Haematologic and Haemostatic Effect of Aqueous Extracts of *Combretum Platypterum* Leaves in Albino Wistar Rats

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ABSTRACT

Combretum platypterum is a straggling scandent shrub with ethnomedicinal analgesic, antimicrobial and haemostatic activities. This study was designed to evaluate the effects of aqueous leaf extract of Combretum platypterum on haematological and haemostatic parameters in albino Wistar rats. Experimental rats were shared into five groups, blood samples from the groups were collected by cardiac puncture on days 0, 14 and 28. This study used the automated ERMA autoanalyzer PCE-210N in analyzing the haematological parameters. Prothrombin time (PT) and partial thromboplastin time with kaolin (PTTK) was carried out using the visual clot detection method. Analysis of data on day 14 showed significant decrease in granulocyte count of groups 2 and 3 compared to the control ($p<0.05$). The platelet count also significantly increased ($p<0.05$) compared to control with group 2 having the highest increase. The PT and PTTK significantly decreased ($p<0.001$) compared to control with group 2 having the highest decrease. On day 28 across the groups, the percentage of lymphocytes significantly increased ($p<0.001$) while the percentage of monocyte and granulocyte significantly decreased ($p<0.001$) compared to control. The platelet count across the groups significantly increased ($p<0.002$) compared to control. The PT of groups 4 and 5 showed significant increase ($p<0.001$) compared to control. The PTTK of groups 3, 4 and 5 significantly increased ($p<0.001$) compared to control. It was observed that consumption of Combretum platypterum at low doses resulted in procoagulant activity but on lengthy periods at high doses, prolonged clotting time resulted.

Keywords: Combretum platypterum leaves, haematological indices, haemostatic indices

INTRODUCTION

A plant extract's blood-related actions can be explained using haematological and haemostatic measures. Blood can serve as a pathogenic reflection as well as an indicator of an animal's physiological state.[1]Haematologicaldisordersare on the rise, yet conventional treatments arenot readily available. This has led to a rise in the use of easily available medicinal herbs in the treatment of blood diseases.[2]Haemostasis is a physiological process that prevents excessive blood loss. The haemostatic system is a delicate balance of pro- and anticoagulant mechanisms, as well as a fibrinolytic process. Platelets, coagulation factors, coagulation inhibitors, and clotting factors are the major components of the haemostatic system.[3]

Combretum platypterum, like other terrestrial plants, has ethnopharmacological value and has been used by the locals to treat a variety of ailments. It's a straggling scandent shrub or forest liana with a stem up to 10cm in diameter and a length of up to 10m. The leaves are opposite or alternate, simple and whole, with no stipules; the petiole is 6-13mm long and belongs to the Combretaceae family.[4]*Combretum platypterum* has a wide range of distribution and appears to be common. It can be found from sea level to 450 meters above sea level in rain forest, secondary forests, and scrub savanna, as well as swampy areas.[5]It is reputed locally for its analgesic, antiarthritic, antimicrobial, and antimalaria effects. The leaves are prepared for herbal remedies such as hot water decoctions andcold water extracts.[6,5]

The medicinal value of *Combretum platypterum* has been established traditionally but there is no dearth of information on its effects on haematological and haemostatic profiles. As a result, extensive scientific research is required to assess its effects on certain blood indices, efficacy and potential toxicity. Hence this study evaluates the haematologic and haemostatic effect of aqueous extracts of *Combretum platypterum* leaves in albino Wistar rats.

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Date manuscript was received: 22/5/2022
Date manuscript was accepted: 2/7/2022

MATERIALS AND METHODS

Plant materials and authentication

Fresh leaves of *Combretum platypterum* were obtained from the University of Benin Farmhouse, identified and authenticated by Dr. A.O. Akinnibosun of the Department of Plant Biology and Biotechnology, Faculty of Life Sciences, University of Benin, Benin City.

Ethical consideration

Ethical approval was sought and obtained from the Faculty of Pharmacy Ethics Committee, University of Benin, Benin City.

Preparation of extract

About 3.65kg leaves were pulverized (after drying) by a commercial blender and (665g of powder obtained), soaked in distilled water using 1g of powder: 4ml of distilled water and allowed to stand for 24hours at room temperature. The extract was filtered using Whatman's (Nitro cellulose 45; 0.45µm pore size) filter paper; the filtrates were concentrated to dryness at 100°C in a water bath and stock solution made. Thereafter, it was put in an airtight container and refrigerated until use.

Experimental animals

Fifty-eight (58)Wistar rats weighing between 150-200g were procured from the Faculty of Pharmacy, University of Benin, Benin City. The rats were fed with rat pellets and tap water *adlibitum*.

After randomization to various groups and before initiation of experiment, the rats were acclimatized for seven days under standard environmental conditions (temperature, relative humidity and dark/light cycle).

Six millilitres (6mls) of blood samples were collected for analysis from each Wistar rat, at the start of the experiment, on the fourteenth and twenty-eight days by cardiac puncture as well as from the abdominal aorta. Three millilitres (3mls) of blood obtained was dispensed into Becton Dickinson (BD) vacutainer® (BD Plymouth, UK) sample bottles containing Ethylene diamine tetraacetic acid (EDTA) and the remaining 3mls of blood sample dispensed into BD Vacutainer® Citrate tubes containing Sodium citrate for the haematologic and haemostatic assays, respectively.

Acute toxicity

The method of Lorke, (1983)[7] was used for the acute toxicity test of the aqueous extracts of leaves of *Combretum platypterum*. Eighteen (18) albino Wistar rats were used for this study. The test involved two phases. In phase one, the animals were grouped into three (3) groups of three rats each and were given 10, 100 and 1000mg/kgb.w of the extracts respectively daily for seven (7) days. In the second phase, the animals were grouped into three (3) groups of three rats each and were given 1600, 2900 and 5000mg/kg b.w of the extracts respectively daily for seven (7) days.

Animal groups and Extract administration

Forty (40) rats were randomly distributed into five (5) groups of eight rats each. Administration was done orally with the aid of a metal oropharyngeal cannula. The groups and daily doses administered are summarized below:

Group 1(control group) was given tap water*ad libitum*.

Group 2 were given 250mg/kg b.w of the aqueous extract of *Combretum platypterum* leaves. Group 3 were given 500mg/kg b.w of the aqueous extract of *Combretum platypterum* leaves. Group 4 were given 1000mg/kg b.w of the aqueous extract of *Combretum platypterum* leaves. Group 5 were given 2000mg/kg b.w of the aqueous extract of *Combretum platypterum* leaves.

On day seven (7) of acclimatization before treatment, two Wistar rats from group 1 were euthanized with 95%w/v chloroform and blood withdrawn by cardiac puncture as well as from the abdominal aorta for the baseline parameters. Subsequently, an even number of samples from each group was collected at two (2) weeks intervals during the period of treatment. The treatment lasted for twenty-eight (28) days; analyses were

done on days 0,14 and 28 within 4 hours of sample collection.

Haematological analysis

Haematological indices were determined from unclotted blood samples using standard protocols as described by Tietz *et al*., (1994)[8] and were determined using the automated ERMA haematology auto analyzer PCE-210N (Diamond Diagnostic; Holliston, USA).

Haemostatic analysis

Partial Thromboplastin Time with Kaolin: After centrifugation and citrated plasma collected, 0.1ml of plasma was dispensed into a clean test tube 0.1ml of pre-warmed kaolin/ platelet substitute (BIOLABO Diagnostics, Maizy, France) aliquot was added to the test tube and incubated at 37°C in a water bath for two (2)minutes. The sample was re-calcified with 0.1ml of 0.025M calcium chloride and a stopwatch started instantly, tilting the tube back and forth and observing for clot formation. The watch was stopped at the first sight of clot formation and the result was recorded in seconds.

Prothrombin time

This was performed by pipetting 0.1ml of the citrated plasma into a test tube and incubating it in a water bath at 37°C for 2 minutes. Then 0.2ml of the pre-warmed thromboplastin/ calcium chloride reagent (BIOLABO Diagnostics, Maizy, France) was added to the test tube using an automatic pipette and the stopwatch started simultaneously while holding the tube in the water bath, tilting back and forth. The watch was stopped at the first sight of clot formation and the result was recorded in seconds.

Statistical analysis

The various results obtained from this study were expressed as Mean ± S.E.M. The data were subjected to a one-way analysis of variance (ANOVA); The ANOVA was performed using SPSS (Version 16.0) statistical software package analysis of data. Differences were considered statistically significant at an error probability of less than or equal to 0.05.At $P \geq 0.05$ (not significant); $P \leq 0.05$ (significant).

RESULTS

The results obtained in this study are shown in Tables 1- 4 and Figure 1. Table 2 shows the mean ± SEM haematological variables on the effects of *Combretum platypterum* aqueous leaf extract on albino rats at day 14. The percentage granulocyte of Group 2(3.9 ± 0.42) and Group 3(4.4 ± 0.3317) significantly decreasedwhen compared to Group 1(9.367 ± 0.47)($p<0.05$).The platelet count of group 5 (568 ± 52.03) showed a significant decreasewhen compared to group 2(838 ± 20.77) only ($p<0.05$). Also, the mean platelet volume (MPV) of group 2 (5.85 ± 0.07) showed a significant decrease when compared to group 1(7.2 ± 0.53) only ($p<0.05$). Finally, the percentage platelet distribution width (PDW) group 4(10.58 ± 0.9978) significantly increased when compared to group 2(6.6 ± 0.041)($p<0.05$).

The comparison of haematological variables on the effects of Combretum platypterum aqueous leaf extract on albino rats at day 28 is shown in table 3.The total white blood cell (TWBC) count of group 4(19.08 ± 0.446) revealed a significant increase when compared to the basal group (12.35 ± 1.65), group 1(14.63 ± 0.5364), group 2(11.93 ± 0.2626) and group 3(12.33 ± 1.621) only ($p<0.05$).Also, the percentage granulocyte count of group 2(2.7 ± 0.495), group 3(2.25 ± 0.1658), group 4(2.775 ± 0.075) and group 5(2.5 ± 0) significantly decreased when compared to the basal group (7.3 ± 2.2) and group 1(9.367 ± 0.4667) ($p<0.05$). The haemoglobin concentration (HB) of group 2(15.1 ± 0.4062) and group 3(14.8 ± 0.1) revealed a significant decrease when compared to the basal group (12.4 ± 0.2) and group 1(12.2 ± 0) only ($p<0.05$). Furthermore, the packed cell volume (PCV) of group 2(48.65 ± 2.244) showed a significant increase when compared to the basal group (38.2 ± 0.6) and group 1(38.23 ±

1.732) only ($p<0.05$). The platelet count of group 3(1299 ± 131.8) and group 4(1181 ± 103.2) showed a significant increase when compared to the basal group (602 ± 74.5) and group 1(624 ± 59.1) only ($p<0.05$). The mean platelet volume (MPV) of group 5 (5.725 ± 0.075) significantly decreased when compared to group 1(7.233 ± 0.5548) and group 3(6.675 ± 0.04787) only ($p<0.05$). Furthermore, the platelet distribution width (PDW) of group 1(10.93 ± 1.068) revealed a significant increase when compared to the basal group (8.05 ± 0.65) only ($p<0.05$).

Comparing the mean ± SEM prothrombin time (PT) and partial thromboplastin time with kaolin (PTTK) at day 14 and 28; group 2, 3, 4 and 5 showed significant increase in PT values when comparing day 14(12.5 ± 0.2887; 13.5 ± 0.6445; 14.75 ± 0.478; 19.75 ± 0.85) to day 28(15.5 ± 0.6455; 16.75 ± 0.62; 23 ± 1.291; 30.25 ± 0.853)($p<0.05$). Likewise, the PTTK values of group 2, 3, 4 and 5 showed significant increase when comparing day 14(33.75 ± 0.8539; 36 ± 0.4082; 38.25 ± 1.109; 47 ± 2.483) to day 28(42 ± 0.9129; 58.75 ± 1.315; 66 ± 1.472; 69 ± 1.354) ($p<0.05$).

Figure 1 shows the mean ± SEM weight on the effects of *Combretum platypterum* aqueous leaf extract on albino rats on days 14 and 28; there was a significant increase in groups 3, 4 and 5 on day 14 when compared with control. However, on day 28, there was a significant decrease in groups 2, 3, 4 and 5 compared to control.

Table 1: Acute toxicity of Combretum platypterum aqueous leaf extract

	Group	**Dosage (mg/kg.bw)**	**Weight initial (g)**	**Weight after (g)**	**Mortality**
Phase 1	1	10	160	170	
	2	100	160	170	0/3
	3	1000	150	155	
Phase 2	1	1600	150	155	
	2	2900	150	155	0/3
	3	5000	150	150	

Table 2: Mean ± SEM haematological variables on the effects of *Combretum platypterum* aqueous leaf extract on albino rats on day 14.

Parameters	Basal Group	Group 1	Group 2	Group 3	Group 4	Group 5	P-value
TWBC ($X10^9$/l)	12.35±1.65	12.23±2.66	8.6±0.33	10.98±0.48	15.08±4.474	12.95±2.593	0.604
Lymphocytes (%)	85.25±0.75	80.33±2.65	90.53±4.01	91.08±0.90	87.18±2.217	85.35±1.688	0.091
Monocytes (%)	7.45±1.45	7.667±0.85	3.075±1.29	4.525±0.95	6.6±1.471	7±1.285	0.118
Granulocytes (%)	7.3±2.2	9.367±0.47	3.9±0.42^b	4.4±0.3317^b	6.1±1.079	7.4±1.028	<0.05
RBC ($\times10^9$/l)	6.465±0.015	6.11±0.31	7.538±0.21	7.015±0.60	7.203±0.433	6.808±0.2845	0.25
HB (g/dl)	12.4±0.2	12.17±0.03	12.85±0.24	13.95±0.64	13.33±0.705	13.2±0.5958	0.313
PCV (l/l)	38.2±0.6	38.3±1.79	41.93±0.74	41.45±1.92	41.43±1.281	39.75±1.788	0.456
RDW (%)	18.15±2.05	16.13±2.67	17.9±0.29	15.33±0.05	17.65±0.8005	16.5±0.5339	0.438
Platelets ($\times10^9$/l)	602.5±74.5	615.7±67.42	838±20.77	764.8±53.32	579.3±83.53	568±52.03^c	0.021
MPV (fl)	6.7±0.5	7.2±0.53	5.85±0.07^b	6.85±0.10	6.1±0.1291	6.725±0.34	<0.05
PDW (%)	8.05±0.65	8.967±0.87	6.6±0.041	8.05±0.89	10.58±0.9978^c	9.45±0.9179	0.021
MCV (fl)	59.15±0.85	57.37±0.84	59.85±1.23	59.2±0.19	57.9±2.232	58.4±1.027	0.798
MCH (pg)	19.15±0.25	19.33±0.34	17.58±0.58	18.98±0.47	18.53±0.5266	19.3±0.09129	0.095
MCHC (g/dl)	32.4±0.00	32.2±1.22	30.43±1.37	31.83±0.28	32.08±0.7465	33.18±0.4589	0.374

Key: p≤0.05-Significant;p≥0.05-Not significant. a represent significance with Group 1; b represents significance with Group 2; c represents significance with Group 3; d represents significance with Group 4; e represents significance with Group 5. TWBC, total white blood cell; RBC, red blood cell; PCV, packed cell volume; HB, haemoglobin; MCV, mean corpuscular volume; MCHC, mean corpuscular haemoglobin concentration; MPV, mean platelet volume; PDW, platelet distribution width; MCH, mean corpuscular haemoglobin; RDW, Red cell distribution width.

Table 3: Mean ± SEM haematological variables on the effects of *Combretum platypterum* aqueous leaf extract on albino rats on day 28

Parameters	Basal Group	Group 1	Group 2	Group 3	Group 4	Group 5	p-value
TWBC ($X10^9$/l)	12.35±1.65	14.63±0.5364	11.93±0.2626	12.33±1.621	19.08±0.446^{abcd}	11.75±0.3279^e	<0.05
Lymphocytes (%)	85.25±0.75	83.6±1.266	95.4±1.046^{ab}	96.2±0.2121^{ab}	95.43±0.3224^{ab}	95.7±0^{ab}	<0.001
Monocytes(%)	7.45±1.45	7.933±0.9684	1.9±0.5523^{ab}	1.55±0.0866^{ab}	1.8±0.2483^{ab}	1.8±0^{ab}	<0.001
Granulocytes (%)	7.3±2.2	9.367±0.4667	2.7±0.495^{ab}	2.25±0.1658^{ab}	2.775±0.075^{ab}	2.5±0^{ab}	<0.001
RBC ($\times10^9$/l)	6.465±0.015	6.47±0.05859	8.345±0.3873^{ab}	7.595±0.08732	7.493±0.418	6.773±0.08035^c	<0.05
HB (g/dl)	12.4±0.2	12.2±0	15.1±0.4062^{ab}	14.8±0.1^{ab}	13.5±0.5196c	11.95±0.09574^{cde}	<0.001
PCV (l/l)	38.2±0.6	38.23±1.732	48.65±2.244^{ab}	46.3±0.8737^b	43.75±1.735	36.4±0.1225^{cde}	<0.001
RDW (%)	18.15±2.05	16.17±2.64	16.63±0.1493	16.53±0.047	16.83±0.478	19.38±0.137	0.234
Platelets ($\times10^9$/l)	602.5±74.5	624±59.1	1050±135.7	1299±131.8^{ab}	1181±103.2^{ab}	910.8±3.637	0.002
MPV (fl)	6.7±0.5	7.233±0.5548	6.3±0.05774	6.675±0.04787	6.35±0.06455	5.725±0.075^{bd}	0.006
PDW (%)	8.05±0.65	10.93±1.068^a	7.75±0.2062^b	8.25±0.05^b	7.575±0.1109^b	5.6±0^{abcde}	<0.001
MCV (fl)	59.15±0.85	59.03±2.167	58.28±0.04787	60.93±0.7941	58.5±0.9548	53.7±0.108^{abcde}	0.001
MCH (pg)	19.15±0.25	18.83±0.1764	18.1±0.3512	19.43±0.2428^c	18±0.324^d	17.55±0.028^{abd}	<0.001
MCHC (g/dl)	32.4±0	31.87±1.525	31.08±0.6074	31.95±0.5393	30.8±0.0707	32.55±0.028	0.343

Key: p ≤0.05 -Significant; p≥0.05- Not significant. a represent significance with Group 1; b represents significance with Group 2; c represents significance with Group 3; d represents significance with Group 4; e represents significance with Group 5.

Table 4: Comparison of mean ± SEM prothrombin and partial thromboplastin times with kaolin on the effects of *Combretum platypterum* aqueous leaf extract on albino rats on days 14 and 28.

	PT (secs)			PTTK (secs)		
	Day 14	Day 28	P value	Day 14	Day 28	P-value
Group 1	20.33±0.3333	19.33±0.33	0.433	44.67±1.856	44.67±1.856	>0.05
Group 2	12.5±0.2887	15.5±0.6455	0.001	33.75±0.8539	42±0.9129	<0.001
Group 3	13.5±0.6455	16.75±0.62	<0.001	36±0.4082	58.75±1.315	<0.001
Group 4	14.75±0.478	23±1.291	<0.001	38.25±1.109	66±1.472	<0.001
Group 5	19.75±0.85	30.25±0.853	<0.001	47±2.483	69±1.354	<0.001

Key: $p \leq 0.05$ Significant; $p \geq 0.05$- Not significant.
PT- Prothrombin Time
PTTK-Partial Thromboplastin Tim ewith Kaolin.

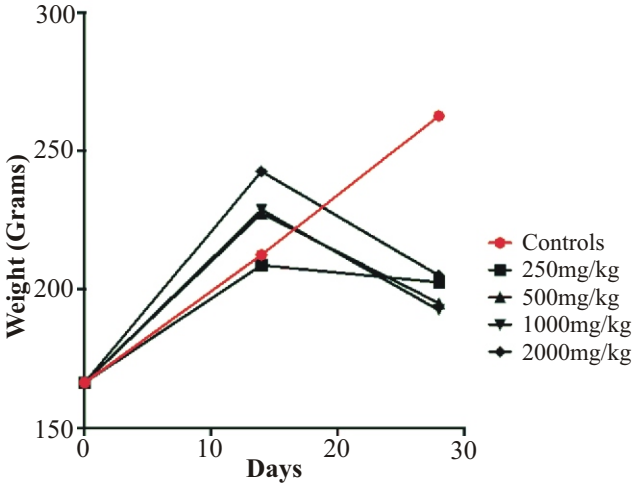

Figure 1: Mean ± SEM weight (expressed in grams) on the effects of *Combretum platypterum* aqueous leaf extract on albino rats on days 14 and 28.

DISCUSSION

The acute toxicity of the aqueous leaf extract of *Combretum platypterum* was estimated in two (2) phases on eighteen (18) albino Wistar rats; three (3) per concentration using the standard method of Lorke.[7]There was neither sign of toxicity nor mortality as such the median lethal dose of the aqueous extract of *Combretum platypterum* was estimated to be over 5000mg/kg b.w (Table 1).

Because blood works as a pathogenic reflector and an indicator of man's physiological status, haematological measurements are employed to explain blood-related functions of a plant.[1]Monocyte is a key component of the innate immune response, which serves as a connection between the innate and adaptive immune systems by presenting antigens to lymphocytes. Monocytes and the granulocytes (neutrophil and eosinophil) are known to originate from a common myeloid progenitor, before being released into the peripheral blood where they circulate for some days before entering the tissues and replenishing the tissue macrophage population.[10]

The platelet count of group 5 (2000mg/kg b.w) was significantly reduced ($p<0.05$) when compared to group 2 (250mg/kg b.w) but showed no significant difference ($p>0.05$) when compared to the control; this suggest that the low dose had a better megakaryopoiesis stimulatory activity(Table 2). This is in line with the finding of Choi *et al*., that platelets are formed from megakaryocytes within four (4)to six (6)days under standard healthy body conditions.[11] The reduced platelet count in

group 5 can relatively increase clotting and bleeding time when compared to lower doses of the extract (Table 2).

The MPV and PDW(%) of all groups when compared to the control revealed no statistical significance ($p>0.05$), this rules out platelet activation seen during inflammation. Platelet activation causes morphological changes in shape and pseudopodia formation in platelets, when platelets are activated in an inflammatory environment(Table 2).[12]

On day 28, the granulocyte(%) and monocyte(%) arising from the same common progenitor significantly decreased ($p<0.001$) when compared to the control. This may be due to the inhibitory effect of *Combretum platypterum* on the haematopoietic growth factor responsible for monocyte and granulocyte proliferation and differentiation in the bone marrow (Table 3).[13]

There was a significant increase ($p<0.001$) in lymphocyte count (%) when compared with the control, this may be due to the stimulatory effect of *Combretum platypterum* on interleukin-9 upon continuous exposure.[14]The resultant increase in lymphocytes may account for its ethnomedicinal usage in treating conjunctivitis and sexually transmitted diseases.[4] Lymphocytes are the main effector cells and memory cells of the immune system. The increased lymphocyte count may aid in the enhancement of immune effector cells, inflammation (as in conjunctivitis) and infections.[15] (Table 3).

The RBC, HB, and PCV of group 2 (250mg/kg b. w) significantly increased ($p<0.05$) when compared to the control; also the HB and PCV of group 3 (500mg/kg b.w) significantly increased ($p<0.05$) when compared to control. The HB, MCV and MCH of group 5 (2000mg/kg b.w) significantly decreased when compared to the control group ($p<0.05$) (Table 3), this may suggest an anaemic effect, upon accumulation of a high dose of *Combretum platypterum.*[15] The relative anaemia observed in group 5, maybe due to the toxic accumulation of saponin which has been reported to potentiate the haemolytic activity of plant parts by hydrolysis of glycosidic bonds and disruption of the red cell membrane.[16] It may also be due to the activity of accumulated glycoside in reducing the bioavailability of trace metals such as iron needed for red blood cell synthesis.[17](Table 3).

The platelet count across the groups significantly increased ($p<0.05$) compared to the control; also the significant decrease in PDW ($p<0.001$) and MPV ($p<0.006$) may suggest active inflammation as revealed by the association between platelet indices (PCT, MPV and PDW) and inflammation; with PDW reported by Vagdatli *et al.* to be a more specific marker for platelet activation as it does not increase upon simple swelling.[18,19] Platelet activation occurs during inflammation. Mean platelet volume (MPV) and platelet distribution width (PDW) have been reported to decrease during active inflammation, while the number of platelets also increases, but they become more monotypic and smaller; supporting the increased platelet count (Table 3).[18]

Prothrombin time (PT) and partial thromboplastin time with kaolin (PTTK) are used to assay the integrity of the intrinsic and extrinsic clotting pathways respectively.[20]The prothrombin time of all groups significantly decrease ($p<0.001$) across the groups with group 1 (250mg/kg b.w) possessing the highest procoagulant activity. This may be due to the presence of phytochemicals such as tannin which has been reported in *Anacardium occidentale* and *Jatropha Curcas*[21] to arrest bleeding from damaged or injured vessels by precipitating clotting proteins to form vascular plugs(Table 4).[22]

The PTTK of groups 2 and 3 when compared with control significantly reduced ($p<0.001$) supporting its procoagulant activity. The PTTK results of group 5 significantly increased ($p<0.001$) when compared to group 2, 3 and 4 but was not significant ($p>0.05$) with the control; this may suggest that the liver was not able to adequately metabolize and bio transform high doses of the plant extract within a very short period resulting in lack of procoagulant activity in group 5; however, this did not pose

any hemorrhagic risk as it was relatively reduced compared to control (Table 4).

On day 28, the PT values of group 5 (2000mg/kg b.w) significantly increased ($p<0.001$) when compared to the control, also the PTTK of groups 3, 4 and 5 significantly increased ($p<0.001$) when compared to the control and group 2 (Table 4). This prolonged PT and PTTK may suggest a deficiency in one or more of the clotting factors needed in normal haemostasis and this may be due to hepatic dysfunction or production of autoantibodies as the liver is needed in clotting protein synthesis, however, this study did not include a histological examination.

Juxtaposing the haematological, haemostatic parameters of group 5 and the weight reduction possibly suggests an active inflammation occurring due to continuous accumulation of high doses of *Combretum platypterum*.

CONCLUSION

The present study showed that oral administration of aqueous leaf extract of *Combretum platypterum* in apparently normal Wistar rats resulted in increased lymphocyte, decreased monocyte and granulocyte counts and increased platelet count. In addition, anaemia upon prolonged administration at high doses was observed. Haemostasis study revealed it has a procoagulant activity at low dose upon brief administration; however, high dose withprolonged consumption revealed inflammation, thus the haematological and haemostatic activities observed are dose-dependent. This study supports the usage of *Combretum platypterum* leaves in managing haematological and haemostatic indices, based on further and possibly, human research.

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