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Cannabidiol Oil and Prednisolone Treatment Altered Hematologic Indices, Serum Urea, Creatinine and Cellular Architecture of Kidney on Cadmium Induced Toxicity in Male Wistar Rats

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

This study investigated the impact of CBD oil and prednisolone on hematologic indices, urea, and creatinine among cadmium-induced toxicity in male rats. Forty male rats weighing 150g to 200g were assigned into 8 groups (1-8) with five rats each. Group 1 served as control, Group 2-8 received 1mg/kg body weight of prednisolone; 1.5mg/kg bw of cadmium; 1mg/kg bw of prednisolone + 0.2mg/kg bw of CBD-oil; 0.2mg/kg bw of CBD-oil + 2mg/kg bw of cadmium; 3mg/kg bw of Pred + 2mg/kg of cadmium; 0.1mg/kg bw of CBD-oil and 0.2mg/kg bw of CBD-oil respectively. The administration was done using gavage for 14 days. The present results revealed that PCV, haemoglobin, and RBC count of the treated groups were decreased significantly ($p<0.05$) comparedto the control. TWBC count significantly increased in treated groups than in control. Platelet count significantly increased in groups treated with pred+ cd, CBD-oil (0.1ml), and CBD-oil (0.2ml) than control. Neutrophil count was significantly reduced in groups treated with CBD oil (0.1ml) than in control and other groups. Lymphocyte count significantly increased in groups treated with cadmium+ CBD oil and CBD oil (0.1ml) than in other groups. Eosinophil count significantly decreased in groups treated with prednisolone and pred +CBD oil than control. Monocyte count significantly increased in groups treated with cadmium, pred +cadmium, and CBD oil (0.1ml) than in control. There was a significant decrease in groups treated with pred +CBD-oil, cadmium + CBD-oil, and CBD-oil (0.2ml) than control. Serum urea significantly decreased in the group treated with pred + CBD oil than control. Serum creatinine significantly increased in groups treated with cadmium + CBD oil and CBD oil (0.2ml) compared to the control and prednisolone groups. Histology of the kidney revealed mesangial expansion, hypertrophy of renal corpuscle, hemorrhage, and lymphocyte infiltration in groups treated with pred+ CBD oil and CBD oil (0.1ml) compared to the control. We conclude that CBD oil, prednisolone, and cadmium administration at different doses induced biochemical alterations, altered hematologic indices, and cytoarchitecture of the kidney. Therefore, if these results apply to humans, combined use of CBD oil and prednisolone should be supplemented with blood tonics, especially in chronic kidney disease.

Keywords: CBD oil; prednisolone; cadmium; hemoglobin; lymphocyte.

1. INTRODUCTION

The consumption of prednisolone and cannabis products especially cannabidiol (CBD) oil a combined remedy in the management of some disorders such as obstructive respiratory disorder, depression and insomnia associated with hypertension, nausea and vomiting associated with cancer chemotherapy, anorexia and cachexia in HIV/AIDS patients, neuropathic pain, allergic, inflammation and spasticity in multiple sclerosis [1] is on the increase in southern Nigeria. This has increased concern about their likely physiologic adverse effects on blood parameters and kidney function.

Cannabidiol is the major non-psychoactive component of *Cannabis sativa* [2]. It was reported that CBD which is an isomer of tetrahydrocannabinol (THC) acts as a balancing force to regulate the strength of the psychoactive agent (THC) and also regulates the body's metabolism of THC by inactivating cytochrome p450 which is an enzyme that metabolizes drugs [2]. The CB2 receptors are present only in the cells of the immune system which are more prevalent in B-cells, natural killer cells, and monocyte, but may be found in polymorphonuclear neutrophil cells, T8 cells, and T4 cells [3]. The endocannabinoid system is an important biological regulatory system that is highly conserved from lower invertebrates to higher mammals [4]. The Endocannabinoid family contains enzymes for biosynthesis and degradation of the ligands and also for immunoregulation. Manipulation of endocannabinoids and or use of exogenous cannabinoids in vivo can constitute a potent treatment modality against inflammatory disorders [4]. Obembe et al., [5], reported that consumption of Cannabis sativa altered hematologic indices by causing thrombo-embolism, production of immature monocytes and reduced white blood cell count, increased red blood cell (RBC), packed cell volume (PCV), and Hemoglobin counts. Omayma [6], reported an increased total white blood cell (TWBC) count on heavy Cannabis users. Amna and Nabiela [7], reported decreased RBC and TWBC count in Cannabis sativa-treated rats with no significant

change in hemoglobin concentration. The kidney is important in the maturation of blood cells because it produces growth factors such as erythropoietin, leucopoietin, and thrombopoietin which are essential for blood cell maturation [8].

Prednisone is a synthetic, anti-inflammatory glucocorticoid derived from cortisone. It is biologically inert and converted to prednisolone in the liver. Prednisolone is an anti-inflammatory agent used to treat immunosuppression, rheumatism, dermatologic, allergic, ophthalmic, respiratory, hematologic, neoplastic, edematous, gastrointestinal, and acute exacerbations of multiple sclerosis [9]. Prednisolone decreases inflammation via suppression of the migration of polymorphonuclear leukocytes and reversing increased capillary permeability. It also suppresses the immune system by reducing the activity and volume of the immune system [9]. Hence, this study investigated the impact of prednisolone and CBD oil on haematologic indices, urea and creatinine on cadmium-induced toxicity in male Wistar rats.

2. MATERIALS AND METHODS

Drugs: prednisolone used for this study was purchased from Unicure pharmaceutical limited, Lagos, Nigeria. The cadmium chloride was purchased from Sigma-Aldrich Limited Germany with EC number 233-296-7. Cannabidiol (CBD) oil was purchased from TEEMU Premium, California, USA.

2.1 Laboratory Animals

Forty male Wistar rats, weighing 150–200g were used for this study. The animals were housed in the Department of Physiology animal house, University of Calabar, Nigeria. Standard animal cages (435 x 290 x150) with wood shavings as bedding were used in housing the animals. They were allowed ad libitum access to rat chow and clean water, and exposed to 12/12-hr light/dark cycle. The animals were acclimatized for 7 days. The animals were kept in line with laid down principles for animal care as prescribed in Helsinki's 1964 declaration. The animal ethics committee of the University of Calabar approved our study protocol with approval number 040PHY3719.

2.2 Experimental Design and Administration of Drugs

The animals were randomly assigned differently into 8 separate groups (n = 5). After 7 days of acclimatization, CBD oil, prednisolone, and cadmium administration commenced. The drugs were administered via oral route using an orogastric tube (gavage), once, every day, to animals in the treatment groups (2 to 8), using the doses outlined in Table 1, while the control group received feed and 0.5ml normal saline as a vehicle. The administration of CBD oil and prednisolone solution lasted for fourteen (14) days, whereas, the administration of cadmium chloride solution lasted only 2 days before the rats were killed and samples were collected for analysis.

2.3 Evaluation of Hematologic Indices

Hematological parameters assayed for are packed cell volume (PCV), total white blood cell count (TWBC), platelet count, and red blood cell count.

2.3.1 PCV

The packed cell volume is the proportion of whole blood occupied by red cells, expressed as a ratio (L/L). PCV was assayed by filling ¾ of the capillary tube with well-mixed EDTA blood, sealing the unfilled end, place in a microhematocrit rotor, and centrifuging for 5 minutes. Immediately after centrifuging, the PCV was read using the microhematocrit reader. Hemoglobin is measured by dividing the PCV value by 3 HB units: mg/dl. The mean cell hemoglobin concentration (MCHC) gives the concentration of Hb in g/l in 1 liter of packed red cells. Hb = MCHEg/L. Mean cell volume (MCV) provides information on red cell size, measured in femtolitre (Fl). Mean cell hemoglobin (MCH) gives the amount of Hb in a picogram (pg.) in average red cells. Method was used by Obembe et al., [5].

2.3.2 Assay for RBC count X10^{12}/L

Procedure: About 4.0ml of formal citrate (diluting fluid) was measured and dispensed into a test tube. About 0.02ml of well-mixed EDTA blood was added and mixed. The counting chamber was assembled and filled with well-mixed samples and left the chamber undisturbed. It was examined using an x10 objective lens. Count the red cells in small squares and read the number of red cells per liter. RBC count = N x 201 X109. Where N=Number counted, 201 is the diluting factor, 0.2mm2=Area. 0.1mm = depth of the chamber. Method was used by Obembe et al., [5].

Table 1. Study design and drugs administration

Groups	No. of rats	Treatment
Group 1 (Control)	5	Feed + 0.5ml of normal saline as a vehicle throughout the experiment.
Group 2	5	1mg/kg bw of prednisolone
Group 3	5	1.5mg/kg bw of Cadmium
Group 4	5	1mg/kg bw of prednisolone + 0.2mg/kg bw of CBD Oil.
Group 5	5	0.2mg/kg bw of CBD oil + 2mg/kg bw of cadmium
Group 6	5	3mg/kg bw of prednisolone + 2mg/kg of cadmium
Group 7	5	0.1mg/kg bw of CBD Oil low dose
Group 8	5	0.2mg/kg bw of CBD oil high dose

2.3.3 Assay for total WBC count unit*10^9/L

Principle: Whole blood dilutes 1 in 20 in an acid reagent which hemolyzes the red cells. Nucleated red cells were not counted as white cells were counted. White cells were counted microscopically using an improved Neubauer counting chamber and the number of WBC per liter of blood was calculated.

Procedure: Pipette 0.38ml of diluting fluid into test tubes and add 0.02ml of well-mixed EDTA blood and mix. Then assemble the counting chamber and re-mix the dilute blood sample using a Pasteur pipette fill one of the grids of the chamber with the sample. Then leave the chamber undisturbed for 20 minutes to allow time for the white cells to settle. Examined using X10 objective lens. The cells were counted in four large squares of the chamber and the number of white cells per liter was recorded. WBC count (per liter) = N x DfX106/A*D; Where N = No of cell counted, Df = Dilution factor, A = Area counted, D = Depth of chamber. Method was used by Obembe et al., [5].

2.3.4 Assay for platelet count unit *10^9/L

Principle: Whole blood is diluted 1:20 in an Ammonium oxalate reagent which lyses the red cells. Platelets are counted microscopically using an improved Neubauer counting chamber and the number of platelets per liter of blood is calculated.

Procedure: Pipette 0.38ml of diluting fluid into a test tube, then add 0.02ml of well-mixed EDTA blood and mix, assemble the counting chamber and fill with the well-mixed sample. The chamber was left undisturbed for 20mms, to prevent drying of the fluid place the chamber in a Petri dish on dampened tissue & cover it with a lid. Examine using X10 objective lens, count the platelet in the small squares & report the number of platelets per liter. Method was used by Obembe et al., [5].

2.4 Determination of Serum Urea

Principle: Urea was measured using Urease-Berthelot Method (mmol/L). Urea in serum was hydrolyzed to ammonia in the presence of urease. The ammonia was then measured photometrically by Berthelot's reaction.

Procedure: Label the tubes as test, standard, and blank. Pipette 0.1ml of the right (R1) into all the tubes and add 10ul of the samples, standard, and d/w into appropriate tubes and then mix and incubate at 37'c for 10mms. Pipette 2.5ml of right (R2) and right (R3) to all the tubes. Mix and incubate at 25'c for 15mins. Read and record the absorbance at 546nm.

2.5 Determination of Serum Creatinine

Principle: Creatinine was measured using Direct End-Point Method (umol/L). Creatinine reacts with picric acid in an alkaline solution to form a colored complex. The amount of complex formed is directly proportional to the creatinine concentration.

Procedure: Label the tubes as a test, standard and blank; Pipette 2.0ml of reagent into all the tubes. Add 0.1ml of the sample, standard, and d/w into respective tubes. Mix and after 30 seconds, read the absorbance of the standard and sample. Exactly 2mins later read the absorbance of the standard and sample. A2 of standard and sample. A1–A2=D.

2.7 Histological Examination of the Kidney

The kidney of the control and treated rats were fixed with 10% buffered formaldehyde for 48 hours. Sections were obtained and stained with

hematoxylin and eosin (H & E) stains. The microscopic slides were labeled appropriately. Photomicrographs were taken at ×500 magnifications using a light microscope (Leica DM 750, Switzerland). Method was recently used by Mobisson et al., [10]; Mobisson et al., [11].

2.8 Statistical Analysis

All results are presented as mean ± SEM, n=5. One-way analysis of variance (ANOVA) was utilized in comparing the difference within groups, followed by post hoc multiple comparisons. Computer software SPSS version 17.0 and Excel analyzer were used for the analysis. The level of significance was placed at p<0.05. Method was used by Mobisson et al., [12].

3. RESULTS

3.1 Comparison of Hematological Indices in Control and Different Experimental Groups

Fig. 1 shows packed cell volume (PCV) concentration in the different experimental groups. The mean PCV concentration was significantly (p<0.05) decreased in treated rats compared to control. However, rats fed with prednisolone, cadmium, and 0.1ml CBD oil were significantly (p<0.05) decreased compared to other treated groups. Fig. 2 illustrates the mean hemoglobin (HB) concentration in the different experimental groups. The mean hemoglobin concentration was significantly (p<0.05) decreased in treated rats compared to control. Although, rats treated with prednisone +CBD oil and prednisolone + cadmium were significantly (p<0.05) increased when compared with other treated groups. Figure 3 depicts the mean red blood cell (RBC) count in the different experimental groups. The mean RBC level was significantly (p<0.05) reduced in all treated groups compared to the control. Although, groups treated with prednisolone, prednisolone + cadmium, and CBD oil (0.2ml) showed a significant increase compared to rats treated with prednisolone + CBD oil and cadmium + CBD oil respectively. Furthermore, rats treated with CBD oil (0.1ml) significantly decreased compared to other treated groups. Figure 4 shows the mean total white blood cell (TWBC) concentration in control and different experimental groups. The TWBC in all treated rats was significantly (p<0.05) increased compared to control. Furthermore, rats treated with cadmium, CBD oil (0.1ml), and CBD oil (0.2ml) increased when compared with other treated groups. Figure 5 shows the mean Platelet count concentration in the different experimental groups. The platelet count was significantly (P<0.05) increased in rats treated with Prednisolone + cadmium, CBD oil (0.1ml), and CBD oil (0.2ml) compared with the control.

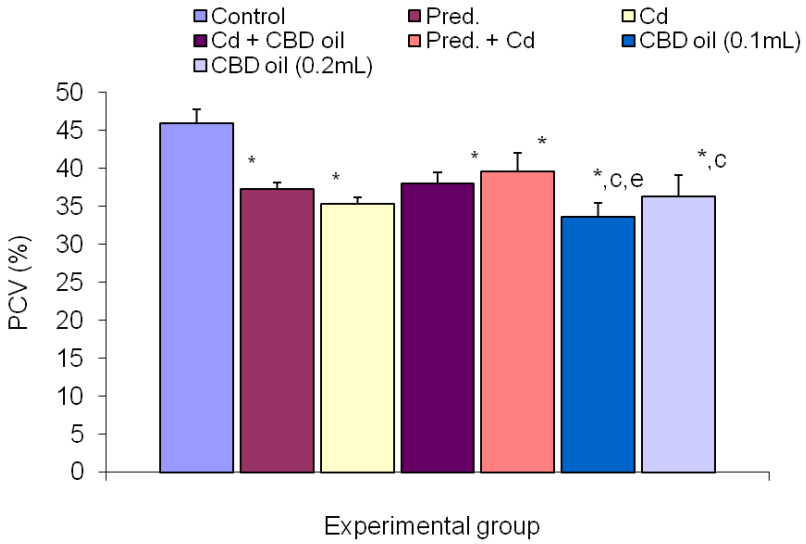

Fig. 1. Packed cell volume (PCV) of the different experimental groups

Values are expressed as mean SEM, n =5
** = p<0.05 vs control;*
c = p<0.05 vs Pred. + CBD oil
e = p<0.05 vs Pred. + Cd

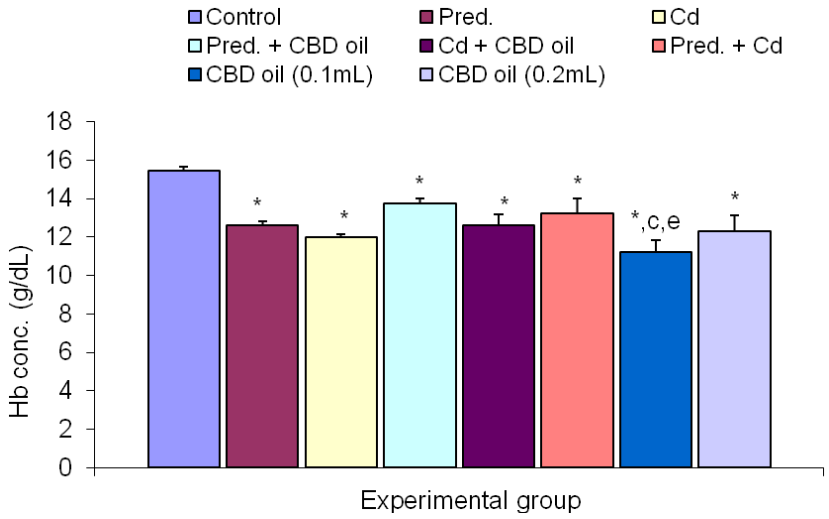

Fig. 2. Haemoglobin (Hb) concentration in the different experimental groups

Values are expressed as mean SEM, n =5.
** = p<0.05 vs control;*
c = p<0.05 vs Pred. + CBD oil
e = p<0.05 vs Pred. + Cd

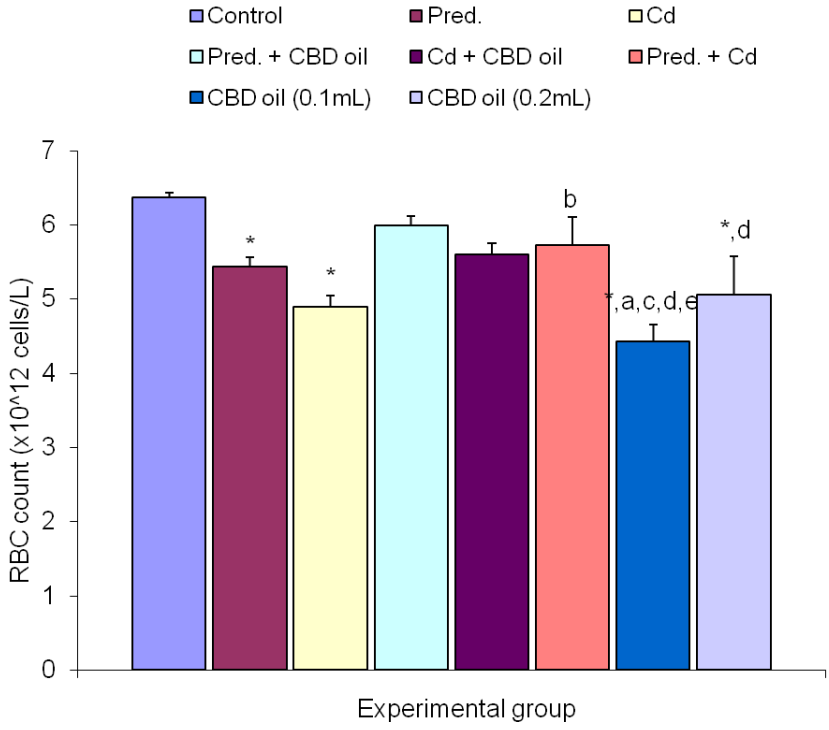

Fig. 3. Red Blood Cell (RBC) count of the different experimental groups

Values are expressed as mean ±SEM, n =5.
** = p<0.05 vs control;*
a = p<0.05 vs Pred.
b = p<0.05 vs Cd
c = p<0.05 vs Pred. + CBD oil
d = p<0.05 vs Cd + CBD oil
e = p<0.05 vs Pred. + Cd

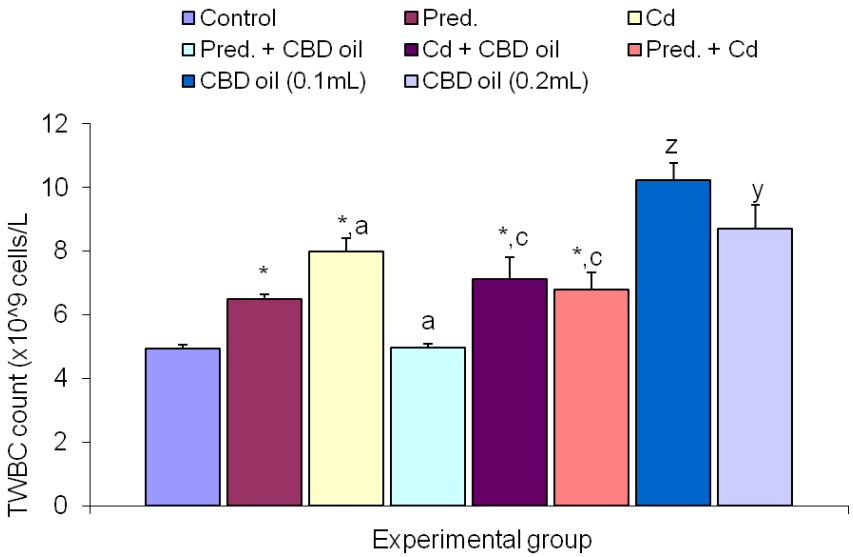

Fig. 4. Total White Blood Cell (TWBC) count of the different experimental groups

Values are expressed as mean SEM, n = 5
** = p<0.05 vs control;*
a = p<0.05 vs Pred;
c = p<0.05 vs Pred. + CBD oil
z = p<0.05 vs all other groups
y = p<0.05 vs other group except with Cd

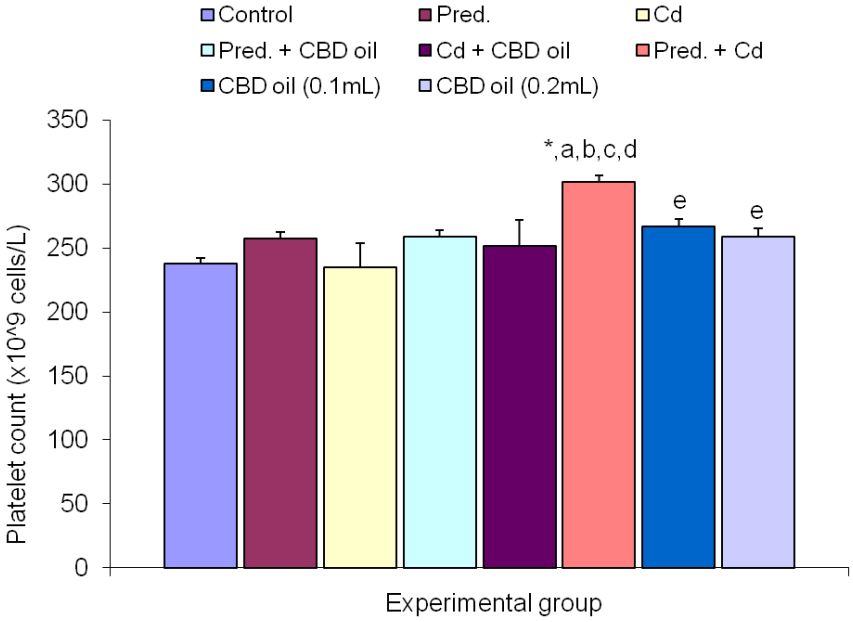

Fig. 5. Platelet count of the different experimental groups

Values are expressed as mean ±SEM, n = 5.
** = p<0.05 vs control;*
a = p<0.05 vs Pred.
b = p<0.05 vs Cd
c = p<0.05 vs Pred. + CBD oil
d = p<0.05 vs Cd + CBD oil
e = p<0.05 vs Pred. + Cd

3.2 Comparison of Differential White Blood Cell Counts of Control and Different Experimental Groups

Neutrophil count was significantly reduced in groups treated with CBD oil (0.1ml) than in control and other groups. Lymphocyte count significantly increased in groups treated with cadmium+ CBD oil and CBD oil (0.1ml) than in other groups. Eosinophil count significantly decreased in groups treated with prednisolone and pred +CBD oil than control. Monocyte count significantly increased in groups treated with cadmium, pred +cadmium, and CBD oil (0.1ml) than in control. There was a significant decrease in groups treated with pred +CBD-oil, cadmium + CBD-oil, and CBD-oil (0.2ml) than control.

3.3 Comparison of Serum Urea and Creatinine Concentration in Control and Different Experimental Groups

Fig. 6 showed a significant decrease ($p<0.05$) in serum urea concentration in the group administered prednisolone + CBD oil compared to the control. However, there was a significant increase in the groups administered cadmium + CBD oil, CBD oil (0.1ml), and CBD oil (0.2ml) compared with the group administered prednisolone + CBD oil. Figure 7 showed a significant decrease ($p<0.05$) in serum creatinine concentration in the group administered with prednisolone compared to control. Furthermore, groups treated with cadmium, prednisolone+ CBD oil, cadmium + CBD oil, prednisolone+ cadmium, CBD oil (0.1ml), and CBD oil (0.2ml) were significantly increased compared to rats treated with prednisolone.

3.4 Histological Examination of the Kidney in Control and Experimental Groups after Administration

Plate 1a control (group 1) revealed normal renal corpuscles and renal tubules. The renal corpuscle (RC) consists of the glomerulus (G) and Bowman's capsule (BS). Renal tubules-proximal convoluted tubule (PCT), loop of Henle, and distal convoluted tubule (DCT) are seen. Plate 1b (group 2) showed a photomicrograph of prednisolone-treated rats with normal renal corpuscle and renal tubules. Plate 1c (group 3) showed cadmium-treated rats with normal renal corpuscle and renal tubules. Plate 1d (group 4) revealed pred+CBD oil-treated rats with mesangial expansion, Hypertrophy of renal corpuscle, and lining epithelia of renal tubules. Plate 1e (group 5) showed cadmium+ CBD oil-treated rats with normal renal corpuscle and renal tubules. Plate 1f (group 6) revealed pred+cadmium treated rats with normal renal corpuscle and renal tubules. Plate 1g (group 7) revealed CBD oil (0.1ml) treated rats with hemorrhage and lymphocyte infiltration. Plate 1h (group 8) showed CBD oil (0.2ml) treated rats with no visible tissue damage in renal corpuscles and renal tubules.

4. DISCUSSION

In recent times, the combined use of cannabidiol oil and prednisolone in Southern Nigeria is on the increase for the management of Asthma and other respiratory obstructive conditions [13]. Though, prednisolone is a known anti-inflammatory and auto-immune drug employed in the treatment of inflammatory conditions [9]. Conversely, the combined use of prednisolone and cannabidiol oil has elicited questions concerning possible adverse effects, especially on the haematologic indices and kidney. This study investigated the impact of CBD oil and prednisolone use on cadmium-induced toxicity in male rats. The parameters assessed include haematologic indices, serum urea and creatinine, and histological examination of the kidney.

The decrease in PCV, RBC, and hemoglobin counts in treated rats may be likely linked to the toxic effects of the cadmium, prednisolone, and CBD oil which may have caused hemolysis or inhibition of erythropoietic growth factors. This result is in contrast with Obembe et al., [5], which reported increased PCV, RBC, and hemoglobin on Cannabis fed rats. However, it corresponds with the result of Amna and Nabiela [7], which reported decreased RBC count in heavy cannabis users. However, Leise et al., [14] reported that blood chemistry parameters were not adversely affected in CBD oil treated mature Horses. Ognjanović et al., [15], reported decreased hemoglobin in rats exposed to cadmium chloride. Though, the reduction in hemoglobin (HB) can be probably due to the production of reactive oxygen species (ROS) under the influence of the dose-dependent drugs leading to the destruction of the red blood cell membrane and its function. The significant increase in TWBC count and altered differential WBC count may be an indication of immune stimulation due to prednisolone, CBD oil, and cadmium administration. The adverse effects of

these agents may have elicited an immune response thereby increasing the WBC concentration. This result corresponds with Omayma [6], who reported increased TWBC in cannabis-fed rats and contradicts the result of Amna and Nabiela [7] that reported decreased TWBC count in Cannabis users. Furthermore, Shnawa et al., [16] reported a significant increase in eosinophilic count and a non-significant increase in lymphocytes and neutrophils in smokers compared to non-smokers. Cannabis was suggested to mediate this effect via its CB2 receptors which are mostly found on the cells of the immune system and are more prevalent on B-cells, natural killer cells, and monocyte, but may be found on polymorphonuclear neutrophil cells, T8 cells, and T4 cells [3]. Furthermore, Prednisolone may decrease inflammation via suppression of the migration of polymorphonuclear leukocytes and reversing increased capillary permeability. It also suppresses the immune system by reducing the activity and volume of the immune system [9]. The significant increase in platelet count in rats treated with pred+CD, CBD oil (0.1ml), and CBD oil (0.2ml) may be linked to increased total WBC count in these groups. The increase in platelet count may be a sign of possible thrombo-embolism as reported by Obembe et al., [5].

The significant increase in urea and creatinine in this study may be an indication of possible kidney damage due to cadmium, prednisolone, and CBD oil treatment. Accumulation of urea and creatinine which are waste products of metabolism is a possible indication of renal dysfunction [8]. However, Ho et al., [17] reported that cannabinoid may pose significant health risk specially in patient with chronic kidney disease. The increase in the level of creatinine concentration may be an indication of renal toxicity which may likely be linked to the significant decrease in the concentration of packed cell volume, hemoglobin, and RBC count recorded in this study. The kidney is the site for the synthesis of erythropoietin which is vital in erythropoiesis [8]. This agrees with the report by Paul et al., [18] that the elevation in the level of creatinine concentration indicates possible toxins that could lead to renal dysfunctions. Moreover, Park et al., [19] suggested a possible effect of cannabinoids on the kidney. The decrease in creatinine concentration in Prednisolone treated groups may be due to a problem associated with the muscles or liver. However, it was reported that Endocannabinoids, such as anandamide influences renal hemodynamics and tubular sodium reabsorption via CB1 receptor activation [20].

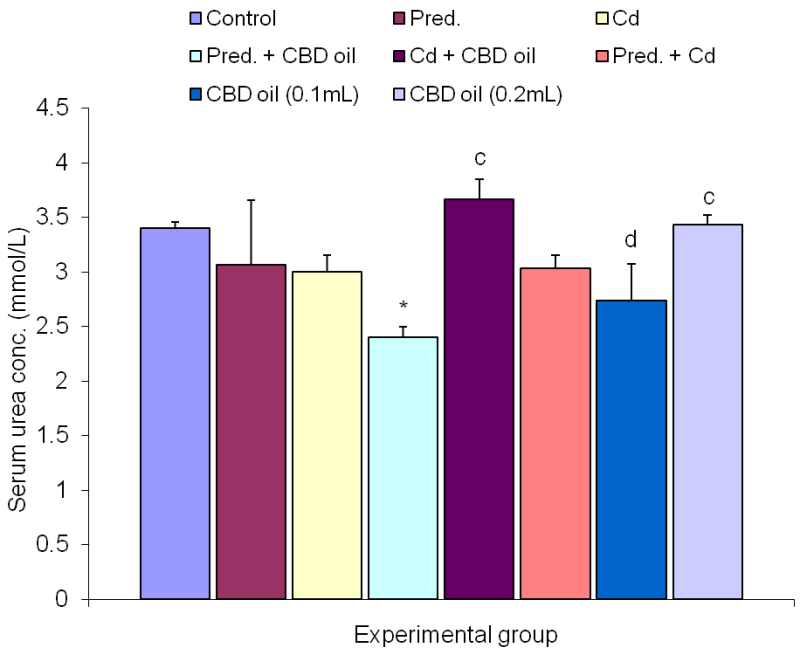

Fig. 6. Serum urea concentration in the different experimental groups

Values are expressed as mean SEM, n = 5
** = p<0.05 vs control;*
c = p<0.05 vs Pred. + CBD oil
d = p<0.05 vs Cd + CBD oil

Table 2. The comparison of differential white blood cell counts of control and experimental groups

Parameters	Group 1 Control	Group 2 prednisolone	Group 3 cadmium	Group 4 pred + CBD oil	Group 5 cadmium+ CBD oil	Group 6 pred+ cadmium	Group 7 CBD oil (0.1ml)	Group 8 CBD oil (0.2ml)
Neutrophil count (%)	28.67±0.88	35.00±1.73	34.33±3.84	36.33±0.88	30.67± 3.53	32.67±2.85	21.33±1.86^{z}	30.67±4.33
Lymphocyte count (%)	62.67±1.45	56.67±0.88	53.67±3.76*	55.67±1.20	64.00±3.06^{b}	57.00±2.52	69.00±2.08^{a,b,c,e}	61.67±5.24
Eosinophil count (%)	3.33±0.33	1.83±0.17*	3.33±0.33^{a}	2.00±0.00*	2.67±0.33^{a}	2.67±0.33^{a}	3.67±0.33^{a,c,d,e}	2.33±0.33*^{,b,f}
Monocyte count (%)	6.00±0.58	5.33±0.33	7.00±0.58^{a}	4.67±0.33^{b,c}	4.67±0.33*^{,b,d}	7.67±0.33*^{,a,c,d}	7.33±0.33*^{,a,c,d}	4.33±0.33*^{,b,f}

*Values are expressed in mean ± SEM, n = 5. *=represents values with significant differences*
** = p<0.05 vs control; a = p<0.05 vs Pred.; b = p<0.05 vs Cd; c = p<0.05 vs Pred. + CBD oil;*
d = p<0.05 vs Cd + CBD oil; e = p<0.05 vs Pred. + Cd; f = p<0.05 vs CBD oil (0.1mL);
z=P<0.05 VS all other groups;

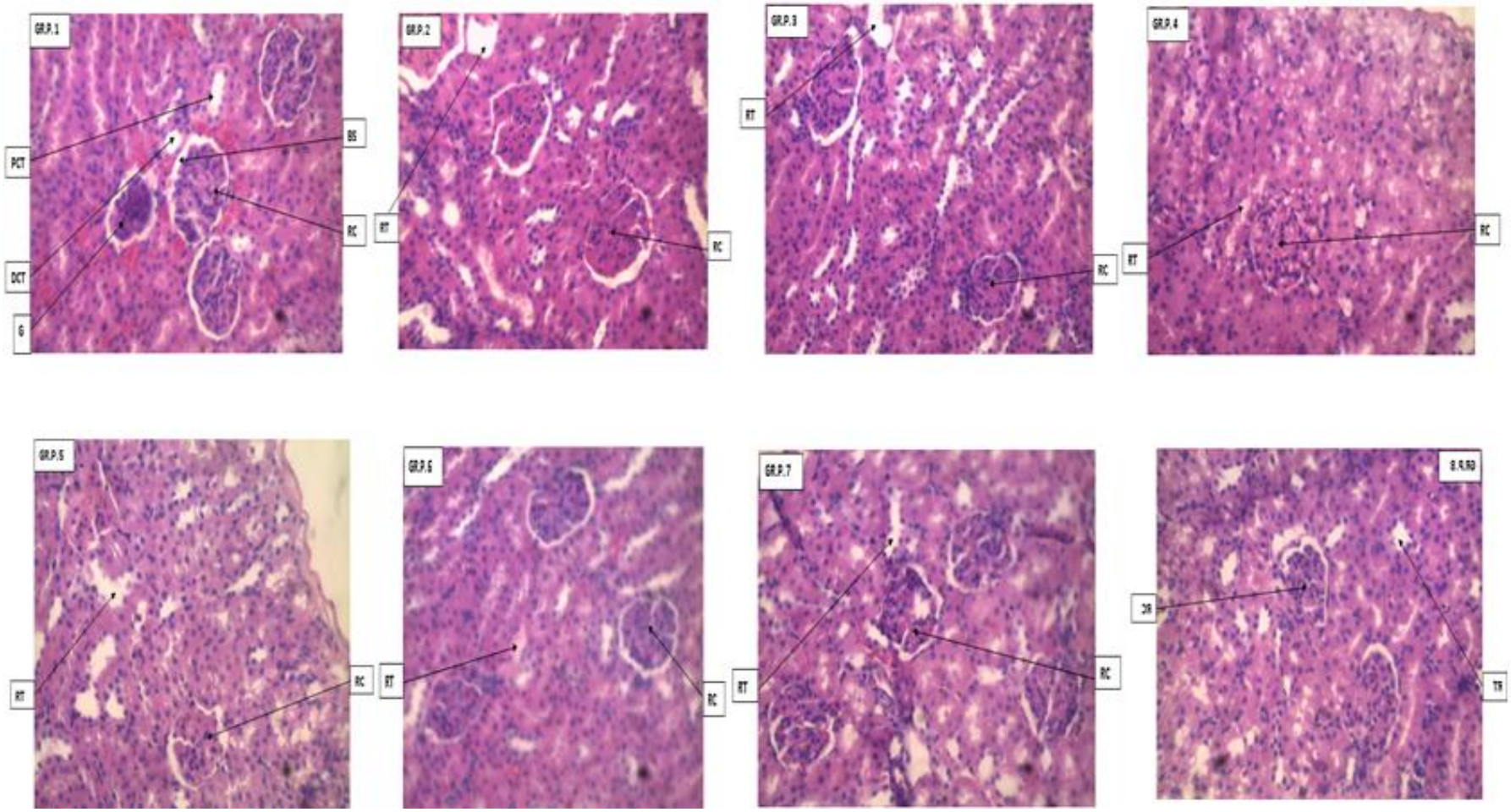

Plate 1(a to h). Photomicrographs of the kidney in control and different experimental groups after CBD oil, prednisone, and cadmium administration. Magnification: x500

Key: G: Glomerulus, PCT: Proximal Convoluted Tubules, RC: Renal Corpuscle
DCT: Distal Convoluted Tubules, RT: Renal Tubules, BC: Bowman's Capsule, GL: Glomerular Late

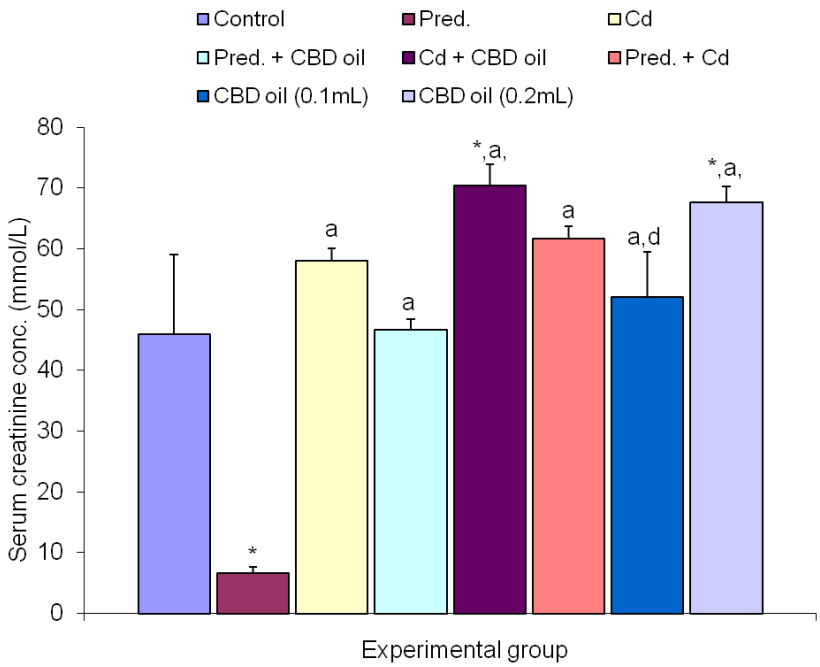

Fig. 7. Serum creatinine concentration in the different experimental groups

Values are expressed as mean SEM, n = 5
** = p<0.05 vs control;*
a = p<0.05 vs Pred.
c = p<0.05 vs Pred. + CBD oil
d = p<0.05 vs Cd + CBD oil

The visible histopathologic changes such as mesangial expansion, hypertrophy of renal corpuscle and lining epithelia of renal tubules, hemorrhage, and lymphocytes infiltration in rats treated with pred+CBD oil and CBD oil (0.1ml) could be linked to increased TWBC, increased platelet count, altered differential WBC count, increased urea and creatinine recorded in these groups. It may also be linked to the toxic effects of the dose-dependent drugs in these groups. Animal models of kidney diseases have also demonstrated that an imbalance of Cannabinoids receptor signaling with dominant CB1 receptor activation over CB2 receptor activation can lead to deleterious effects such as oxidative stress, inflammation, cell dysfunction, apoptosis, and fibrosis [21,22].

5. CONCLUSION

Administration of CBD oil, prednisolone, and cadmium at different doses caused significant decrease in PCV, RBC, and Hemoglobin values and significantly increased TWBC, platelet count, serum urea, and creatinine concentrations and altered the cytoarchitecture of the kidney in male rats. The alteration in the concentration of blood parameters may likely be an indication of anemia, compromised immune system and possible kidney damage. Therefore, if these results are to be applicable in humans, consideration and precaution should be applied in combined use of CBD oil and prednisolone in management of certain illnesses as they adversely affect blood parameters and renal function. Further studies should be conducted to ascertain the possible physiologic mechanism through which cannabis products mediated their effects in the kidney.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The animal ethics committee of the University of Calabar approved our study protocol with approval number 040PHY3719.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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