EFFECT OF AQUEOUS EXTRACT OF *Musa paradisiaca* ON THE KIDNEY OF ADULT WISTAR RATS

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A PROJECT SUBMITTED TO THE DEPARTMENT OF ANATOMY, SCHOOL OF BASIC MEDICAL SCIENCES, UNIVERSITY OF BENIN, BENIN CITY, EDO STATE, NIGERIA.

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DEDICATION

This work is dedicated to God Almighty, the Giver of life for keeping me alive throughout my academic journey and especially throughout the duration of this research.

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ABSTRACT

Musa paradisiaca (plantain) is widely used in traditional medicine and consumed as food, yet its renal safety profile remains poorly characterized. This study evaluated the dose dependent effects of its aqueous extract on kidney function and oxidative stress in adult Wistar rats. Twenty-five rats were divided into five groups (A–E) and administered control, 100, 500, 750, and 1000 mg/kg of *Musa paradisiaca* extract orally for 16 days. Serum urea, creatinine, antioxidant enzymes—superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx)—and malondialdehyde (MDA) were assayed. Kidney weights, reno-somatic index (RSI), and histological features were evaluated. Serum urea increased significantly ($p < 0.05$) in rats receiving 750 mg/kg and 1000 mg/kg extract compared with control. Antioxidant enzyme activities (SOD, CAT, and GPx) declined notably at higher doses, whereas MDA levels had no significantly, indicating absence of enhanced lipid peroxidation and oxidative stress. The RSI was elevated in the 1000 mg/kg group, although body weights were unaffected. Histological sections showed preserved renal architecture across groups, suggesting functional rather than structural injury at higher doses. In conclusion the aqueous extract of *Musa paradisiaca* is largely safe at low to moderate doses but elicits biochemical signs of nephrotoxicity at higher concentrations. The findings justify the need for dosage regulation and caution in prolonged or high dose use of plantain based remedies.

CHAPTER ONE
INTRODUCTION

1.1 Background of Study

Plants have long been directly connected to scientific discoveries and numerous studies as a source of medicine. Medicinal plants constitute one of the main sources of new pharmaceutical and healthcare products; there has been an increase in the demand for phytopharmaceuticals all over the world due to the side effects of allopathic drugs.

The WHO referred to herbal medicine as "herbs, herbal materials, herbal preparations and finished herbal products that contain as active ingredients parts of a plant and other plant materials or combinations". According to studies, more than 60% of consumers use herbal remedies because they have a strong faith in its efficacy and safety and do not seek medical advice before doing so. (Amorha *et al*., 2018)

The kidney plays a very vital role in ensuring the body is in balance by excretion of wastes, balancing of electrolytes and fluid levels. Even when kidney functions becomes muddled up, either by toxins, drugs or metabolic ailments, it continues to be a significant worldwide health issue. Recently, scientists have resorted to natural plant substances as possible regulators of kidney activity with references to their antioxidant and anti-inflammatory activities. *Musa paradisiaca* (plantain) is one of these plants which have attracted attention due to its extensive food use and its acceptance as a traditional medicine.

Musa paradisiaca is a perennial herb, which grows in tropical and subtropical areas. Besides being a delicious snack, its fruit, peel, pseudostem, and leaves are taken as folk medicine against problems such as ulcers, diarrhea, inflammation, high blood pressure and kidney issues. Lab data indicate that the plant extracts in water include flavonoids, tannins, phenolics, alkaloids, saponins

and glycosides- all of which can function as antioxidants, anti-ulcers, antimicrobials and kidney protectants (El-Said *et al*., 2022; Ugbogu *et al*., 2021).

A few studies have been conducted investigating the effects of *Musa paradisiaca* on kidney of animals. Panigrahi *et al*. (2012) discovered that kidney stones, and increased antioxidants in rats administered with ethylene glycol could be prevented by an aqueous plantain extract. Similarly, El-Said *et al*. (2022) reported that a leaf extract treated mice with a cadmium-induced liver and kidney damage by alleviating oxidative stress and repairing antioxidant enzymes. A protective effect on kidney structure and function was also observed in even gentamicin treated rats after the intake of plantain. (Edenta *et al*., 2022).

Such encouraging outcomes are marred by reports of dose-related harms. Edenta *et al*. (2022) noted that some cultivars produced aqueous peel extracts, which increased serum urea and creatinine, which were indicative of kidney toxicity at certain doses or strains. Although the acute toxicity tests indicate that fermented aqueous extracts have an LD 50 greater than 5,000 mg/kg, higher doses repeatedly provoke disturbances in kidney biochemistry. This inconsistency supports the necessity of standardized tests of aqueous *Musa paradisiaca* extracts, particularly the impact of dosage on the result.

The adult Wistar rats are a favorite model in the study of toxicity and drugs due to their well-known behavior and their ability to handle and provide reproducible outcomes. A dose response trial involving aqueous extract of *Musa paradisiaca* in such rats will assist in describing its nephrotoxicity and therapeutic efficacy. By experimenting with different doses on healthy animals, we will be able to identify the point at which it is protective or harmful- information that is vital both in traditional and modern utilization of the plant.

Briefly, although the literature suggests that *Musa paradisiaca* may have a protective effect on kidneys, the inconsistency among cultivar and doses requires a systematic study. This experiment will evaluate the effect of varying levels of aqueous plantain extract on the test subjects, adult Wistar rats, on blood tests and tissue analysis to determine the health and integrity of the kidneys.

1.2 Statement of Research Problem

The significance of medicinal plants remains a dominant trend in medical research and we are always excavating the impact of plants on the major organs such as the kidneys. One common food is plantain (*Musa paradisiaca*), which is also used in folk medicine (e.g. in high blood pressure, diabetes, gut problems, etc.). The interesting fact is that its action is believed to be a rich blend of phytochemicals, such as alkaloid, flavonoid, tannin and phenol compounds, which tend to serve as antioxidants. However, no one has successfully pinned down the actual impact of the compound on the health of kidneys at varying concentrations.

Musa paradisiaca has been indicated in a few recent animal experiments to have protective effects on the kidneys. In one study, rats with kidney damage caused by arsenic, responded positively to being given an aqueous extract of the plant, improving serum creatinine and urea levels, kidney structure and antioxidant enzymes (Hossain *et al*., *2015*). A different article showed that the urea and creatinine of rats given unripe plantain supplements were reduced following iron overload and that the kidneys of the kids appeared to be healthier as well (Ezeanyika *et al*., 2019). In another model, *Musa paradisiaca* pseudo stem extract significantly decreased urea and creatinine concentrations, restored oxidative stress markers, and improved histopathological damage in rats with experimentally induced urolithiasis (Panigrahi *et al*., 2012).

Nevertheless, there are still significant questions. The majority of the studies are done on the protective action of the plant in the presence of stressful conditions and toxin-containing environment rather than on whether the plant would in fact cause damage to the kidneys in case you have excessive doses of it. Even the essential biomarkers such as urea, creatinine, antioxidant enzymes (superoxide dismutase, catalase, glutathione) have not even a clear dose-response curve. It is quite a large margin since kidney tissue is extremely sensitive to both stimulators and depressants and the same herbal extract might go either way depending on the amount and duration of the usage.

Then the systematic study would be to investigate the effects of aqueous extracts of unripe *Musa paradisiaca* on the kidneys of adult Wistar rat at various doses. This will assist us to determine whether the plant is truly kidney-friendly at safe doses or whether high doses would be toxic. This information is vital in determining the way people could safely use the plant as food or medicine. Furthermore, the findings will contribute to the broader scientific understanding of how bioactive compounds in commonly consumed foods influence vital organs such as the kidneys.

1.3 Aim of Study

To evaluate the effects of aqueous extract of *Musa paradisiaca* on the kidneys of adult Wistar rats across graded doses, assessing functional, biochemical, and histological outcomes.

1.4 Objectives of Study

The specific objectives of this study were.

- To investigate the electrolytes, urea and creatinine levels in adult Wistar rats treated with and without *Musa paradisiaca*

- To investigate the body and organ weight changes in adult Wistar rats treated with and without *Musa paradisiaca*

- To investigate the histology of kidney in adult Wistar rats treated with and without *Musa paradisiaca*

- To investigate the oxidative stress markers in adult Wistar rats treated with and without *Musa paradisiaca*

1.5 Significance of Study

This study is important because it contributes to the body of scientific work and general health. Plantain *(Musa paradisiaca*) is a common food with many individuals consuming it daily and it has also been utilized in traditional medicine to cure all sorts of issues. However, despite its popularity, there is not much hard scientific data concerning its impact on kidney functioning, particularly when you administer it as an aqueous extract in various dosages. Since the kidneys are extremely essential to the body, in terms of detoxification, fluid balance, and waste disposal, anything that we consume regularly must be screened in terms of potential protective or damaging effects on the kidney

CHAPTER TWO
REVIEW OF RELATED LITERATURE

This chapter comprises of detailed description of the aqueous extract, including reviews of the previous work involving the plant extract, and the organ(Kidney)

2.1 Introduction

Plants have long been directly connected to scientific discoveries and numerous studies as a source of medicine. Medicinal plants constitute one of the main sources of new pharmaceutical and healthcare products; there has been an increase in the demand for phytopharmaceuticals all over the world due to the side effects of allopathic drugs.

The WHO referred to herbal medicine as "herbs, herbal materials, herbal preparations and finished herbal products that contain as active ingredients parts of a plant and other plant materials or combinations". According to studies, more than 60% of consumers use herbal remedies because they have a strong faith in its efficacy and safety and do not seek medical advice before doing so. (Amorha *et al*., 2018)

Some studies have reported that components of herbal medicine cause renal tubular lesions such as inflammatory cell infiltration, degeneration, and necrosis of renal tubular epithelial cells(Luo Y *et al*.,2018). In another study where rats were exposed to plant extracts, histopathologic changes in the kidney were that of acute tubular necrosis with diffused interstitial and glomerular hemorrhage This suggests that irreversible cellular injury affecting the epithelial parenchyma and endothelial cells occurred. (Lloyd *et al*.,2013) *Musa paradisiaca* commonly known as 'plantain' is the hybrid between *Musa acuminata* and *Musa balbisiana*. Premature plantain is heavily consumed in Nigeria in many ways. While it may be a useful herbal remedy in treating different ailments, hyperglycemia in diabetes and peptic ulcer disease. It may also be associated with

adverse reactions and there is not enough reliable information on its effect on the kidney. Hence the need for this study.

The kidney is essential for controlling blood pressure, fluid and electrolyte balance, and the removal of waste products from metabolism. Because of their high vascularization and metabolic activity, the nephrons are especially vulnerable to harm from medications, poisons, and food ingredients (Zhou *et al*., 2017). Both structural changes in renal tissues and functional abnormalities like increased creatinine, urea, or issues with electrolyte handling can be signs of nephrotoxicity. A number of natural products and herbal remedies have also been linked to nephrotoxicity, even though many synthetic medications, including aminoglycosides, NSAIDs, and chemotherapeutics, are well known for their nephrotoxic potential (Ali *et al*., 2019). Therefore, to determine safe consumption levels and therapeutic margins, the safety evaluation of dietary and medicinal plants is required.

2.2 BOTANICAL DESCRIPTION

2.2.1 Musa paradisiaca

Musa paradisiaca is a species as well as a cultivar, originating as the hybrid between *Musa acuminata* and *Musa balbisiana*, cultivated and domesticated by humans during the early ages. Most cultivated bananas and plantains are polyploid cultivars either of this hybrid or of *Musa acuminata* alone. Linnaeus originally used the name *Musa paradisiaca* only for plantains or cooking bananas, but the modern usage includes hybrid cultivars used both for cooking and as dessert bananas. Linnaeus's name for dessert bananas, *Musa sapientum*, is thus a synonym of *Musa* × *paradisiaca* (Wikipedia,2025)

The genus Musa (family: Musaceae) comprises bananas and plantains, which are staple foods in many tropical regions, particularly in Africa, Asia, and South America. *Musa paradisiaca*, commonly referred to as plantain, is highly valued for its carbohydrate-rich fruit, which serves as a major source of energy (Eleazu *et al*., 2015). In addition to macronutrients, plantain is rich in micronutrients such as potassium, magnesium, and vitamins A, C, and B6. Potassium is known to promote cardiovascular and renal health by modulating blood pressure and fluid balance. This nutritional profile underscores its significance in diets, particularly in West Africa where plantain-based meals are consumed daily

***Musa paradisiaca*(plantain) plant**

2.2.2 Origin

Almost all cultivated plantains and many cultivated bananas are cultivars of the hybrid between two wild species, *Musa acuminata* and *Musa balbisiana*. It is believed that Southeast Asian farmers first domesticated *Musa acuminata*. When the cultivated plants spread north-west into areas where *Musa balbisiana* was native , hybrids between the two species occurred and were then developed further into a wide range of cultivars.(Ploetz *et al*., 2007)

Hundreds of cultivars of two species are known, possessing characteristics that are highly variable, but broadly intermediate between the ancestral species. They are typically 2–9 metres (7–30 ft) tall when mature. The above-ground part of the plant is a "false stem" or pseudostem, consisting of leaves and their fused bases. Each pseudostem can produce a single flowering stem. After fruiting, the pseudostem dies, but offshoots may develop from the base of the plant. Cultivars of banana are usually sterile, without seeds or viable pollen.(Nelson *et al*., 2006)

Common Names: Plantain, True banana, Cooking banana

Local Names: Agada(Hausa,Nigeria), Ogedeobani(Etuno), Matoke(Swahili,East Africa), Ogede agbagba(Yoruba,Nigeria), Ogede(Igbo,Nigeria)

2.2.3 Taxonomy

Banana plants were originally classified by Linnaeus into two species, which he called *Musa paradisiaca* for those used as cooking bananas (plantains), and *Musa sapientum* for those used as dessert bananas. It was later discovered that both of his "species" were actually cultivated varieties of the hybrid between two wild species, *Musa acuminata* and *Musa balbisiana*, which is now called *Musa* × *paradisiaca L*. The circumscription of the modern taxon *Musa* × *paradisiaca*

thus includes both the original *Musa paradisiaca* and *Musa sapientum*, the latter being reduced to a synonym of *Musa* × *paradisiaca*.

At one time, to deal with the great diversity of cultivated bananas and plantains, botanists created many other names which are now regarded as synonyms of *Musa* × *paradisiaca*, such as *Musa corniculata Lour*., used for a group of plantains with large fruit resembling the horns of a bull. Cultivated varieties are now given cultivar names, with the cultivars classified into groups and subgroups. Thus *Musa* × *paradisiaca* is a species of banana as well as a cultivar (Ploetz *et al*., 2007).

Taxonomical classification

Kingdom: Plantae

Subkingdom: Tracheobionta

Superdivision:Spermatophyta

Division: Magnoliophyta

Class: Liliopsida

Subclass: Zingiberidae

Order:Zingiberales

Family: Musaceae

Genus: Musa L.

Species: *Musa paradisiaca* L.

2.2.4 Morphology

Musa paradisiaca is a large, perennial herbaceous plant in the Musaceae family, often mistaken for a tree due to its height of 3–8 m. It is a hybrid of *Musa acuminata* and *Musa balbisiana*:

· Pseudostem: Robust, 20–30 cm in diameter, formed by tightly packed leaf sheaths, green to reddish

· Leaves: Broad, 1–3 m long, 30–60 cm wide, spirally arranged, easily torn by wind, bright green

· Flowers: Borne in drooping inflorescences, 1–2 m long, with reddish-purple bracts; female flowers develop into fruit

· Fruit: Elongated, curved, 15–30 cm long, green ripening to yellow, starchy, typically cooked

2.3 ETHNOMEDICINAL USES

Beyond its nutritional roles, *Musa paradisiaca* holds significant value in ethnomedicine. As many traditional ailments can be gotten from this plant. The unripe fruits is traditionally used to manage diabetes, ulcers, and diarrhea due to its high starch content and hypoglycemic properties(Ayodele,2011). The ripe fruits is used as laxatives (Oanhwange *et al*.,2009) while the cooked plantains are used for treating hypertension and kidney problems (Odenigbo *et al*.,2012). Fresh leaves are used in treating burns, wounds, and skin irritations because of their cooling effects (Shodehinde and Oboh, 2012). Stem juice of this plant is used for treating diarrhoea, dysentery, cholera, otalgia, and the flower is used in dysentery, diabetes and menorrhagia (Ghani, 2003). The root can also help to manage blood disorders, venereal diseases (Ghani, 2003).

2.4 PHYTOCHEMICAL COMPOSITION

Carbohydrates have been isolated from *Musa sapientum* (Anhwange, 2008). Catecholamines such as norepinephrine, serotonin, dopamine (Waalkes *et al*., 1958; Vettorazz, 1974), tryptophan, indole compounds (Shanmugavelu and Rangaswami, 1962), pectin have been found in the pulp. Several flavonoids and related compounds (Leucocyanidin, quercetin and its 3-O-galactoside, 3-O-glucoside, and 3-O-rhamnosyl glucoside) were isolated from the unripe pulp of plantain (Lewis *et al*., 1999; Lewis and Shaw, 2001; Ragasa *et al*., 2007). Serotonin, nor-epinephrine, tryptophan, indole compounds, tannin, starch, iron, crystallizable and non-crystallizable sugars, vitamin C, B-vitamins, albuminoids, fats, mineral salts have been found in the fruit pulp of *Musa paradisiaca* and *Musa sapientum* .(Imam and Akter, 2011)

Other commonly investigated phytochemicals in the Musa genus are anthocyanins, lutein, α-, and β-carotenes. Neoxanthin, cryptoxanthin, coumarin, and β-sitosterol. Also terpenes are another common phytochemical investigated the genus Musa. (Begashaw *et al*., 2023)

Cellulose, hemicelluloses, arginine, aspartic acid, glutamic acid, leucine, valine, phenylalanine and threonine have been isolated from pulp and peel of *Musa paradisiaca* (Ketiku, 1973; Emaga *et al*., 2007). Hemiterpenoid glucoside (1,1-dimethylallylalcohol), syringin, (6S, 9R)-roseoside, benzyl alcohol glucoside, (24R)-4α, l4 α,24-trimethyl-Sacholesta-8,25(27)-dien-3β-o1 have been isolated from flower of *Musa paradisiaca*. (Duita *et al*., 1983; Martin *et al*., 2000)

Phytochemicals	Pharmacological use
Tannic acid	Used for the treatment of burns
Catechin	Enables LDL to oxidation
Gallic acid	Antioxidant and hepatoprotective
coumaric acid	
Quercetin	
Ferulic acid	
Carotene	Reduce the risk of CVD and cancer
Serotonin	Increase wellbeing and happiness
Catecholamines	Used to increase blood pressure, glucose level, heartbeat rate
Sitosterol	Used in the management of benign prostate hyperplasia
Campesteroland Stigmasterol	Used for the reduction of cholesterol absorption

2.5 PHARMACOLOGICAL ACTIVITIES

2.5.1 Antimicrobial activity

The antimicrobial activities of the plantain (*Musa paradisiaca*) have been demonstrated in several investigations, with a wide variety of organisms serving as probable test subjects (most commonly fungus and bacteria, but also parasites and viruses). Asoso *et al*. (2016) demonstrated the antimicrobial activity of plantain peel and fruit extracts against *Escherichia coli*, *Staphylococcus aureus*, *Salmonella*, *Shigella*, *Klebsiella pneumoniae*, and *Bacillus subtilis*. The researchers used the agar well diffusion method to conduct their research. The minimum inhibitory concentration (MIC) for the ethanolic peel extract ranged between 150 and 200 mg/ml when tested against *Staphylococcus aureus* strain 25923 ATCC, *Salmonella typhi* strain 22648 ATCC, and *Klebsiella pneumonia* strain 34089 ATCC. The minimum inhibitory concentrations (MICs) of fruit ethanol extracts ranged from 200 to 300 mg/ml. On the other hand, the minimum inhibitory concentrations (MICs) for methanolic extracts of peels and fruit were 100 and 200

mg/ml, respectively, whereas the MICs for fruit extracts ranged from 150 to 250 mg/ml. (Kemisetti *et al*., 2022)

Extracts of acetone generated either from fruit peels or fruits themselves did not exhibit any antibacterial activity against the various test isolates. Even though there was indications of activity, differentiation based on Gram reactivity to the cell wall could not be found. This suggests that the mechanism of activity did not include cell wall lysis as one of its components. An ethanolic extract of peel powder has been shown to be beneficial against opportunistic skin infections such as Propionibacterium acnes, which is now known to be Cutibacterium acnes, and Staphylococcus epidermidis. This potential use is supported by Prakash *et al*. (2017), who discovered an inhibitory effect against *Aspergillus niger*, the fungus that is now believed to be responsible for cases of tinea capitis (Chokoeva *et al*., 2016). In order to determine whether or not the ethanolic and ethanolic and aqueous (1:1) extracts of *Musa paradisiaca* flowers are effective against fungus, Jawla *et al*. (2012) conducted a microdilution experiment. The MIC values for these extracts ranged from 5.62-25.81 µg/mL and 7.61-31.58 µg/mL, respectively. The minimum inhibitory concentration (MIC) of *Candida albidus* MTCC-2661 was determined to be 6.49 and 7.61 µg/ml for ethanolic extracts and ethanolic and aqueous extracts, respectively. *Candida albicans* MTCC-183 fared marginally better than the other strains, with ethanolic extracts average 8.62 g/mL and extracts including a mixture of ethanol and water (1:1) averaging 9.88 µg/mL. The minimum inhibitory concentrations (MICs) for ethanol in three different bacterial isolates Pseudomonas aeruginosa ATCC-9027, Bacillus subtilis MTCC-121, and *Bacillus cereus* MTCC-430 ranged from 5.62 to 7.95 µg/ml, respectively, whereas *Salmonella typhimurium* MTCC-98 showed the highest ethanolic MIC. The MIC for *Escherichia coli* MTCC-443 was found to be the highest in both the ethanolic and the aqueous (1:1) extracts.

Streptococcus pneumoniae MTCC-2672 came in second place with a value of 24.86 µg/mL, and then Proteus mirabilis MTCC-1429 came in third with a value of 22.13 µg/ml. (Kemisetti *et al*., 2022)

2.5.2 Antidiabetic activity

The methanolic extract of mature, green *Musa paradisiaca* fruits (100-800 mg/kg p.o.) had a hypoglycemic effect in normal and streptozotocin treated diabetic mice(Ojewole and Adewunmi 2003). Ethanol and ethanol:water (1:1) extracts of *Musa paradisiaca* flowers were given to normal and alloxan-treated diabetic rats. Blood glucose levels were measured daily following oral administration of extracts at doses of 100, 250, and 500 mg/(kg.d). Both extracts reversed alloxan-induced diabetic rats' permanent hyperglycemia within a week. The ethanol extract (250 mg/kg) was discovered to be 7.69% more potent hypoglycemic effect than the standard oral hypoglycemic drug, glibenclamide 0.2 mg/kg b.w.respectively.Jawla *et al*., 2012

A group of researchers isololated syringin from the tepal (flower) extract of *Musa paradisiaca* and tested its antidiabetic activity by oral administration (50 mg/kg/day for 30 days) in streptozotocin (STZ)-induced diabetic rats. They found that syringin significantly reversed the diabetes associated rise in blood glucose and HbA1c, and restored the diabetes-induced drop in plasma insulin and hemoglobin toward normal levels. Importantly, syringin treatment also normalized markers of renal and liver dysfunction in these rats: blood urea, serum creatinine, plasma protein, uric acid, and the activities of serum transaminases and alkaline phosphatase were brought back to near normal levels. (Krishnan *et al*.,2014)

A study evaluated the hypoglycemic effect of an aqueous extract of *Musa paradisiaca* stamen by giving 100, 200, or 400 mg/kg orally to normal and STZ-nicotinamide diabetic rats. In normal (non-diabetic) rats, the highest dose (400 mg/kg) blunted the rise in blood glucose during an oral glucose tolerance test within 30–60 minutes of a glucose challenge (2 g/kg) without causing hypoglycemia. In Steptozocin-nicotinamide diabetic rats, the 400 mg/kg dose also significantly lowered the elevated blood glucose levels. Thus, the *Musa paradisiaca* stamen extract showed a dose-dependent glucose-lowering effect in diabetic animals, without inducing hypoglycemia in healthy rats. (Ashish *et al*.,2016)

2.5.3 Analgesic activity

The in vivo analgesic activity of aqueous and ethanolic leaf extracts from *Musa sapientum* and *Musa paradisiaca* (400 mg/kg i.p.) significantly increases reaction time in the hot plate method when compared to the vehicle treated group. Acetic acid can be used to induce a writhing syndrome, which provides analgesia. Because of this process, the body releases endogenous substances that stimulate the pain nerve endings. The dose dependent analgesic effects of the aqueous extract of *Musa paradisiaca* indicate the presence of two components, one working centrally and the other acting through the peripheral pathway..The maximum analgesic effect of *Musa sapientum* extracts was observed after two hours.(Kemisetti *et al*, 2022)

2.5.4 Anticancer activity

Cancer, often described as a malignancy or tumour, remains one of the major health challenges worldwide, claiming millions of lives each year through progressive and often painful outcomes. This burden has driven scientists to search more actively for natural sources, particularly plants, that might slow down or suppress the growth of cancer cells. Among the many plants investigated for such properties is the plantain *(Musa paradisiaca*).

Nutrition has long been recognised as a key factor in cancer development and prevention. In particular, insufficient intake of dietary fibre and antioxidants has been linked to an increased risk of colorectal cancer. On the other hand, diets rich in fibre and antioxidant compounds are considered protective and play an important role in managing and preventing colon cancer.

Preliminary screenings of agricultural by-products have shown that plantain flowers are a rich source of both dietary fibre and anxidants. This finding suggests that they may offer a valuable alternative to other agro-residues commonly studied for health applications. To explore this further, researchers examined the methanolic extract of plantain inflorescence (PIMET) in colon cancer cell lines (HT29). Their findings not only confirmed its anticancer potential but also shed light on the biological mechanisms through which PIMET exerts its effects, offering a promising avenue for future therapeutic development. (Yakubu *et al*., 2015)

2.5.5 Antioxidant activity

The aqueous extracts obtained from roasted and boiled plantains were evaluated for their phenolic and flavonoid composition as well as their antioxidant activities. Results showed that the total phenolic content of the roasted and boiled plantain extracts were 89.06 ± 0.03 mg/100 g and 93.12 ± 0.01 mg/100 g, respectively. Similarly, the total flavonoid content was 48.34 ± 0.01 mg/100 g for the roasted sample and 61.03 ± 0.01 mg/100 g for the boiled sample. Statistical analysis revealed that boiling significantly, ($P < 0.05$) increased the phenolic concentration and reducing power of the flour, whereas roasting resulted in a higher vitamin C content (379.21 ± 0.30 vs 247.04 ± 0.04 mg/100 g). Despite these variations, no significant difference was observed between the ABTS antioxidant activity of the roasted and boiled plantain extracts. The antioxidant activities of the aqueous extracts of unripe plantain *(Musa paradisiaca*), were studied using their inhibitory action on sodium nitroprusside induced lipid peroxidation in rat pancreas in

vitro. The results showed that all the aqueous extracts possessed antioxidant activity (Al-Snafi *et al*., 2023)

2.5.6 Hypolipidemic activity

Oral administration of flavonoids (1 mg/100 g body weight) extracted from unripe fruits of *Musa paradisiaca* demonstrated significant hypolipidemic effects in male rats. Treatment markedly reduced serum cholesterol, free fatty acids, phospholipids, and triglycerides across the serum, liver, kidney, and brain. In addition, it enhanced the activity of HMG-CoA reductase while significantly lowering the activities of glucose-6-phosphate dehydrogenase and malate dehydrogenase. The extract also promoted lipoprotein lipase and plasma LCAT activities, alongside notable increases in hepatic and fecal bile acids as well as fecal neutral sterols. These changes suggest an accelerated degradation of cholesterol, thereby highlighting the lipid-lowering potential of *Musa paradisiaca* flavonoids (Vijayakumar *et al*., 2009).

2.5.7 Antihypertensive activity

Hypertension, or high blood pressure, is a significant medical condition linked to long-term cardiovascular risks such as heart attack, stroke, and heart failure. A key player in its pathophysiology is the Renin-Angiotensin System (RAS), a hormone pathway that regulates blood pressure and fluid balance. In this system, the enzyme Angiotensin-Converting Enzyme (ACE) plays a critical role by converting angiotensin I into angiotensin II, a potent vasoconstrictor (Borges et al., 2005).

While *Musa paradisiaca* has a history of use in traditional medicine for managing hypertension, scientific validation, particularly for the peels—which often pose a waste management issue—has been limited. Research has since worked to characterize the interaction between aqueous peel extracts and ACE, an established therapeutic target for controlling high blood pressure (Kaou et

al., 2008). The findings suggest that water-soluble phytochemicals in the peels possess highly inhibitory effects on ACE, indicating a potential therapeutic mechanism.

Furthermore, animal studies have provided supporting evidence. Research conducted by Parmar and Kar (2007) demonstrated the hypotensive effects of ripe banana pulp in rats with drug-induced hypertension. They proposed that this effect may be linked to the fruit's high content of tryptophan and carbohydrates, which can elevate serotonin levels—a neurotransmitter known to mediate natriuretic (sodium-excreting) effects. In a separate investigation, Oric and colleagues (as cited in the review) established that an aqueous extract of plantain induces a concentration-dependent hypotensive effect. This was observed in isolated rat tissues, where the extract relaxed aortic rings and portal veins that had been pre-contracted by agents like norepinephrine and potassium chloride.

Collectively, these studies substantiate the traditional use of *Musa paradisiaca* and highlight its potential for further investigation and development into nutraceuticals aimed at managing hypertension.

2.5.8 Wound healing activity

A study was carried out to evaluate the wound healing activity of the methanolic extract of *Musa paradisiaca Linn*. stem using a burn wound model in Wistar albino rats. The burns were induced by applying a red hot steel rod to the hind limb region, and the healing process was monitored daily. Wound contraction rates were assessed through histopathological examination. The findings demonstrated that treatment with the methanolic extract of *Musa paradisiaca Linn*. resulted in significantly enhanced healing compared to the control group, indicating its potential as an effective wound healing agent in burn injuries. (Amutha and Selvakumari, 2016)

In addition, a study demonstrated the wound healing potential of both methanolic and aqueous extracts of plantain (*Musa sapientum var*. *paradisiaca*) in rats. Administration of the extracts led to significant increases in hydroxyproline, hexuronic acid, hexosamine, superoxide dismutase, wound breaking strength, and reduced glutathione levels. In addition, they reduced wound size, scar formation, and lipid peroxidation. These beneficial effects were attributed to the strong antioxidant properties of plantain, which support tissue repair and regeneration. (Agarwal *et al*.,2009)

2.5.9 Antiallergic activity

The pseudo stem powder of *Musa paradisiaca* was suspended in acacia solution (10 mg/mL) for experimental purposes. Acute oral toxicity tests were conducted in both male and female rats, while female mice were sensitized against ovalbumin. A single dose of the powder (60 mg/kg body weight) or ketotifen (3 mg/kg body weight) was administered one hour prior to the induction of systemic anaphylaxis by intravenous injection of ovalbumin. In addition, the test product (0.6, 2.6, and 20 mg/kg body weight per day) was administered to mice throughout the immunization period, followed by either induction of systemic anaphylaxis or evaluation of passive cutaneous anaphylaxis titers in rat models using mouse antisera. No mortality or signs of toxicity were observed in rats treated with *Musa paradisiaca* powder. Unlike ketotifen, a single oral dose of the plant product did not inhibit systemic anaphylaxis in mice; however, daily oral administration significantly reduced both active and passive anaphylactic responses. These findings indicate that pseudostem powder of *Musa paradisiaca* possesses antiallergic properties. (Garcia *et al*., 2019)

2.5.10 Anti-ulcerative activity

Elango *et al*. (2007) investigated the antiulcer activity of the Siddha preparation *Musa paradisiaca* Bhasma (derived from the ripe fruit) using both acute and chronic ulcer models in

rats. Acute gastric ulcers were induced with 80% ethanol, while chronic ulceration was produced using 10% acetic acid. In the acute model, the bhasma was administered orally at doses of 10 and 20 mg/kg one hour prior to ulcer induction, whereas in the chronic model, treatment was given once daily for ten consecutive days. The results demonstrated significant antiulcer activity, evidenced by a reduction in ulcer index and an increase in gastric mucin levels. Antioxidant assays, including catalase, superoxide dismutase, and lipid peroxidation measurements, further confirmed the protective effect of the formulation. (Kemisetti *et al*.,2022)

Similarly, Herbert *et al*. examined the cytoprotective effects of a methanolic extract of *Musa paradisiaca* in indomethacin-induced peptic ulcer models. Using pylorus ligation techniques in rats, the extract was shown to exhibit both cytoprotective and antisecretory properties, thereby attenuating gastric ulceration. Collectively, these findings support the antiulcer potential of *Musa paradisiaca*, mediated through its antioxidant, cytoprotective, and antisecretory activities. (Kemisetti *et al*.,2022)

2.5.11 Anti-inflammatory activity

The methanolic extract of *Musa paradisiaca* stem, given orally at doses of 200 and 400 mg/kg, exhibited significant and dose-dependent anti-inflammatory effects in models of xylene-induced ear edema, carrageenan-induced paw edema, and dextran-induced paw edema when compared with the control. (Biswas *et al*., 2012)

2.5.12 Antiurolithiatc activity

Researchers evaluated the antiurolithiatic efficacy of an aqueous-ethanol extract of *Musa paradisiaca* pseudostem in a rat model of hyperoxaluria induced urolithiasis. Urolithiasis was induced by administering 0.75% ethylene glycol in drinking water for 28 days, with 1% ammonium chloride given during the first 14 days. This treatment significantly increased

markers of stone formation and renal stress including crystalluria, oxaluria, hypercalciuria, polyuria, urinary crystal deposition, and elevated serum urea, creatinine, nitric oxide, and erythrocyte lipid peroxidation. Co-treatment with the *Musa paradisiaca* extract dose dependently reversed these abnormalities in kidney function, yielding effects comparable to those of the standard antiurolithiatic drug cystone. (Panigrahi *et al*., 2012)

2.5.13 Reproductive activity

Alabi *et al*. (2013) investigated the effects of administering powdered mature green fruits of *Musa paradisiaca*, dissolved in distilled water, on semen quality in adult male Wistar rats at doses of 500 mg/kg and 1000 mg/kg. A significant improvement in semen parameters was observed at the lower dose, whereas rats treated with the higher dose showed a marked reduction in sperm concentration and the percentage of morphologically normal spermatozoa. (Alabi *et al*., 2013)

In a related study, Yakubu *et al*. (2013) examined the impact of oral administration of the aqueous root extract of *Musa paradisiaca* on testicular function in male rats. The extract produced a significant ($p < 0.05$) increase in the testes-to-body weight ratio, total protein, sialic acid, glycogen, cholesterol, alkaline phosphatase, γ-glutamyltransferase, acid phosphatase activities, and testicular testosterone concentration. Conversely, serum luteinizing hormone and follicle-stimulating hormone levels were reduced. These findings indicate that oral administration of *Musa paradisiaca* root extract at doses of 25, 50, and 100 mg/kg enhances testosterone-dependent testicular function and supports reproductive performance in male rats. (Yakubu *et al*., 2013)

2.5.14 Nephroprotective effects

A study explored the nephroprotective activity of methanolic extracts prepared from different parts of plant including the bract, flower, trachea, and tracheal fluid, using a gentamicin-induced nephrotoxicity model in mice. As expected, gentamicin administration led to sharp increases in blood urea nitrogen, blood urea, and serum creatinine, alongside clear histopathological damage in kidney tissue. Interestingly, treatment with the bract extract at doses of 100 and 250 mg/kg body weight, as well as the flowering stalk (trachea) extract at 250 and 500 mg/kg, significantly counteracted these biochemical disturbances and improved the renal histology. These results suggest that *Musa paradisiaca* extracts may provide protective effects against drug-induced kidney injury, most likely through mechanisms linked to their bioactive constituents. (Abbas *et al*.,2017)

Akinnuga *et al*. (2012) demonstrated that aqueous extract of plantain peel improved renal histology in alloxan-induced diabetic rats by reducing oxidative stress and restoring tubular architecture. Similarly, Osunde *et al*. (2017) reported reduced serum creatinine and urea in rats treated with unripe plantain extract following nephrotoxin exposure, suggesting protective effects against chemically induced renal injury.

2.5.15 Nephrotoxic effects

A recent study reported that 14-day oral administration of ethanolic extract of premature plantain pulp in female Wistar rats produced histological alterations in kidney tissue, with damage increasing in severity at higher doses. This suggests potential nephrotoxicity when plantain pulp extract is used for extended periods or at high doses. (Victor *et al*.,2023)

2.6 ORGAN OF STUDY(KIDNEY)

2.6.1 Description

The kidneys are also called renes from which we have the derivative renal; and nephros from which we have the terms nephron, nephritis, etc. The kidneys are a pair of excretory organs situated on the posterior abdominal wall, one on each side of the vertebral column, behind the peritoneum. They remove waste products of metabolism and excess of water and salts from the blood, and maintain its pH.

The kidneys occupy the epigastric, hypochondriac, lumbar and umbilical regions Vertically they extend from the upper border of twelfth thoracic vertebra to the centre of the body of third lumbar vertebra. The right kidney is slightly lower than the left, and the left kidney is a little nearer to the median plane than the right. The transpyloric plane passes through the upper part of the hilus of the right kidney, and through the lower part of the hilus of the left kidney. Each kidney is about 11 cm long, 6 cm broad, and 3 cm thick. The left kidney is a little longer and narrower than the right kidney. On an average the kidney weighs 150 g in males and 135 g in females. The kidneys are reddish brown in colour.

2.6.2 Relations

Superiorly, on top of each kidney and separated by renal fascia, are the suprarenal glands (adrenal glands), the right pyramidal suprarenal gland oriented apically on the right kidney and the left crescentic suprarenal gland oriented more medially on the left kidney. The right kidney is posterior to the ascending colon, the second part of the duodenum medially, and the liver, separated by the hepatorenal recess. The left kidney is posterior to the descending colon, its renal hilum lateral to the tail of the pancreas, superomedial aspect adjacent to the greater curvature of the stomach, and left upper pole adjacent to the spleen and connected by splenorenal ligaments (Soriano *et al*.,2025)

The diaphragm overlies the superior third of each kidney posteriorly, with the 12th rib crossing the upper pole. The kidneys rest between the medial border of the psoas muscle and the lateral margin of the quadratus lumborum, while the proximal ureters descend along the psoas en route to the pelvic cavity. (Coffin *et al*.,2015)

At the medial margin of each kidney lies the renal hilum, where the renal artery enters, and the renal pelvis and vein leave the renal sinus. The renal vein is found anterior to the renal artery, which is anterior to the renal pelvis. The renal pelvis is the flattened, superior end of the ureter. It receives 2 or 3 major calyces, each of which receives 2 or 3 minor calyces. The minor calyces are indented by the renal papillae, which are the apices of the renal pyramids. A pyramid and its cortical tissue comprise a lobe. (Soriano *et al*.,2025)

2.6.3 Capsules of the kidney

From within outwards, the kidney is surrounded by four capsules/coverings as follows

1.Fibrouscapsule(truecapsule).

2.Perirenal(perinephric)fat.

3.Renalfascia(falsecapsule).

4.Pararenal (paranephric) fat.

- Fibrous capsule: The kidney is surrounded by a thin fibrous capsule formed by condensed connective tissue at the periphery of the organ. Under normal conditions, this capsule can be easily separated from the renal surface. It extends through the hilum to line the renal sinus and continues with the walls of the

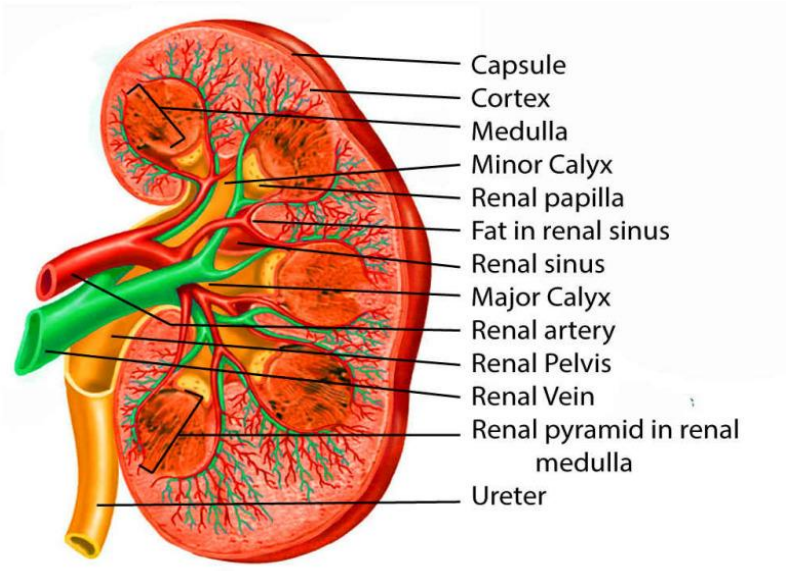
calyces at their attachment sites. In cases of inflammation, however, the capsule adheres firmly to the kidney and cannot be removed. (Singh, 2020)

- Perinephric fat: The perinephric fat is a layer of adipose tissue that surrounds the fibrous capsule of the kidney. It occupies the space within the renal fascia, which loosely encloses both the kidney and the suprarenal gland. This fatty capsule is thickest along the renal borders and extends inward through the hilum into the renal sinus. In cases of chronic debilitating disease, depletion of this fat may result in downward displacement of the kidney, sometimes causing ureteral kinking. (Singh, 2020)

- Renal Fascia: Conventionally, the perirenal fascia was characterized to possess a pair of layers: the posterior fascia of Zuckerkandl, and the anterior fascia of Gerota. It was believed that these two layers merged laterally to form the lateral conal fascia which then proceeded anterolaterally of the colon and joined the parietal peritoneum. Newer studies however, propose that the fascia is not merely a mixture of distinct layers but a one multilaminar structure. Posteromedially, it is joined to the muscular psoas major/ quadratus lumborum. It runs behind the kidney in the form of a bilaminar sheet, which divides variably to form a thinner anterior perirenal fascia which wraps around the front of the kidney and a thicker posterior layer continuing anterolaterally as the lateral conal fascia. Past perceptions were based on the fact that the anterior and posterior perirenal fascia above the suprarenal gland merged and connected to the diaphragmatic fascia. The existing evidence though indicates that the better part of the perirenal space is open and communicated with the bare right liver area and the left subphrenic

extraperitoneal space. The anterior fascia joins the inferior coronary ligament and the bare area of the liver at the upper pole of the right kidney and the gastrophrenic ligament at the left side. The fascia is affixed posteriorly on the right and left to the quadrate lumbarum and psoas majora fasciae, and the diaphragmatic fascia. The anterior layer extends to the other kidney medially and the posterior layer extends along the backbone. Beneath, the two layers run along the ureter and at the terminal fuse with the iliac fascia.(Chaurasia,2019)

- Paranephric fat: It consists of a variable amount of fat lying outside the renal fascia. It is more abundant posteriorly and towards the lower pole of the kidney. It fills up the paravertebral gutter and forms a cushion for the kidney.(Chaurasia,2019)



Structure of the Kidney

2.6.4 Structure

The kidney is composed of two regions: the cortex and medulla. The cortex is composed of renal corpuscles, convoluted tubules, straight tubules, collecting tubules, collecting ducts, and vasculature. Medullary rays, comprised of straight tubules and collecting ducts, extend into the cortex from the medulla. The medulla also contains the vasa recta, a network of capillaries integral to the countercurrent exchange system. Pyramids are conical structures formed by the collecting of tubules in the medulla, oriented with the base towards the cortex and apices towards the hilum. The papillae at the apices of the pyramids extend into minor calyces and drain via the collecting ducts at their tips, the area cribrosa. A collecting duct and the group of nephrons that it drains is referred to as a lobule. (Soriano *et al*.,2025)

The functional units of the kidney are known as nephrons of which in an average adult kidney are two million. The nephrons in every case start with a renal corpuscle composed of the glomerulus which is a capillary tuft fed by the afferent arteriole and Bowman's capsule, a two-layered epithelial structure. The glomerulus empties into an efferent arteriole and this produces the vasa recta that nourishes the tubules. The nephron segments following Bowman's capsule are proximal convoluted tubule, proximal straight tubule (thick descending limb), thin descending limb of the loop of Henle, thin ascending limb, distal straight tubule (thick ascending limb), distal convoluted tubule, collecting tubule, cortical collecting duct, medullary collecting duct, papillary duct and culminating with the urinary drainage system comprising of minor calyx, major calyx, renal pelvis and ureter. The nephron tubules are usually originated in the cortex, then extended to the medulla, hairpin looped and then making an upward shape back to the cortex around the parent corpuscle.(Soriano *et al*.,2025)

The glomerular corpuscle also harbors the glomerular filtration barrier comprising of three components namely the fenestrated endothelium of the glomerular capillaries, the trilaminar glomerular basement membrane (GBM) and the visceral layer of the Bowman capsule composed of podocytes. The interdigitating podocyte foot develops filtration slits, which are spanning under the slit diaphragm. The GBM is grouped into lamina rara externa, lamina rara interna and lamina densa. Bowman has a parietal layer of the capsule which is made of simple squamous epithelium and the space between it and visceral layer is Bowman space. The mesangial cells, which are extracapillary cells that are found in the renal corpuscle, offer structural and regulatory support. Each corpuscle has the juxtaglomerular apparatus (JGA), a combination of juxtaglomerular cells and specialized mesangial cells plus the macula densa of the thick ascending limb (TAL) that goes back to its parent glomerulus and links with the afferent arteriole.(Soriano *et al*.,2025)

2.6.5 Functions

Kidneys have various vital roles in homeostasis. They also produce metabolic waste products, such as urea and ammonia and control the levels of electrolytes and acid-base. They play an important role in regulating blood pressure and the intravascular volume maintenance through the renin-angiotensin-aldosterone system. Besides, the kidneys help in the reabsorption of some important substances including amino acids, glucose, electrolytes, calcium, phosphate, and water. They also function as endocrine glands and secrete hormones such as calcitriol that controls the metabolism of calcium and erythropoietin that controls the production of red blood cells.(Soriano *et al*.,2025)

2.6.6 Arterial supply

Kidneys have a high vascular demand as they receive about 20 percent of the cardiac output. The blood is supplied to each kidney by a renal artery, which is a branch of the abdominal aorta just below the superior mesenteric artery and enters the renal hilum at the L2 level. The right renal artery is bigger and runs behind the inferior vena cava. Both renal arteries branch into five segmental ones near the hilum. The anterior segment of the kidney is fed by the first branch, the posterior segmental artery. The anterior branch then splits into four segmental arteries that are named after the regions which they supply: superior, anterosuperior, anteroinferior and inferior segmental arteries. The accessory renal arteries remain in approximately 25% of patients as a result of underdevelopment of embryonic vessels. These other arteries normally emerge either out of the aorta or the renal artery and are typically serving the kidney poles.(Lung and Lui, 2023)

2.6.7 Venous drainage

The renal veins course anterior to the renal arteries as they return blood to the inferior vena cava. The left renal vein is notably longer than the right, as it crosses the midline to drain into the inferior vena cava at approximately the L2–L3 level. This anatomical difference makes the left kidney the preferred choice for transplantation, since its longer vein facilitates graft procedures. The left renal vein commonly receives tributaries from the left gonadal vein, left suprarenal vein, and left inferior phrenic vein, while branches from the lumbar or hemiazygos veins join it in about 75% of individuals. As it travels, the left renal vein passes posterior to the superior mesenteric artery and anterior to the aorta, a relationship that predisposes it to compression—known clinically as renal vein entrapment or “nutcracker” syndrome. In contrast, on the right

side, the gonadal and renal veins typically drain separately into the inferior vena cava.(Soriano *et al*.,2025)

2.6.8 Lymphatics

The lymphatic drainage of the kidney follows the renal vessels. Lymph from the renal cortex and medulla drains into lymphatic channels that accompany the renal veins and arteries, ultimately reaching the lateral aortic (lumbar) lymph nodes around the origin of the renal arteries from the abdominal aorta. From there, drainage continues into the cisterna chyli and then the thoracic duct. This pathway is clinically important because renal malignancies and infections may spread via these lymphatic routes to the para-aortic and interaortocaval lymph nodes.(Standring, 2021)

2.6.9 Nerve supply

The kidneys, together with parts of the proximal ureters and the suprarenal glands, receive autonomic input through the renal plexus, which carries both sympathetic and parasympathetic fibers. The sympathetic contribution arises from the abdominopelvic splanchnic nerves, and these fibers are distributed throughout the renal vasculature and nephrons, with dense innervation around the afferent arterioles, thick ascending limbs, and distal convoluted tubules.(Soriano *et al*.,2025)

Sensory (afferent) nerves are mainly located in the renal pelvis, where they follow the course of the renal artery or proximal ureter toward the pelvic wall. These afferents play a key role in sympathetic activity and blood pressure regulation. Their pathways vary as some run parallel to the ureter and pelvis, while others form circumferential networks all the while supplying the pelvic wall, renal arteries, and renal veins. Only a few sensory fibers are found in the renal cortex, and none in the medulla.(Soriano *et al*.,2025)

Visceral afferent fibers transmit pain signals alongside the sympathetic fibers to the spinal cord levels T11–L2. Because of this, renal pain is often perceived in the corresponding dermatomes, presenting as flank pain. Such pain is usually due to obstruction with distension, ischemia, inflammation, or infection. In contrast, small non-obstructing renal stones typically do not produce pain or colic.(Soriano *et al*.,2025)

2.7 HISTOLOGY

2.7.1 The Renal Corpuscles

The renal corpuscle is the filtration apparatus of the nephron. Each corpuscle consists of two main elements; the glomerulus and glomerular (Bowman's) capsule.

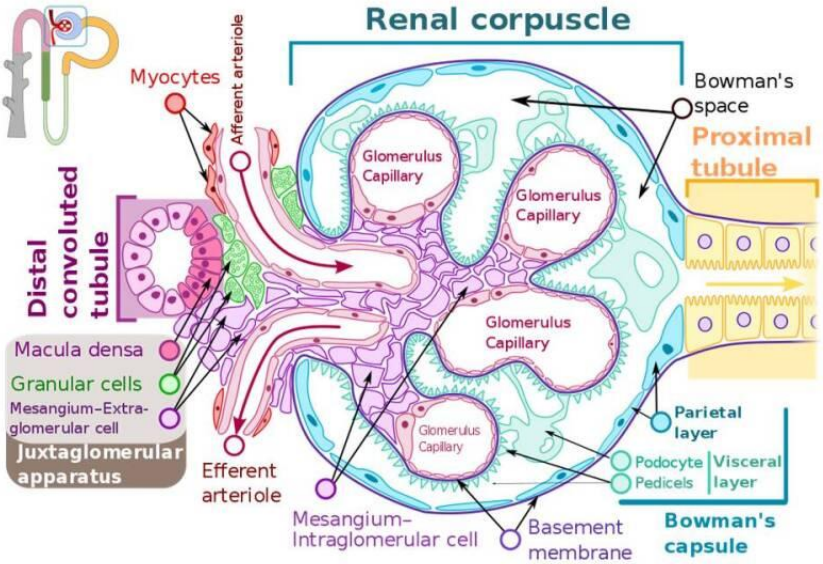


Diagram of the Renal Corpuscle

2.7.1.1 Glomerulus

The glomerulus is made up of a tuft of looped capillaries situated in the center of the renal corpuscle. These vessels bring blood into the filtration unit and provide a broad surface area specialized for filtration. Because the capillaries lie between two resistance arterioles—the afferent and efferent—they are able to maintain a relatively stable glomerular filtration rate across a wide range of blood pressures. Their structure further enhances this role: the endothelial lining is fenestrated, containing pores about 60 nm in diameter that cover nearly half of the surface area, allowing efficient passage of filtrate. Despite the pore size, the negatively charged glycocalyx on the luminal surface prevents larger molecules (over ~100 nm) from crossing. Unlike most capillaries, those of the glomerulus are not firmly embedded in a supporting matrix but instead are suspended within Bowman's capsule. Appropriately, the name "glomerulus" is derived from the Greek word for "filter."(Pirie and McLaren,2023)

2.7.1.2 Bowman's capsule

Bowman's capsule is composed of two distinct layers: the visceral and the parietal. The visceral layer closely surrounds the glomerular capillaries and is made up of specialized epithelial cells called podocytes, which have a characteristic stellate appearance. The parietal layer, on the other hand, consists of a thin lining of simple squamous epithelium. The space that lies between these two layers serves as the site where the initial filtrate of urine is collected.(Pirie and McLaren,2023)

2.7.1.3 Intraglomerular mesangial cells

Intraglomerular mesangial cells provide structural support for the glomerular capillaries by occupying the spaces beneath the basement membrane. They are usually positioned opposite the podocytes within the glomerulus. Because the glomerular capillaries lack surrounding interstitial tissue and the kidney contains very few stromal cells, this specialized support system is necessary. Mesangial cells are typically small and irregular in shape, with limited cytoplasm and indented, heterochromatic nuclei. Together with the extracellular matrix they produce, these cells form the mesangium. In certain renal disorders, mesangial cell proliferation leads to narrowing of the capillary lumina and a reduction in the available filtration surface.(Pirie and McLaren,2023)

2.7.1.4 Glomerular filtration

The kidney filtration apparatus is formed by three layers of tissue; endothelium of the glomerular capillaries, glomerular basement membrane (GBM) and podocytes (visceral layer of renal capsule). Glomerular capillaries are composed of fenestrated endothelium. Fenestrations function as pores. The GBM is more complex than other epithelial basal membranes. It consists of three layers; a thick central lamina densa and two thinner layers (lamina rara interna and lamina rara externa).(Murray and Paulini, 2025)

2.7.1.5 Glomerular basement membrane

The glomerular basement membrane is the third component of the filtration barrier, along with the capillary endothelium and podocytes. It is a fused basement membrane of the endothelial cells and podocytes, and also offers some support to the glomerular capillaries. Thus it is thicker (240 to 270 nm) than other capillary basement membranes (40 to 80 nm) . It is a gel-like material containing an organized fibrous mesh-like network forming heterogeneous pores of 10 nm. The

primary component is type IV collagen but contains other proteins such as laminin, and heparan sulfate, glycoproteins, and the proteoglycans agrin and perlecan. The mesh-like structure and negative charges form a molecular sieve or barrier, preventing high molecular weight proteins such as albumin and globulin (antibodies)s from leaving the circulation . The precise role of the glomerular basement membrane in selective permeability has recently come under debate, but it undisputedly restricts fluid flux.(Murray and Paulini, 2025)

2.7.1.6 Podocytes

Podocytes line the glomerular capillaries, extending finger-like processes known as pedicels that interlock with one another. The spaces between them, called filtration slits, are bridged by a slit diaphragm that contributes to the kidney's selective filtration barrier. Working in concert with the capillary endothelium and the glomerular basement membrane, this system ensures that only molecules of appropriate size and charge cross into the renal tubules. Larger elements such as blood cells, platelets, many proteins, and negatively charged molecules are retained within the circulation, while water and small solutes move into the tubular system. The residual blood then exits the glomerulus through the efferent arteriole and re-enters the venous network.(Pirie and McLaren,2023)

2.7.1.7 Juxtaglomerular apparatus

The juxtaglomerular apparatus (JGA) is a specialized structure situated at the vascular pole of the glomerulus, playing a critical role in regulating renal blood flow and filtration. It is composed of three main components.

The macula densa is a thickened segment of the distal convoluted tubule characterized by closely packed columnar cells with apically located nuclei. These cells monitor the sodium

chloride concentration of the tubular fluid and mediate tubuloglomerular feedback, thereby adjusting the glomerular filtration rate (GFR) of the associated nephron.

The juxtaglomerular (granular) cells, located in the walls of the afferent arteriole, are modified smooth muscle cells. They synthesize and release renin in response to decreased renal perfusion pressure or sympathetic stimulation, initiating the renin-angiotensin-aldosterone system (RAAS) to help regulate systemic blood pressure.

The lacis cells, also known as extraglomerular mesangial cells, are positioned in the region between the afferent and efferent arterioles near the macula densa. They share structural and supportive functions with intraglomerular mesangial cells and are believed to participate in signaling between the macula densa and juxtaglomerular cells.(Pirie and McLaren,2023)

2.7.2 The Renal Tubule

The renal tubule system is the portion of the nephron responsible for transforming the glomerular ultrafiltrate into urine. This is achieved through the selective reabsorption of essential substances and the secretion of metabolic wastes and excess ions. The tubule system is divided into three major segments:

Proximal tubule – subdivided into a convoluted portion and a straight portion; this segment reabsorbs the majority of water, electrolytes, and nutrients such as glucose and amino acids.

Nephron loop (loop of Henle) – composed of descending and ascending limbs; it plays a crucial role in generating the osmotic gradient within the medulla, which is necessary for water reabsorption.

Distal tubule – consisting of a straight portion and a convoluted portion; it is primarily involved in the fine regulation of sodium, potassium, and acid–base balance before filtrate passes into the collecting ducts.

2.7.2.1 Proximal tubule

The proximal tubule represents the first segment of the nephron's tubular system and begins directly after the capsular space of the renal corpuscle. It is divided into two regions: the proximal convoluted tubule, which lies within the renal cortex, and the proximal straight tubule, also known as the thick descending limb, which extends into the medulla. Both segments are lined by simple cuboidal epithelium containing numerous mitochondria and a prominent brush border of microvilli. These structural features support the tubule's primary functions of absorption and secretion. The proximal tubule is responsible for reabsorbing more than half of the water, ions, and small molecules initially filtered by the glomerulus, returning them to the bloodstream to maintain homeostasis

2.7.2.2 Nephron loop

The nephron loop, often referred to as the loop of Henle, is a U-shaped segment of the nephron that dips into the renal medulla before returning to the cortex. Histologically, it is composed of two thin limbs—the descending and ascending portions. Both are lined by simple squamous epithelium, with cells that contain few organelles, have minimal or absent microvilli, and demonstrate limited secretory activity. (Mescher, 2018)

Functionally, the two limbs exhibit complementary properties. The descending limb is highly permeable to water but relatively impermeable to solutes, while the ascending limb shows the

opposite characteristics, facilitating selective solute transport but restricting water movement. Together, these segments, in concert with the vasa recta, generate and maintain the osmotic gradient of the medulla, a process critical for concentrating urine and regulating salt and water balance. Some sources use “nephron loop” interchangeably with “loop of Henle,” whereas others broaden the definition to include the proximal straight tubule, the nephron loop itself, and the distal straight tubule.(Hall and Hall, 2020)

2.7.2.3 Distal tubule

The distal tubule is divided into two segments: a straight portion and a convoluted portion. The straight segment, also known as the thick ascending limb, arises from the thin ascending limb of the nephron loop at the boundary between the inner and outer medulla. The convoluted portion extends back into the renal cortex. Both segments are lined with simple cuboidal epithelium, resembling the proximal tubule in general structure but with distinct differences. (Mescher, 2018)

Unlike the proximal tubule, the epithelial cells of the distal tubule possess fewer and less prominent microvilli, resulting in a smoother luminal surface. Although both reabsorption and secretion occur in this segment, they are less extensive than in the proximal tubule. The cells are rich in mitochondria, which provide the energy needed for active transport processes, enabling the reabsorption of essential electrolytes and the secretion of remaining metabolic by-products. Importantly, sodium reabsorption in this region is regulated by the hormone aldosterone, linking the distal tubule to systemic electrolyte balance and blood pressure regulation (Hall and Hall, 2020).

CHAPTER THREE
MATERIALS AND METHODS

3.1 COLLECTION OF PLANT SAMPLE

Unripe fruit of the experimental item *Musa paradisiaca* was gotten from uselu market, Benin, Nigeria. It would be taxonomically identified and authenticated at the herbarium unit of the Department of Plant biology, Faculty of Life Sciences, University of Benin, Benin City Nigeria.

3.2 EXTRACT PREPARATION

Aqueous extraction of Unripe *Musa paradisiaca* fruits was performed using a freeze-drying technique. Unripe fruits were first air-dried at room temperature, then milled into a fine powder using an electric blender. Five hundred grams (500 g) of the powdered sample were soaked in 2 liters of distilled water for 24 hours. The mixture was filtered using white filter paper to separate the residue from the liquid extract. The resulting filtrate was concentrated in the medical laboratory of the University of Benin, Benin City.

3.3 EXPERIMENTAL ANIMALS

Twenty adult Wistar rats were procured from the Animal House, Department of Anatomy, School of Basic Medical Sciences, College of Medical Sciences, University of Benin, Edo State. The rats will be allowed to acclimatize for 2 weeks before commencement of the experiment. During this period, the animals will be allowed free access to standard animal feed (Topfeeds grower mash) and clean water ad libitum. The animals will be weighed weekly throughout the duration of the experiment (so as to get the cumulative weight required for experimental use). All experimental procedures involving the animals will be carried out in accord with approved protocols and compliance with the recommendations for the proper management and utilization of laboratory animals used for research

3.4 EXPERIMENTAL DESIGN AND ADMINISTRATION.

In this research, the animals were classified into five groups; A, B, C, D, E with each group experimental period spanned for 16 days. The rats will be administered with *Musa paradisiaca* extract simultaneously for 16 days. Twenty (20) adult wistar rats weighing between 127g and

GROUPS	DOSAGE
Group A	Control, fed with Animal feed and water only
Group B	Received 100mg/kg of extract daily for 16 days.
Group C	Received 500mg/kg of the extract daily for 16 days.
Group D	Received 750mg/kg of extract daily for 16 days.
Group E	Received 1000mg/kg of extract daily for 16days.

TABLE 1.0 EXPERIMENTAL DESIGN

282g will be separated into five(5) groups of randomized patterns with four (4) rats in each group.

3.5 METHOD OF SACRIFICE AND SAMPLE COLLECTION

At the end of the experimental period, the animals were grossly observed for general characteristics and weighed using a top loader weighing balance. After 16 days of administration, the final weights of the rats was taken using the compact digital scale. The rats were put under mild anaesthesia for about two minutes. This procedure was carried out by placing them in an enclosed container containing cotton wool soaked in chloroform. After the rats had been anaesthetized, an abdomino-thoracic incision was made to expose the viscera and thereafter, this incision was made after the rat had been placed in a supine position on the dissecting table. Blood samples was collected from the Inferior Vena Cava and put in heparin bottles for the kidney function analysis.

The kidneys were harvested from the retroperitoneal region of the abdomen. After the sample had been harvested, they were prepared for both oxidative stress and histochemical analysis. The kidney sample for antioxidant analysis were homogenized with normal saline for antioxidant enzymes analysis while the sample for histochemical analysis were fixed with 10% formal saline

for about 24 hours for routine hematoxylin and eosin histological processing. The extracted organs (kidneys) would then be sent to the University of Benin, Anatomy department's Histopathology Laboratory for tissue processing and functional investigation.

3.6 HISTOLOGICAL PROCEDURE

3.6.1 PARAFFIN TISSUE PROCESSING

- After the fixation of the harvested tissue in 10% formal saline, the tissues will undergo the following processing steps:

- The tissues were dehydrated using a series of alcohol gradients (70% to 90% and absolute alcohol) with ethanol as the alcohol of choice.

- Xylene was used as a clearing agent to remove the alcohol completely, with two changes of xylene ensuring thorough clearance.

- The tissues were then infiltrated with molten paraffin wax in three stages at a temperature of 65-70°C. Each stage lasted for 15 minutes, with the final stage lasting 30 minutes.

- Embedding was performed by pouring the molten paraffin wax into an embedding mould, where the tissues will be placed in a longitudinal orientation to create longitudinal sections.

- The molten paraffin wax was allowed to cool and solidify, forming tissue blocks.

- Following trimming, the tissue blocks was sectioned using a rotary microtome to produce thin ribbon-like sections with a thickness of 5 microns.

3.6.2 HEMATOXYLIN AND EOSIN STAINING METHOD

• Tissue sections that were of satisfactory quality and appeared as ribbons were chosen and placed in 20% alcohol to spread the paraffin sections, which was then cut and floated in a water bath at 30°C.

• The sectioned tissues were then transferred onto slides and allowed to air-dry.

• The tissue sections were immersed in xylene for 15 minutes to eliminate excess paraffin wax, followed by hydration by passing through decreasing concentrations of alcohol (100%, 90%, 70%) and then into water, each step lasting 5 minutes.

• Hematoxylin was used to stain the tissues for 10 minutes.

• The tissues undergone a washing process in running tap water (referred to as blueing).

• The sections were then counter-stained with 1% Eosin for 5-10 minutes.

• After rinsing in water, the tissues were rapidly dehydrated through a series of alcohol concentrations (70% to absolute alcohol) for 5 minutes.

• Subsequently, the tissues were cleared with xylene for 5 minutes, and the slides were mounted with a glass cover slip using an appropriate mounting medium, Distyrene-Plasticizer-Xylene (DPX).

3.6.3 PHOTOMICROGRAPHY

The sections of the kidney were obtained and examined under Leica DM750 research microscope with a digital camera (LeicaCC50) attached. Digital photomicrographs of the tissue sections were then taken at x40, x100 and x400 objective magnifications.

3.7 STATISTICAL ANALYSIS

Data was subjected to statistical analysis using GraphPad Prism version 9.0 statistical package and relevant statistical values were obtained. One-way analysis of variance (ANOVA) was carried out and data was presented as mean ± standard error of mean (SEM). Least significant difference (Fisher's LSD) post-hoc test will be used. Values of $P<0.05$ were considered statistically significant. The statistical values obtained were then converted into graphical representation in form of bar charts.

CHAPTER FOUR
RESULTS

Histological Results
GROUP A(CONTROL)

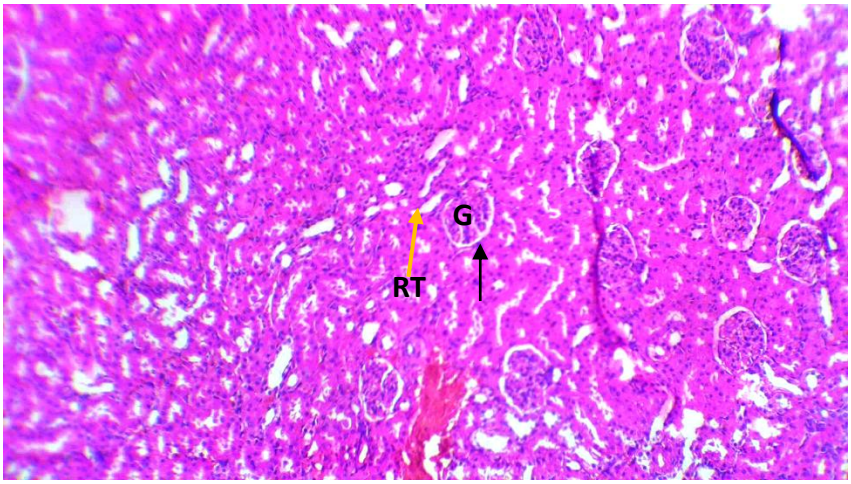


Plate 1. Kidney: glomerulus (G), urinary space (black arrow), renal tubules (RT)(Hand E x100)

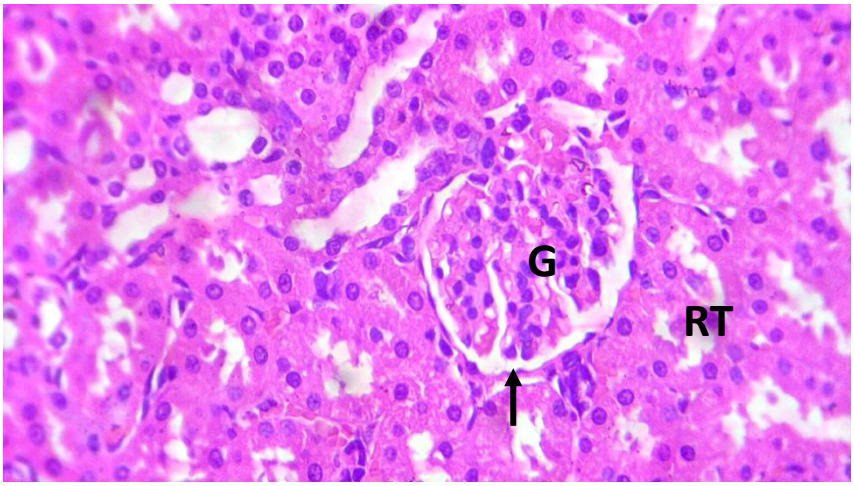


Plate 2. Same slide: glomerulus (G), urinary space (black arrow), renal tubules (RT) (Hand E x400)

GROUP B

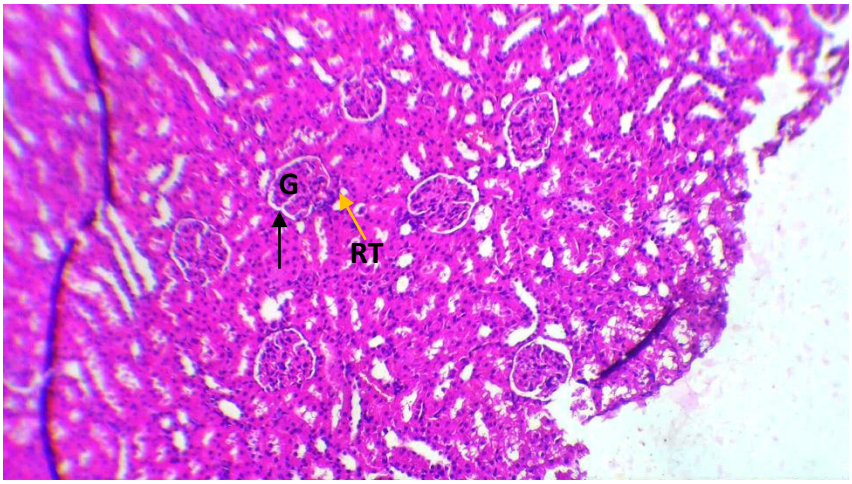


Plate 3. Rats given 100mg/kg of extract: glomerulus (G), urinary space (black arrow), renal tubules (RT) (Hand E x100)

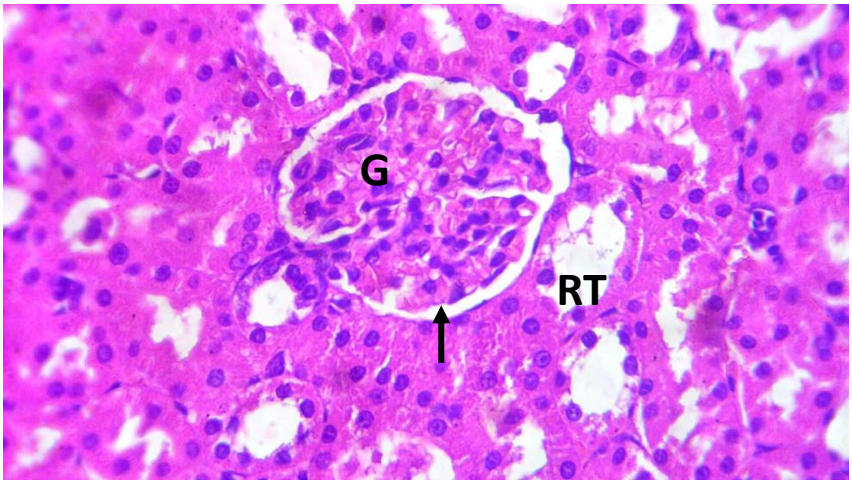


Plate 4. Same slide: glomerulus (G), urinary space (black arrow), renal tubules (RT) (Hand E x400)

GROUP C

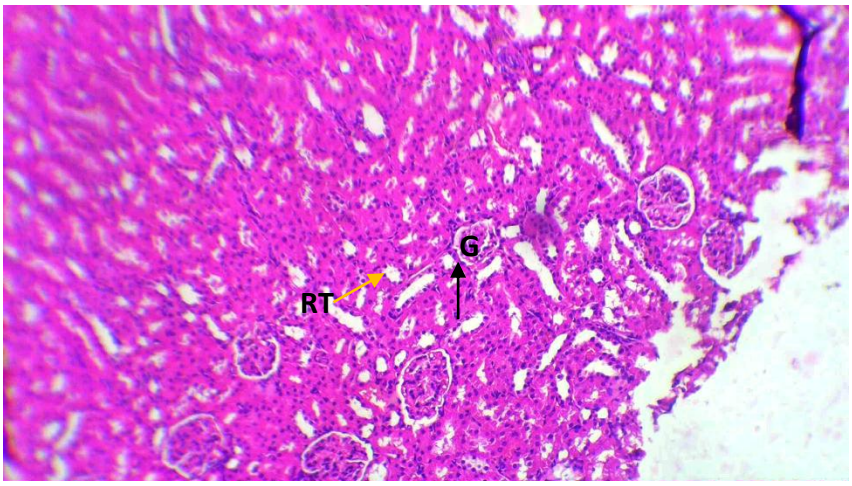


Plate 5. Rats given 500mg/kg of extract: glomerulus (G), urinary space (black arrow), renal tubules (RT) (Hand E x100)

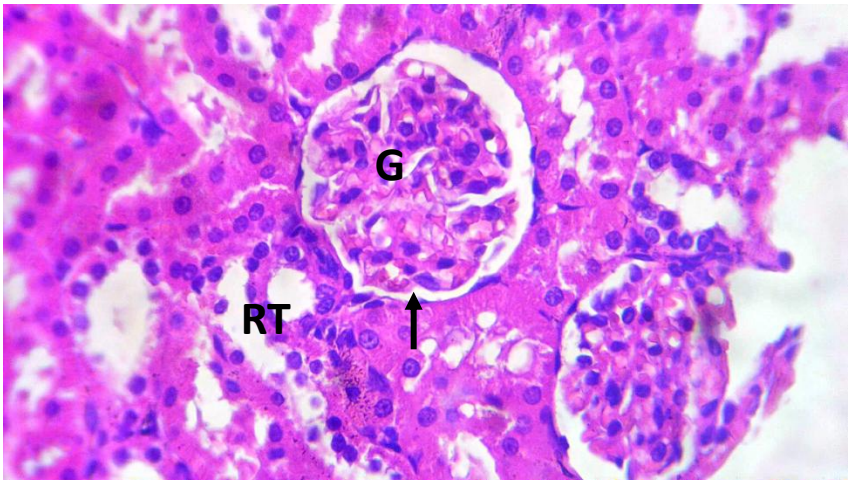


Plate 6. Same slide: glomerulus (G), urinary space (black arrow), renal tubules (RT) (Hand E x400)

GROUP D

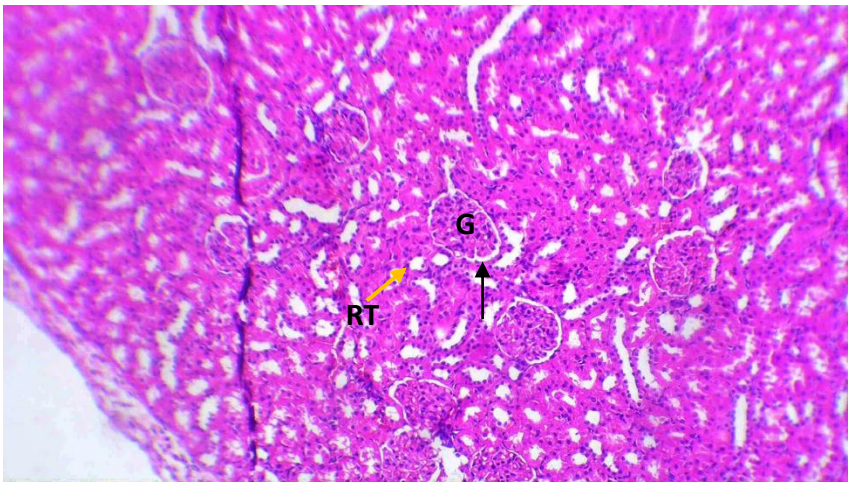


Plate 7. Rats given 750mg/kg of extract: glomerulus (G), urinary space (black arrow), renal tubules (RT) (Hand E x100)

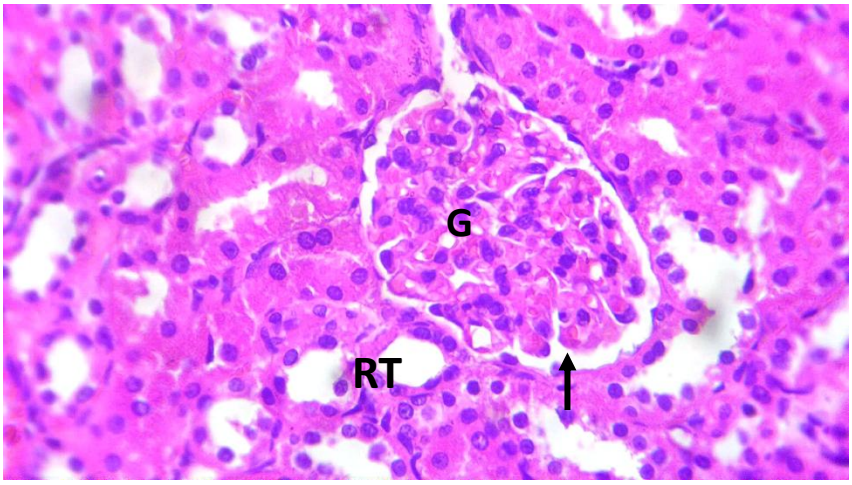


Plate 8. Same slide: glomerulus (G), urinary space (black arrow), renal tubules (RT) (Hand E x400)

GROUP E

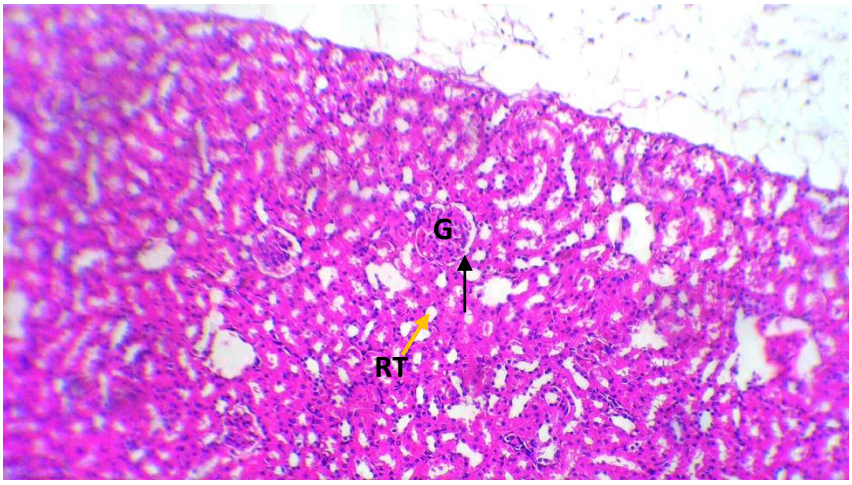


Plate 9. Rats given 1000mg/kg of extract: glomerulus (G), urinary space (black arrow), renal tubules (RT) (Hand E x100)

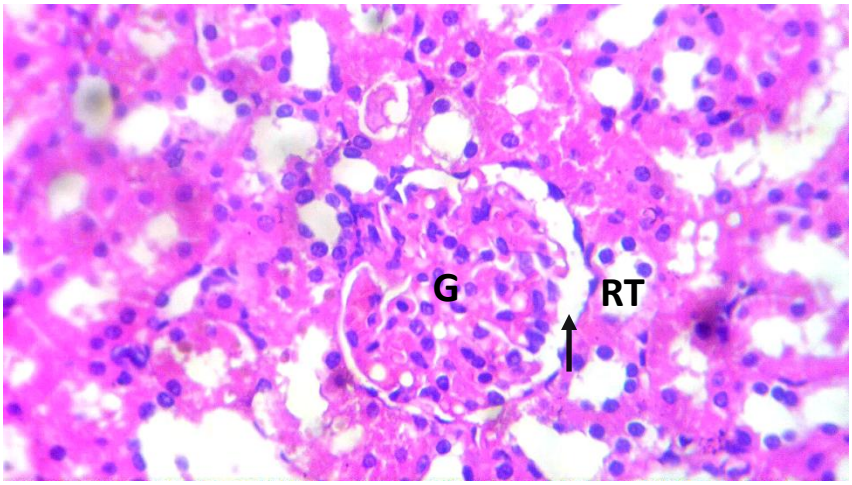


Plate 10. Same slide: glomerulus (G), urinary space (black arrow), renal tubules (RT)(Hand E x400)

Biochemical results

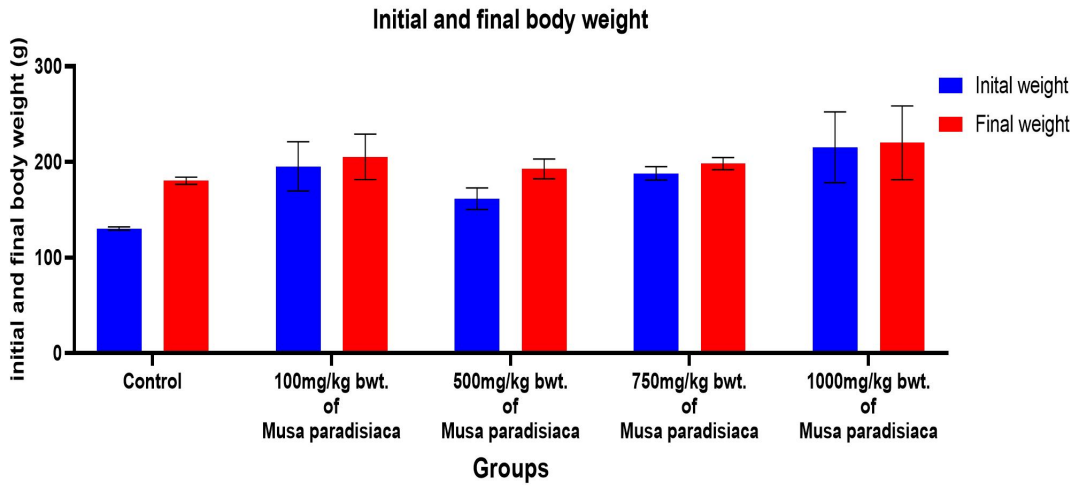


Chart 1: Initial and Final weight after 16 days of administration.

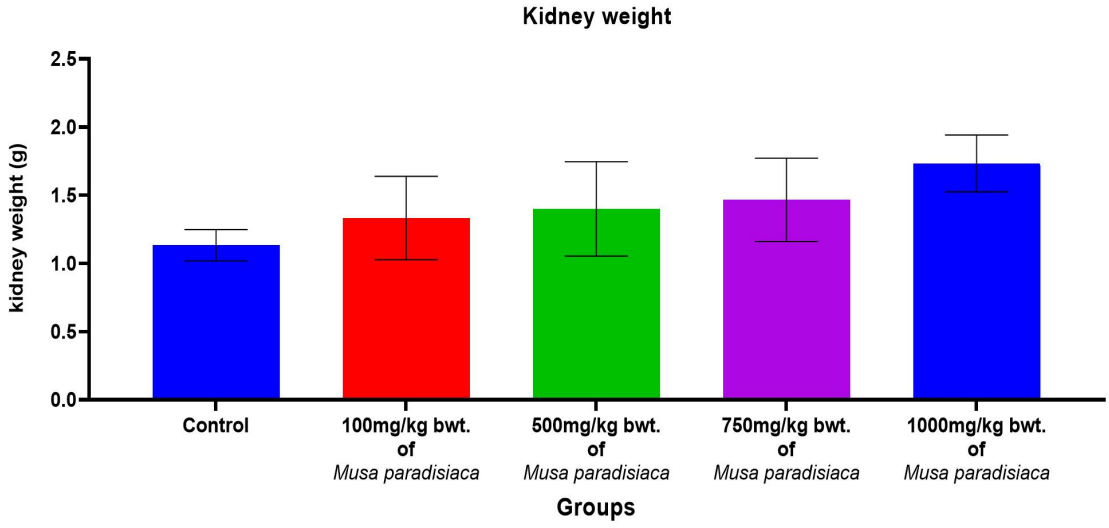


Chart 2: Kidney weight after 16 days.

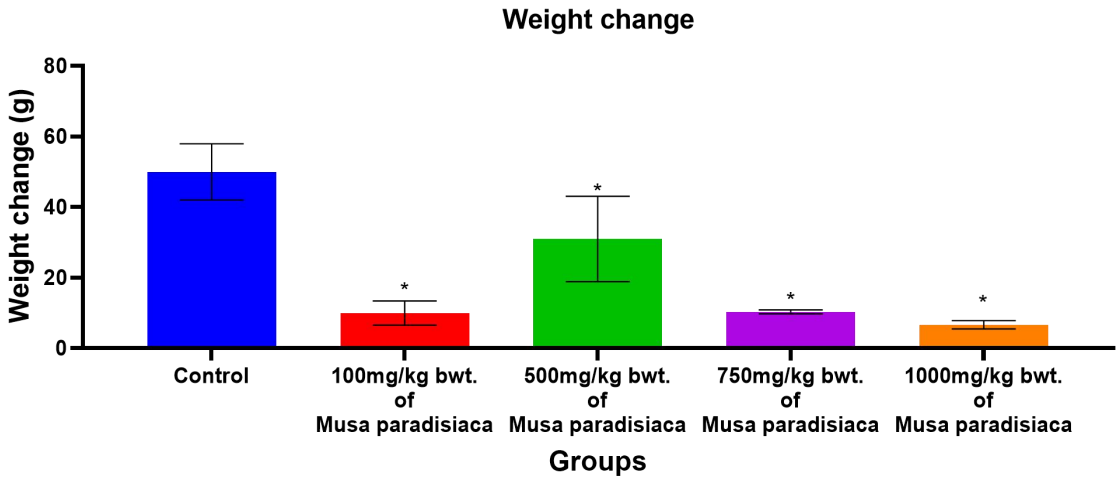


Chart 3: weight change after 16 days. Values are given as mean ± SEM. * $p< 0.05$ compared with the control group.

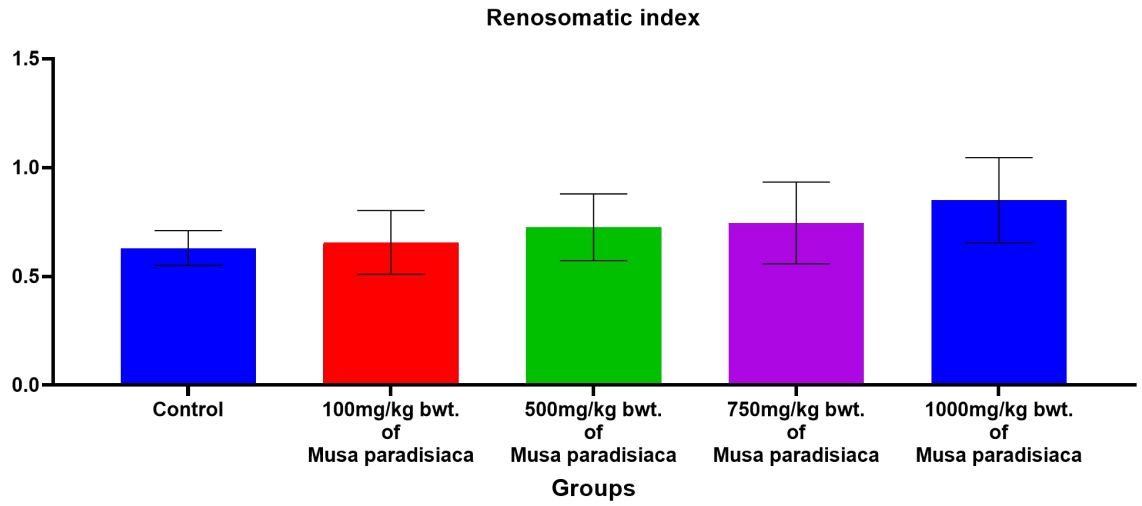


Chart 4: Reno-somatic index of control and treatment groups after 16 days.

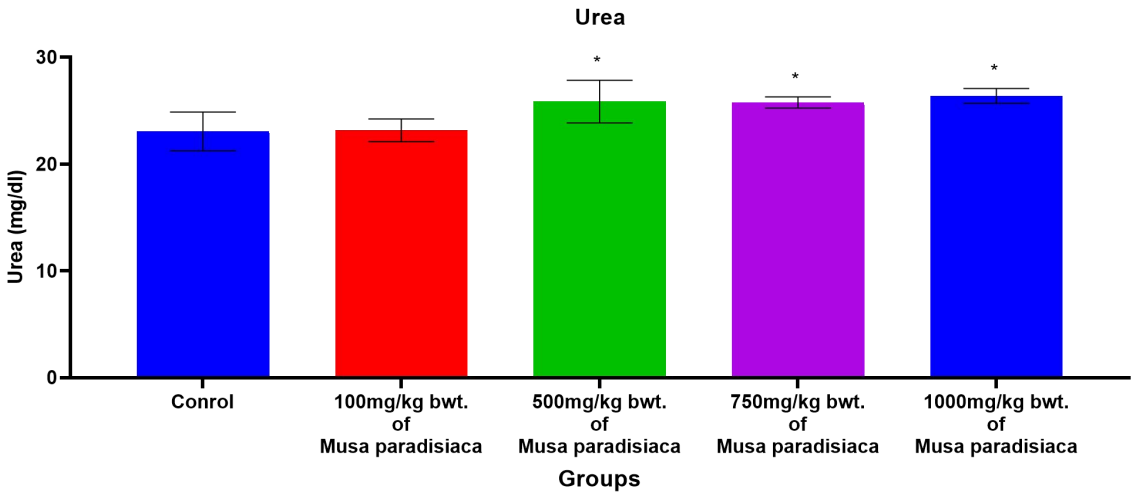


Chart 5: Activity of Urea in the Kidney of control and treatment groups after 16 days. Values are given as mean ± SEM. $^{*}p< 0.05$ compared with the control group.

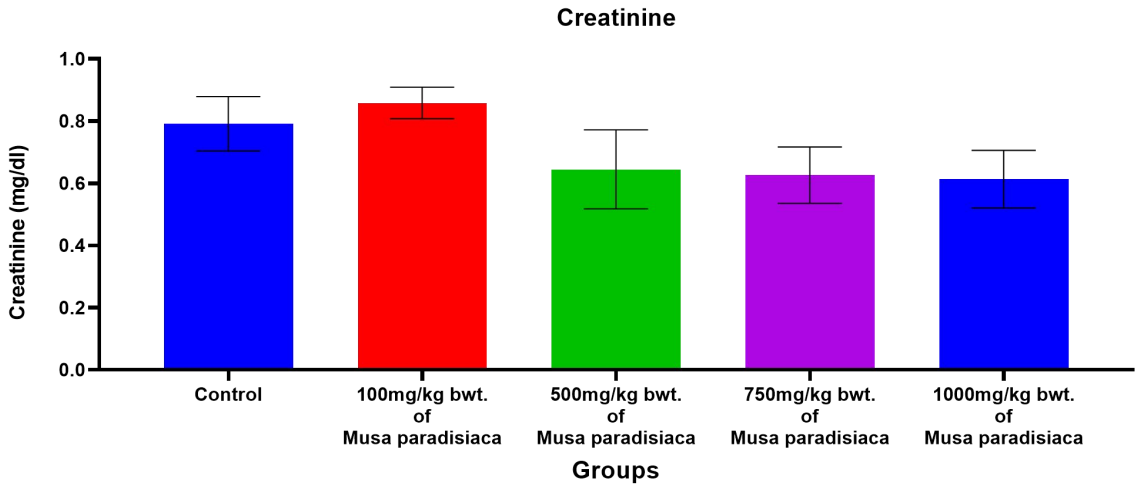


Chart 6: Activity creatinine in the kidney of control and treatment groups after 16 days.

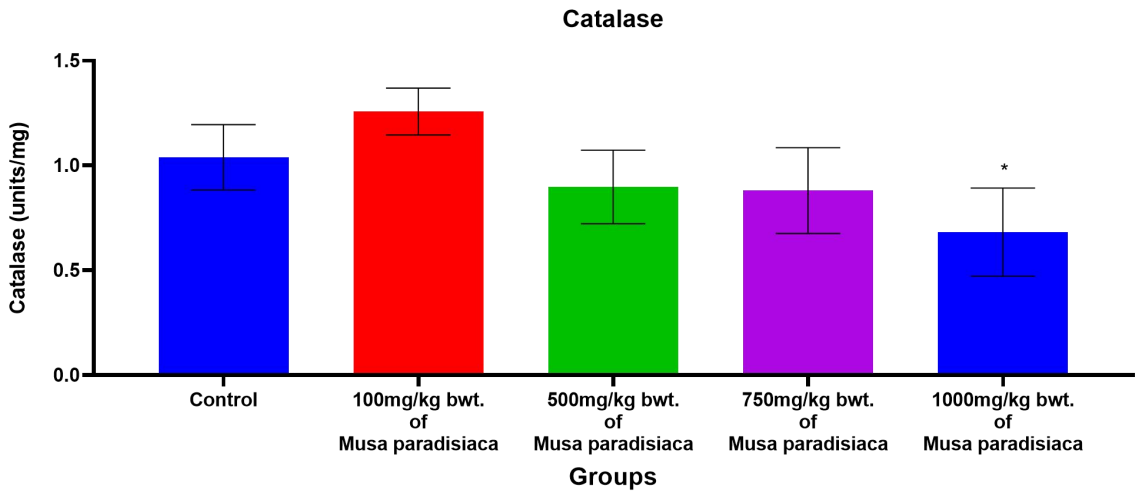


Chart 7: Catalase activity in the Kidney of control and treatment groups after 16 days. Values are given as mean ± SEM. $^{*}p< 0.05$ compared with the control group.

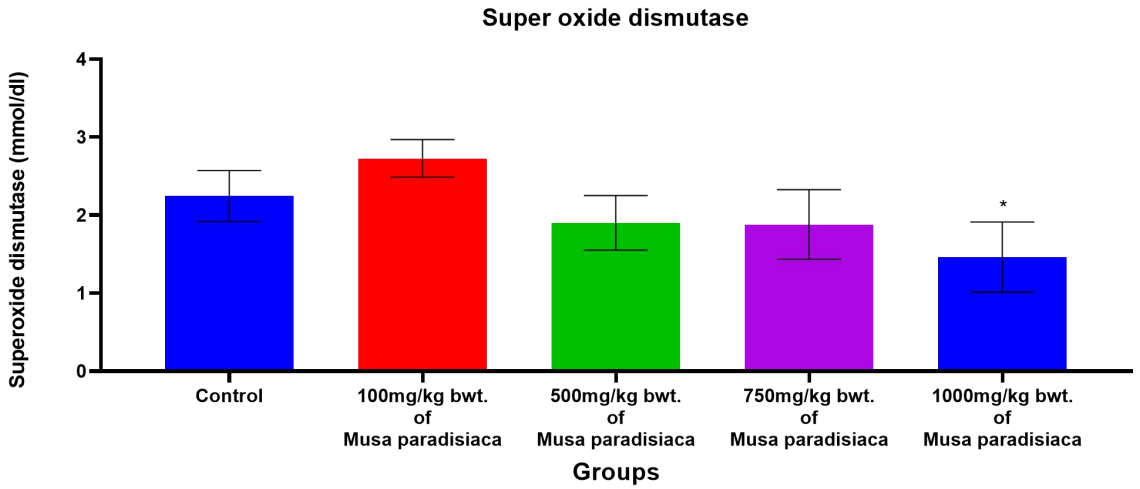


Chart 8: Superoxide dismutase activity in the Kidney of control and treatment groups after 16 days. Values are given as mean ± SEM. $^{*}p< 0.05$ compared with the control group.

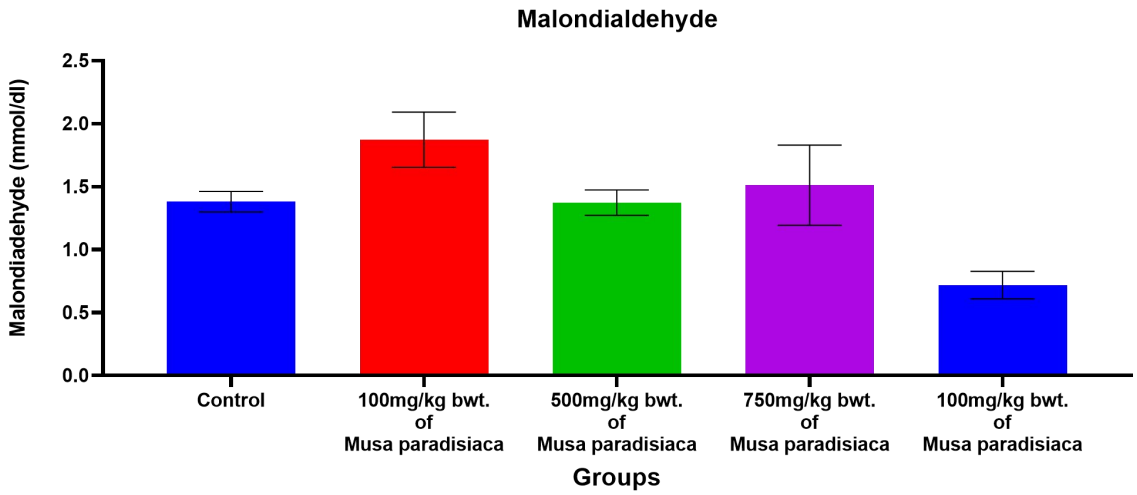


Chart 9: Lipid peroxidation activity in the Kidney of control and treatment groups after 16 days. Values are given as mean ± SEM. $^{*}p< 0.05$ compared with the control group.

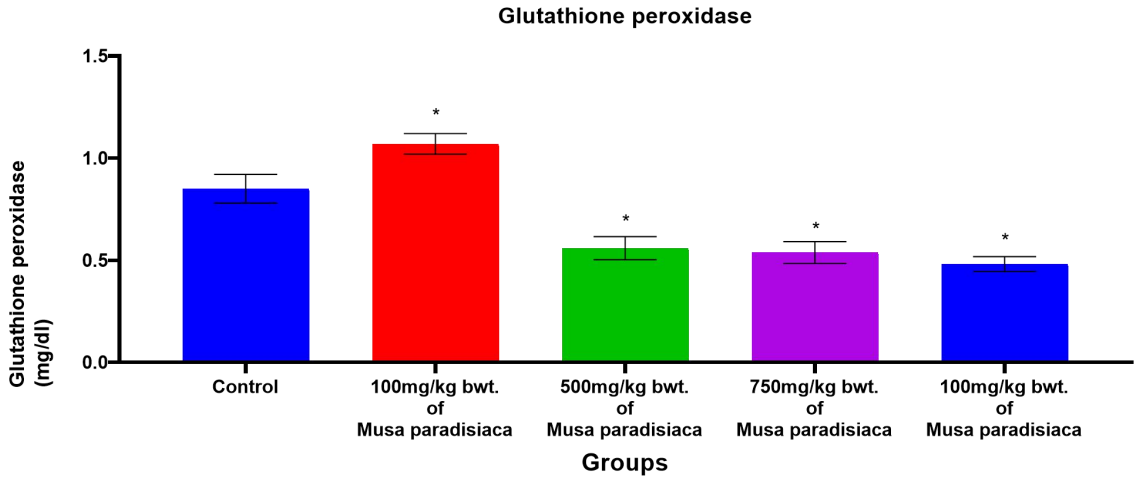


Chart 10: Glutathione Peroxidase activity in the Kidney of control and treatment groups after 16 days. Values are given as mean ± SEM. $^{*}p< 0.05$ compared with the control group.

CHAPTER FIVE
DISCUSSION, CONCLUSION AND RECOMMENDATION

5.1. Interpretation of Major Findings

This study was designed to evaluate the dose related effects of an aqueous extract of unripe *Musa paradisiaca* on the kidneys of adult Wistar rats. The central finding is a clear demonstration of a dose dependent dual effect: lower doses (100 and 500 mg/kg) exhibited a safe profile with no significant adverse changes, while higher doses (1000 mg/kg) induced marked nephrotoxicity, as evidenced by significant biochemical alterations. The absence of specific histological changes at the magnifications assessed suggests that the toxicity at high doses is primarily functional and biochemical, potentially representing an early stage of injury before overt structural damage becomes visible.

The results directly address the research problem by establishing a clear dose response curve and identifying the toxicity threshold, thereby resolving the inconsistencies highlighted in the literature regarding the plant's impact on renal health.

5.2. Discussion of Key Results in Relation to Objectives and Literature

5.2.1. Renal Functional Biomarkers: A Clear Threshold of Toxicity

The most definitive evidence of nephrotoxicity in this study comes from the dose dependent elevation of serum urea and creatinine levels (Charts 5 and 6). These markers are the clinical cornerstones for assessing glomerular filtration rate (GFR). Their significant rise in Groups D (750 mg/kg) and E (1000 mg/kg) indicates a decline in renal function.

Comparison with Literature on Toxicity: This finding provides robust confirmation and quantification of the dose related harms suggested by earlier reports. Our data directly align with Edenta *et al*.(2022), who noted that certain plantain cultivars increased serum urea and creatinine, indicative of kidney toxicity. Our study builds upon this by precisely demonstrating that this effect is dose dependent, beginning at 750 mg/kg for the aqueous extract. Furthermore, it corroborates the work of Victor *et al*.(2023), who reported histological alterations and implied functional decline with ethanolic pulp extracts. While our study did not show overt histological damage, the significant functional impairment we observed at 1000 mg/kg is consistent with their findings, suggesting that biochemical dysfunction may precede visible structural change.

Comparison with Literature on Protection: Conversely, the stability of urea and creatinine in Groups B (100 mg/kg) and C (500 mg/kg) validates the safety of lower doses. This is crucial for contextualizing the many studies that report nephroprotection. For instance, Panigrahi *et al*. (2012) and El-Said *et al*. (2022), demonstrated protective effects using plantain extracts in models of ethylene glycol-induced urolithiasis and cadmium-induced damage, respectively. Their positive results were likely achieved using doses within a safe range, similar to our Groups B and C. Our study confirms that in a healthy, non-stressed kidney, these doses do not cause harm, thereby defining the safety window within which the previously reported protective mechanisms can operate without risk.

5.2.2. Oxidative Stress Markers: The Mechanistic Core of Toxicity

The results for oxidative stress markers provide a compelling mechanistic explanation for the observed functional toxicity and align with the established pathway of many nephrotoxins.

Antioxidant Enzymes (SOD and Catalase): The significant decrease in the activities of Superoxide Dismutase (SOD) and Catalase in Groups D and E (Charts 7 and 8) indicates a state of oxidative overwhelm. This finding is in direct contrast to the nephroprotective studies. For example, El-Said *et al*.(2022) reported that plantain leaf extract alleviated oxidative stress and repaired antioxidant enzymes in cadmium treated mice. Our high dose results show the opposite effect, demonstrating that when a certain concentration threshold is crossed, the extract itself becomes the source of oxidative insult, suppressing these critical defense enzymes.

Lipid Peroxidation(MDA) and Glutathione Peroxidase(GPx): The significant decrease in Malondialdehyde (MDA) in Group E (Chart 9) is a direct biomarker of no oxidative damage to renal cell membranes. This is not a classic sign of toxic injury, commonly reported in studies of known nephrotoxins like gentamicin (Ali *et al*., 2019). The concurrent reduction in Glutathione Peroxidase (GPx) activity (Chart 10) further crippled the kidney's ability to detoxify peroxides. When compared to the study by Abbas *et al*. (2017), who found that methanolic extracts counteracted gentamicin induced oxidative stress, our high dose results reveal the plant's Janus-faced nature: it can combat oxidative stress in a compromised system at low doses but can induce it in a healthy system at higher doses.

5.2.3. Body Weight, Kidney Weight, and Reno-somatic Index

The significant increase in the Reno-somatic Index (RSI) in the high dose group (Group E, 1000 mg/kg) (Chart 4) could be an indicator of renal stress, often pointing to organ hypertrophy, inflammation, or edema. This finding, in the presence of stable final body weight, suggests a specific targeted effect on the kidney. It reinforces the biochemical data, indicating that the organ

was undergoing a pathological response to the high dose insult, even in the absence of specific histological changes in the tubules or glomeruli at the resolution used.

5.3. Reconciling the Dual Nature: The Pro-Oxidant Shift

The stark contrast between the safety of low doses and the toxicity of high doses can be explained by the phytochemical composition of *Musa paradisiaca*. The plant is rich in flavonoids, phenolics, and alkaloids (El-Said *et al*., 2022), which are known to have concentration-dependent effects.

At Low Doses (Protective/Safe Zone): These compounds act as potent antioxidants, donating electrons to stabilize free radicals. In a healthy kidney, they are effectively metabolized, causing no disruption and potentially even bolstering endogenous defenses.

At High Doses (Toxic Zone): The same phytochemicals can exhibit pro-oxidant activity. When present in excess, they can auto-oxidize, generating quinones and semiquinone radicals that deplete cellular antioxidant reserves like (Glutathione) and directly damage proteins and DNA (Galati and O'Brien, 2004). This pro-oxidant shift overwhelms the renal cells, leading to the observed oxidative stress and functional impairment. This mechanism explains why the extract is protective in models where an external toxin has already created an oxidative burden, but is toxic when it itself creates an unsustainable oxidative load in a healthy system.

5.4. Conclusion

This study therefore indicates that, the aqueous extract of *Musa paradisiaca* demonstrated no significant effects in adult Wistar rats after administration across the tested dosages. This is evidenced by the preserved renal function, indicated by stable levels of kidney urea and creatinine; the absence of significant oxidative damage, shown by unchanged antioxidant

enzyme activities and lipid peroxidation; and the maintenance of structural integrity, supported by a normal reno-somatic index and total protein content. Therefore, the extract can be considered safe for the kidneys at the concentrations used in this study. The key implication of this research is the critical importance of dosage. It validates cautious traditional use but sounds a strong warning against the unregulated consumption of high concentration plantain extracts. The toxicity observed is primarily functional and oxidative, suggesting that chronic administration at high doses could potentially progress to irreversible structural damage.

5.5. Recommendation for Future Research

Based on these findings, it is recommended that future research should focus on longer term studies to confirm the safety of the extract and investigate its effects at higher dosage levels to establish the full safety margin. Furthermore, the demonstrated safety profile warrants exploration into the potential therapeutic or protective benefits of the extract on the kidneys under conditions of induced toxicity or disease. Further investigation into the specific phytochemicals responsible for the pro-oxidant effect is also warranted to fully understand the safety profile of *Musa paradisiaca.*

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