42 *	5.20 ± 0.54
RBC × 10^{12}/l	7.56 ± 0.72	7.34 ± 0.36	8.12 ± 0.40	8.160 ± 0.3803	7.34 ± 0.14
PLT × 10^9/l	474.20±12.15	457.40 ± 32.52	569.00 ± 21.70	590.20 ± 16.19	495.80 ± 11.60
MCV (fl)	54.28 ± 1.78	56.16 ± 0.87	56.82 ± 0.77	56.000 ± 1.590	52.620 ± 3.45
PCV (%)	49. 20 ± 0.09	49. 39 ± 0.05	48. 50 ± 0.09*	48. 20 ± 0.09*	49. 20 ± 0.79
HGB (g/dl)	13.10 ± 0.32	12.38 ± 0.17	12.40 ± 0.2121	13.120 ± 0.3216	12.56 ± 0.25
MCHC	28.94 ± 0.53	31.10 ± 0.66	31.40 ± 0.1761	31.740 ± 1.66	28.92 ± 0.49

Sacrificed 14 days after the last administration of the suspension. Results are presented as mean ± SEM. Significance relative to the control, WBC= white blood cell count, RBC= red blood cell count, PLT= platelets, MCV= mean corpuscular volume, PVC= packed cell volume, HGB= haemoglobin, MCHC = mean corpuscular haemoglobin concentration, 0(group I) = control, 78 (treatment) = group II, 158 (treatment) = group III, 312 (treatment) = group IV, PRG = Post Recovery Group: (group V) * ($p < 0.05$) = significant

level in group II and an increase in serum albumin level in group IV when compared to the control group. There was a decrease in serum albumin concentration in group V (Fig 1).

DPP significantly increased the serum cholesterol level in all groups significantly ($p<0.001$) in groups II to IV and $p<0.01$ in group V indicating that the extract has the predisposition to increase serum cholesterol levels significantly at the concentrations indicated (Fig.2).

Administration of DPP showed a significant ($p<0.001$) decrease in serum total protein in groups III, IV and V when compared to the control group. There was no significant difference in the total protein in group II (Fig.3).

Serum triglyceride (TG) levels were altered at different rates in the different groups following the administration of DPP extract. In group II, there was a significant ($p<0.001$) decrease in serum TG when compared to the control group. The levels further decreased significantly ($p<0.001$) in group III but started to increase in group IV, although significantly ($p<0.001$) lower than the control group. There was a further increase in the TG levels of rats which were in group V but still significantly ($p<0.001$) lower than the control group (Fig. 4).

Serum High density lipoprotein (HDL) levels were significantly ($p<0.001$) decreased in groups II and III when compared to the control group. The values increased in groups IV and V but was still significantly ($p<0.001$) decreased in group V. HDL concentration in group IV was not significant in group IV when compared to the control group (Fig. 5).

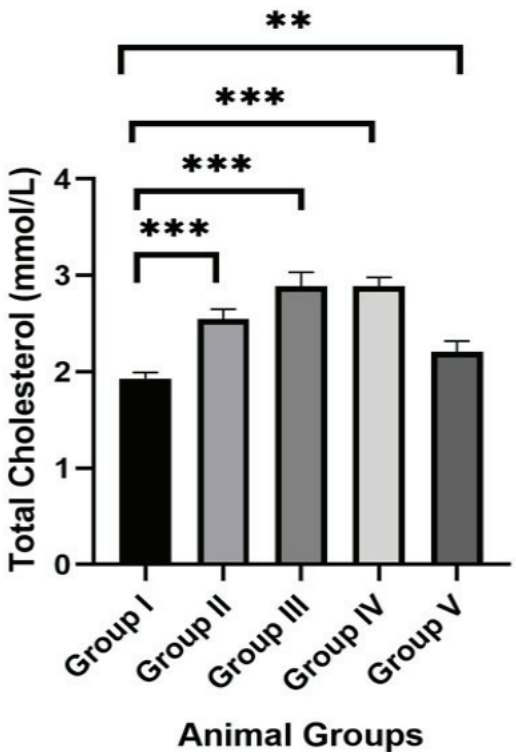

Figure 2. Showing the serum total cholesterol level in all groups. (***- $p<0.001$, ** - $p<0.01$, * - $p<0.05$).

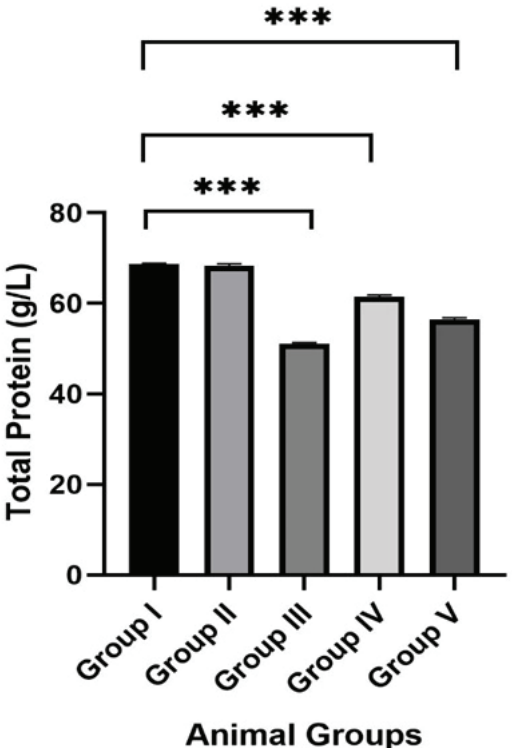

Figure 3. Showing the serum total protein level in all groups. (***- $p<0.001$, ** - $p<0.01$, * - $p<0.05$).

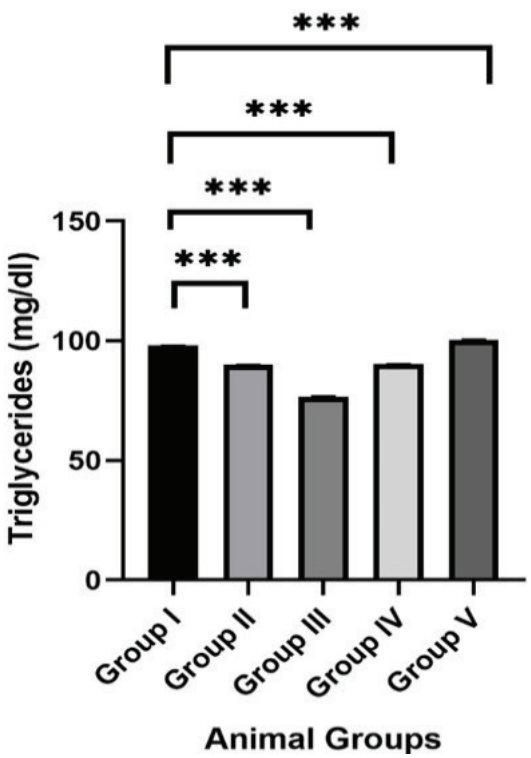

Figure 4. Showing the serum triglyceride level in all groups. (***- $p<0.001$, ** - $p<0.01$, * - $p<0.05$).

by the administration of DPP to the animals in groups I – IV. There was a significant ($p<0.01$) decrease in the aspartate transferase level observed in group V (Fig.7).

Alanine aminotransferase (ALT) levels were sigbificaantly ($p<0.001$) increased in groups I-IV

Low Density Lipoprotein (LDL) levels were significantly ($p<0.001$) increased in all groups (II-V) following the administration of DPP. The levels decreased after DPP was discontinued and there was a slight but significant ($p<0.001$) increase above the control group observed in group V (Fig.6).

Aspartate transferase (AST) levels were not altered compared to the control group but in group V, there was a significant ($p<0.001$) decrease compared to the control group (Fig. 8).

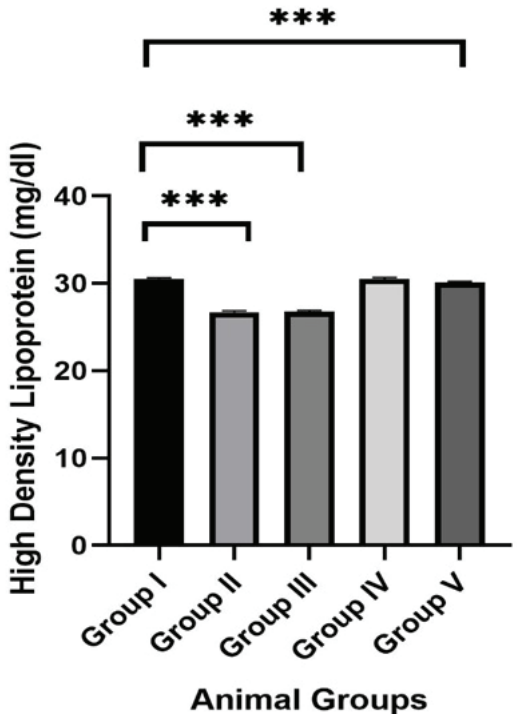

Figure 5. Showing the high density lipoprotein level in all groups. (***- $p<0.001$, ** - $p<0.01$, * - $p<0.05$).

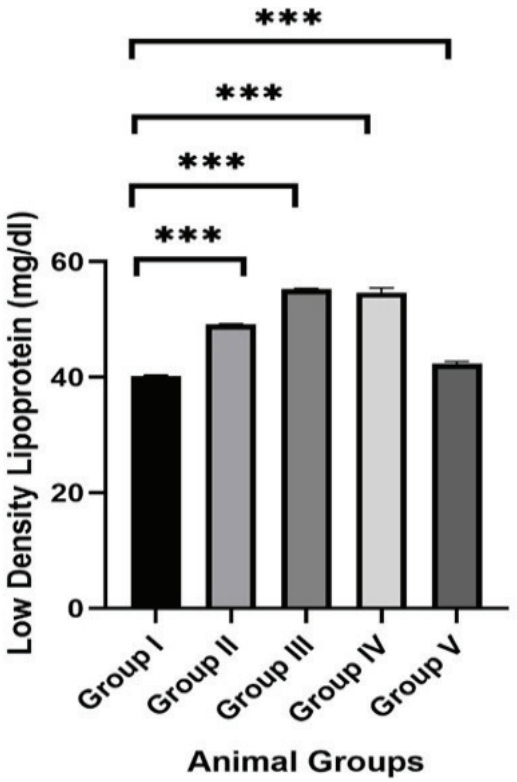

Figure 6. Showing the low density lipoprotein level in all groups. (***- $p<0.001$, ** - $p<0.01$, * - $p<0.05$).

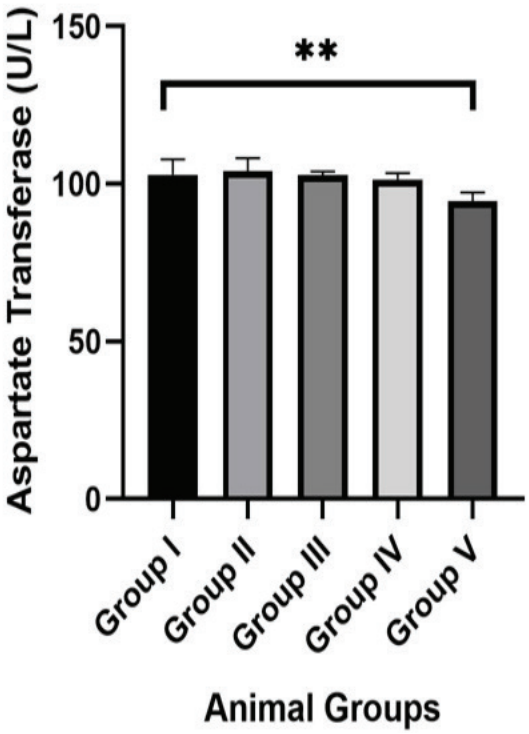

Figure 7. Showing aspartate transferase level in all groups. (***- $p<0.001$, ** - $p<0.01$, * - $p<0.05$).

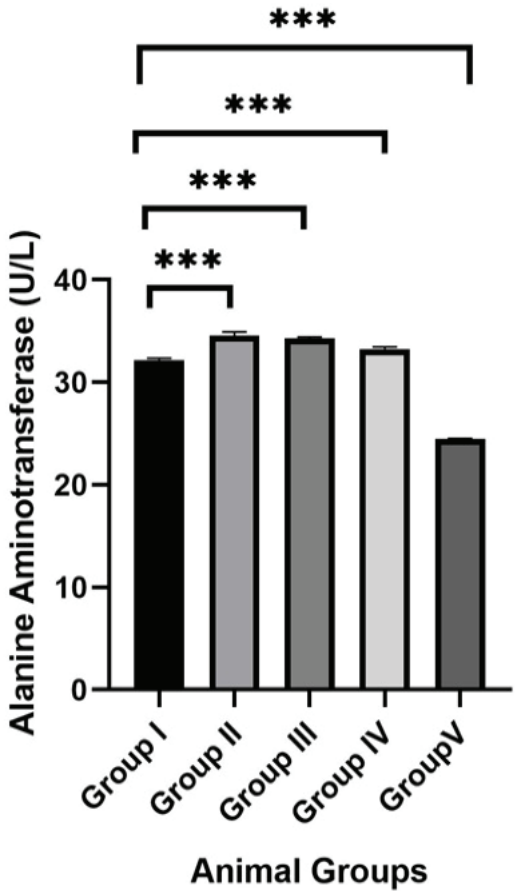

Figure 8. Showing alanine aminotransferase level in all groups. (***- $p<0.001$, ** - $p<0.01$, * - $p<0.05$).

The results for Alkaline phosaphate (ALP) was similar to the result obtained for ALT as a significantly ($p<0.001$) increase in the level of ALP was observed in the groups administered DPP (groups I-IV) and in group V, there was a decrease in the serum level of ALP (Fig. 9).

Effects of Administration of the Aqueous Suspension of DPP on Serum Electrolytes, Urea and Creatinine in Female Rats

Serum pottasium levels were also significantly ($p<0.001$) increased in groups administered DPP when compared to the control group (Fig. 10). Administration of DPP did not cause any significant change in the serum sodium concentration in all groups when compared to the control group (Fig. 11). Serum chloride ion was significantly ($p<0.001$) increased in groups I-IV when compared to the control. Serum chloride ion concentration was decreased in group V (Fig. 12).

Serum creatinine concentration in groups I-IV did not show any significant change when compared to the control group, but in group V, there was a significant ($p<0.05$) decrease in the serum creatinine level (Fig. 13). Serum urea concentration was significantly elevated in all groups compared to the control group (Fig. 14).

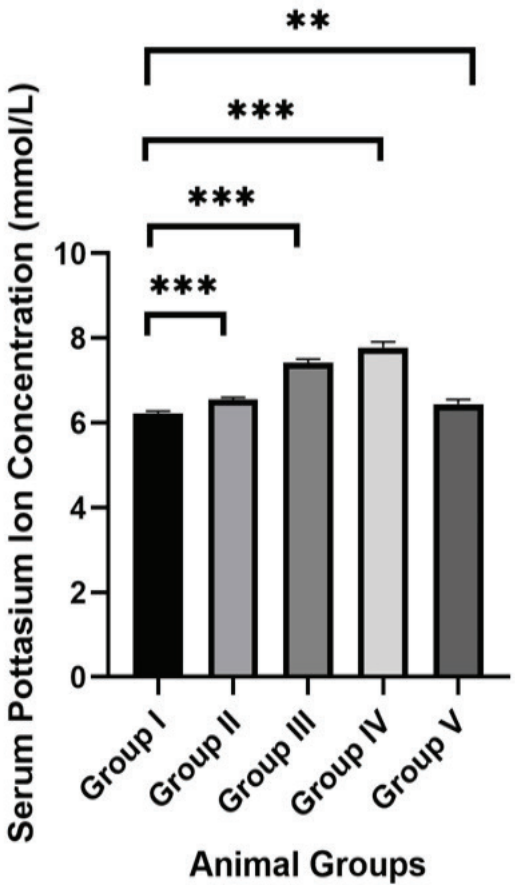

Figure 10. Showing serum pottasium level in all groups. (***- p<0.001, ** - p<0.01, * - p<0.05).

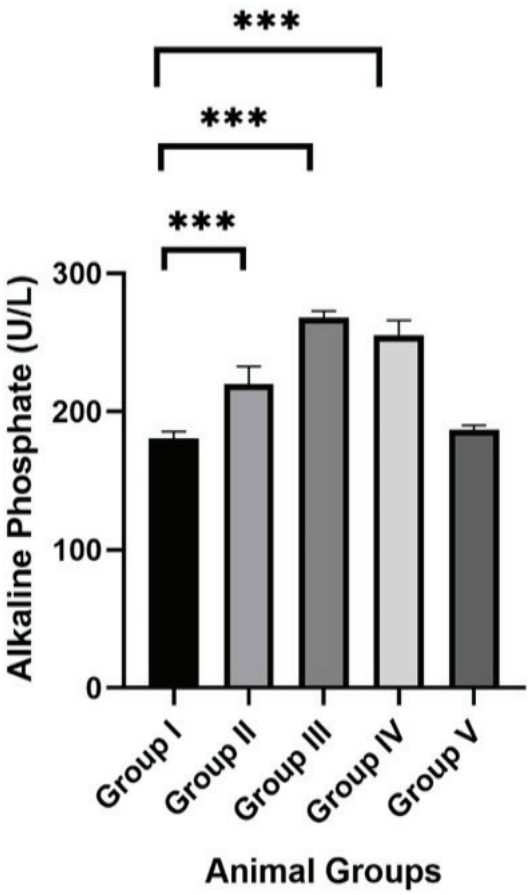

Figure 9. Showing alkaline phosphate level in all groups. (***- p<0.001, ** - p<0.01, * - p<0.05).

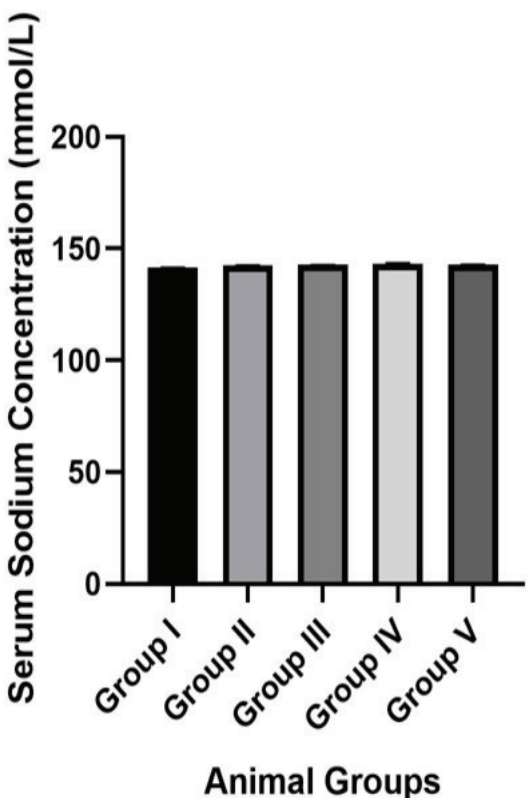

Figure 11. Showing serum sodium level in all groups. (***- p<0.001, ** - p<0.01, * - p<0.05).

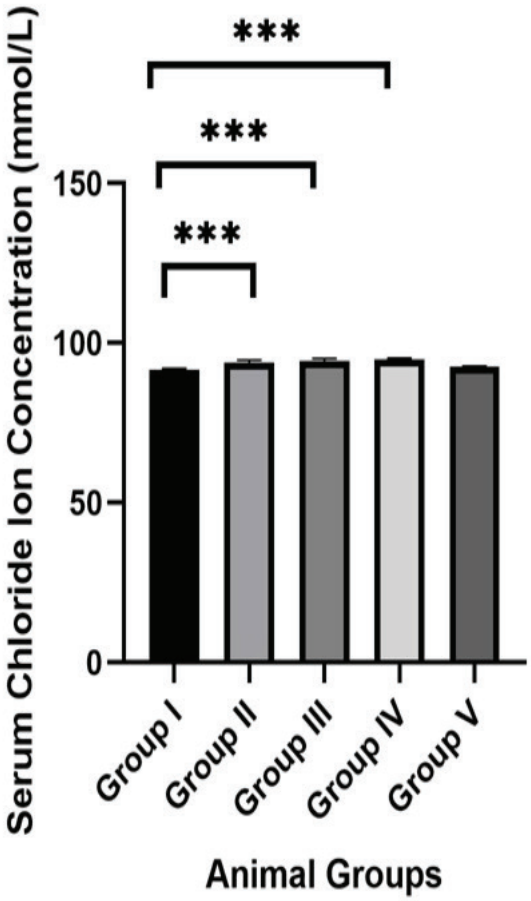

Figure 12. Showing serum chloride level in all groups. (***- p<0.001, ** - p<0.01, * - p<0.05).

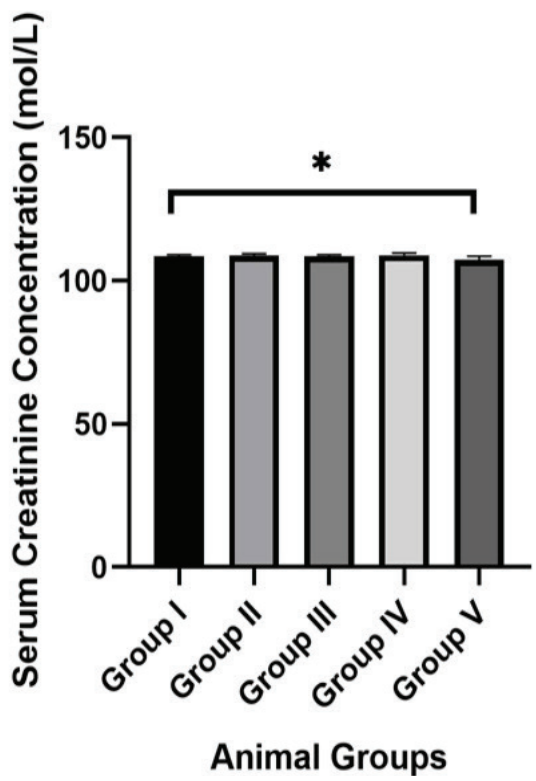

Figure 13. Showing serum creatinine level in all groups. (***- p<0.001, ** - p<0.01 *-p<0.05).

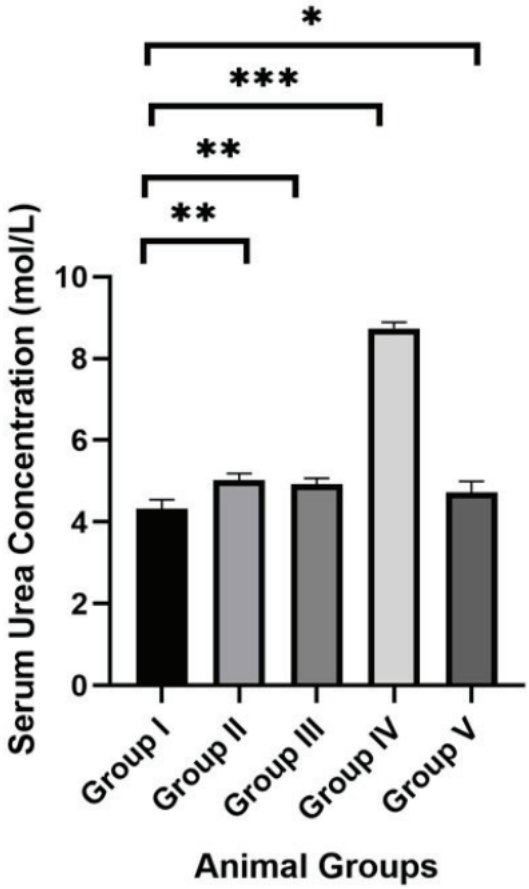

Figure 14. Showing serum urea level in all groups. (***- p<0.001, ** - p<0.01, * - p<0.05).

Suspension of DPP on the Histomorphology of the Liver, Brain, Kidney and Splenic Tissues

Microscopic observation of the kidney tissue of rats in all groups revealed little change in the histoarchitecture of the renal tissue. The tuft of vascular tissue that constituted the glomerulus was encapsulated within Bowman's capsule and surrounded by Bowman's space which was slightly dilated in group VI (Fig15).The histomorphology of the brain tissue in groups II and III were similar to the control group. The granular layer in groups IV and V was thinner when compared to the other groups. The molecular layer showed degeneration and vacuolated cells in group IV. The purkinje layer was same in all groups (Fig. 16). The liver tissue showed the same histoarchitecture in all groups with the cords of sinusoids radiating towards the central vein separated by sinusoids. The central vein appeared more dilated in the liver tissue of rats in group IV (Fig. 17). The micrograph of the splenic tissue showed aggregates of lymphoid follicules of the white pulp embedded in the red pulp of the splenic parenchyma. The white pulp appeared more diffuse in the spleen tissue of rats in group II compared to the other groups (Fig. 18).

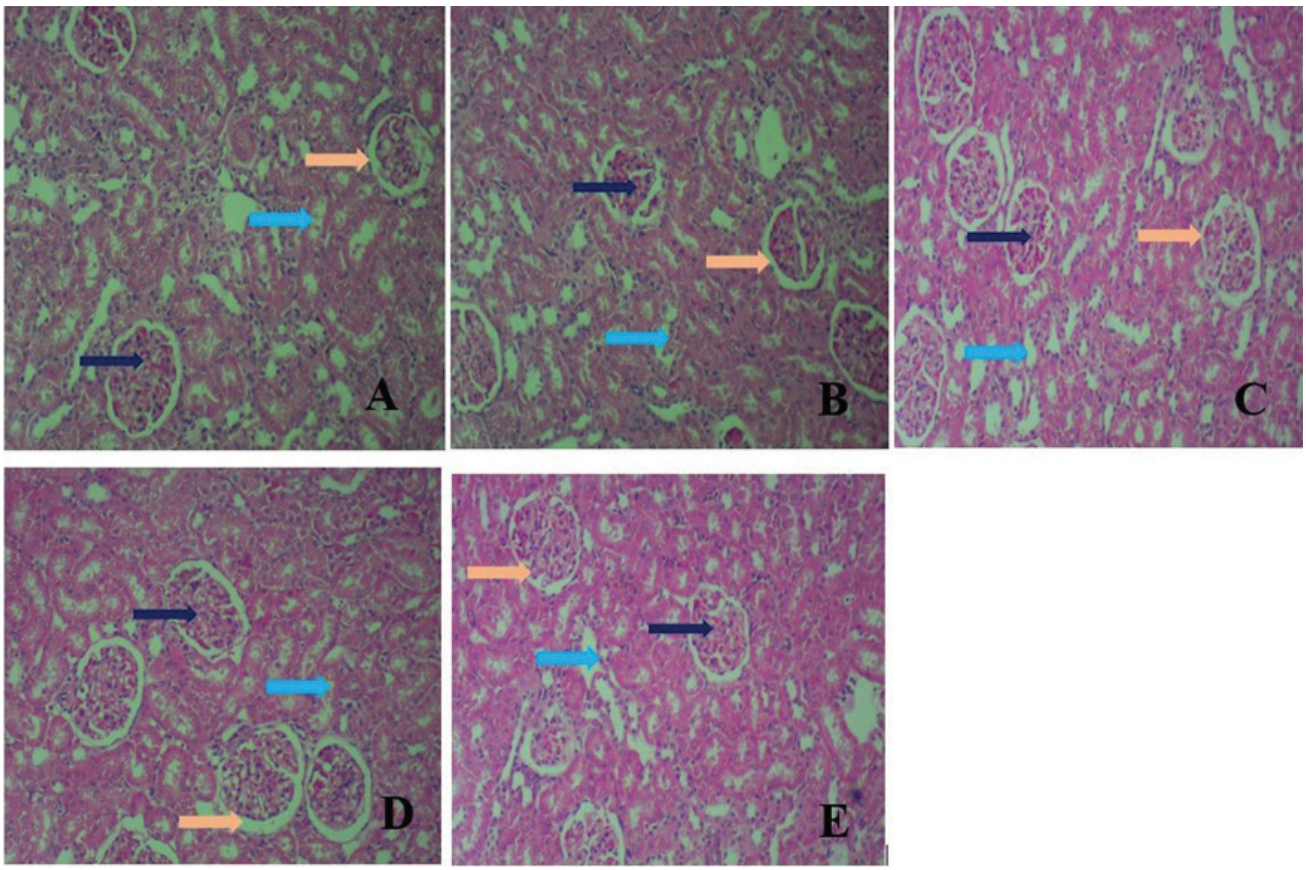

Figure 15. A-E Showing the micrograph representing the kidney tissue in all groups. There was little changes observed in the histology of the glomerus (navy arrow). Bowman's capsular space (orange yellow) appeared wider in group IV) when compared to group I. The renal tubules (blue arrow) were same in all groups. H & E X100.

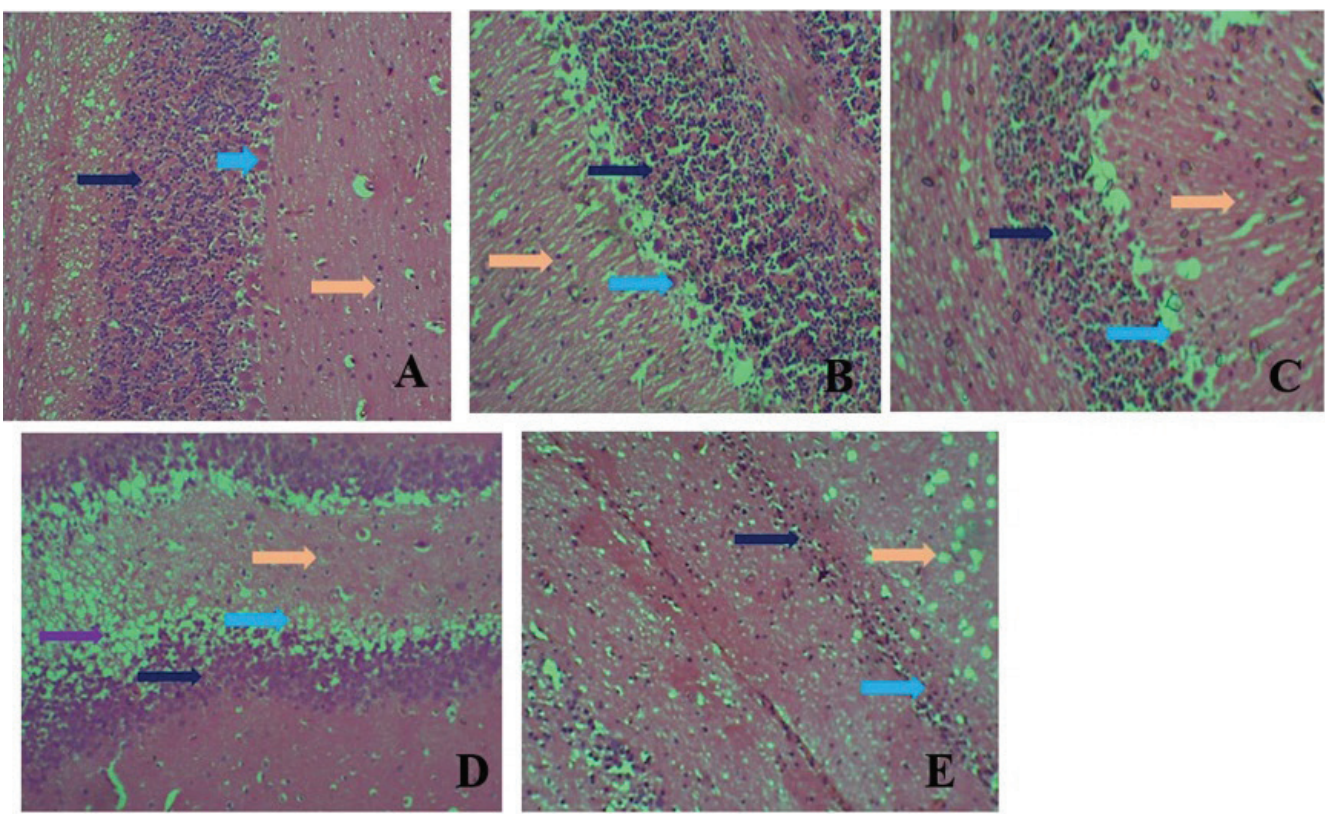

Figure 16. A-E Showing the photomicrograph of the brain tissue of rats in groups I-V. The granular layer (navy arrow) showed a similar arrangement with the control group in rats in groups II and III (Fig 16 B and C). the granular layer was thinner in thickness in groups IV and V (Fig. 16 D and E). The molecular layer in group IV showed a region of degeneration (purple arrow in fig. 16 D). The purkinje layer (blue arrow) remained same in all groups. H & E X 100.

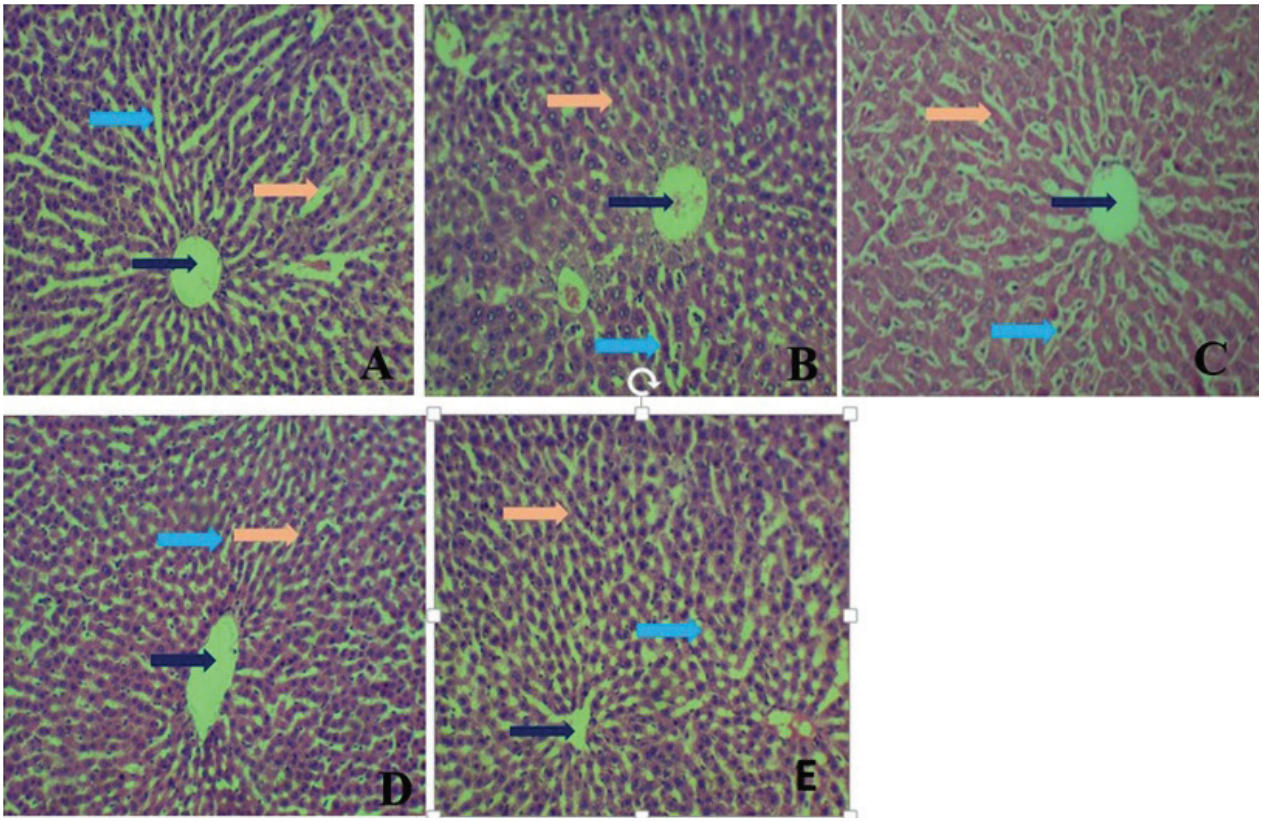

Figure 17. A-E Showing the photomicrographof the liver of rats in groups I-V. The histoarchitecture of the liver tissue was unaltered by administration of the extract. The central vein (navy arrow) was clear in groups I-III. The vein was slightly dilated in group IV (fig. 17D). The sinusoids (orange arrow) were surrounded on both sides with cords of hepatocytes (blue arrow) radiating towards the central vein. H&E X 100

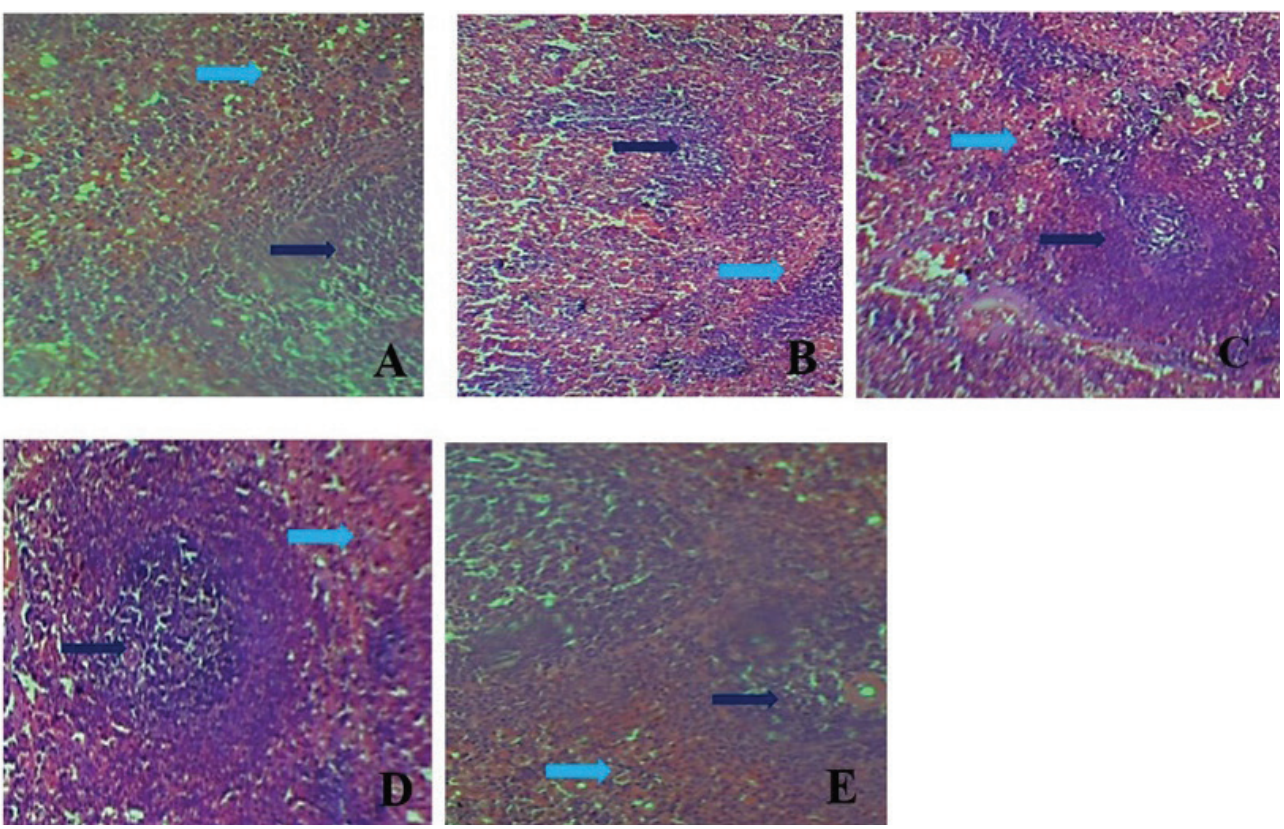

Figure 18. A-E Showing the photomicrograph of the spleen showing the splenic histoarchitecture in all groups. There was no changes observed in the histology of the spleen as the white pulp (navy arrow) was embedded in the red pulp (blue arrow) of the splenic parenchyma. The white pulp in group II appeared more diffuse than in other groups. H & E X100

Discussion

Date palm pollen (DPP) has been consumed for many centuaries for its numerous health benefits. In the current study, DPP is administered to female albino rats to detemine its effect on the weight, hematological parameters, serum electrolytes, renal and hepatic biomarkers. DPP did not have a significant effect on the weight of albino rats in any group after administration of the extract for the duration of the study This result differed from other studies that showed that DPP increased body weight in the male rats used in the study. Different studies[2,15,16,17] demonstrated that methanolic extracts of DPP increased the body weight in the male rats used. This difference could be attributed to the fact that males and females have different energy metabolism and susceptibility to pathophysiological conditions and response to the experimental protocol as reported by Dacie and Lewis[18].

Oral administration of DPP in the current study caused insignificant changes in the red blood cell count, haemoglobin concentration, mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC) in the rats administered DPP extract when compared with the control. The hematological values in this study agreed with similar reference values conducted in a study as reported by Orabi and Shawky[19]. Other studies[20,21] demonstrated that frequent oral administration of date palm pits caused a substantial increase in the concentration of mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, and hemoglobin in the rats used in the study. The extract appeared to decrease white blood corpuscle (WBC) count in a dose dependent manner; a decrease in WBC count may suggest immunosuppression and consequent decline in immune system's response to infection or antigens.

Serum albumin consists of a single species of proteins representing approximately 60% of the total protein. It is synthesized exclusively in the liver and functions as a regulator of blood oncotic pressure, as a carrier for many cations and water insoluble substances, and as a pool of amino acids for caloric or synthetic purposes. The values obtained from the present study showed that the extract could play a role in maintaining serum oncotic pressure.

Deterrmining the lipid profile in the research animals gives an indication of the levels of circulating lipids as well as ascertaining the likelihood of cholesterol-related diseases. The lipid profile valuable information about the levels of cholesterol present in blood. HDL is one of the major classes of plasma lipoproteins that are composed of a number of heterogeneous particles, including cholesterol and vary with respect to size and content of lipid and apolipoprotein. HDL removes cholesterol from the peripheral cells to the liver, where the cholesterol is converted to bile acids and excreted into the intestine. DPP increased serum cholesterol, decreased serum triglycerides levels at lower doses (78 $mgkg^{-1}$ and 156 $mgkg^{-1}$) but increased the levels at a higher dosage (312 $mgkg^{-1}$). The extract had a similar effect on serum high density lipoprotein (HDL) concentration at the lower dosages (78 $mgkg^{-1}$, 156 $mgkg^{-1}$) but at the concentration of 312 $mgkg^{-1}$, the serum HDL concentration increased. Low density lipoprotein (LDL) levels were increased significantly in all groups. at a concentration of 156 $mgkg^{-1}$ and 312 $mgkg^{-1}$. LDL and HDL levels returned back to normal after the extract administration was discontinued in group V. Elevated LDL levels as a result of the administration of DPP indicated an increased risk for coronary heart disease (CHD), peripheral artery disease or stroke. Abdel-Shaheed *et al.*[22] reported no significant difference in the lipid profile in rats administered with aqueous extract of date palm wheras Uchida *et al.*[23] reported that hydroethanolic extracts of DPP decreased LDL levels in diabetic rats and concluded that DPP and its hydroethanolic extract may have hypolipidemic effects which may be due to its known constituents, such as phytosterols, polyunsaturated fatty acids (which decreased plasma total and LDL-c compared with saturated fatty acids). In the present study however, LDL levels were elevated after administration of the extract.

ALT is considered to be liver specific and is present in large concentrations in the cytoplasm of hepatocytes while AST is present in many tissues and is useful in evaluating muscle and liver tissue damage in small and large animals. Administration of DPP caused no significant difference in serum AST concentration, when the extract administration was discontinued, there was a significant decrease in AST concentration in that group. Serum ALT and ALP concentration was significantly increased in all groups following administration of the extract. The elevation in the levels of these biochemical markers (ALT and ALP) in female rats. Ferreira-Gonzalez *et al.*[24] reported that psychologic stress in rats and mice results in approximately fourfold increases in liver biomarkers. This may also be a response to emotional stress, preanalytical effects (handling) as well as physical inturbations or muscle injury that is not detected by histopathology. The insignificant increase in the levels of AST is an indication that the extract is not hepatotoxic as elevation in this parameter is an indicator of hepatocellular injury.

Serum ALP originates mostly from liver and bone while excessive serum cholesterol provides supportive evidence for hepatic disease[25]. In accordance with the current study, Al-Samarai *et al.*[5] reported that DPP caused a significantly diminished the elevated serum hepatic and renal enzymes and lipid profiles in paracetamol-induced hepatorenal toxicity. Maliver*et al.*[26] also reported an increase in liver enzyme levels in test animals. Increase in serum level of AST in brain,

kidney, skeletal muscle and liver may be due to damage in these tissues and can cause increase in serum AST activity. When sudden increase in the levels of AST is observed without a concurrent increase in ALT, this may suggest physical and psychological stress effects and not due to pathological changes[27].

Creatinine is a waste product formed in muscle from a high-energy storage compound, creatinine phosphate. Creatine phosphate can be stored in muscle at approximately four times the concentration of adenosine triphosphate. In muscles, it spontaneously undergoes degradation to form a cyclic anhyride-creatinine. The blood concentration of creatinine and its excretion in urine are remarkably constant in normal individuals. Therefore, serum creatinine level is used as an indicator for assessing kidney function. Urea contributes most of the body's non-protein nitrogen, accounting for about 45% of the total amount. It is the major end-product of protein catabolism in humans and synthesized in the liver, released into circulation and excreted by the kidneys. Measurement of urea in blood is also a useful indicator of renal and hepatic integrity.

From the present study, there was a significant increase in the serum levels of potassium and urea. In the group that received the highest dose, there was a very noticable spike in the serum sodium concentration. There was no significant increase in sodium, chloride ion, and creatinine concentrations in the administered groups.

The kidney functioning capacity was assessed in this study by measuring the levels of electrolytes, creatinine and urea in the serum of the rats. The absence of any significant effect of DPP on the weight of the kidney as well as serum concentrations of sodium, chloride and creatinine of the rats suggested normal functioning of the organ. The slight increase observed in the serum levels of potassium and urea, especially following the administration of the highest dose may be attributed to slight destruction of cells, with a concomitant redistribution of potassium from the intra-to extracellular compartment, leading to haemolysis as observed also in a study carried out by Kessel *et al.*[8]. Many herbal preparations have been found to exhibit renal tubular necrosis showing extensive interstitial fibrosis and severe tubular loss most prominent in the outer cortex[29,30]. Abdel-Shaheed *et al.*[22] also demonstrated that DPP elevated serum uric acid, creatinine and urea concentrations in studies carried out.

Histopathological changes of the tissues can confirm results obtained from the biochemical analysis. In the renal tissue, very little changes were observed in all groups following the administration of DPP. The cerebellum showed a degeneration of the molecular and granular layers and in the spleen tissue, the white pulp was more diffuse in the group administered DPP extract. The liver tissue in the group that ingested the highest dosage also showed very little histological changes in the tissue with dilations observed in the central group in this group[31]. Aboul-Ela *et al.*[32] showed that date fruit and seed extracts produced significant improvement in liver morphology in streptozotocin induced diabetic rats. Al-Asmari *et al.*[1] and Raji KB *et al.*[4] showed that DPP treatment curtailed paracetamol acetaminophen-induced oxidative stress in both hepatic and renal tissue by ameliorating redox-sensitive tissue damage. It was concluded that the protective role of DPP could be due to its antioxidant, membrane stabilizing as well as antihyperlipidemic actions exerted through modulation of biochemical markers.

In the current study, administration of a dosage of 312 $mgkg^{-1}$ showed deleterious effects as observed in the biochemical analysis of serum for renal and hepatic biomarkers. The effects were greatly reduced after the treatment was discontinued in group V.

Conclusion

The present study examined the effect of date palm pollen (DPP) on heamatological indices, organ weight, serum and renal biomarkers as well as histoachitecture of several tissues in female albino rats. Results obtained showed that at a concentration of 312 $mgkg^{-1}$, DPP elevated hepatic and renal biomarkers as well as serum electrolytes. When the extract administration was stopped for a period of two weeks and the same tests were carried out, the results of the tests carried out read as normal again. Histopathological analyses showed no major changes in all groups. From the results obtained from this study, DPP is safe and even beneficial at a lower concentration.

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