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Original Research Article

Phytochemical Constituents of Methanol Leaf Extract of *Ficus capensis* and the Assessment of Its Toxicity on Adult Wistar Rats

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Abstract

Purpose: This study aimed to evaluate the phytochemical constituents and conduct a detailed toxicological assessment of *Ficus capensis* methanolic leaf extract in Wistar rats. The primary objective was to document its previously undocumented toxicity profile and potential for genetic damage, given its recognized therapeutic and medicinal value.**Methods:** *Ficus capensis* leaf was methanol-extracted for phytochemical screening and proximate analysis. Toxicity assessment involved acute (up to 5000 mg/kg) and 28-day sub-chronic studies. In the sub-chronic phase, twenty Wistar rats per group received oral doses of 10, 100, or 1000 mg/kg body weight, with a control group receiving distilled water. Post-treatment, rats were sacrificed, and tissues were analyzed for biochemical parameters (ALT, AST, ALP, total protein, bilirubin), hematology, histopathology, and genotoxicity (Comet Assay).**Results:** Phytochemical analysis confirmed tannins, phenols, flavonoids, alkaloids, saponins, and cardiac glycosides. Proximate analysis showed 19.69% protein and 37.15% carbohydrates. Acute toxicity tests revealed no mortality or toxicity signs at up to 5000 mg/kg. The sub-chronic study demonstrated no significant changes in biochemical or hematological parameters across treated groups. Histopathological analysis showed no adverse effects on the liver or kidney. Crucially, the Comet assay indicated no genetic damage, with no significant differences in % Tail DNA or Tail moment.**Conclusion:** These findings strongly suggest that *Ficus capensis* leaf extract exhibits no toxicity or DNA damaging effects. This comprehensive toxicological assessment underscores its potential as a safe therapeutic alternative, with active compounds that may offer protective benefits against toxicity.

Keywords: *Ficus capensis* , Genotoxicity, Therapeutic , Subtoxicity, Histopathological

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INTRODUCTION

Medicinal plants are unique plants with diverse chemical compositions, known to facilitate various biological activities when administered and contribute to the biological and therapeutic value.[1,2] They are known for their healing effect in ailing conditions, bringing longevity to fast-declining organs.[3] Given their biological diversity, medicinal plants are a rich source of organic drugs typically exhibiting therapeutic action.[4] These organic drugs are largely transformed into the current conventional medications.[5] The compositions of these diverse compounds being referred to as phytochemicals are naturally distributed based on the species and family origin of the plant.[6] The saponins, flavonoids, phenols, alkaloids, steroids, tannins, glycosides, anthraquinones, terpenoidsetc constitute major members of this family.[7,8] The concentration, availability and percentage abundance relatively, of the phytochemicals in any plant species determined their therapeutic and nutritive significance.[9]

Several plants among the native African continents and sub-continents have been investigated empirically, on account of phytoconstituents and diversities, and at the same time contributing significantly to human health and nutrition.[10,13] More plants daily are systematically discovered, validated and further investigated on their scientific value and relevance on a large scale. *Ficus capensis* is a unique plant belonging to the Moraceae family.[14,15] It is a deciduous tree with spreading roots, branches and broader leaves.[16] Apart from the wide use of *F. capensis* in folk medicine in the treatment of inflammatory diseases, reports of its antibacterial,[17] anti-anaemic effect,[18] are documented in the literature.

Further information also showed that the plant's leaves are being treasured among most of the ethnic nationalities in the South-Southern part of Nigeria in treating various ailments arising from pathogenic organisms.[17] The preventive ability of plants against sickling of red blood cells was reported.[18] However, to the best of our knowledge, analysis of the phytochemical-constituents concerning the methanolic leaf extract of *F. capensis* and its effects on haematological, hepatic, and as well as genotoxic potential on Wistar rats are yet to be fully studied, hitherto. Bringing to fullness, the aim of the current study; phytochemical constituents and toxicological assessment of methanolic leaf extract of *F. capensis* in Wistar rats.

Generally, as part of the research focus, alteration in the genetic permutation is a known factor influencing individual susceptibility to adverse cellular derangements.[19] Mutations in DNA could spontaneously arise due to chemical action from either endogenous or exogenous origin.[20]Genotoxicity is a property of chemical agents with damaging effects on genetic machinery in a cell, resulting in mutations.[21] The enormous ability of any agent to sequester DNA arrangement, showcases the genotoxicity ability of that agent.

Figure 1: Image of fresh leaf of *F. capensis*

MATERIALS AND METHODS

Chemicals

All chemicals and reagents used were of analytical grade and were obtained from a reputable scientific chemical organization.

Animal Procurement

Fifty healthy adult male and female Wistar rats weighing 200-220g were purchased from the animal house unit of the Biochemistry Department, Federal University of Agriculture, Makurdi. The rats were maintained in cages under 12/12-hour light/dark cycles at normal laboratory conditions of a temperature of 25-26°C. They were fed with a rat pellet diet and clean water. Experiments were conducted in strict compliance with internationally accepted principles for laboratory animal use and care, as all experiments were performed according to "Principles of Laboratory Animal Care" (NIH Publication No. 85; rev. 1985) and ethics of College of Health Sciences Research Ethics Committee (CHSREC), Kogi State University Anyigba, Nigeria.

Ethical approval
Ethical approval was obtained from the College of Health Sciences Research Ethics Committee (CHSREC), Kogi State University Anyigba. Following a reference protocol number, CREC-CHS/PAAU/2025/0001 for the approval of handling live rats.

Plant Collection and Identification:
Fresh leaves of *F. capensis* were collected from Kogi State University Staff quarter, Kogi State, Nigeria, in January 2024 and were identified by a taxonomist at the Department of Biological Sciences, Kogi State University Anyigba, Nigeria (KSU), and the voucher number is PT-149. The leaves were air-dried at room temperature in Medical Biochemistry, KSU, for two weeks and pulverized to a coarse powder using an electric grinding machine.

Experimental Design
Preparation of Plant Extract
Five hundred grams (500 g) of the pulverised leaves of *F. capensis* were soaked in conical flask cork methanol (1:5, w/v) and filtered after 48 hours using a Watman no. 1 filter paper. The filtrate obtained was evaporated in an electric oven at 45ºC. The dried extract was stored in clean, airtight sample containers and kept in a refrigerator at 20°C until it was required to be used.
The percentage yield of the extract was calculated using the relation:
Percentage Yield %=Weight of extract weight of pulverized leaves g×100

Qualitative Phytochemical Screening
Phytochemical screening of the leaf extract Tannin, flavonoids, alkaloids, cardiac glycosides, saponins, and phenols was done according to the method described by Seriki.[22] andSofowora.[23]The quantitative phytochemical determination of tannin, phenolic content, flavonoids, cardiac glycosides, saponin, alkaloid by Ibeabuchi.[24]

Proximate Analysis
Proximate analysis on the leaf was determined according to the standard method of AOAC, (2000) as described by Waleed.[25]The outlined procedure was used for moisture, protein, fat, ash, fibre and carbohydrate contents analysis.

Toxicological studies
Acute Toxicity
The acute toxicity of methanol extract (LD_{50}) was studied in Wistar rats using the method of Lorke.[26] Thirty-six (36) Wistar rats of both sexes, were randomly divided into three groups (n = 6) in the first phase and orally administered methanol extract at graded doses (10, 100, and 1000 mg/kg body weight). They were observed for 24 hrs. On account no death was recorded, further high doses of 1,600, 2,900, and 5,000 mg/kg b. w of methanol extract was administered to another set of rats of animals (n = 6), and the number of deaths within 24 hrs grace observation was recorded. The LD50 was calculated as the geometric mean of the maximum dose producing 0% mortality (D0) and a minimum dose producing 100% mortality (D100), as mathematically expressed below:
$LD50 = \sqrt{(D0 \times D100)}$
D0 = the maximum dose-producing mortality and
D100 = the minimum dose that produced mortality

Subchronic Toxicity
Subchronic toxicity study of methanol leaf extract on male Wistar rats was determined according to the method described by Aniagu et al.[27]Following this procedure, animals were sacrificed, the liver was harvested, while blood, processed into serum for biochemical estimations (aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin, total protein creatinine, urea and uric acid).

Biochemical Estimation
Analysis using an Automated Analyzer (LabmaxPlenno, Labtest Co. Ltd., Lagoa Santa, Brazil), following the respective instructions of the commercial assay kits specified for each assay in accordance with the manufacturer's protocol, AST, ALT, ALP, total bilirubin, total protein, creatinine, urea and uric acid were estimated.

Determination of Haematological Parameters
A method of McCrea & Baker [28] was adopted for the determination of the haematological parameters. This consists of a rat's blood collected in an EDTA bottle, maintained at 10°C in ice. Analysis was done using an automated SysmexHaematologyanalyser(Sysmex kox1: Sussex corporation, Kobe, Japan, Xp 300 Series, Code No: AC580857).

Histological Examination of the Liver
The histological examination of the rats' liver was conducted following an outlined method of Rockey .[29] An initial staining, following haematoxylin and eosin(H & E)for the identification of nuclei (blue) and cytoplasm and fibrous tissue (pink) was conducted in line with the previously reported protocols.[30,31]

Determination of Genotoxicity Using the Comet Assay

The genotoxicity determination employing comet assay on liver cells was by an outlined methodology of Tice.[32] Briefly, it involved a fragment of the liver in PBS (10 mL) and a cell suspension (10 mL). 10 mL of each of the suspended tissue was added to 120 mL of 0.5% agarose at 37°C, complemented with a pre-coated slide layered with 1.5% regular agarose and capped for proper solidification. A mixture containing 2.5 M NaCl, 100 mM EDTA, 10 mMTris–HCl buffer, 1% sodium sarcosinate, 1% Triton X-100, and 10% DMSO was added to the solidified existing mixture at pH 10 for 60 mins. Following the incubation period, the layers were cleansed with cold PBS, left without agitation for 5 mins and subsequently, transferred into the electrophoresis buffering medium (0.3 mMNaOH and 1 mM EDTA, pH > 13) for 20 mins to unwind the constituents DNA. After a successful electrophoretic migration (set up at 25 V; 0.86 V/cm and 300 mA), a 0.4 M Tris, following, is an addition of visualizing agents to enhance resolution and visualization. An image analysis was carried out using Comet Assay II, Perceptive Instruments, Suffolk, Haverhill, UK in line with the manufacturer's instructions to measure the proportions of DNA damage.

Statistical Analysis

The data from the experiments were analyzed with GraphPad Prism version 5.0 and expressed as mean ± SEM. One-way ANOVA was employed for statistical analysis, with significance defined as $p < 0.05$.

RESULT AND DISCUSSION

This study reports phytochemical analysis (Table 1 and 2), revealing the presence of tannin, total phenol, flavonoid, alkaloid, saponin, and cardiac glycosides of *F capensis* leaf extract. The results validate previous reports, [33,34] on the plant under the current investigation. The current findings indicated that the extract possessed some biologically active compounds, which could serve as a potential source of drugs in applications.[35]The presence of alkaloids (1.0%in amount, under the condition of our investigation) in the extract supports the earlier findings [36] that the antibacterial activity of this plant could be attributed to the presence of alkaloids. Alkaloids are being reported given their possession of several pharmacological activities, which include antihypertensive effects, antiarrhythmic effects, antimalarial, and anticancer activity. [37,38]

Table 1: Qualitative Phytochemical Screening

Phytochemical Constituent	Value
Tannin	+
Total phenol	+
Flavonoid	+
Alkaloid	+
Saponin	+
Cardiac glycosides	+

Key: Detected

Table 2: Quantitative Phytochemical Screening

Phytochemical Constituent	Value
Tannin (mg of GAE/g)	21.47±0.01
Total phenol (mg of GAE/g)	148.89±0.04
Flavonoid (mg of QE/g)	67.00±0.06
Alkaloid (%)	1.06±0.00
Saponin (mg DE/g)	62.94±0.05
Cardiac glycosides (mg SeS/g)	4.60±0.00

Results are expressed as Mean ± Standard error of mean (SEM).

Pure isolated alkaloids and their synthetic compounds have been used in medicine as analgesic, antispasmodic, and bactericidal agents.[39,40] Saponins from fruits and vegetables are important dietary supplements and are known to exhibit antimicrobial activities and protect plants from microbial pathogens.[41]The crude extract of *F capensis* is taught to modulate blood lipids, and risk of cancer propagation, and improve blood glucose levels as well, as antioxidant activity.[42,43] Data obtained in the current study aligned with the published report by Ogundare and Akinyemi.[44] Cyanogenic glycosides containing plants are used as flavouring agents in pharmaceutical preparations .[45] The finding of glycoside (4.6 mg/100g) and tannins (687.64 mg/100 g)in Table 2) in the current investigation on the. capensis crude supports its pharmacological use as a flavouring agent and as well confers on the leaf a treatment agent against wounds emanating from varicose ulcers and haemorrhoids.[46] The flavonoids content of the leaf of *F.capensis* (67.00 ± 0.06mg of QE/g) in this finding attest to its protection against diverse diseases such as cancer,

inflammation, and [47,48] confirming the ethnopharmacological use of *F. capensis*.

The high carbohydrates, protein, moderate ash, fibre content, and substantial fat in the leaf of *F. Capensis*(table 3) are implicated in energy requirements for the body processes.[49,50] These nutrient contents also contributed to weight gain, as seen in the results, which is in agreement with Dickson et al.[51] A high protein content probably, contributes to the various body functions such as body development, maintenance of fluid balance, formation of hormones, synthetic proteins, and sustaining of strong immunity. [52] The fibre content could aid in the absorption of trace elements in the gut flora and therefore increase intestinal bowel movement[53] and play a vital role in the reduction and prevention of constipation.[54]

Table 3: Proximate Analysis

Component	Value
Moisture (%)	11.66±0.04
Ash (%)	13.50±0.25
Lipid (%)	7.80±0.10
Protein (%)	19.69±0.09
Fibre (%)	10.20±0.10
Carbohydrate (%)	37.15±0.21

Results are expressed as Mean ± Standard error of mean (SEM).

In Table 4 the acute toxicity result of the extract of 10-5000 mg/kg b.w produced no significant physical signs of toxicity, such as writhing, weakness, anorexia, gasping, palpitation, decreased respiratory rate, or death within 24 hours of post-administration. Hence, the oral median lethal dose (LD50) of the extract was estimated to be >5000 mg/kg. The result of this study is in agreement with the report of Dickson [51] where the result of LD50 was greater than 5000 mg/kg, showing that *F. capensis* extract is safe for human consumption. In the sub-chronic toxicity study, there was no death or sign of toxicity all through the period of administration. Changes in body weight (Figure 2) and general behaviour are early indicators of toxicity and are therefore critical for objectively evaluating a compound's effect on test animals There were no yet apparent noxious signs in the animals treated with the extracts of *F. capensis.*

Table 4: Acute Toxicity Study of the Methanol leaf Extract of *F. capensis*

Group	Treatment (mg/kg)	D/T
1	10	0/6
2	100	0/6
3	1000	0/6
Phase II		
1	1600	0/6
2	2900	0/6
3	5000	0/6

D/T: Number of deaths/ number of rats treated

Biochemical investigation in animal experiments regarding liver functional status, AST, ALT, ALP, bilirubin, and total protein levels are effective indicators of liver health (Figure 3-7). A release of ALT and AST from the cytosol signals injury to the hepatocytes compartment, while a decrease in the level of total protein is an indication of tissue injury and reflection of hepatic toxicity, complimented by a corresponding bilirubin, cholesterol elevation in the serum. An elevated ALP corresponds to bile duct obstruction or bone disorders.[56,57] Similarly, creatinine, urea and uric acid (table 5) are reported for their renal assessment. [58]

Table 5: Effect of Methanol Leaf Extract of *F. capensis* on biomarkers of kidney Function on *Wistar* Rats

Treatment	CREATININE (mg/dl)	UREA (mg/dl)	Uric Acid (mg/dl)
Group 1	0.55±0.35b	38.52±0.94a	9.63±1.88d
Group 2	0.24±0.05a	38.25±1.44a	5.81±1.10b
Group 3	0.91±0.71c	41.80±2.06ab	6.75±0.26c
Group 4	0.24±0.06a	42.89±0.98ab	5.31±0.46a

Assessment of haematological parameters aids diagnosis of anaemia and infection.[59] More importantly, a reduction in red blood cells is a complication leading to a reduction in the oxygen binding and its carrying capacity to the tissues.[60] The extract showed (Table 6) no significant effect on the RBC, HGB, HCT, MCV, MCH, and MCHC, thus confirming that the extract may not be toxic to the erythropoietic system. A slight elevation in white blood cell (WBC) counts observed in rats treated with varying dosages of the extract, suggests a potential immunomodulatory response indicative of cellular mobilization against exogenous substances. This observation aligns

with other researchers who demonstrate that plant extracts can elicit immune responses, often characterized by changes in WBC populations.[61]

Table 6: Shows Effect of Methanol Leaf Extract of *Ficus capensis* on haematological parameters of *Wistar Rats*

Treatment	RBC ($x10^6$/µL)	HGB (g/dL)	HCT (%)	PLT ($x10^3$/µL)
Group 1	7.76 ± 0.19[a]	14.30± 0.47[a]	39.16± 1.18[a]	817.33±1 28.22[b]
Group 2	7.93± 0.12[a]	13.23± 0.38[a]	38.21± 2.41[a]	722.33±6 1.55[ab]
Group 3	8.04± 0.45[a]	13.60± 0.63[a]	40.02± 3.64[a]	498.31±8 2.67[a]
Group 4	8.55± 1.05[a]	12.63± 1.50[a]	44.58± 5.2[b]	841.00±4 2.33[b]

Data are presented as the mean ± standard error of the mean (SEM), with six samples per group (n=6). Within each column, means with differing superscript letters indicate statistically significant differences when compared to the control group (Group 1) ($p < 0.05$

Table 7: Effect of Methanol Leaf Extract of *Ficus capensis* on MCV, MCH and MCHC

Treatment	MCV (fL)	MCH (Pg)	MCHC(g/dL)
Group 1	68.4±2.99[a]	16.7±0.90[a]	24.4±0.61[a]
Group 2	68.1±2.70[a]	16.7±0.41[a]	24.5±0.40[a]
Group 3	66.4±2.60[a]	16.0±0.33[a]	24.1±0.49[a]
Group 4	73.4±5.28[a]	17.6±0.73[a]	24.1±0.78[a]

Data are presented as the mean with its standard error (SEM), using a sample size of six (n=6). Within each column, means bearing distinct superscript letters indicate a statistically significant difference from the control group ($p < 0.05$)

The WBC population, encompassing its differential components, is crucial in mediating immune function, primarily through phagocytic clearance of foreign pathogens.[62]Further investigation is warranted to elucidate the specific mechanisms by which the extract influences WBC dynamics and to determine the clinical significance of these findings.The histological result in plates 2 and 3 reveals the histological components of the kidney and liver respectively.

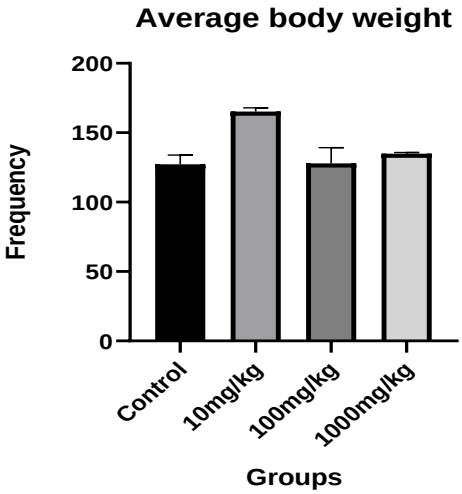


Figure 2: Effect of Methanol leaf Extract of *Ficus capensison* Average Body Weight of *Wistar Rats*

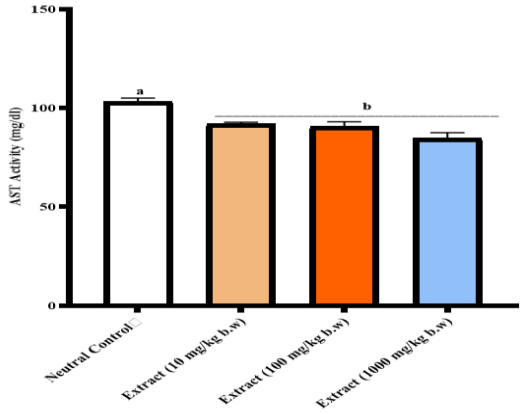


Figure 3: Effect of Methanol Leaf Extract of *Ficus capensis* on the activity of AST

After 28 days of administration, the effect of methanol leaf extract of *F. capensis* on 88the histological appearance of the kidney and liver was microscopically evaluated after staining with haematoxylin and eosin stain. Plates 2 and 3(a-d) show the photomicrographs of the kidney and liver of the control and treated rats, respectively. Histopathological examination of the kidney and liver(Plate 2) revealed no remarkable changes in

the structural architecture in the control group and the groups treated with methanol leaf extract. These findings showed that methanol leaf extract of *F. capensis* was not able to induce histopathological changes in the kidney and liver of Wistar rats at the various doses administered.

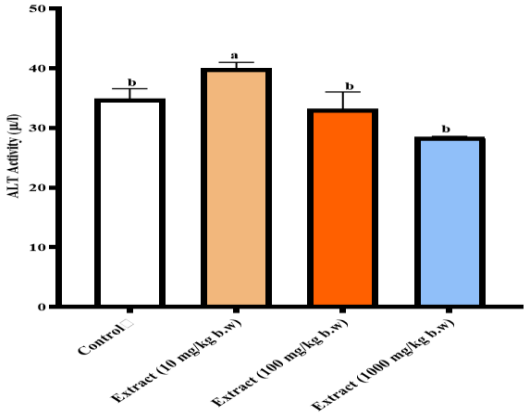


Figure 4: Effect of Methanol Leaf Extract of *Ficus capensis* on the activity of ALT in *Wistar* rats

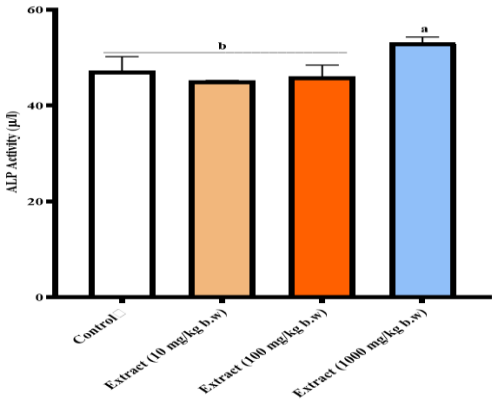


Figure 5: Effect of Methanol Leaf Extract of *Ficus capensis* on the activity of ALP in *Wistar* rats

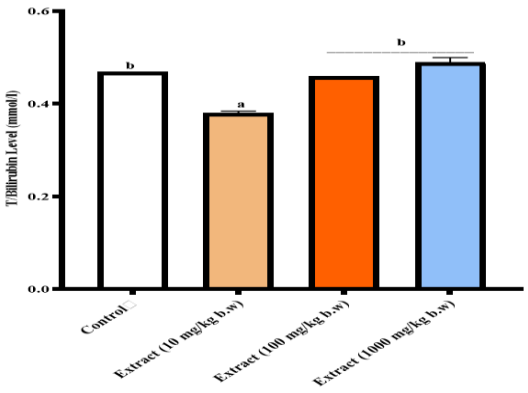


Figure 6: Effect of Methanol Leaf Extract of *Ficus capensis* on the Total bilirubin level of *Wistar* rats

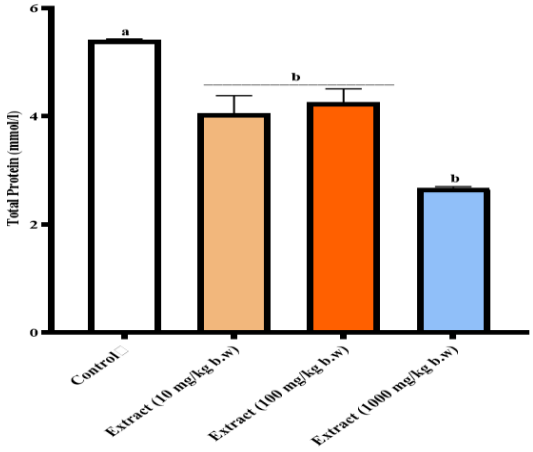


Figure 7: Effect of Methanol Leaf Extract of *Ficus capensis* on the Total Protein level of *Wistar* rats.

The genotoxicity of methanol leaf extract from *F. capensis* was evaluated using the single-cell gel comet assay. Given that peripheral blood is the initial site of exposure to xenobiotics, DNA damage was measured in these cells using percentage tail DNA and tail moment. It is well-recognised that the single-cell gel comet assay can detect genotoxins even at low concentrations.[63] The results in plate 1 show no significant differences in the group treated with the plant extract at 10 mg when compared to the control however results showed a significant difference in rats administered with 100 mg and 1000 mg/kg.bw when compared with control thus methanol leaf extract of *F. capensis* did not induce genetic damage in the liver tissues.

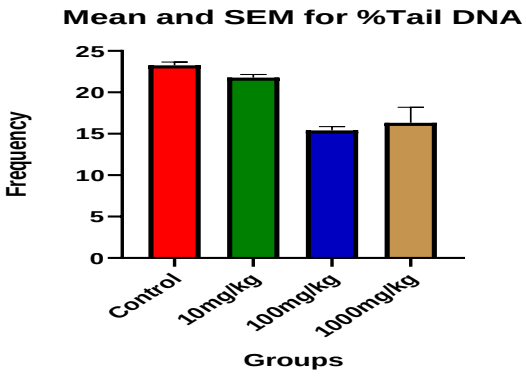


Figure 8: Comet assay of Methanol Leaf Extract of *Ficus capensis*

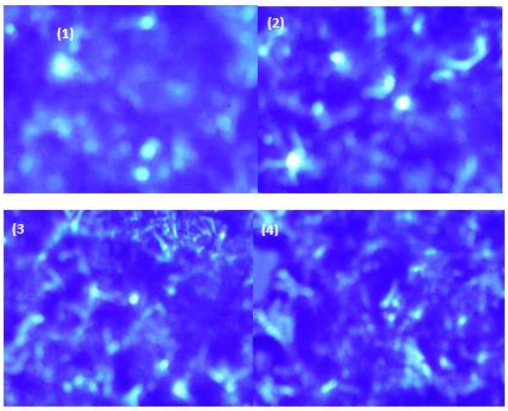
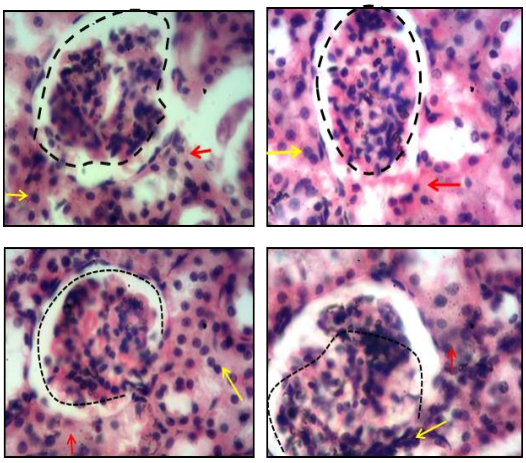


Plate 1: Photomicrograph of comet assay for (1) Control rats, animal that received (2)10 mg/kg of extract (3) 100 mg/kg of extract (4) 1000 mg/kg of extract.



Plates 2: Histopathology of the kidney of rat of control and group administered with methanolicextract of *F. capensis*Microscopic images (200x magnification) revealed normal kidney structure across all groups: (1) control, (2) 10 mg/kg extract, (3) 100 mg/kg extract, and (4) 1000 mg/kg extract. In each, the renal corpuscles displayed typical cellular boundaries, distribution, density, and staining properties. (Convoluted tubule: red arrow, podocytes: yellow arrow, glomerular capsule space: black dotted line).

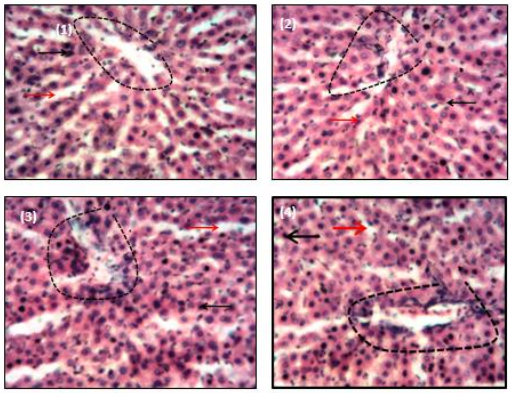


Plate 3: Microscopic examination (200x magnification) of liver tissue revealed normal structural characteristics in all groups: (1) control, (2) 10 mg/kg extract, (3) 100 mg/kg extract, and (4) 1000 mg/kg extract. Specifically, each showed a central vein with a typical surrounding clear zone (halo), and densely packed hepatocytes. In the 1000 mg/kg group, slight enlargement of the sinusoidal spaces was observed. (Central vein: dotted circle, sinusoidal space: red arrow, hepatocyte: black arrow)

CONCLUSION

This study provides a comprehensive phytochemical, toxicological, biochemical, haematological, histological, and genotoxic evaluation of the methanol leaf extract of *F. capensis*. The extract demonstrated rich phytochemicals, which likely contribute to its reported ethnomedicinal uses. The acute and subchronic toxicity assessments revealed a high safety margin (LD_{50}> 5000 mg/kg), with no significant adverse effects observed on biochemical, haematological and histological analysis in rats' liver. The extract displayed a non-genotoxic effect at a moderate dose suggesting its risk assessment profile at a high dose. These findings present *F. capensis* leaf extract as a reserve bioactive compound with therapeutic and nutritional benefits. Hence, structural elucidation; isolating, characterizing and purification of the specific bioactive compound(s) responsible for the observed effects in this study is recommended for further studies, given its potential pharmaceutical applications.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHORS DECLARATION

The authors hereby declare that the works presented in this article are original and that any liability for claims relating to the content of this article will be borne by them.

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