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Research Article
Dennettia tripetala Extracts Up-regulate Haematopoiesis against Carbon Tetrachloride Toxicity

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Abstract

Background and Objective: The use of *Dennettia tripetala* in ethnomedicine to manage pain, inflammation and fever have been attributed to its analgesic effects. In this study, we evaluated the effect of *Dennettia tripetala* extracts on hematopoiesis against carbon tetrachloride-induced toxicity. **Materials and Methods:** Thirty Wistar experimental rats were weighed and randomized into six groups of five rats each. The rats were treated as described below in strict accordance with the NIH guidelines for the care and use of laboratory animals. **Results:** Administration of aqueous extract of *Dennettia tripetala* and subsequently carbon tetrachloride resulted in significant ($p<0.05$) increases in white blood cell count, percentage monocytes, percentage granulocytes and decreases in percentage Lymphocytes. Administration of the ethanolic extract and subsequently carbon tetrachloride resulted in significant ($p<0.05$) increases in white blood cells, percentage monocytes and granulocytes. Administration of the 250 mg kg^{-1} with carbon tetrachloride resulted in significant ($p<0.05$) increases in red blood cells and haemoglobin while the 1000 mg kg^{-1} ethanolic *Dennettia tripetala* extract alone caused Hematocrit and mean corpuscular volume to increase and mean corpuscular hemoglobin concentration to decrease significantly. **Conclusion:** *Dennettia tripetala* extracts at low doses up-regulated hematopoiesis which possibly prevented the harmful effects of carbon tetrachloride.

Key words: Carbon tetrachloride, Complete blood count, *Dennettia tripetala*, differential leukocytes, Immune parameters, haematological parameters

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Carbon tetrachloride exposure could be lethal because it causes degeneration of the liver and kidneys[1-3]. It can also affect the central nervous system and under prolonged exposure results in coma or death[4], while under chronic exposure cancer could occur[5]. The metabolism of carbon tetrachloride generates free radicals which target the cell membranes of major organs or tissues where the blood components are usually produced[6-8]. Hematological parameters can be used as indices to evaluate the extent of damage caused by poisonous compounds in the body[9] and blood-related functions[10]. In herbal and traditional medicine, plants or herbs of medicinal values have been used in the management of various disorders resulting from exposures to this poisonous compounds[11].

Dennettia tripetala (DT) is a medicinal plant whose fruit (Pepperfruit) is consumed for its spicy taste and medicinal values. It belongs to the *Annonaceae* family and grows widely in Nigeria[12]. The use of DT in herbal medicine to manage pain and fever has been attributed to its analgesic effects which are comparable to that of morphine, aspirin and indomethacin. Its oil has been found to relieve inflammation with edema in experimental animals with a mechanism similar to that of dexamethasone[13]. DT fruit has also been shown to elicit hepatoprotective, nephroprotective and hypoglycemic effects in experimental rats exposed to carbon tetrachloride (CCl_4)[8,12,14,15]. DT, due to its saponins tannins and flavonoid contents, also possesses antimicrobial and anti-inflammatory properties[16,17]. The ethyl acetate extract of DT is effective in managing diabetes and reducing the plasma glucose level in drug-induced hyperglycemia in experimental rats[15,18].

Toxicity study carried out by Ikpi and Nku shows the LD_{50} of DT to be moderately high at about 251.19 g kg^{-1} b.wt., however, this was relieved at an increased dose of administration[19]. Also, an LD_{50} of about 1120 mg kg^{-1} was determined from the intraperitoneal administration of the ethyl acetate root extract of DT[20]. The extract was shown to be mildly toxic to the kidney, liver, spleen and blood cells. However, at increased exposure time, the extract was shown to be cardio-protective[20]. Anyaele and Amusan[21] pointed out the potential use of DT essential oil in producing insecticides- due to the toxic effects of the hexanoic extracts of the fruits against the larvae of Aedes aegypti mosquito. Although Ikpi and Nku[19] demonstrated the hematotoxic effects of low doses of ethanolic extracts in normal healthy rats, this study focused on the effects of graded doses of aqueous or ethanolic extracts of *Dennettia tripetala* (DT) on haematopoiesis against carbon tetrachloride-induced toxicity, using experimental rats.

MATERIALS AND METHODS

Study area: The study was carried out in the Department of Biochemistry, Faculty of Life Sciences, University of Benin, Edo State, Nigeria.

Plant materials and preparation of plant extracts: Fresh fruits of *Dennettia tripetala* were prepared into a fine powder and weighed amount soaked in 2.5 L of distilled water or absolute ethanol. The filtrates (aqueous and ethanolic extracts) were concentrated and stock solutions of 200 mg mL^{-1} were prepared by dissolving 20 g of the freeze-dried extract in 100 mL of distilled water[8,14,22].

Preparation of CCl_4 stock solution: Carbon tetrachloride was dissolved in olive oil (serving as a vehicle) in a 1:1 (volume/volume) ratio. The CCl_4-olive oil preparation was administered to the experimental rats as applicable, at a dose of 3 mL kg^{-1} body weight[8,14,22].

Experimental animal and design: Thirty female Wistar albino rats, obtained from the animal house of the Department of Anatomy, University of Benin, were used for the study. The experimental animals were housed in clean disinfected cages in the animal house of the Department of Biochemistry. They were allowed unhindered access to normal feed (product of Bendel Feeds and Flour Mill, Ewu, Edo State, Nigeria) and water all through the duration of the experiment. The animals were weighed and randomized into six groups of five animals each. They were allowed to acclimatize to the new environment for 14 days before the commencement of the experiment. The animals were grouped and treated as defined below:

Group A (Control) : Given only feed and water

Group B : treated orally with the aqueous or ethanolic extract of *Dennettia tripetala* fruit at a dose of 250 mg kg^{-1} body weight daily for 14 days prior to the administration of a single oral dose of CCl_4 (3 mL kg^{-1} b.wt.)

Group C : Treated orally with the aqueous or ethanolic extract of *Dennettia tripetala* fruit at a dose of 500 mg kg^{-1} b.wt. daily for 14 days prior to the administration of a single oral dose of CCl_4 (3 mL kg^{-1} b.wt.)

Group D : Treated orally with the aqueous or ethanolic extract of *Dennettia tripetala* fruit at a dose of 1000 mg kg^{-1} b.wt.

daily for 14 days prior to the administration of a single oral dose of CCl_4 (3 mL kg^{-1} b.wt.)

Group E : Treated orally with the aqueous or ethanolic extract of *Dennettia tripetala* fruit at a dose of 1000 mg kg^{-1} b.wt. daily for 14 days

Group F : Given a single dose of CCl_4 (3 mL kg^{-1} b.wt.) on day 14 without prior treatment with *D. tripetala*.

All experimental animals were handled in strict accordance with the NIH guidelines for the care and use of laboratory animals. The procedures and protocols of the study were approved by the Research Ethics Committee of the College of Medical Sciences, University of Benin, Benin City.

Sample collection and preparation: The experimental animals were sacrificed on day 15 under chloroform anesthesia after an overnight fast. Blood samples were collected from cardiac puncture into heparinized and plain bottles.

Hematological analysis and procedure: The hematological analysis was carried out using the Abacus Junior Hematology Analyzer S/N 111749 P/D 02/2009, Diatron, GmbH, Wein Austria. The blood samples were diluted in a buffered electrolyte solution and measured volumes passed through an aperture tube between two electrodes.

The interruption of the current by the non-conducting blood cells altered the electrical charge thereby producing a pulse. The amplitude of the resulting pulse was proportional to the volume of the cell which caused it. A threshold circuit ensured only those pulses exceeding the pre-set threshold level were counted. The cell count was determined from the total number of pulses obtained from a measured volume of blood.

Statistical analysis: Statistical analysis was carried out using GraphPad Prism 6. Results are expressed as Mean±SEM. The differences among means were analyzed using one-way ANOVA followed by Tukey's test. Statistical significance was set at $p<0.05$.

RESULTS

The effects of aqueous or ethanolic extracts of *Dennettia tripetala* (DT) on White Blood Cells (WBC), Lymphocytes (LY), Monocytes (MO), Granulocytes (GR), Red Blood Cells (RBC), Heamoglobin (Hgb), Hematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Corpuscular Heamoglobin (MCH), Mean Corpuscular Heamoglobin Concentration (MCHC). Red Cell Distribution Width (RDW), Platelet Count (PLT), Plateletcrit (PCT), Mean Platelet Volume (MPV) and Platelet Distribution Width (PDW) of experimental rats treated with a single dose (one-time administration) of carbon tetrachloride (CCL_4) (3 mL kg^{-1} b.wt.; diluted 1:1 in olive oil) are as shown in the tables below.

In Table 1, the administration of aqueous extract of DT for 14 days with subsequent administration of CCl_4 at day 14 resulted in significantly ($p<0.05$) lower WBC in the group given only 1000 mg dL^{-1} of DT, as compared with the other groups. Groups F (given CCl_4 only), D and B, showed significantly lower LY (%), as compared with that of groups E, C and A (control). Also, groups A and E showed significantly lower MO (%) as compared with the other groups.

Table 2 shows that in groups F, E, D and C, their WBCs were significantly higher than that of the control group, as well as that of the group given the lowest dose and CCl_4. Percentage Monocytes (MO) were significantly higher in all the treated groups as compared with the control group. Also, the group that was given CCl_4 only showed significantly lower MO compared with the other groups given CCl_4 and graded doses of the ethanolic extract of DT. Administration of 1000 mg kg^{-1} ethanolic DT extract only resulted in a non-significant decrease while administration of 500 mg kg^{-1} with CCl_4 resulted in a significant decrease in percentage GR as compared with the control group. However, the groups that were given CCl_4 and graded doses of ethanolic extract of DT showed percentage GR that was significantly higher than that of the control.

Table 1: Effects of aqueous extract of DT and CCl_4 on the differential leukocyte of the experimental rats

Group	Description	WBC ($\times 10^3$ μL^{-1})	LY ($\times 10^3$ μL^{-1})	MO ($\times 10^3$ μL^{-1})	GR ($\times 10^3$ μL^{-1})	LY (%)	MO (%)	GR (%)
A	Control	5.40±0.61^a	4.20±0.55	0.43±0.18	-0.43±0.19	78.37±6.54^a	2.50±4.45^a	-9.70±3.05
B	Aqueous 250 DT+CCL_4	7.07±0.70^a	3.83±0.62	0.77±0.13^a	0.87±1.97	44.30±9.17^b	12.33±0.90^b	32.90±19.58
C	Aqueous 500 DT+CCL_4	6.17±0.95^a	4.07±0.47	0.80±0.20^a	-0.97±0.33	62.40±2.97	11.33±1.03^b	-24.43±4.29
D	Aqueous 1000 DT+CCL_4	6.23±0.23^a	2.20±0.10	0.73±0.03	3.17±0.18	39.33±4.32^b	13.30±1.82^b	25.10±28.85
E	Aqueous 1000 DT only	-2.90±0.45^b	3.33±0.38	0.13±0.03^b	-0.27±0.03	87.10±0.62^a	-2.33±0.27^a	-9.30±0.25
F	CCL_4	6.90±1.23^a	3.23±0.07	0.53±0.09	2.57±1.66	52.20±11.32^b	8.27±0.35^b	30.93±20.46

Values represent Mean±SEM (n = 6), Means with different superscripts, ^{a,b}Along columns are significantly different ($p<0.05$), WBC: White blood cells, LY: Lymphocytes, MO: Monocytes, GR: Granulocytes

Table 3 shows that RBC, Hgb and HCT were significantly higher in groups treated with CCl_4 and graded doses of the extract as compared with the control group. MCHC was significantly higher in all the treated groups compared to the control group.

In Table 4, RBC and Hgb were significantly higher in groups F, D and B as compared with the control. However, administration of ethanolic extract of DT only at a dose of 1000 mg kg^{-1} b.wt. for 14 days resulted in a significantly lower Hgb concentration as compared to the control and other treated groups. Percentage HCT was significantly lower in the group given only aqueous DT at 1000 mg kg^{-1} compared to other groups, while groups F, D and B showed significantly higher values compared to other groups. MCV was significantly higher in the group given only aqueous DT at 1000 mg kg^{-1} as compared with the control and other treated groups. Administration of 1000 mg kg^{-1} ethanolic extract of DT with CCl_4 resulted in a significantly higher MCHC compared to administration of 1000 mg kg^{-1} ethanolic extract of DT only.

Administrations of CCl_4 only resulted in significantly lower PDW in comparison with the control group. Also, the groups treated with aqueous DT and CCl_4 showed PDW significantly lower than that of the control and the group that was given only 1000 mg kg^{-1} aqueous DT. However, the RDW, PLT, PCT and MPV values were not significantly affected in all the groups irrespective of the treatments as compared with the control (Table 5).

Table 2: Effects of ethanolic extract of DT and CCl_4 on the differential leukocyte of the experimental rats

Group	Description	WBC ($\times 10^3$ μL^{-1})	LY ($\times 10^3$ μL^{-1})	MO ($\times 10^3$ μL^{-1})	GR ($\times 10^3$ μL^{-1})	LY (%)	MO (%)	GR (%)
A	Control	-2.60±0.53^a	2.97±0.20	0.20±0.06	-0.167±0.03	92.33±1.25	0.767±1.72^a	-5.17±0.44^a
B	Ethanolic 250 DT+CCL_4	2.13±2.87^a	1.67±0.22	0.63±0.13	0.433±1.35	34.70±4.52	12.80±1.57^b	34.17±23.23^b
C	Ethanolic 500 DT+CCL_4	8.03±1.27^b	4.27±1.22	1.20±0.10	0.667±1.63	61.90±5.60	13.77±1.14^b	-18.17±3.02^b
D	Ethanolic 1000 DT+CCL_4	8.13±0.95^b	2.97±0.12	1.00±0.12	3.100±1.82	36.23±2.76	12.03±0.33^b	34.17±20.64^b
E	Ethanolic 1000 DT only	7.60±1.72^b	4.50±0.98	1.17±0.61	0.967±1.57	65.00±8.61	12.73±4.37^b	-14.93±5.26^a
F	CCL_4	7.90±1.36^b	3.63±1.13	0.63±0.03	2.467±1.42	33.37±31.90	7.37±1.52^{bc}	35.97±20.78^b

Values represent Mean±SEM (n = 6), Means with different superscripts, ^{a,b,c}Along columns are significantly different (p<0.05), WBC: White blood cells, LY: Lymphocytes, MO: Monocytes, GR: Granulocytes

Table 3: Effects of aqueous extract of DT and CCl_4 on the haematological parameters of the experimental rats

Group	Description	RBC ($\times 10^6$ μL^{-1})	Hgb (g dL^{-1})	HCT (%)	MCV (fl)	MCH (pg)	MCHC (g dL^{-1})
A	Control	7.10±0.09^a	13.10±0.44^a	40.30±1.40^a	-56.77±2.46	-19.10±0.36	31.97±0.32^a
B	Aqueous 250 DT+CCL_4	8.14±0.06^b	15.30±0.58^b	43.83±0.12^b	-53.03±1.20	-19.03±0.26	35.13±0.43^b
C	Aqueous 500 DT+CCL_4	8.07±0.20^b	15.90±0.25^b	46.77±0.26^b	-57.23±1.81	-19.63±0.43	34.17±0.23^b
D	Aqueous 1000 DT+CCL_4	8.21±0.20^b	16.20±0.38^b	46.22±0.70^b	-55.60±0.55	-19.77±0.03	35.43±0.22^b
E	Aqueous 1000 DT only	7.06±0.31^a	14.50±0.29^a	42.07±0.60^a	-55.30±0.76	-19.13±0.35	34.33±0.19^b
F	CCL_4	8.19±0.23^b	16.13±0.32^b	45.57±0.20^b	-56.90±1.04	-19.93±0.22	34.83±0.54^b

Values represent Mean±SEM (n = 6), Means with different superscripts, ^{a,b}Along columns are significantly different (p<0.05), RBC: Red blood cells, Hgb: Heamoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, MCH: Mean corpuscular heamoglobin, MCHC: Mean corpuscular heamoglobin concentration

Table 4: Effects of ethanolic extract of DT and CCl_4 on the haematological parameters of the experimental rats

Group	Description	RBC ($\times 10^6$ μL^{-1})	Hgb (g dL^{-1})	HCT (%)	MCV (fl)	MCH (pg)	MCHC (g dL^{-1})
A	Control	7.48±0.14^a	14.70±0.10^a	42.33±0.13	-54.63±1.27^a	-19.10±0.21	35.00±0.17
B	Ethanolic 250 DT+CCL_4	8.63±0.14^b	16.77±0.37^b	47.27±1.30^a	-55.47±0.48^a	-19.43±0.32	34.93±0.33
C	Ethanolic 500 DT+CCL_4	8.23±0.21^a	15.80±0.36^a	44.40±0.77	-52.57±1.73^a	-18.93±0.15	35.20±0.26
D	Ethanolic 1000 DT+CCL_4	8.65±0.24^b	17.00±0.23^b	46.40±0.17^a	-52.70±0.50^a	-19.43±0.26	36.70±0.21^b
E	Ethanolic 1000 DT only	7.30±0.09^a	14.13±0.26^c	40.23±1.88^b	21.67±35.83^b	-18.97±0.27	34.73±0.64^a
F	CCL_4	8.74±0.15^b	17.23±0.24^b	46.97±0.90^a	-53.60±0.15^a	-19.63±0.20	36.63±0.57

Values represent Mean±SEM (n = 6), Means with different superscripts, ^{a,b,c}Along columns are significantly different (p<0.05), RBC: Red blood cells, Hgb: Heamoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, MCH: Mean corpuscular heamoglobin, MCHC: Mean corpuscular heamoglobin concentration

Table 5: Effects of aqueous extract of DT and CCl_4 on the differential platelet of the experimental rats

Group	Description	RDW (fl)	PLT ($\times 10^3$ μL^{-1})	PCT (%)	MPV (fl)	PDW (fl)
A	Control	40.20±1.06	546.30±48.89	0.286±0.02	-5.33±0.12	-7.93±0.12^a
B	Aqueous 250 DT+CCL_4	39.07±0.73	647.00±40.08	0.365±0.02	-5.50±0.12	-8.80±0.20^b
C	Aqueous 500 DT+CCL_4	40.17±0.17	611.30±147.80	0.315±0.05	-5.60±0.25	-9.17±0.15^b
D	Aqueous 1000 DT+CCL_4	39.90±1.82	590.70±47.88	0.326±0.02	-5.50±0.06	-8.60±0.17
E	Aqueous 1000 DT only	38.40±1.06	623.00±98.17	0.396±0.03	-5.30±0.15	-8.09±0.15^a
F	CCL_4	39.40±1.82	718.00±31.48	0.386±0.00	-5.33±0.22	-8.27±0.09^b

Values represent Mean±SEM (n = 6), Means with different superscripts, ^{a,b}Along columns are significantly different (p<0.05), RDW: Red cell distribution width, PLT: Platelet count, PVT: Plateletcrit, MPV: Mean platelet volume and PDW: Platelet distribution width

Table 6: Effects of ethanolic extract of DT and CCl_4 on the differential platelet of the experimental rats

Group	Description	RDW (fl)	PLT ($\times 10^3$ μL^{-1})	PCT (%)	MPV (fl)	PDW (fl)
A	Control	13.70±24.66	684.70±54.47	0.329±0.01	-4.73±0.13	-7.33±0.09[a]
B	Ethanolic 250 DT + CCL_4	39.40±0.57	643.70±31.64	0.336±0.01	-5.40±0.20	-8.77±0.17[b]
C	Ethanolic 500 DT + CCL_4	13.83±24.27	564.00±45.65	0.315±0.02	-5.37±0.33	-8.83±0.41[b]
D	Ethanolic 1000 DT + CCL_4	37.43±0.33	530.70±45.17	0.298±0.02	-5.53±0.07	-8.57±0.32[b]
E	Ethanolic 1000 DT ONLY	38.27±0.60	620.00±75.11	0.304±0.02	-5.03±0.19	-7.67±0.09[a]
F	CCL_4	-11.07±24.10	775.00±138.80	0.377±0.06	-4.97±0.22	-8.10±0.00

Values represent Mean±SEM (n = 6), Means with different superscripts, [a,b]Along columns are significantly different ($p<0.05$), RDW: Red cell distribution width, PLT: Platelet count, PVT: Plateletcrit, MPV: Mean platelet volume and PDW: Platelet distribution width

Table 6 indicates that the administration of ethanolic extract of DT with CCl_4 resulted in significantly lower PDW compared to the control and administration of 1000 mg kg^{-1} dose of ethanolic DT extract only.

DISCUSSION

The complete blood count (white blood cell count, red blood cell count, platelet count, hematocrit, hemoglobin concentration, differential white blood count, red blood cell indices, etc.) and differential leukocyte count form the basis of any laboratory evaluation. For example, the HCT (a test that measures the volume of blood in percent that is comprised of the RBC), MCV (the average size of the RBCs expressed in femtolitres), MCH (the average amount of hemoglobin inside an RBC expressed in pictograms), MCHC (the average concentration of hemoglobin in the RBC), MCV (the mean of the RBC distribution histogram, based on electrical impedance), RDW (the coefficient of variation, or sometimes the standard deviation of the RBC), etc. These hematological analyses help in the diagnosis of blood-related diseases such as anemia, certain blood cancers, acute and chronic illness, white blood cell disorders (e.g., leukemia) and inflammatory diseases. They provide important information about the blood and to some extent the bone marrow and help in monitoring blood loss, infection and inflammation.

In this study, the administration of aqueous DT extract for 14 days at different doses with subsequent administration of CCl_4 resulted in increases in WBC count, percentage MO, percentage GR and decrease in percentage LY of the experimental rats. These were similar to the effect of the CCl_4 administration alone. The effect of the CCl_4 was not different from those of the different doses of the extract. However, the 1000 mg kg^{-1} dose of the aqueous extract elicited the least response while the 250 mg kg^{-1} dose with CCl_4 elicited the highest response. Equally, administration of ethanolic extract of DT with CCl_4 affected the WBC concentration of the test animals. The WBC level of the test animals was higher than that of the control animals. However, the lowest dose did not considerably affect the WBC level. Percentage MO and GR were equally affected by the ethanolic extract. WBCs play different roles in response to inflammation and an elevated WBC count normally indicates the response of bone marrow to an inflammatory process[23]. Cherfane *et al.*[24] showed that elevated absolute monocytic count and low lymphocyte to monocyte ratio are good predictors of disease activity. It has been suggested that elevation of monocyte counts occurs when there is active inflammation[25]. The increases due to the administrations are indications that there were immune responses, although for the 1000 mg kg^{-1} dose, the GR level was not significantly affected. These findings indicate that the administration of DT extracts (aqueous or ethanolic) at low doses with subsequent administration of CCl_4 probably triggered immune responses in the test animals. It has been observed that at low to moderate doses, DT may be hematotoxic to rats, although the observed toxicity seemed to be relieved at increased doses of DT[19]. The effects of CCl_4 were not pronounced as it seemed not to contribute meaningfully to the observed effects in the test animals, probably due to attenuation by the plant extracts. It may however be inferred that the administration of the extracts before subsequent administration of the CCl_4 possibly prevented the CCl_4 from eliciting any meaningful effect. Previously, we showed that under experimental conditions, carbon tetrachloride caused damage to the kidney mainly by inducing inflammation, swelling of the tubules and necrosis of the tubular lining[8]. Our study also indicated that aqueous or ethanolic extract of DT ameliorated the harmful effects of carbon tetrachloride to varying degrees, although the highest dose was shown to be least effective[8]. The histological study also showed that the administration of different doses of the extracts of DT caused mobility of large numbers of immune cells to the regions of the liver that were damaged by carbon tetrachloride[8]. The immune cells, as observed in the present study, probably moved from the liver into the blood, which was detected on analysis of the blood.

At the highest dose of only the aqueous extract (1000 mg kg^{-1}), the RBC, Hgb and HCT were not significantly affected while for the other doses with CCl_4, they were significantly increased. But the MCHC was elevated in all the

treated groups, irrespective of the treatment. Also, the administration of the 250 and 1000 mg kg^{-1} ethanolic DT doses with CCl_4 increased the RBC and Hgb levels while the 1000 mg kg^{-1} ethanolic DT extract alone resulted in increases in the HCT and MCV levels. The MCHC level was only affected (reduced) by the administration of the ethanolic extract alone at 1000 mg kg^{-1} dose. The plant extracts alone likely had little or no effects on the blood parameters as indicated. However, it is a different picture when CCl_4 was administered following the extract administration, as these parameters were significantly affected. Studies have shown the presence of saponins in the ripe *Dennetia tripetala* fruit powder and extracts (aqueous or ethanolic)[26,27]. Saponins have the potential of inducing hemolysis and act as antifungal agents[26]. Hemolysis of the red blood cells possibly due to the effects of either, CCl_4, the plant extracts, or both acting synergistically may bring about increases in Hgb concentrations as observed. Alternatively, the effects of the various treatments on the reticulocyte (as indicated by the RBC, Hgb, HCT and MCHC) show the possible interference of the CCl_4 and the extracts with the activities of the bone marrow. This is because the number and characteristics of the reticulocytes in the peripheral blood reflect the activity of the bone marrow[28]. The reticulocyte count is a fundamental part of the evaluation of patients with hematopoietic disease[28].

MCH, RDW, PLT, PCT and MPV were not significantly affected in all the treated groups as compared with the control group, irrespective of the treatments. PDW was significantly lower in all the groups given CCl_4 and graded doses of the aqueous extract but not significantly affected by the highest dose of the aqueous extract which was administered alone. The MCH, RDW, PLT, PCT and MPV levels were also not significantly affected by the ethanolic extract of DT with CCl_4, at the doses administered. But, PDW was significantly affected (decreased) by all the doses with CCl_4. These observations are possible indications that the plant extracts administered at different doses ameliorated the immune reactions or inflammations possibly triggered by the CCl_4. This may be associated with the flavonoid content of the plant as shown in our previous study[27]. *In-vitro* studies have shown that flavonoids show anti-cancer activities[29], anti-microbial and anti-inflammatory activities, as well as potential to be biological response modifiers[30,31]. Findings from this study show that DT is an effective medicinal herb that can be used in ethnomedicine for the management of immune reactions or inflammations triggered by toxic agents like CCl_4. However, it is recommended that further studies be carried out on the plant to determine the active constituents responsible for its various effects and possibly derive useful drugs from it.

CONCLUSION

Our findings indicated that the administration of DT extracts (aqueous or ethanolic) at low doses triggered increased hematopoiesis in the test animals which possibly prevented the subsequent administration of CCl_4 from eliciting any harmful effect. Thus, indicating the preventive effects of DT on the haematotoxicity or inflammations possibly triggered by the CCl_4.

SIGNIFICANCE STATEMENT

This study reveals the possibility of *Dennettia tripetala* to trigger increase in hematopoiesis as a protective measure against CCl_4 toxicity. This study further gave credence to the use of *Dennettia tripetala* in ethnomedicine.

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