

Proactive Study on the Toxicity of *Ficus benghalensis* Leaf Extract in Rat Models Preceding the Exploration of Therapeutic Benefits

Kalyan Acharjya^{1*}, Sushila Arya², Neetha SS³

*¹Assistant Professor, Maharishi School of Engineering & Technology, Maharishi University of Information Technology, Uttar Pradesh, India, Email Id- kalyan.acharjya@gmail.com, Orcid Id- 0000-0001-7802-7332

²Assistant Professor, School of Agriculture, Dev Bhoomi Uttarakhand University, Dehradun, Uttarakhand, India, Email Id- agri.sushila@dbuu.ac.in, Orcid Id- 0000-0001-7492-4757

³Assistant Professor, Department of Computer Science and Information Technology, Jain (Deemed to be University), Bangalore, India, Email Id- neetha.s.s@jainuniversity.ac.in, Orcid Id- 0000-0003-3751-9597

Abstract

Traditional Indian medicine has made extensive use of the Banyan tree, scientifically called *Ficus benghalensis* to cure several diseases. For diarrhea, Charaka recommended soaking the Nyagrodha (*Ficus benghalensis*) leaf buds in water. The leaves of the *Ficus benghalensis* tree can offer analgesic, antipyretic, and anti-ulcerogenic properties, according to recent studies. Finding the oral toxicity profile of a methanol extract of the *Ficus benghalensis* plant's leaves in Wistar albino rats was the aim of the study. *Ficus benghalensis* leaf extract (FbLEx) was administered orally to the rats once, at 100, 500, 1000, 2000, 4000, and 5000 mg/kg. Over a span of fourteen days, we monitored overall behavior and harmful symptoms. The acute toxicity of FbLEx, animals were given a diluted solution of the extract in methanol. At the end of the fourteen days of therapy, there were no reports of mortality or behavioural abnormalities. Furthermore, no negative effects were seen throughout the clinical testing, indicating that the extract was administered orally at a dosage exceeding 5,000 mg/kg body weight without causing any damage. However, the histology study found tiny alterations in the heart and kidneys. In conclusion, more investigations on the repeated dose toxicity of *Ficus benghalensis* leaves are needed to confirm their long-term safety. However, according to toxicological tests, the methanol extract of the plant was shown to be quite safe when taken orally.

Keywords: *Ficus benghalensis*, Rat, Toxicity, Diabetes Mellitus (DM)

INTRODUCTION

The scientific name for the banyan tree is *Ficus Benghalensis*, and it belongs to the Moraceae family. In India, this tree holds great religious importance. A significant toxicological concern for many years has been the liver damage caused by different hepatotoxins (1). Injuries to the liver can alter these metabolic processes. With its drooping branches and many aerial roots that serve as support roots, this tree is capable of reaching a height of 30 meters. The bark has a greenish white hue, and the leaves are alternate and simple, often seen in bunches at the ends of branches (2). The origins of the practice of food as medicine back hundreds of years. The "not modern" people's conventional wisdom on disease prevention and treatment was based on natural, organic remedies, is evident from ancient texts. It's really global reach is shown by the widespread adoption of natural product treatments throughout different regions of the globe, mostly referred as Ayurveda and Traditional Chinese Medicine. The use of natural substances as medicine or protection against disease is central to all of these practices, although the names can differ (3). The genus *Ficus* is well-known for its enormous diversity; it includes around 800 tree, vine, shrub, epiphyte, and hemi epiphyte species. Common names for fig trees and figs are both derived from the genus *Ficus* (4). Among these species, *Ficus benghalensis* stands out as a revered symbol of spiritual wisdom and everlasting life in India, where it is known as India's National Tree. The latex-like sticky substance found in the vasculatures of most *Ficus* species is involved in defense mechanisms and self-healing after physical damage (5). Common uses for latex include making

detergents for the home. These receptacles grow into many fruits with duplets collected. In general, when mature, the fresh fruits have a juicy, sugary texture and a delicate, fleshy exterior that can be any shade of red, pink, purple, or any other color found in the fruit's native species (6). Traditional Indian medicine relies heavily on plant remedies. A wide range of medical conditions have found their way into plant-based remedies and cures. Traditional Indian medicine and folklore employ a variety of plants to cure burns, scrapes, and other injuries. Wound healing is facilitated by several herbal plants. Due to their ability to promote the body's inherent healing systems, plants are more effective healers. Banyan trees, or *Ficus benghalensis* L., are among the most widely used plants (7, 8). Herbal medicine has been around for a while and is still used today. It involves using plant extracts as a medication. Plants have traditionally served as the primary source of treatment in systems such as Ayurveda, homeopathy, and allopathy. Early 20th-century researchers tended to favor allopathic pharmaceuticals, but in the last few decades, there has been a shift toward alternative approaches. The use of cosmetics and medications produced from plants, such as herbs on the rise. A quarter of all pharmaceuticals have their origins in plants (9). All around the world, traditional and folkloric medicines are integral parts of healthcare systems. A staggering 75% of the global population gets some of their medical treatment from plants or plant extracts. India has a vast network of forests, which are home to a wide variety of plant life (10). There are a number of plants that have traditional medicinal uses. New opportunities in contemporary healthcare arise from the logical design of innovative pharmaceuticals derived from conventional medicine. According to Ayurveda, India's ancient medical system, there are certain plants that boost the immune system of the host. A massive tree belonging to the Moraceae family, *Ficus benghalensis* can reach heights of 20 to 30 meters and has branches that stretch out wide and have aerial roots (11). A decoction made from the aerial roots of the *Ficus benghalensis* tree has been used by traditional healers in rural areas of Maharashtra to build up the immune system and protect against a variety of illnesses. Unfortunately, there has been a lack of research on the pharmacological and photochemical properties of the aerial roots to support this approach (12). Traditional healers in India have relied on the country's abundant medicinal plants for centuries, the country's verdant forests. As a remedy for diarrhea, they employed several plant components from the genus *Ficus*. For the purpose of testing its antidiarrheal effects in animal models, this plant was chosen based on its historical usage as an antidiarrheal in the *Ficus* genus. Rats utilized in this research were Wistar albinos, which typically weigh between 180 and 200 grams. Two experimental models, one using castor oil and the other using magnesium sulfate, were used to assess the antidiarrheal activity (13). Hyperglycemia and irregularities in the metabolism of carbohydrates, lipids, and proteins are hallmarks of the metabolic diseases known together as diabetes mellitus (DM). Problems with insulin production, insulin sensitivity, or insulin action can lead to this condition.

The herb *Combretum micranthum* has several uses, including those of an antidiabetic, antioxidant, and anti-inflammatory (14). A substantial risk factor for disorders affecting every organ system is diabetes, a chronic condition. There are a lot of conventional pharmaceuticals on the market for this issue, but they should look at how herbal remedies work (15). In the family Marceau, the genus *Ficus* is among the most numerous and massive plant families. This evaluation set out to please review the two main species in this genus and their pharmacological effects, therapeutic applications, and photochemistry, specifically, the *benghalensis* and religious varieties of *Ficus*. According to the results of the chemical study, many different types of phytoconstituents were found in *Ficus* species. such as glycosides, sugar, proteins, volatile and essential oils, terpenoids, tannins, alkaloids, saponins, and phenols substances, oils, and anabolic steroids. In sum, the evaluation exploring the significance of *Ficus benghalensis* as a medicinal plant from a broader therapeutic perspective in addition to maintaining optimal oxygen level in the air (16). One popular name for *F. benghalensis* is barged, and it is grown as a spiritual or garden tree. Ayurveda medicine makes use of *F. benghalensis* leaves for a variety of conditions, including ulcer protection, leprosy, fever, and inflammations. In addition to its usage in aphrodisiacs, tonics, vulnerable maturants, nasal disorders, and gonorrhoea, the milky juice has other medicinal properties (17). Biliousness, syphilis, Styptic, and diarrhea inflammation of the liver are symptoms of yunani's aerial root. While several parts of *F. benghalensis* have

been the subject of pharmacological studies, other historically significant medicinal benefits of the plant have yet to be verified by scientific means. For example, as pain relievers, fever reducers, anti-ulcerogenic, anti-inflammatory, antibacterial, and antidiabetic effects. The chemical components of *F. benghalensis* include leucocynidine glycoside, flavonoids, and Bengalenosides (18). Finding effective hepatoprotective medicines is crucial because liver disorders are a major health burden on a worldwide scale. Using thioacetamide (TAA)-induced hepatotoxicity models, the examined the hepatoprotective effects of Hiptage benghalensis Ethanol Fraction of Extract (EFEE) (19). Indian women have long relied on the aerial roots of the Banyan Fig (*Ficus benghalensis*), the country's official tree, to alleviate problems related to their reproductive health. Nevertheless, there is no pharmacological evidence to support this traditional usage. Furthermore, there was no documentation of extensive metabolite profiling for aerial roots of *Ficus benghalensis*'s (20).

MATERIALS AND METHODS

The study was to identify any symptoms of toxicity, which shed light on *Ficus benghalensis*'s safety profile and laid the groundwork for future research into its medicinal uses. This first toxicity evaluation helps in developing therapeutic treatments in a reasonable manner and provides a foundation for a comprehension of the plant's biological effects as shown in figure (1).

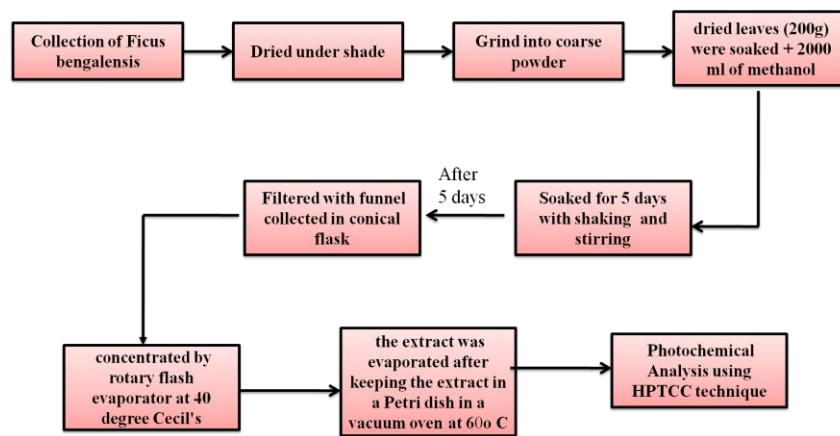


Figure (1). Preparation of plant extract

(Source: author)

Experimental animals

The Experimental rat's weight was 180 ± 20 g when they were 12 weeks old. Within their own polypropylene cages, the animals were housed in an environment with a temperature of $25 \pm 2^\circ\text{C}$, a humidity level of 55-65 percent and a cycle of twelve hours of light and darkness. The animals were given seven days prior to the actual studies to acclimatize to the settings in a clean, controlled environment. This was done to provide safe and healthy conditions for the animals. Free water and fertilizer were provided.

The study of acute oral toxicity

The following dose levels are predetermined: 100, 500, 1000, 2000, and 4000 milligrams per kilogram of body weight. Select one of these amounts to serve as the starting dosage for your patient. For LD_{100} calculation, a limit dosage of 5000 mg/kg physical weight was employed, and four dosages were selected from the available

alternatives. The conducted acute toxicity tests on female rats in accordance with OECD 4000. For the aim of determining the significance of the LD₁₀₀ value in female rats, five groups of rats were used, with each group consisting of three female rats. The medication was given to the animals after they had been fasting for the previous night. A garing tube was used to administer a single dose of the graded FBLEx to the animals, who were brought inside the garage. As can be seen in table (1), the methanol leaf extract of *Ficus benghalensis* was diluted to maintain the volume of dosage at 3 milliliters per 300 grams.

Table (1). The specifics of the groups and the doses given per kilogram

(Source: author)

Collection	The number of female rats	Dosage (mg/kg)
Group I	5	Distilled water
Group II	5	100
Group III	5	500
Group IV	5	1000
Group V	5	2000
Group VI	5	4000
Group VII	5	5000

Observation of animals

At a minimum, general clinical observations were carried out on a daily basis over the course of the 14-day trial period, which took into consideration the anticipated amount of time for effects to manifest after the administration of the dose. Every animal was closely observed for any indications of disease or death, such as abnormal motor activity, changes in the amount of water or food that was consumed, writhing, streptokinase reaction, sleepiness, diarrhea, piloerection, opisthotonus, exophthalmoses, and tremors. At a minimum of twice each day, these inspections were carried out.

Sacrifice of animals

On the fifteenth day, each and every animal group that had been evaluated and it was sent to a humane slaughterhouse. After conducting a comprehensive postmortem examination, the following organs were removed for the purpose of histological examination: the brain, liver, lungs, intestine, heart, ovary, kidney, stomach, and spleen.

RESULTS AND DISCUSSION

Analyses: The methanol leaf extract of *Ficus benghalensis* was subjected to high-performance thin-layer chromatography (HPTLC) for the purpose of conducting a photochemical examination. The findings of this research revealed the presence of Coumadins, anthracites, glycosides, bitter components, anthracenes, and flavonoids.

Pathology: In comparison to the group that served as the subject of the control, the rats that were examined at necropsy did not exhibit any pathological abnormalities that were noticeable. This was the case even after they had been given a dose of 5000 mg/kg. As can be seen in figure (2), these organs exhibited a normal architecture of the kidney's tubules, as well as occasional thickening of the mesangium and atrophy of the glomerular.

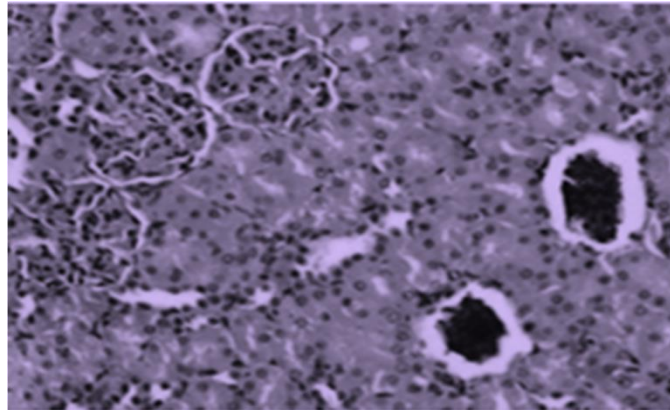


Figure (2). Kidney

(Source:

https://www.bing.com/images/search?view=detailV2&insightstoken=bcid_r5AH76ulzm8GvQ*ccid_kAfvq6XO&form=ANCMS1&iss=SBIUPLOADGET&selectedindex=0&id=1005602332&ccid=kAfvq6XO&exph=385&expw=512&vt=2&sim=1)

Note: The kidneys exhibit thickening of the mesangium and atrophy of the Glomerular, making them seem black and compressed, and in rare cases, the Glomerular tuft disappears entirely. There was mild to moderate congestion.

As illustrated in figure (3), the cardiac fibers, exhibited inter-muscular edema, discontinuance of the fibers at specific spots, loss of cross striations, and a rise in eosinophilic sarcoplasm, which provide evidence of necrosis.

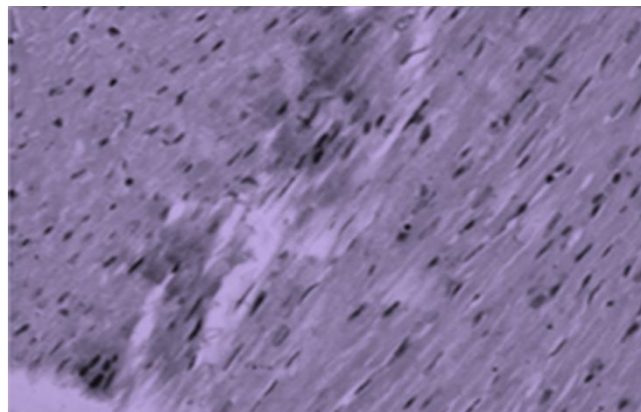


Figure (3). Heart

(Source: https://www.bing.com/images/search?view=detailV2&insightstoken=bcid_r-Yuh5NaW8Gwg*ccid_79i6Hk1p&form=ANCMS1&iss=SBIUPLOADGET&selectedindex=0&id=-651807021&ccid=79i6Hk1p&exph=373&expw=510&vt=2&sim=1)

Note: A heart with edema between the muscles, fibers that no longer connect, missing cross striations, and an increase in eosinophilic sarcoplasm, which point to necrosis

Evaluation of acute toxicity: After twenty-four hours of receiving methanol leaf extract from *Ficus benghalensis*, none of the experimental groups exhibited any signs of toxicity or death. This was the case regardless whether or not they had participated in the experiment. The therapy groups were subjected to observation for a period of fourteen days, and each and every one of them was monitored. The clinical indications of toxicity or mortality were not observed in any of the groups that were the subject of the investigation at the dose and duration that was suggested. Table (2) shows that both *Ficus benghalensis* methanol leaf extracts had LD₁₀₀ values over 5 g/kg in rats.

Table (2). Fatality trend in the FBLEx acute oral toxicity investigation involving female rats

(Source: author)

Collection	The number of female rats	Dosage (mg/kg)	Mortality (%)	Mortality observed
Group I	5	Distilled water	-	-
Group II	5	100	-	-
Group III	5	500	-	-
Group IV	5	1000	-	-
Group V	5	2000	-	-
Group VI	5	4000	-	-
Group VII	5	5000	-	-

The first stage evaluating a substance's hazardous properties is to determine its acute oral toxicity. It details the potential risks to health from oral exposure over a short period of time. By giving preliminary information on the mechanism of hazardous action of a chemical, it is a stage in determining a dose regimen in further research. In spite of the fact that it was administered at the highest possible dose of 5000 mg/kg, it was discovered that the methanol leaf extract of *Ficus benghalensis* did not result in any forms of death or clinical symptoms of toxicity. Microscopic examination revealed inter-muscular edema, fiber discontinuation in certain areas, loss of cross striations, and an increase in eosinophilic sarcoplasm, which are indicators of necrosis in cardiac tissue. Specifically, this was proved by the occasional thickening of the mesangium as well as the atrophy of the glomerular tissue, which ultimately led to a condensed mass inside the kidney tissue. OECD Technical Group 423 considers substances having LD₁₀₀ values beyond 5 g/kg essentially non-toxic. It is generally accepted that substances with LD₁₀₀ values over 5 g/kg of body weight are not hazardous. This is the consensus among industry experts. Consequently, the methanol leaf extract of *Ficus benghalensis* is one of the chemicals that does not contain a high level of toxicity, nor does it have a high level of adverse effects. Rather, it is one of the substances that cause harm.

CONCLUSION

The aforementioned findings suggest that a dose of 5000 mg/kg of *Ficus benghalensis* leaf extract did not cause mortality. This exploratory analysis may assist to clarify toxicological facts on FBLEx. Chronic toxicity studies of FBLEx might be the subject of future research to assess its potential long-term consequences. Finally, we have learned a great deal from our proactive investigation into the toxicity of *Ficus benghalensis* leaf extract in rat models, assuring safety before investigating treatment options. To pave the road for prospective uses in health and medicine, future research should concentrate on clarifying the extract's medicinal advantages.

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