

Acute Toxicity Evaluation of *Ficus Platyphylla* Methanolic Leaf Extract on Wistar Rats

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Abstract

Medicinal plants are extensively used in traditional medicine globally, necessitating thorough safety evaluations to ensure therapeutic benefits outweigh risks. *Ficus platyphylla*, a West African medicinal plant, is traditionally used for various ailments including insomnia, epilepsy, and inflammation. However, its safety profile requires scientific validation. This study aimed to investigate the acute toxicity and median lethal dose (LD₅₀) of the methanol leaf extract of *Ficus platyphylla* in Wistar rats and to assess its phytochemical composition, effects on organ weight, and hepatic enzyme activities. The methanol leaf extract was orally administered to Wistar rats in two phases using Lorke's method: phase one doses of 10, 100, and 1000 mg/kg, and phase two doses of 1500, 3000, and 5000 mg/kg. Animals were monitored for behavioral changes, toxicity signs, and mortality over 24 hours and 14 days. Qualitative phytochemical screening was conducted. Organ weights and serum activities of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured. Phytochemical analysis revealed alkaloids, flavonoids, tannins, saponins, phenols, steroids, cardiac glycosides, and terpenoids. No mortality occurred at any dose, although transient toxicity signs including shivering, hair loss, and dizziness appeared at 5000 mg/kg. There were no significant changes ($p > 0.05$) in body weight, relative organ weights, or serum ALT and AST activities between treated and control groups, indicating low hepatotoxic potential. The oral LD₅₀ was estimated to exceed 5000 mg/kg. *Ficus platyphylla* methanol leaf extract demonstrated a high margin of acute safety in Wistar rats, supporting its ethnomedicinal use. The absence of significant toxicity and liver enzyme elevation suggests minimal risk under short-term exposure. Further sub-chronic and chronic toxicity studies are recommended for comprehensive safety evaluation.

Keywords: Acute toxicity, *Ficus platyphylla*, liver enzymes, methanol leaf extract, phytochemical screening

1.0 Introduction

Medicinal plants have been integral to human healthcare for centuries, serving as a primary source of treatment in many traditional medical systems worldwide [1]. In Africa, they remain a vital part of cultural heritage and continue to provide therapeutic, economic, and nutritional value [2]. The growing demand for herbal remedies has accelerated research into their pharmacological and toxicological properties, particularly in relation to safety, efficacy, and potential adverse effects [3]. Despite their perceived safety, some medicinal plants contain bioactive compounds that can exert toxic effects on

vital organs, underscoring the need for rigorous evaluation [4].

Toxicity studies, including acute, subacute, subchronic, and chronic assessments, are essential in establishing the safety profile of medicinal plant extracts. These studies help define the lethal dose (LD₅₀), identify target organ toxicity, and determine safe dosage ranges for human or animal use [5]. Acute toxicity testing, in particular, provides a rapid estimate of potential hazards associated with single-dose exposure and guides subsequent long-term investigations.

Ficus platyphylla, locally known as “Gamji” in Northern Nigeria, is a deciduous tree widely distributed across the West African savannah [6]. It has been traditionally employed in the management of insomnia, epilepsy, psychosis, depression, pain, and inflammation. Preparations typically involve the use of stem or root bark decoctions, cold-water extracts, or powdered plant material taken orally or via inhalation [7]. Phytochemical screenings of *Ficus platyphylla* have revealed the presence of saponins, flavonoids, tannins, and steroids, compounds known for their analgesic, anti-inflammatory, and central nervous system activities [8,9].

Although previous studies have reported the therapeutic potential of *Ficus platyphylla*, concerns remain regarding its safety profile. Prolonged administration has been linked to possible renal damage and histopathological alterations in the glomeruli of rat kidneys [10]. Other studies have suggested that extracts may influence haematological parameters, including reductions in white blood cell counts and lymphocytes [11]. Studies on *Ficus exasperata*, a closely related species, have also reported potential toxicity at high concentrations, with mortality increasing progressively at doses of 4000–8000 ppm despite safety at lower doses [12]. These findings highlight the importance of controlled toxicity studies to establish a safe dosage range and guide its medicinal use.

The present study was designed to evaluate the acute toxicity and LD₅₀ of the methanol leaf extract of *Ficus platyphylla* in Wistar rats. The research also assessed phytochemical composition, organ weight variation, and hepatic enzyme activity to provide baseline safety data and identify potential risks associated with short-term consumption.

2. Materials and Methods

2.1 Plant Collection and Authentication

Fresh mature leaves of *Ficus platyphylla* were collected in November 2023 during the dry season from the Federal University Birnin Kebbi permanent campus, Kebbi State, Nigeria. The plant was identified and authenticated by a taxonomist in the Department of Biological Sciences, and a voucher specimen (FUBK-H-60) was deposited in the Departmental herbarium for reference.

2.2 Preparation of Methanolic Leaf Extract

The leaves were washed, air-dried at room temperature, and pulverised into a fine powder using a mechanical grinder (Model MG-500, Crown Star, China). Extraction was carried out by macerating 500 g of the powdered material in 2.5 L of methanol for 72 h with intermittent shaking. The mixture was filtered through Muslin cloth followed by Whatman No. 1 filter paper. The filtrate was concentrated under reduced pressure using a rotary evaporator at 40°C and stored at 4°C until use.

2.3 Phytochemical Screening

Qualitative phytochemical analysis of the methanolic extract was performed using standard methods to detect the presence of alkaloids, flavonoids, tannins, steroids, saponins, terpenoids, cardiac glycosides, and phenols [13].

2.4 Experimental Animals

Adult Wistar rats (*Rattus norvegicus*) (150–200 g) of both sexes (equal distribution of males and females in each group) were obtained from the animal house of the Department of Biochemistry, Federal University Birnin Kebbi. The animals were acclimatized for 7 days before the experiment and housed in clean cages under standard laboratory conditions (25 ± 2°C, 12 h light/dark cycle) with free access to standard pellets (Vital Feed, Lagos, Nigeria) and water *ad libitum*. These animals were approved for use by the Animal Facility Centre (AFC) committee of Federal University Birnin Kebbi after reviewing the protocol for good laboratory practice and animal handling, which is in compliance with the National Institutes of Health Guide for the care and the use of laboratory animals (Publication No. 85-23, revised 1985).

2.5 Experimental Design

The acute toxicity study was conducted using “Lorke (1983)” in two phases. In phase one, three groups of two females and one male sex Wistar rats (n = 3) received oral doses of 10, 100, and 1000 mg/kg body weight of the extract. In phase two, three additional groups received 1500, 3000, and 5000 mg/kg body weight. Animals were closely observed for signs of toxicity and behavioral changes at 30 minutes, 1 hour, 2 hours, 4 hours, and 24 hours after dosing. Thereafter, the animals were monitored daily for a period of 14 days to assess delayed toxicity and mortality.

2.6 Organ Weight Determination

At the end of the observation period, animals were anaesthetised using chloroform inhalation and dissected. The liver, kidneys, pancreas, spleen, and lungs (selected for their relevance in acute toxicity as sites of metabolism, excretion, endocrine function, immune response, and respiratory function, respectively) were excised, rinsed in saline, blotted dry, and weighed immediately to avoid dehydration artifacts. Relative organ weights were calculated as organ weight (g) per 100 g body weight.

2.7 Biochemical Analysis

Blood samples were collected via cardiac puncture into plain tubes, allowed to clot, and centrifuged at 3000 rpm for 10 min to obtain serum. Liver enzymes, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activities were measured in duplicate using Randox Laboratories Ltd. (Crumlin, United Kingdom) diagnostic kits according to the manufacturer's instructions with internal quality controls.

2.8 Statistical Analysis

Data were expressed as the mean $\pm$ standard error of the mean (SEM). Statistical differences between groups were determined using one-way analysis of variance (ANOVA) followed by Duncan's multiple range test. A p -value < 0.05 was considered statistically significant.

3. RESULTS

3.1 Phytochemical Composition

The extraction process yielded 11.09% (w/w) at room temperature. The obtained results of the qualitative phytochemicals screening of crude methanol extract of *Ficus platyphylla* leaf extract revealed the presence of alkaloids, tannins, flavonoids, saponins, phenols,

steroids, cardiac glycosides and terpenoids (Table 3.1).

Table 3.1: Qualitative phytochemical composition of *F. platyphylla* methanolic leaf extract

Phytochemicals	Interference
Flavonoids	+++
Tannins	++
Cardiac glycosides	++
Saponins	+++
Steroids	++
Terpenoids	+
Alkaloids	+
Phenols	+++
Anthraquinones	-
Coumarins	-
Quinones	-
Xanthoproteins	-

Keys: +: Present in a trace concentration; ++: Present in a medium concentration; +++: Present in a high concentration; -: Absent.

3.2 Effect on Body and Organ Weights

3.2.1 Body weight

Mild signs of toxicity, including shivering, hair loss and dizziness were observed 24 hours post-administration at the 5000 mg/kg body weight dose. No toxicity signs were observed at lower doses. Changes in the weight in both treated groups and control groups were also observed (Table 3.2). The percentage weight gain observed across treatment groups ranged from 22.59% to 38.33%, with FP3000 showing statistically significant difference ($p < 0.05$) compared to control, while other groups showed no significant difference ($p > 0.05$). However, these variations fall within normal growth ranges and do not indicate toxicity. Relative organ weights for the liver, kidney, and heart showed no significant variation ($p > 0.05$) across all treatment groups compared to controls, indicating absence of gross organ toxicity.

Table 3.2: Weight change of rats after seven days of administration of *Ficus platyphylla* methanolic leaf extract

	Day 1	Day 7	% Change
Control	96.12 $\pm$ 1.85	126.03 $\pm$ 0.96	31.17 $\pm$ 1.57 ^a
FP1600	109.54 $\pm$ 0.60	151.50 $\pm$ 3.49	38.33 $\pm$ 3.72 ^a
FP3000	118.49 $\pm$ 0.99	145.28 $\pm$ 5.35	22.59 $\pm$ 4.13 ^b
FP5000	99.10 $\pm$ 0.74	133.7 $\pm$ 8.31	34.84 $\pm$ 7.57 ^a

All results are presented as Mean $\pm$ SEM. Where applicable, the same superscript with the control indicates no significant difference ($p > 0.05$) while the different superscripts with the group indicate significant difference ($p < 0.05$).

Keys: FP1600: *F. platyphylla* at 1600mg/kg b.w; FP3000: *F. platyphylla* at 3000mg/kg b.w; FP5000: *F. platyphylla* at 5000mg/kg b.w.

3.2.2 Organ Weights

Relative organ weights for the liver, pancreas, spleen, kidneys, and lungs are presented in Table 3.3. The liver, spleen, and kidneys showed no significant variation ($p > 0.05$) across all treatment

groups compared to controls. However, statistically significant differences were observed in pancreatic weights for FP1600 and FP5000 groups, and in lung weight for the FP3000 group ($p < 0.05$). Despite these statistical differences, the organ weights remained within normal physiological ranges, indicating absence of gross organ toxicity.

Table 3.3: Effect of *Ficus platyphylla* methanolic leaf extract of on organ weights in Wistar rats

	Liver	Pancreas	Spleen	Kidneys	Lungs
Control	5.24 ± 0.36 ^a	0.45 ± 0.11 ^a	1.14 ± 0.02 ^a	1.20 ± 0.05 ^a	1.24 ± 0.07 ^a
FP1600	5.40 ± 0.19 ^a	0.14 ± 0.04 ^b	1.02 ± 0.20 ^a	1.18 ± 0.02 ^a	1.22 ± 0.05 ^a
FP3000	5.75 ± 0.3 ^a	0.38 ± 0.13 ^a	1.15 ± 0.09 ^a	1.21 ± 0.09 ^a	1.40 ± 0.11 ^b
FP5000	4.73 ± 0.10 ^a	0.23 ± 0.05 ^b	1.23 ± 0.16 ^a	1.11 ± 0.06 ^a	1.17 ± 0.01 ^a

All results are presented as Mean ± SEM. Where applicable same superscript with the control indicates no significant difference ($p > 0.05$) while the different superscripts with the group indicate significant difference ($p < 0.05$).

Keys: FP1600: *F. platyphylla* at 1600mg/kgb.w; FP3000: *F. platyphylla* at 3000mg/kgb.w; FP5000: *F. platyphylla* at 5000mg/kgb.w.

3.3 Liver Enzyme Activity

Table 3.3 shows the liver enzymes of the rats treated with the extract. The results revealed no significant changes in ALT levels were observed across dose groups compared to the control. A slight but statistically significant decrease in AST was observed at 3000 mg/kg compared to the control group (Table 3.4).

Table 3.4: Effect of *F. platyphylla* methanolic leaf extract on ALT and AST levels in rats

	ALT (U/L)	AST (U/L)
Control	21.98 ± 4.76 ^a	41.17 ± 1.89 ^a
FP1600	25.07 ± 0.76 ^a	41.34 ± 1.56 ^a
FP3000	22.16 ± 1.44 ^a	36.25 ± 0.29 ^b
FP5000	21.67 ± 0.70 ^a	44.91 ± 7.91 ^a

All results are presented as Mean ± SEM. Where applicable, the same superscript with the control indicates no significant difference ($p > 0.05$) while the different superscripts with the group indicate significant difference ($p < 0.05$).

Keys: FP1600: *Ficus platyphylla* at 1600mg/kg b.w; FP3000: *Ficus platyphylla* at 3000mg/kg b.w; FP5000: *Ficus platyphylla* at 5000mg/kg b.w.

4. Discussion

Qualitative phytochemical screening of the methanolic leaf extract of *Ficus platyphylla* revealed the presence of alkaloids, flavonoids, tannins, steroids, saponins, terpenoids, cardiac glycosides, and phenols, while anthraquinones, coumarins, quinones, and xanthoproteins were absent (Table 3.1 and Figure 1). These findings align with earlier reports on *Ficus platyphylla* stem bark and leaves [8, 13]. Similar phytochemical profiles have been reported for related *Ficus* species, including *Ficus*

exasperata, which demonstrated comparable levels of flavonoids, saponins, tannins, and phenols in studies conducted in Nigeria [12]. The detected phytochemicals are known to possess diverse pharmacological activities, such as anti-inflammatory, analgesic, and antioxidant effects [9]. The presence of saponins and flavonoids may contribute to the plant's ethnomedicinal uses, given their free radical scavenging and membrane-stabilising properties [14].

No mortality was recorded in any dose group during the 14-day observation period. Rats administered the highest dose (5000 mg/kg) exhibited transient signs of toxicity including shivering, hair loss, and reduced activity within the first 24 h, but these resolved without intervention. Based on Lorke's method, the oral LD₅₀ of the methanolic leaf extract is estimated to be greater than 5000 mg/kg body weight, indicating a high safety margin for acute exposure. Similar non-lethal profiles have been reported for *Ficus platyphylla* methanolic stem bark extract at comparable doses [10]. The absence of mortality indicated that the extract is relatively safe in the short-term exposure. However, caution is warranted as sub-chronic or chronic administration may reveal delayed toxic effects, as observed in other plant species containing similar bioactive constituents [13]. Studies on *Ficus exasperata* demonstrated that while single low-to-high doses showed minimal toxicity, prolonged administration at high concentrations (4000-8000 ppm) resulted in increased mortality and biomarkers of organ damage [12].

Body weight changes were not statistically significant ($p > 0.05$) across most treatment groups compared to controls (Table 3.2), except for FP3000 which showed a significant but not biologically concerning difference. Relative organ weights for the liver, pancreas, spleen, kidneys, and lungs are presented in Table 3.3. While some organs (pancreas and lungs) showed statistically significant differences in certain treatment groups, these variations remained within normal physiological ranges. Stability in major organ weights (liver, kidneys, spleen) typically indicates the absence of gross toxicity or organ swelling/shrinkage, which are common in hepatotoxic or nephrotoxic reactions [18].

Serum ALT and AST activities did not increase in a dose-dependent manner and remained comparable to control values ($p > 0.05$) (Table 3.4). Elevated transaminases are reliable indicators of hepatocellular injury [16]. Thus, the absence of significant changes suggests the extract does not adversely affect liver function during acute exposure. The hepatoprotective trend observed here may be attributed to the antioxidant activity of flavonoids and phenolics present in the extract [15]. This aligns with the hepatoprotective potential reported for other flavonoid-rich medicinal plants [17] and is consistent with findings from related *Ficus* species studies [12].

Phytochemical and Acute Toxicity Study of *Ficus platyphylla*

Methanolic Leaf Extract Safety Profile

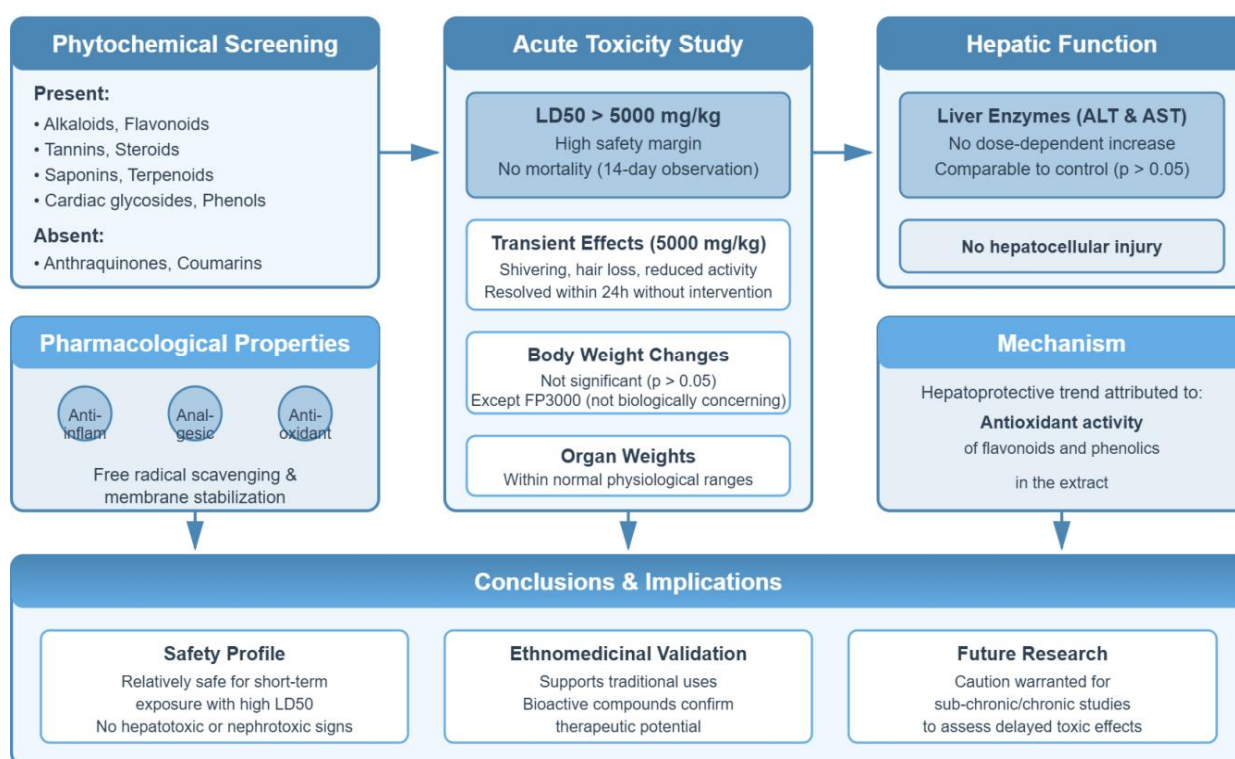


Figure 1: Discussion Chart

5. Conclusion

The methanolic leaf extract of *Ficus platyphylla* exhibited no mortality or severe adverse effects in Wistar rats at doses up to 5000 mg/kg body weight, indicating a high margin of acute safety. Phytochemical analysis confirmed the presence of bioactive compounds with potential therapeutic

benefits, while stability in body and organ weights, as well as unchanged serum ALT and AST activities, suggest minimal risk of hepatotoxicity under short-term exposure. These findings support the ethnomedicinal use of *Ficus platyphylla*, particularly for acute therapeutic applications. However, further studies involving sub-chronic and

chronic administration, as well as histopathological assessments, are necessary to establish its long-term safety profile.

6. Recommendations

Future studies on the impact of this plant's leaf extracts on hematological and histopathological parameters are recommended. In order to expand on our understanding of the medicinal profile of *Ficus platyphylla* leaf, it is recommended that future research concentrate on the separation, purification, and characterization of the extract's active ingredients, as well as sub-chronic and chronic toxicity investigations to establish comprehensive long-term safety data.

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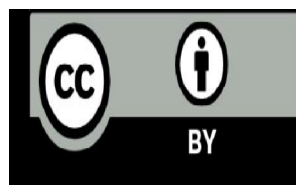
8. Conflict of Interest

We declare that there is no conflict of interest in the article.

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