

Effect of Ethyl acetate fraction of crude ethanol extract of *Ficus capensis* on haematological and biochemical indices of phenylhydrazine-induced anaemic rats

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Abstract

Introduction: Traditionally, the leaves of *Ficus capensis* has been used for the treatment of anaemia due to its blood boosting effect. This study investigated the effect of *Ficus capensis* leaf fraction in phenylhydrazine-induced anemic rats.

Methods: Anaemia was induced in the rats by intraperitoneal injection of 20 mg/kg phenylhydrazine for four consecutive days. Graded doses of the ethyl acetate fraction of *F. capensis* were given by oral gavage once a day continuously for 14 days. At the end of the treatment, blood was collected for hematological (haemoglobin, packed cell volume, red blood cells, platelets, white blood cells and white blood cell differentials) and biochemical analysis (lipid profile, kidney function test, liver function test, electrolytes and lactate dehydrogenase assay).

Results: The results of LD₅₀ showed that the plant is safe for the treatment of anaemia. The fasting blood glucose of both the treated and untreated groups were within normal. There was a significant increase ($p < 0.05$) in haemoglobin, packed cell volume and red blood cell count of the groups treated for a period of 14 days with the fraction compared with the untreated group. The biochemical parameters were observed to be within the normal range for the treated groups compared to the untreated group.

Conclusion: The results suggest that ethyl acetate fraction of *F. capensis* can boost blood parameters without having a drastic effect on the biochemical parameters. This study therefore validates the traditional claim that the leaf extract of *F. capensis* is useful in the treatment of anaemia.

Keywords: Anaemia; Leaves; Intraperitoneal; Haemoglobin; Platelets; Glucose

1. Introduction

The use of plants in the management and treatment of several ailments is gaining global attention, especially in developing countries that rely majorly on traditional medicine to meet their health needs [1]. A huge number of researchers have documented that plant metabolites are effective in the management of many health issues especially anemic conditions [2,3,4,5]; this is believed to be partly due to its numerous bioactive compounds viz-a-viz phytochemicals [6]. Anaemia is a common nutritional deficiency disorder and global public health problem, affecting one third (over 2 billion) of the global populations, both in developing and developed countries with major consequences of human health, social and economic development [7].

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The occurrence of anaemia has been characterized with various red cell defects such as production defect (aplastic anaemia), maturation defect (megaloblastic anaemia), defects in haemoglobin synthesis (iron deficiency anaemia), genetic defects of haemoglobin maturation (thalassaemia) or due to the synthesis of abnormal haemoglobin (haemoglobinopathies, sickle cell anaemia and thalassaemia) and physical loss of red cells (haemolytic anaemias) [8,6] which could range from being mild to severe.

Although, the use of synthetic drugs to combat this condition has gained wide improvement, varying side effects and their high cost has impaired on its accessibility, especially in developing countries such as Nigeria; and this has shifted the attention of the populace to herbal products, which is believed to easily accessible with little or no side effects [1,9]. Findings have revealed that *Ficus capensis* is one of the promising plants that could help to ameliorate this diseased condition.

Ficus capensis commonly called Bush fig tree, is a fast growing, deciduous tree with spreading roots, branches and broad green leaves that usually grow to about 5-12 metres in height but may attain a height of 35-40 metres. In Nigeria, it is locally known "Asakakoro" in Igbo, "Opoto" in Yoruba and "Uwaryara" in Hausa. It is cultivated in all part of the country but most abundant in the Middle-belt (North-central) of Nigeria [10,11].

Traditionally, *Ficus capensis* has been used extensively in the treatment of anaemia although there is only few literatures backing up its use as a crude extract. However, no existing study has been done to test its efficacy when fractionated with ethyl acetate. Although *F. capensis* has found applications in the treatment of a number of disease conditions ranging from wounds, eye problems, toothache, body pain, lung and throat problems [12], anti-diarrhea [13] antibacterial [14], immune booster [15] to anti-sickling effect [16], its role in the management of anemic conditions has not been well explored and documented in the literature. Hence, the need for research to focus on exploring the effect of this plant on hematological parameters and its continuous role in influencing biochemical parameters. This study therefore aimed at exploring the effect of ethyl acetate fraction of crude ethanol extract of *Ficus capensis* on haematological and biochemical indices of phenylhydrazine-induced anaemic rats.

2. Materials and methods

2.1. Sample collection and identification

The leaves of *F. capensis* were collected from Ifite, Awka North Local Government Area, Anambra State, Nigeria. The sample was identified by a taxonomist in the Department of Botany, Nnamdi Azikiwe University, Awka. A voucher specimen (NAU 164) was deposited in the herbarium of the department.

2.2. Preparation of ethanol leaf extract of *F. capensis*

The leaves were properly washed and air dried at room temperature for two weeks. The dried leaves were pulverized into powder using corona manual grinding machine. Exactly 1.5 kg of the pulverized leaf powder of *F. capensis* was soaked in 6 litres of 70% ethanol for 24 hrs for ethanol extraction. The ethanol mixture was sieved using muslin cloth and filtered using Whatman no 1 filter paper. The filtrate was concentrated using water bath at 50°C. The biological yield of the extract after extraction was 125.7g. The ethanol extract was stoppered in universal bottles and preserved in the refrigerator for use.

2.3. Fractionation of leaf extract of *F. capensis*

The crude ethanol leaf extract (125.7g) was fractionated by the method of Wu *et al.* [17]. The method involved successive extraction by increasing polarity with n-hexane, chloroform, ethyl acetate, n-butanol and water. Twenty grams (20g) of the ethanol extract was dissolved in 250ml of Methanol/Water (MeOH/H₂O) (1:1) mixture and shaken with n-hexane (3 x 200ml). Combined extract was left to dry on the bench to yield n-hexane fraction. Methanol (MeOH) was further fractionated by successive solvent extraction with chloroform (2 x 200ml), ethyl acetate (1 x 200ml) and n-butanol (2 x 200ml). Each fraction was left to evaporate to dryness on the bench to yield n-hexane fraction (2.61g), chloroform fraction (4.29g), ethyl acetate fraction (7.82g), n-butanol fraction (2.18g) and water fraction (3.10g).

2.4. Experimental animals

Thirty-eight (38) Wistar albino rats weighing between 150–180 g was obtained from Chris Farm Ltd Mgbakwu, Awka, Anambra State. They were housed in standard cages with housing conditions of 12:12 light: dark cycles. They were fed with vital grower's mash pellets and water *ad libitum*. The weights of the experimental animals were monitored before,

during, and after the experiment. All the experimental procedures and protocols used for this study were in accordance with the guidelines and principles of Nnamdi Azikiwe Animal Care Ethics.

2.5. Acute toxicity (LD₅₀) evaluation

The median lethal dose (LD₅₀) for each of the extracts was determined using Lorke's method [18]. Thirteen (13) rats were used for the LD₅₀ study. This method tests acute toxicity in two steps. In the initial investigations the range of doses are administered to calculate an established dose. Based on these results, further specific doses are administered to calculate an LD₅₀. The method described here is based on the assumption that the herb or substance to be investigated is completely unknown and that the investigation is to be carried out with a minimum number of experimental animals. The first phase involved administration of single low doses of 10, 100 and 1000 mg/kg to different group of rats and monitoring for 24 hours for signs and symptoms of toxicity. If no death was recorded after 24 hours, higher single doses of 1600, 2900 and 5000 mg/kg was administered. The first phase required three animals in each group to determine the toxic range. The result of this test was used as a basis for selecting the subsequent doses.

2.6. Animal grouping for anaemia studies

Twenty-five male Wistar rats were randomized into five groups of five rats each and used for the study. The grouping were as follows:

- Group A: Normal Control
- Group B: Anemic untreated
- Group C: Anaemia + Standard drug (1 ml/kg Emzoron)
- Group D: Anaemia + 100 mg/kg ethyl acetate fraction of *F. capensis*
- Group E: Anaemia + 200 mg/kg ethyl acetate fraction of *F. capensis*

2.7. Dose preparation and treatment

The ethyl acetate fraction of the leaf of *F. capensis* was solubilized with distilled water. Emzoron was administered to the to the positive control group (group C) as a reference drug, distilled water was given to the anaemic untreated group (Negative control-group C). Two doses of the ethyl acetate fraction and drug were administered to the rats orally for fourteen consecutive days with water and feed *ad libitum* [19].

2.8. Induction of anaemia

Anaemia was induced intraperitoneally in experimental rats using 20mg/kg body weight of phenylhydrazine for four consecutive days. The animals were confirmed to be anemic on the 5th day before the commencement of treatment. Blood was collected from the *media cantus* vein for hematological analysis before and after the induction of anaemia to monitor the animals for the symptoms of anaemia before the commencement of treatment.

2.9. Collection of blood sample for bioassay studies

At the end of the experiment, the experimental animals were anaesthetized with chloroform vapor, and sacrificed. A 5ml sterile syringe with needle was used for the collection of blood via cardiac puncture and was used for bioassay studies.

2.10. Random blood glucose concentration

The blood glucose levels of the rats were checked before the induction of anaemia, during, and after treatment using One Touch Glucometer (Life Scan, USA) and test strips based on the method of Trinder, [20].

2.11. Haematological analysis

Haematological parameters were determined using automated haematology analyzer [Mindray-BC-5300]. The parameters analysed include haemoglobin, packed cell volume, red blood cells, platelets, mean corpuscular volume, mean corpuscular haemoglobin, Mean corpuscular haemoglobin concentration, white blood cells, neutrophils, lymphocytes, monocytes, eosinophils, basophils.

2.11.1. Lipid profile

The lipid profile (Total Cholesterol, Triglycerides, High-Density Lipoprotein-cholesterol, Low-Density Lipoprotein-cholesterol and Very Low-Density Lipoprotein-cholesterol) were determined using Randox test kits ^[20,21]. Low-density Lipoprotein-cholesterol (LDL-c) was calculated using a standard formula ^[22].

2.11.2. Electrolyte concentration

The serum electrolyte [Potassium ion (K⁺), Sodium ion (Na⁺), Chloride ion (Cl⁻), Bicarbonate ion (BCO₃⁻), Total Calcium (T^{cal}) and Ionized Calcium (n^{cal})] concentration was analyzed using AFT-300 electrolyte analyzer.

2.11.3. Liver function test

Serum biochemical indices (Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), direct and total bilirubin) were determined using Randox diagnostic test kits.

2.11.4. Kidney function test

Urea and creatinine were analyzed using Randox test kits.

2.11.5. Lipid peroxidation

Lipid peroxidation was determined by the thiobarbituric acid-reacting substances (TBARS) assay method of Buege and Aust ^[23]. The reaction depends on the formation of complex between malondialdehyde and thiobarbituric acid (TBA). 0.4ml of serum was collected into the test tubes; 1.6ml of 0.25N HCl was added together with 0.5ml of 15% trichloroacetic acid and 0.5ml of 0.375% of thiobarbituric acid and then mixed thoroughly. The reaction mixture was then placed in 100°C boiling water for 15 minutes, allowed to cool and centrifuged at 3000 rpm for 10 minutes. The supernatant was collected and the optical density recorded at 532nm against reagent blank containing distilled water.

The lipid peroxidation activity was calculated using the formula:

$$\frac{\text{Optical density}}{\text{Time}} \times \frac{\text{extinction co-efficient}}{\text{amount of sample}}$$

Where the extinction coefficient value is $1.56 \times 10^{-5} \text{M}^{-1} \text{CM}^{-1}$

The unit is expressed as $\mu\text{mol}/\text{MDA}/\text{mg}$ of protein.

2.11.6. Lactate dehydrogenase

Serum lactate dehydrogenase enzyme was determined using Randox diagnostic test kits.

2.12. Data analysis

Data obtained in the research were analyzed using the Statistical Package for Social Sciences software for windows version 25 (SPSS Inc., Chicago, Illinois, USA). All the data collected were expressed as Mean $\pm$ SEM. Analysis of variance (ANOVA) was carried out on the results and significance was accepted at $p < 0.05$.

3. Results

The result of acute toxicological test of the plant extract on experimental rats is presented in table 1. The plant extract showed a toxic effect at a dose of 2900 mg/kg when one mortality was recorded. The median lethal dose (LD₅₀) which is the dose required to kill half of the members of a tested population after specified test duration was calculated to be 2154 mg/kg.

Table 1 Acute toxicity studies of ethyl acetate fraction of crude ethanol extract of *F. capensis* leaf

Phase	Dose mg/kg	Death recorded in rats	Observations
First	10	$\frac{0}{3}$	Normal
	100	$\frac{0}{3}$	Normal
	1000	$\frac{0}{3}$	Normal
Second	1600	$\frac{0}{1}$	Normal
	2900	$\frac{0}{1}$	Slightly weak
	5000	$\frac{0}{1}$	Very weak

The effect of ethyl acetate fraction of *F. capensis* on Bodyweight of phenylhydrazine-induced anemic rats was presented in table 2. The result showed a significant $p < 0.05$ weight increase in the treated group animals compared with the untreated group after induction of anaemia.

Table 2 Effect of ethyl acetate fraction of *Ficus capensis* on bodyweight of phenylhydrazine-induced anemic rats

Groups	Weight (g)			
	Before induction of anaemia Day 0	After 4 th day of induction of anaemia Day 5	After 7 th day of treatment Day 12	After 14 th day of treatment Day 19
Normal Control	156.20 ^b ±3.66	167.40 ^b ±2.71	174.60 ^b ±2.56	179.60 ^b ±3.63
Anemic Untreated	153.80 ^c ±3.47	160.75 ^c ±3.52	165.40 ^d ±3.80	171.00 ^c ±2.84
Anaemia + Standard drug (Emzoron)	150.00 ^d ±3.07	156.60 ^d ±3.94	163.78 ^d ±1.65	172.23 ^c ±4.10
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	164.80 ^a ±4.65	175.20 ^a ±1.72	181.60 ^a ±2.19	185.40 ^a ±6.34
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	154.20 ^c ±3.13	165.60 ^b ±5.75	168.00 ^c ±2.58	170.20 ^c ±2.79

Columns with different alphabet superscripts are significantly different at $p < 0.05$; Values are means ± standard error of mean (n=???) (n = 5)

Table 3 presents the effect of ethyl acetate fraction of *F. capensis* on random blood glucose concentrations of phenylhydrazine-induced anemic rats. The result showed a non-significant ($p > 0.05$) difference in glucose levels of experimental animals during fourteen days of treatment compared with the untreated group after induction of anaemia.

Table 3 Effect of ethyl acetate fraction of *F. capensis* on random blood glucose concentrations of phenylhydrazine-induced anemic rats

Groups	Glucose level (g/dl)			
	Before induction Day 0	After 4 th day of induction of anaemia Day 5	After 7 th day of treatment Day 12	After 14 th day of treatment Day 19
Normal control	80.00±4.32	83.20±5.17	92.20±5.56	87.00±3.30
Anemic untreated	78.80±3.12	94.80±5.70	89.00±5.87	90.50±10.82
Anaemia + Standard drug (0.29 ml/kg Emzoron)	91.00±8.21	80.60±2.87	92.00±3.30	109.80±1.07
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	82.00±3.91	79.80±2.80	101.0±5.99	93.60±6.24
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	89.20±3.97	80.00±6.03	106.80±4.42	84.20±6.30

The result the effect of ethyl acetate fraction of *F. capensis* on Haemoglobin (HGB) concentration of phenylhydrazine-induced anemic rats showed a significant increase ($p<0.05$) in the haemoglobin concentration of treated animals after fourteenth day compared with the untreated group (Table 4).

Table 4 Effect of ethyl acetate fraction of *F. capensis* on Haemoglobin (HGB) concentration of phenylhydrazine-induced anemic rats

Groups	HGB (g/dl)		
	Before induction Day 0	After 4 th day of induction of anaemia Day 5	After 14 th day of treatment Day 19
Normal Control	14.00±0.10	14.13±0.23	12.97±0.38
Anemic Untreated	13.93±0.48	8.20±0.67 ^a	10.10±1.21 ^a
Anaemia + Standard drug (Emzoron)	13.50±0.78	8.53±1.24 ^a	12.90±1.08 ^b
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	13.00±0.52	8.80±0.35 ^a	13.80±0.20 ^b
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	13.60±0.42	9.60±0.41 ^a	14.60±0.32 ^b

^aSignificant decrease with respect to Day 0; ^bSignificant increase with respect to Day 5.

The result of the packed cell volume (PCV) of induced anemic rats is presented in table 5. Results indicated a significant increase ($p<0.05$) in the PCV of animals treated after the fourteenth day compared with the untreated group.

Table 5 Effect of ethyl acetate fraction of *F. capensis* on Packed Cell Volume (PCV) of phenylhydrazine-induced anemic rats

Groups	PCV (%)		
	Before induction Day 0	After 4 th day of induction of anaemia Day 5	After 14 th day of treatment Day 19
Normal Control	49.97±1.34	52.40±1.22	39.00±0.93
Anemic Untreated	50.60±1.41	28.83±1.47 ^a	29.00±3.93 ^a
Anaemia + Standard drug (Emzoron)	50.27±1.58	28.70±4.98	37.93±3.47 ^b
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	49.77±0.96	26.40±0.93 ^a	41.53±0.80 ^b
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	42.73±1.26	28.37±1.14 ^a	43.97±0.69 ^b

^aSignificant decrease with respect to Day 0; ^bSignificant increase with respect to Day 5.

The result of the Red Blood Cells (RBC) of induced anemic rats is presented in table 6. Results indicated a significant increase ($p<0.05$) in the RBC of treated animals after the fourteenth day compared with the untreated group.

Table 6 Effect of ethyl acetate fraction of *F. capensis* on Red Blood Cells (RBC) of phenylhydrazine-induced anemic rats

Groups	RBC (g/dl)		
	Before induction Day 0	After 4 th day of induction of anaemia Day 5	After 14 th day of treatment Day 19
Normal Control	8.11±0.10	8.37±0.28	6.78±0.26
Anemic Untreated	8.46±0.27	2.84±0.18 ^a	4.11±0.36 ^a
Anaemia + Standard drug (Emzoron)	8.32±0.41	3.14±0.56 ^a	5.40±0.57 ^b
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	8.26±0.34	4.22±0.63 ^a	6.05±0.32 ^b
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	7.92±0.16	5.30±0.28 ^a	5.93±0.15 ^b

^aSignificant decrease with respect to Day 0; ^bSignificant increase with respect to Day 5.

Table 7 presents the effect of ethyl acetate fraction of *F. capensis* on Platelets (PLT) count of phenylhydrazine-induced anemic rats. The result indicated a significant increase ($p<0.05$) in platelets levels of experimental animals after fourteenth day treatment compared with the untreated group after induction of anaemia.

Table 7 Effect of ethyl acetate fraction of *F. capensis* on Platelets (PLT) count of phenylhydrazine-induced anemic rats

Groups	PLT (10 ⁹ /L)		
	Before induction Day 0	After 4 th day of induction of anaemia Day 5	After 14 th day of treatment Day 19
Normal Control	771.33 ^b ±26.03	812.67 ^b ±55.26	876.00 ^b ±45.57
Anemic Untreated	717.33 ^d ±38.48	741.00 ^c ±9.54	908.33 ^a ±72.46
Anaemia + Standard drug (Emzoron)	780.00 ^a ±10.06	893.33 ^a ±35.30	815.33 ^c ±36.67

Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	742.00 ^c ±27.43	709.33 ^d ±41.06	782.00 ^d ±59.80
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	786.33 ^a ±18.62	891.00 ^a ±101.12	788.00 ^d ±43.32

Columns with different alphabet superscript are significantly different at $p < 0.05$; Values are means $\pm$ standard error of mean

The result of the Mean Corpuscular Volume (MCV) of phenylhydrazine-induced anemic rats is presented in table 8.0. Results indicated a significant increase ($p < 0.05$) in the MCV of treated animals after the fourteenth day compared with the untreated group.

Table 8 Effect of ethyl acetate fraction of *F. capensis* on Mean Corpuscular Volume (MCV) of phenylhydrazine-induced anemic rats

Groups	MCV (fL)		
	Before induction Day 0	After 4 th day of induction of anaemia Day 5	After 14 th day of treatment Day 19
Normal Control	61.40±0.90	62.67±0.72	57.57±0.97
Anemic Untreated	59.57±3.03	102.00±3.52 ^b	69.87±3.83 ^c
Anaemia + Standard drug (Emzoron)	55.53±5.09	91.57±6.30	70.50±1.55
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	62.80±4.36	66.07±12.32	68.93±2.44
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	54.80±3.21	53.63±0.75	74.13±0.72 ^{bd}

^bSignificant increase with respect to day 5; ^cSignificant decrease with respect to day 5; ^dSignificant increase with respect to day 0.

The result of the Mean Corpuscular Haemoglobin (MCH) of phenylhydrazine-induced anemic rats is presented in table 9. Results showed a significant increase ($p < 0.05$) in the MCH of treated animals after fourteenth day compared with the untreated group.

Table 9 Effect of ethyl acetate fraction of *F. capensis* on Mean Corpuscular Haemoglobin (MCH) of phenylhydrazine-induced anemic rats

Groups	MCH (pg)		
	Before induction Day 0	After 4 th day of induction of anaemia Day 5	After 14 th day of treatment Day 19
Normal Control	16.53±0.34	16.90±0.45	19.17±0.23
Anemic Untreated	16.90±0.32	28.87±0.55 ^d	24.37±0.94 ^{cd}
Anaemia + Standard drug (Emzoron)	15.97±0.50	27.43±1.03 ^d	23.97±0.62 ^{cd}
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	16.90±0.68	21.70±2.86 ^d	22.97±1.07 ^d
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	16.33±0.61	18.17±0.48	24.60±0.17 ^{bd}

^bSignificant increase with respect to day 5; ^cSignificant decrease with respect to day 5; ^dSignificant increase with respect to day 0.

The result of the Mean Corpuscular Haemoglobin Concentration (MCHC) of phenylhydrazine-induced anemic rats is presented in table 10. Results showed a significant increase ($p < 0.05$) in the MCHC of treated animals after the fourteenth day compared with the untreated group.

Table 10 Effect of ethyl acetate fraction of *F. capensis* on Mean Corpuscular Haemoglobin Concentration (MCHC) of phenylhydrazine-induced anemic rats

Groups	MCHC (g/dl)		
	Before induction Day 0	After 4 th day of induction of anaemia Day 5	After 14 th day of treatment Day 19
Normal Control	26.97±0.39	26.93±0.55	33.33±0.55 ^{bd}
Anemic Untreated	26.37±0.90	28.40±1.46	34.97±0.63 ^{bd}
Anaemia + Standard drug (Emzoron)	27.57±1.34	30.23±2.36	34.03±0.37 ^{bd}
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	30.87±0.18	33.47±1.94	33.33±0.43
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	29.63±1.60	33.90±0.55	33.17±0.30

^bSignificant increase with respect to day 5; ^dSignificant increase with respect to day 0.

Table 11 presents the effect of ethyl acetate fraction of *F. capensis* on White Blood Cells (WBC) count of phenylhydrazine-induced anemic rats. Results indicated a significant increase ($p<0.05$) in the WBC of treated animals after the fourteenth day compared with the untreated group.

Table 11 Effect of ethyl acetate fraction of *F. capensis* on White Blood Cells (WBC) count of phenylhydrazine-induced anemic rats

Groups	WBC (10 ⁹ /L)		
	Before induction Day 0	After 4 th day of induction of anaemia Day 5	After 14 th day of treatment Day 19
Normal Control	8.08±0.98	9.28±2.30	12.06±1.35
Anemic Untreated	7.53±0.69	17.58±3.70 ^d	29.20±3.65 ^{bd}
Anaemia + Standard drug (Emzoron)	7.64±0.66	20.66±5.31 ^d	22.39±8.59 ^d
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	8.39±1.03	34.28±4.51 ^d	8.78±0.78 ^c
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	9.40±2.20	26.58±4.53 ^d	11.39±3.19 ^c

^bSignificant increase with respect to day 5; ^cSignificant decrease with respect to day 5; ^dSignificant increase with respect to day 0.

Results of the effect of ethyl acetate fraction of *F. capensis* on Neutrophils (NEUT) count of phenylhydrazine-induced anemic rats indicated a significant increase ($p<0.05$) in the neutrophil count of animals treated after fourth day compared with the untreated group (Table 12).

Table 12 Effect of ethyl acetate fraction of *F. capensis* on neutrophils (NEUT) count of phenylhydrazine-induced anemic rats

Groups	Neutrophils (%)		
	Before induction Day 0	After 4 th day of induction of anaemia Day 5	After 14 th day of treatment Day 19
Normal Control	27.80±0.75	27.07±0.49	19.77±3.32
Anemic Untreated	28.13±1.39	38.27±0.98 ^d	36.00±7.91
Anaemia + Standard drug (Emzoron)	29.17±0.88	42.23±5.83 ^d	24.20±4.50 ^c
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	27.70±1.57	47.03±0.38 ^d	19.53±2.73 ^c
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	27.67±0.60	46.00±2.20 ^d	23.27±3.78 ^c

^cSignificant decrease with respect to day 5; ^dSignificant increase with respect to day 0.

Table 13 presents the effect of ethyl acetate fraction of *F. capensis* on Lymphocytes (LYMPH) count of phenylhydrazine-induced anemic rats. Results indicated a significant decrease ($p<0.05$) in the lymphocytes count of treated animals after fourth day with a significant increase after the fourteenth day of treatment compared with the untreated group.

Table 13 Effect of ethyl acetate fraction of *F. capensis* on lymphocytes (LYMPH) count of phenylhydrazine-induced anemic rats

Groups	Lymphocytes (%)		
	Before induction Day 0	After 4 th day of induction of anaemia Day 5	After 14 th day of treatment Day 19
Normal Control	71.03±0.64	70.83±0.27	79.93±3.43
Anemic Untreated	66.33±2.45	51.23±3.01 ^a	50.60±11.44
Anaemia + Standard drug (Emzoron)	65.93±1.62	49.60±0.47 ^a	75.47±4.32 ^b
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	64.90±3.62	55.00±3.58 ^a	80.00±2.76 ^b
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	68.30±1.55	51.13±0.80 ^a	76.63±3.81 ^b

^aSignificant decrease with respect to day 0; ^bSignificant increase with respect to day 5.

The effect of ethyl acetate fraction of *F. capensis* on Monocytes (MON) count of phenylhydrazine-induced anemic rats is presented in table 14. Results indicated a significant decrease ($p<0.05$) in the monocytes count of treated animals after the fourteenth day when compared with the untreated group.

Table 14 Effect of ethyl acetate fraction of *F. capensis* on monocytes (MON) count of phenylhydrazine-induced anemic rats

Groups	Monocytes (%)		
	Before induction Day 0	After 4 th day of induction of anaemia Day 5	After 14 th day of treatment Day 19
Normal Control	0.37±0.03	0.37±0.03	0.00±0.00
Anemic Untreated	0.43±0.09	2.13±0.03 ^d	0.50±0.25 ^c
Anaemia + Standard drug (Emzoron)	0.43±0.03	2.17±0.03 ^d	0.13±0.13 ^c
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	0.30±0.06	2.17±0.03 ^d	0.27±0.13 ^c
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	0.33±0.03	2.07±0.07 ^d	0.00±0.00 ^c

^cSignificant decrease with respect to day 5; ^dSignificant increase with respect to day 0.

The effect of ethyl acetate fraction of *F. capensis* on Eosinophils (EOS) count of phenylhydrazine-induced anemic rats is presented in table 15. Results indicated a significant decrease ($p<0.05$) in the eosinophil count of treated animals after fourteenth day when compared with the untreated group.

Table 15 Effect of ethyl acetate fraction of *F. capensis* on eosinophils (EOS) count of phenylhydrazine-induced anemic rats

Groups	Eosinophils (%)		
	Before induction Day 0	After 4 th day of induction of anaemia Day 5	After 14 th day of treatment Day 19
Normal Control	1.20±0.00	1.23±0.03	0.30±0.12 ^{ac}
Anemic Untreated	1.37±0.23	1.17±0.03	0.23±0.15 ^{ac}
Anaemia + Standard drug (Emzoron)	1.27±0.07	1.47±0.07	0.20±0.10 ^{ac}
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	1.27±0.07	1.27±0.03	0.20±0.00 ^{ac}
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	1.10±0.00	1.13±0.03	0.10±0.06 ^{ac}

^aSignificant decrease with respect to day 0; ^cSignificant decrease with respect to day 5.

The effect of ethyl acetate fraction of *F. capensis* on Basophils (BAS) count of phenylhydrazine-induced anemic rats is presented in table 16. Results indicated a significant decrease ($p>0.05$) in the basophil count of treated animals after fourteenth day when compared with the untreated group.

Table 16 Effect of ethyl acetate fraction of *F. capensis* on basophils count of phenylhydrazine-induced anemic rats

Groups	Basophils (%)		
	Before induction Day 0	After 4 th day of induction of anaemia Day 5	After 14 th day of treatment Day 19
Normal Control	0.17±0.03	0.13±0.03	0.00±0.00 ^{ac}
Anemic Untreated	0.13±0.03	0.30±0.06	0.00±0.00 ^{ac}
Anaemia + Standard drug (Emzoron)	0.13±0.03	0.37±0.03	0.00±0.00 ^{ac}

Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	0.13±0.03	0.37±0.03	0.00±0.00 ^{ac}
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	0.13±0.03	0.40±0.00	0.00±0.00 ^{ac}

^aSignificant decrease with respect to day 0; ^cSignificant decrease with respect to day 5.

Table 17 presents the effect of ethyl acetate fraction of *F. capensis* on the lipid profile of phenylhydrazine-induced anemic rats. Results showed a significant decrease ($p<0.05$) in the LDL-C, triglyceride and VLDL of untreated anaemic animals when compared with the apparently healthy normal control group.

Table 17 Effect of ethyl acetate fraction of *F. capensis* on lipid profile of phenylhydrazine-induced anemic rats

Groups	Total cholesterol (TCHOL) (mg/dl)	High-density lipoprotein (HDL-C) (mg/dl)	Low-density lipoprotein (LDL-C) (mg/dl)	Triglycerides (TRIG) (mg/dl)	Very-low density lipoprotein (VLDL) (mg/dl)
Normal Control	88.00±3.61	46.33±10.52	24.67±2.40	36.73±13.51	4.93±0.48
Anemic Untreated	120.33±5.17 ^e	35.33±4.06	40.67±4.26 ^e	76.87±6.16 ^e	8.13±0.85 ^e
Anaemia + Standard drug (Emzoron)	98.00±4.16 ^h	43.33±2.19	31.00±1.15 ^h	48.47±4.10	6.20±0.23
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	108.70±1.45 ^e	42.33±8.17	34.00±6.43	59.53±7.46	6.80±1.29
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	97.33±7.22 ^h	46.00±3.21	31.04±5.51 ^h	45.13±4.89	6.20±1.10

^eSignificant increase with respect to normal control; ^hSignificant decrease with respect to anemic untreated.

Table 18 presents the effect of the ethyl acetate fraction of *F. capensis* on the electrolyte levels of phenylhydrazine-induced anemic rats. Results showed a significant increase ($p<0.05$) in the sodium, chloride and bicarbonate ions of extract extract-treated groups when compared with the untreated anemic and apparently healthy normal control groups.

Table 18 Effect of ethyl acetate fraction of *F. capensis* on electrolyte levels of phenylhydrazine-induced anemic rats

Groups	Potassium ion (K ⁺) (mmol/L)	Sodium ion (Na ⁺) (mmol/L)	Chloride ion (Cl ⁻) (mmol/L)	Bicarbonate ion (BCO ₃ ⁻) (mmol/L)	Total Calcium (T ^{cal}) (mmol/L)	Ionized Calcium (n ^{cal}) (mmol/L)
Normal Control	5.73±0.15	132.7±2.40	103.33±0.67	19.33±1.45	1.53±0.17	0.77±0.09
Anemic Untreated	7.77±1.72	132.0±1.73	102.67±1.76	21.33±0.88	1.20±0.23	0.60±0.12
Anaemia + Standard drug (Emzoron)	5.13±0.07 ^h	132.33±0.33	97.33±0.33 ^h	18.33±0.88	1.13±0.13	0.57±0.07
Anaemia + 100 mg/kg ethyl	5.93±0.92	135.67±3.21	105.67±0.33 ⁱ	20.33±2.03	1.47±0.29	0.73±0.15

acetate fraction of <i>F. capensis</i>						
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	5.90±0.11	136.33±0.33	106.67±0.67 ^{gi}	21.00±1.53	1.90±0.15 ^{gi}	0.93±0.09 ^{gi}

^fSignificant decrease with respect to normal control; ^gSignificant increase with respect to anemic untreated; ^hSignificant decrease with respect to anemic untreated; ⁱSignificant increase with respect to Standard drug.

Table 19 presents the effect of the ethyl acetate fraction of *F. capensis* on liver function parameters of phenylhydrazine-induced anemic rats. Results showed a significant decrease ($p>0.05$) in the AST, ALT and ALP activities as well as total and direct bilirubin of extract-treated groups when compared with the untreated anemic and apparently healthy normal control groups.

Table 19 Effect of ethyl acetate fraction of *F. capensis* on liver function parameters of phenylhydrazine-induced anemic rats

Groups	Alanine transaminase (ALT) (U/L)	Aspartate transaminase (AST) (U/L)	Alkaline phosphatase (ALP) (U/L)	Total bilirubin (T. BIL) (mg/dl)	Direct bilirubin (D. BIL) (mg/dl)
Normal Control	10.00±1.15	16.33±0.33	31.93±1.68	1.47±0.11	0.36±0.04
Anemic Untreated	22.00±5.13 ^e	31.33±2.60 ^e	52.50±3.84 ^e	1.91±0.05 ^e	0.89±0.05 ^e
Anaemia + Standard drug (Emzoron)	12.33±2.60	19.67±1.76 ^h	36.60±5.71 ^h	1.48±0.04 ^h	0.46±0.08 ^h
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	12.00±1.15	22.00±3.21 ^h	32.30±4.73 ^h	1.51±0.06 ^h	0.35±0.03 ^h
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	11.00±5.13 ^h	18.33±2.33 ^h	34.63±3.11 ^h	1.65±0.19	0.36±0.04 ^h

^eSignificant increase with respect to normal control; ^hSignificant decrease with respect to anemic untreated.

Results of the effect of ethyl acetate fraction of *F. capensis* on kidney function parameters of phenylhydrazine-induced anemic rats showed a significant decrease ($p<0.05$) in the urea and creatinine levels of extract treated groups when compared with the untreated anemic group (Table 20).

Table 20 Effect of ethyl acetate fraction of *F. capensis* on kidney parameters of phenylhydrazine-induced anemic rats

Groups	Urea (mg/dl)	Creatinine (mg/dl)
Normal Control	8.03±0.88	2.40±0.15
Anemic Untreated	13.63±0.80 ^e	4.43±0.12 ^e
Anaemia + Standard drug (Emzoron)	8.67±0.26 ^h	2.67±0.34 ^h
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	9.77±0.38 ^h	2.32±0.03 ^h
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	10.90±0.47 ^h	1.73±0.09 ^h

^eSignificant increase with respect to normal control; ^hSignificant decrease with respect to anemic untreated.

The effect of ethyl acetate fraction of *F. capensis* on malondialdehyde (MDA) in phenylhydrazine-induced anemic rats is presented in table 21. Results showed a significant decrease ($p<0.05$) in the MDA levels of extract-treated groups when compared with the untreated anemic group. The effect of ethyl acetate fraction of *F. capensis* on lactate dehydrogenase (LDH) in phenylhydrazine-induced anemic rats is presented in table 21. Results showed a significant decrease ($p<0.05$) in the LDH activities of extract treated groups when compared with the untreated anemic group.

Table 21 Effect of ethyl acetate fraction of *F. capensis* on malondialdehyde (MDA) concentration and Lactate dehydrogenase (LDH) activity of phenylhydrazine-induced anemic rats.

Groups	Malondialdehyde (MDA) ($\mu\text{mol/L} \times 10^{-8}$)	lactate dehydrogenase (LDH) (U/L)
Normal Control	1.57 $\pm$ 0.20	207.00 $\pm$ 8.89
Anemic Untreated	5.87 $\pm$ 0.22 ^e	363.00 $\pm$ 14.80 ^e
Anaemia + Standard drug (Emzoron)	2.90 $\pm$ 0.78 ^{eh}	276.30 $\pm$ 28.05 ^{eh}
Anaemia + 100 mg/kg ethyl acetate fraction of <i>F. capensis</i>	3.57 $\pm$ 0.38 ^{eh}	255.67 $\pm$ 16.33 ^h
Anaemia + 200 mg/kg ethyl acetate fraction of <i>F. capensis</i>	3.10 $\pm$ 0.36 ^{eh}	246.00 $\pm$ 17.58 ^h

^eSignificant increase with respect to normal control; ^hSignificant decrease with respect to anemic untreated.

4. Discussion

Hematological parameters can be used to determine the level of beneficial or harmful effects of foreign compounds including plant extracts in the blood [24]. The induction of phenylhydrazine in animals has been implicated in the pathogenesis of anaemia. Anaemia is said to be a condition in which the blood does not have enough healthy red blood cells which often leads to reduced oxygen flow to the body's organs. This condition is believed to be alleviated with the use of plant extract especially *Ficus capensis*.

Despite an extensive acceptance that herbal medicine is gaining in recent times, one of the major challenges associated with its use is the absence of scientific evaluation of their safety profiles since many of them have turned out to be toxic [1]. It is therefore crucial that safety assessments of natural products be conducted to ascertain their safe consumption and consequently validate their therapeutic purpose scientifically.

Median lethal dose (LD₅₀) determination has remained a useful tool in safety assessment of substances [25]. Absence of death and normal behavior of experimental animals after an oral administration of 1600 mg/kg body weight (table 1) of *F. capensis* extract suggests that the extract may be largely safe by this route. Previous studies have supported that *F. capensis* is safe for therapeutic purpose at a dose of about 2900 mg/kg body weight [26].

As shown in table 2, oral administration of *F. capensis* extract to the experimental animals showed a significant increase in the body weight of the treatment group compared to the untreated control. This is consistent with the findings of Aja *et al.*, [27] and Ezeigwe *et al.* [28]. Administration of *F. capensis* extract could have possibly caused an increase in satiation state of the animals by plausibly inhibiting the release of cholecystokinin (CCK) which is released in the proximal small intestine and mediate meal termination and early phase satiety [29]. Since CCK is known to reduce meal size and also suppress hunger before meal, inhibiting its release will subsequently lead to increase feed consumption which ultimately leads to weight gain.

Glucose is the most important carbohydrate fuel in a biological system whose majority of it comes from the diet in a fed state. As depicted in table 3, there was significant reduction in the blood glucose of the animals treated with 200 mg/kg body weight of *F. capensis* after 4th and 14th day of induction compared with the untreated control. Since the glucose concentration in the body is normally maintained between 80 to 120 mg/dl (30), the administration of the plant extract used in this study could therefore help to maintain the daily requirement of blood glucose in a biological system.

Hematological parameters are used to determine possible alterations in the levels of biomolecules such as enzymes, metabolic products, normal functioning and histopathology of the organs [31]. Tables 4 to 16 showed the effect of *F. capensis* leaf extract on Haematological parameters. As evident in results above, there was significant increase ($p<0.05$) in the haemoglobin (table 4), packed cell volume (table 5), red blood cell (table 6), Mean Corpuscular Volume (table 8),

Mean Corpuscular Haemoglobin (table 9), Lymphocytes (table 13), levels in the experimental animals treated with 200 mg/kg body weight of *F. capensis* after 14th day of induction when compared with the untreated group while a marked reduction in the Platelets (table 7), Mean Corpuscular Haemoglobin Concentration (table 10), White Blood Cells (table 11), Neutrophils (table 12), Monocytes (table 14) and Eosinophils (table 15) counts in animals treated with 200 mg/kg body weight of *F. capensis* after 14th day of induction was observed when compared with the untreated group.

A significant increase ($p<0.05$) in haemoglobin, packed cell volume, red blood cell, Mean Corpuscular Volume, Mean Corpuscular Haemoglobin and Lymphocytes counts as observed in this study is consistent with the findings of Onu and Aja [32] who reported that garlic and ginger supplemented diet significantly ($p<0.05$) enhanced haematological parameters in rabbit. This is in line with the previous studies involving combination of *Cnidioscolus aconitifolius* and *Ficus capensis* in the treatment of anaemia [33]. Similar observations were made by Aja *et al.* [27] and Njoku-Oji *et al.* [34]. While the red blood cells contain haemoglobin; an iron-containing oxygen-transport metalloprotein in red blood cells of almost all vertebrates as well as the tissues of some invertebrates, saddled with the responsibility of carrying oxygen from the respiratory organs to the rest of the body, packed cell volume is the volume percentage of red blood cells in the blood that is used to estimate and monitor response to treatment. The general increase in haemoglobin, packed cell volume, and red blood cells of rats administered extract of *Ficus capensis* indicates that *Ficus capensis* leaves may contain blood-forming factors that may have stimulated more blood production by the rats that received the extracts than the group that did not receive the extracts.

Although the results on RBC, Hgb, and PCV in this study is in agreement with the findings of Aja *et al.* [27] and Njoku-Oji *et al.* [34], the result of White Blood Cells and its differentials showed a marked increase on administration of leaf extract of *F. capensis* is in contrast with the result of this study.

In clinical practice, effective and intensive lipid-lowering is vital for the prevention of cardiovascular diseases [35]. Extract of *F. capensis* leaf significantly ($p<0.05$) reduced total cholesterol (TC), low density lipoprotein (LDL-c), triacylglycerol (TAG) and very low-density lipoprotein (VLDL-c) with significant increase in high density cholesterol (HDL-c) levels in extract treated groups compared with the untreated control (table 17). These reductions in TC, TAG, LDL-c and VLDL-c levels suggest the ameliorative potential of *F. capensis* extracts in phenylhydrazine-induced anemic rats.

The possible TC-lowering effects of *F. capensis* leaves extracts observed in this study could be attributed to decreased activity of hepatic HMG CoA reductase and/or stimulation of cholesterol-7- α -hydroxylase, which converts cholesterol into bile acids [36]. It could also be due to the presence of saponins, a phytochemical which forms insoluble complexes with cholesterol or their bile salt precursor, thus making them unavailable for absorption [37].

The extract of *F. capensis* leaves could have reduced TAG levels by either activating endothelium-bound lipoprotein lipase which hydrolyses the triglyceride into fatty acid hence decreasing triglyceride levels or inhibit lipolysis so that fatty acids do not get converted to triglyceride. Sikarwar and Patil [38] made similar assertions.

Low density lipoprotein (LDL) is known for transporting cholesterol to body cells and it transports about 60-70% of total cholesterol. Therefore, an increase in TC level consequently increases LDL-c. The findings in this work showed significant ($p<0.05$) reduction in LDL-c levels. This plausibly could be attributed to the presence of phenolics in the plant extract as reported by previous researchers. Phenolics have been said to aid LDL-c receptors densities in the liver binding to apolipoprotein B thereby making liver cells more efficient to remove LDL-c from blood.

HDL-c act as cholesterol scavengers; they pick up excess cholesterol and cholesterol esters from the blood and peripheral tissues to the liver where it is broken down to bile acids. It plays an important role in reducing blood and peripheral cholesterol concentrations and inhibits formation of atherosclerotic plaque in the aorta [39,40]. Hence, they are known as protective cholesterol. The present studies showed a significant ($p<0.05$) increase in HDL-c in the extract treated group compared to the untreated control. This could possibly be due to increasing activity of lecithin-cholesterol acyl transferase (LCAT), an enzyme responsible for incorporating free cholesterol into HDL-c, thereby promoting reverse cholesterol transport and competitively inhibit the uptake of LDL-c. Yokozawa *et al.*, [41] and Geetha *et al.*, [42] made similar assertion in their independent studies.

Electrolytes are minerals in a biological system and its assessment is important in maintaining homeostasis as well as acid/base balance. Electrolytes play a significant role in conducting nervous impulses, contracting muscles as well as keeping the body hydrated. The administration of *F. capensis* extract in the anaemic rats improved the electrolyte (potassium, sodium, chloride and bicarbonate) levels of the animals (table 18). as shown in table 18, there was a significant increase in the potassium level of the extract treated group compared with the control. Potassium is a type

of electrolyte that helps the nerves to function properly and also aid muscle contraction. It also helps to improve the heartbeat as well as move nutrients into cells and waste products out of cells. Potassium has also been said to modulate electrolyte balance and regulate blood pressure through its effects on the distal cell voltage and chloride. Similar observation was made with sodium (table 18). Sodium, a counterpart of potassium, helps to maintain normal fluid levels outside the cells. Another electrolyte worthy of note is the chloride. Chloride assists with fluid balance, acid-base balance and delivery of oxygen to the cells.

Liver injury, if untreated could result to varying liver diseases ranging from steatosis to hepatitis, fibrosis, and necrosis. Viability and the health status of the liver is often assessed by liver biomarkers such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) among others. From the results in this study, there was significant decrease in the activities of ALT, AST, alkaline phosphatase (ALP) as well as total and direct bilirubin levels in the extract-treated groups compared with the untreated control (table 19).

As observed in this study, the elevated levels of AST and ALT observed in the serum of induced untreated group may be due to injuries inflicted on the liver due to the administration of phenylhydrazine. There was a significant ($p < 0.05$) restoration of these liver marker enzyme levels in all the treated groups on administration of the leaf extract. The reversal of these liver marker enzymes towards normalcy by the extracts observed in this study may be due to the prevention of the leakage of intracellular enzymes owing to the presence of polyphenol in the extracts and their membrane stabilizing activity [43,28].

Assessment of the functionality of the liver is often carried out by Hyperlipidemia is one of the disease conditions that are injurious to the liver; it sometimes results in fatty infiltration of the liver leading to a condition known as non-alcoholic fatty liver [44]. Fatty liver is an accumulation of triglycerides and other fats in the liver cells, if not treated leads to inflammation of the liver. It is characterized by varying degree of liver injury from steatosis to hepatitis, fibrosis, and necrosis [45]. It is, therefore, a clear manifestation of hepato-protective effects of the leaf extract.

Creatinine and urea are indices for assessment of kidney function. Creatinine is a waste product formed in muscle by the metabolism of creatine. It is synthesized in the liver, passes into the circulation and is taken up almost entirely by skeletal muscle. Its retention in the blood is evidence of kidney impairment.

Urea is the main end product of protein catabolism. Amino acid deamination takes place in the liver where ammonia is converted into urea and excreted through urine. Urea varies directly with protein intake and inversely with the rate of excretion. The elevated levels of creatinine and urea observed in the serum of induced untreated group rats (table 20) may be because of injuries or damage of the nephron structural integrity due to the accumulation of phenylhydrazine. However, there was a significant ($p < 0.05$) restoration of the kidney serum levels of creatinine and urea in all the treated groups on administration of the leaf extract.

Table 21 showed the effect of ethyl acetate fraction of *F. capensis* on malondialdehyde (MDA) concentration of phenylhydrazine-induced anemic rats. MDA is one of the final products of polyunsaturated fatty acid peroxidation in the cells and it is commonly used as a biomarker of oxidative stress. Increase in free radicals causes overproduction of MDA. The ability of the extract of *F. capensis* to significantly reduce the MDA levels of the treated groups justifies its potential antioxidant activities.

5. Conclusion

The observations from this present study revealed that ethyl acetate fraction of *F. capensis* leaf is largely safe for therapeutic purposes and continuous administration of this plant fraction could help to combat anaemic disorders implicated with the induction of phenylhydrazine, mitigate the release of free radicals and as well protect the integrity of the liver. This could be as a result of active compounds (flavonoids, phenols, tannins, alkaloids) and high levels of vitamins A, B, C, D and carotenoids found in the leaves of *F. capensis*. Further studies will be needed to test the efficacy of the ethyl acetate fraction of *Ficus capensis* in other animal models.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest in this manuscript.

Statement of ethical approval

The research work was approved by the Animal Research Ethics Committee, Nnamdi Azikiwe University. Ethical Code: NAU/AREC/2023/00061.

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Implication for health policy/practice/research/medical education:

The findings of this research indicate that ethyl acetate fraction of *F. capensis* leaves may boost haematological parameters of phenylhydrazine-induced anaemia in Wistar rats without severely upstaging the biochemical parameters. These insights significantly affect health policy, clinical practice, and research. Healthcare personnel should consider incorporating *Ficus capensis* leaves in the daily recommended diet of anemic patients, as it will be a big relief for them without serious adverse effects.

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