EFFECT OF AQUEOUS LEAF EXTRACT OF BRYOPHYLLUM PINNATUM (RESSURECTION PLANT) ON CADMIUM INDUCED KIDNEY DAMAGE IN ADULT WISTAR RATS

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SUPERVISED BY: DR. A. O. R. EHIMIGBAI.

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CERTIFICATION

This is to certify that this research on the "**EFFECT OF AQUEOUS EXTRACT OF *Bryophyllum pinnatum* ON CADMIUM INDUCED KIDNEY DAMAGE IN ADULT WISTAR RAT**" was carried out and submitted by Kennedy David Onyemachi of matriculation number BMS2004961 to the department of anatomy, School of basic medical science in the university of Beninbenin, Benin city in partial fulfilment of the requirement for the award of bachelor of science {B.Sc} Degree in Anatomy.

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{HOD}

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EXTERNAL EXAMINER **DATE**

DEDICATION

This work is dedicated to The Lord in whose power I have over-come and to my family.

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I specially thank my supervisor, **Dr.O.A.R. Ehimigba**i for his patience, encouragement and support all through the course of this work, he is truly a father worthy of emulation.

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ABSTRACT

Bryophyllum Pinnatum is an indigenous and exotic plant used widely by the traditional Practitioner for treating various ailment like renal calculi, hypertension, asthma, cold abscesses, bleeding disorder. This study was aimed to examine the protective effect of aqueous *bryophyllum Pinnatum* on Cadmium-induced renal oxidative damages. The kidney which is an integral part of the drug excretory system. It was reported as one of the targets of Cadmium toxicity in the cell include a decrease in cell membrane fluidity. Thirty male adult Wistar rats weighing 150g and 180g were divided into six groups [A,B,C,D,E,F] where group A [serves as Control] receives animal feed [grower mash] with distilled water for 28 days group B [serves as toxicant] was given 10mg/kg of Cadmium chloride only for 28 days. Group c: receives 200mg/kg of *bryophyllum pinnatum* daily for 28 days. Group D: receoives 400mg/kg of *bryophyllum pinnatum* daily for 28 days. Group E: receives 200mg/kg of *bryophyllum pinnatum* and 10mg/kg of Cadmium chloride daily for 28 days. Group f: receive 400mg/kg of *bryophyllum pinnatum* and 10mg/kg of cadmium chloride daily for 28 days. Cadmium chloride and *bryophyllum pinnatum* extract was administered pro-gastric tube [oral gauge]. Biochemical analysis: renal function test was done and the following electrolytes was assayed. Urea test was done, creatinine test was done. The aqueous extract of *bryophyllum* *pinnatum* demonstrates a protective effect against Cadmium-induced damage in adult Wistar rats. The result mitate oxidative stress and inflammation reduce kidney damage and dysfunction.

CHAPTER ONE

1.0 INTRODUCTION

1.1 BACKGROUND OF THE STUDY

The utilization of medicinal plants is a widespread practice in developing nations, sparking concern and interest among healthcare professionals and researchers (World Health Organization, 2019). One such plant, *Bryophyllum pinnatum*, a succulent perennial herb native to Asia and Africa, has been extensively used in traditional medicine (Kumar *et al*., 2017).In Cameroon's Mbouda subdivision, *Bryophyllum pinnatum* was identified as one of the most frequently used medicinal plants for treating infection disorders (Njouendou *et al*., 2019). Local herbalists and traditional healers employ the plant's leaves or entire plant as an analgesic and to cure various conditions, including burns, convulsions, and dysmenorrhea (Tiwari *et al*., 2014). The plant's diverse traditional applications have earned it the names "life plant," "resurrection plant," and "goodluck" (Jain *et al*., 2011). Phytochemical analysis has revealed the presence of terpenoids and cytotoxic bufadienolides (Sahoo *et al*., 2010).

Bryophyllum pinnatum is widely distributed across tropical Africa, America, India, China, and Australia, where it is used in folkloric medicine (Srivastava *et al*., 2015). In southern India and Bengal, the plant is used to treat renal diseases, serving as a source of Pashanabheda (Parnabeeja), a member of the Crassulaceae family (Warrier *et al*., 2014). Traditional practitioners also employ the plant to treat various ailments, including renal calculi, hypertension, asthma, and bleeding disorders (Kumar *et al*., 2018).

The kidney is a major component of the urinary system, which maintains body homeostasis through filtration, active and passive absorption, and secretion. The final product of the filtration processes is urine which contains eliminated waste metabolic products. The kidneys are equally involved in the regulations of fluid and electrolyte balance, blood pressure and erythropoiesis. Impaired Kidney functions have been reported as one of the most silent feature of *Bryophyllum pinnatum* (Leaf extract) toxicity (Chang *et al*, 1980). Functional deficits in humans that have been associated with excessive *Bryophyllum pinnatum* leaves extract exposure include enzymuria, low and high-molecular weight proteinuria, impaired transport of organic anions and glucose and depressed glomerular filtration rate. A few studies have revealed histopathological features of renal injury in humans, including intranuclear inclusion bodies and cellular necrosis in the proximal tubule and interstitial fibrosis(Biagini and Cramer *et al*,1974). In ras, proximal tubular injury involves the convoluted and straight portions of the tubule with greater severity in the cervical segment (Murakami *et al*, 1983). Typical histological features include the formation of intranuclear inclusion bodies in proximal tbule cells, abnormal morphology (e.g swelling and budding) of proximal tubular mitochondria (Goyer and Krall, 1969), karyomegaly and cytomegaly and cellular necrosis. These changes appear to progress in the chronic phase of toxicity at high dosage. Tubular atrophy, interstitial fibrosis and glomerular sclerosis has also been reported on the excessive usage of *Bryophyllum pinnatum* leaf extract on rodent species (Khalil-Manesh *et al*, 1992). Adenocarinomas of the kidney have been observed in long-term studies in rodents in which animals also developed proximal tubular nephropathy (Goyer *et al*., 1985). The potential toxicity of medicinal plants is however, of great concern (Adedapo *et al*, 2009). This study therefore tested the hypothesis of the aqueous extract of *Bryophyllum pinnatum* leaves on the morphology and functions of the kidney in adult Wistar rats.

1.2 AIM OF THE STUDY

This study aim to evaluate the effect of aqueous extract of *Bryophyllum pinnatum* on cadmium induced kidney damage in adult wistar rat

1.3 SPECIFIC OBJECTIVE

The objective of this study is to:

1. study the changes in body and organ weights of the experimental rats.
2. investigate the effects of aqueous extract of *Bryophyllum pinnatum* fruit extract on the histology of the renal tissues in experimental rats.
3. determine the antioxidant enzymes in experimental rats.
4. estimate the biochemical assay of serum urea and creatinine level in experimental rats.

1.4 STATEMENT OF REASEARCH PROBLEM

Cadmium is a highly toxic heavy metal released into the environment through industrial, agricultural, and domestic activities. Prolonged exposure, even at low concentrations, has been strongly linked to kidney damage, including tubular necrosis, glomerular degeneration, and altered renal biomarkers such as serum creatinine and urea. Cadmium-induced renal injury is primarily mediated by oxidative stress, mitochondrial dysfunction, and accumulation in the proximal tubules (Johri et al., 2010; Satarug et al., 2018).

Bryophyllum pinnatum is a medicinal plant widely used in ethnomedicine and has been reported to possess antioxidant, anti-inflammatory, and cytoprotective properties. Experimental studies have shown that aqueous extracts of B. pinnatum can enhance antioxidant status, reduce lipid peroxidation, and modulate renal function indices in animal models (Akinmoladun et al., 2020; Umeh et al., 2021).

Given the global burden of chronic kidney disease and the essential role of the kidneys in detoxification and homeostasis, it is imperative to explore the protective potential of medicinal plants against cadmium-induced renal injury. This study therefore aims to evaluate the effect of aqueous extract of Bryophyllum pinnatum on cadmium-induced kidney damage in adult Wistar rats, by assessing biochemical markers of renal function (serum creatinine and urea) and histopathological changes, in order to determine its potential nephroprotective efficacy.

CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 BRYOPHYLLUM PINATIUM

https://greeninstitute.ng/plants/2019/2/18/bryophyllum-pinnatum

Bryophyllum pinnatum is a succulent pennial herb found throughout Asia and Africa. *Bryophyllum pinnatum* was one of the most often used medicinal plants in the mbouda subdivision(cameroon) according ti an ethnobotanical assessment of plants used to cure infection disorders (Elufioye *et al*., 2022).

Thus, data gathered directly from local herbalists and traditional healers revealed that the plant leaves or the entire plant is used as an analgesic and to cure a variety of conditions, including burns, convulsion, candidiasis, blennorrhea, jandice, and dysmenorrhea (Sadhana *et al*., 2018).

Its many traditional applications make it appropriate to refer to it as a life plant, resurrection plant (Emeka 2021)

Previous research on phytochemicals found that terepenoids, cytotoxic bufadienolides were present.

Bryophyllum pinnatum is a perennial herb, an indigenous and exotic plant used widely by the traditional practitioners for treating various ailments like renal calculi, hypertension, asthma, cold, abscesses, bleeding disorders.

The local people of southern India and Bengal use the plant in renal diseases as a source of Pashanabheda, which is commonly known as Parnabeeja, a member of Crassulaceae. Plant is found growing widely and used in folkloric medicine in tropical Africa, tropical America, India, China, and Australia.

It is a succulent herb; leaves are variable and leaflets are elliptic. Flowers are reddish purple. Over the years, studies have been carried out to explore various pharmacological activities like Urolithic, Diuretic, Anti-Diabetic, Wound healing property. Besides, phyto-chemical investigations reveal the presence of Alkaloids, cardiac glycoside, Flavonoids.

2.1.1 PLANT CLASSIFICATION

The classification of Bryophyllum is as follows:

Kingdom: Plantae

Subkingdom: Tracheobionta

Division: Spermatophyta

Subdivision: Magnoliophyta

Class: Magnoliopsida

Subclass: Rosidae

Order: Rosales

Family: Crassulaceae

Genus: Bryophyllum

2.1.2 PHYTOCHEMICAL CONSTITUENTS

B.Pinnatum is rich in alkaloids, triterpenes, glycosides, flavonoids, cardienolides, steroids, and lipids

2.1.3 PHARMACOLOGICAL ACTIVITIES

2.1.3.1 Hepatoprotective and Nephro Protective

Recent studies have validated the wisdom of this traditional medicine. Researchers Yadav and Dixit discovered that the leaf juice outperformed a concentrated extract in shielding the liver from harm (Yadav and Dixit, 2003). This breakthrough finding has significant implications for people suffering from liver ailments.

But the benefits don't stop there. The leaf juice has also shown remarkable antioxidant properties, which may help protect the kidneys from damage caused by certain medications (Randjelovic *et al.*, 2012). This is a game-changer for individuals at risk of kidney damage.

These findings are a testament to the power of traditional knowledge, combined with modern scientific research. As we continue to unlock the secrets of this incredible plant, we may discover even more ways to harness its healing properties and improve human health.

2.1.3.2 Antidiabetic Activities

The zinc-rich properties of a particular plant may hold the key to treating diabetes, a debilitating disease caused by insulin failure.

But that's not all - this incredible plant has also shown remarkable pain-relieving and anti-inflammatory properties. In a series of studies, Ojewole and his team tested the plant's aqueous leaf extract on mice and rats, with astonishing results.

The extract demonstrated significant pain-relieving effects, reducing discomfort in mice exposed to painful stimuli. But what's even more remarkable is that the extract also showed potent anti-inflammatory properties, reducing swelling and inflammation in rats.

The plant extract had a profound impact on blood sugar levels in diabetic rats, causing a significant drop in glucose levels. This breakthrough finding offers new hope for people living with diabetes, and could potentially lead to the development of new, more effective treatments.

2.1.3.3 Analgesic, Anti-inflammatory and Wound Healing activity

The age-old practice of using plant extracts to treat wounds and stop bleeding has been validated by science. It turns out that these extracts are rich in saponins, a natural compound that helps blood cells clot and wounds heal faster.

Saponins have some remarkable properties that make them a potent healing agent. They can cause red blood cells to clump together, helping to stop bleeding quickly. They also have a bitter taste and can create a rich lather when mixed with water (Kamboj *et al.,* 2009). These unique traits are what give plant extracts like B. pinnatum their incredible therapeutic powers.

The extracts also contain tannins, which have astringent properties that help soothe and heal irritated tissues. This could explain why traditional healers in southeast Nigeria have long relied on herbs to treat burns and wounds (Agyare et al., 2016). By harnessing the power of nature, these healers have developed effective remedies that promote rapid healing and recovery.

2.1.4 Uterine Contractility

For expectant mothers facing the risk of preterm delivery, finding effective and safe ways to prevent it is a top priority. Fortunately, research has shown that a natural remedy, B. pinnatum, outperforms conventional labor inhibitors in preventing preterm birth, with fewer unwanted side effects. A groundbreaking study led by Plangger and his team put B. pinnatum to the test. They compared its effectiveness in delaying preterm labor with that of beta-agonists, a commonly used medication. The researchers carefully matched 67 pairs of pregnant women who were at risk of preterm labor, ensuring that factors like age, gestational age, and previous preterm labor were similar across both groups.

One group received intravenous B. pinnatum, while the other received beta-agonists. The results were promising: B. pinnatum proved to be a more effective and safer alternative for preventing preterm delivery. This natural remedy offers new hope for expectant mothers and their healthcare providers, who can now consider a more gentle and effective way to prevent preterm birth.

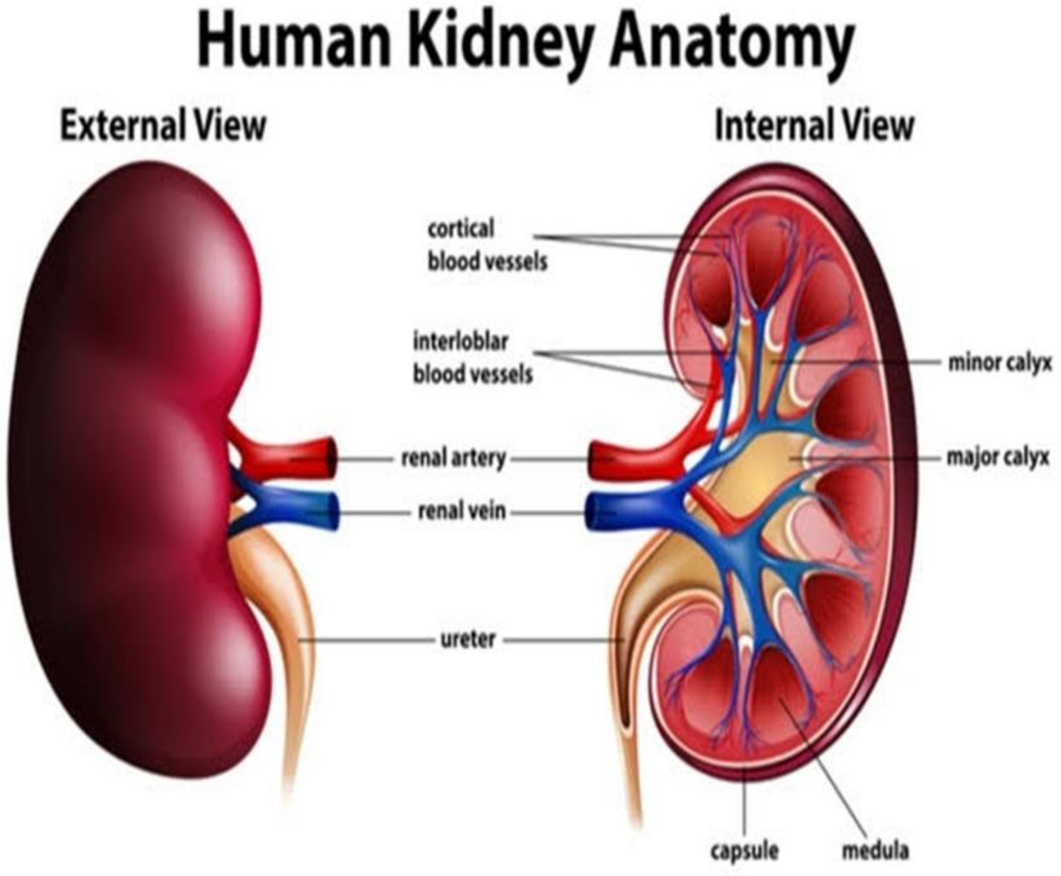
Insecticidal, Fungitoxic

In a study by, Supratman and his team uncovered the secret to B. pinnatum's incredible pest-fighting powers. They isolated two powerful compounds, bryophyllin A and bryophyllin C, which proved to be highly toxic to silkworm larvae(supratman *et a*l.,2001). This breakthrough discovery opens up new possibilities for natural and sustainable pest control methods.

B. pinnatum extracts have also shown remarkable fungicidal and phytotoxic effects. Alabi and his team put the extracts to the test, using them to treat cowpea plants afflicted with wilting diseases in Ago-Iwoye, South Western Nigeria. The results were impressive: the extracts significantly reduced the rate of disease infection in the treated plants.

These findings have far-reaching implications for farmers and gardeners seeking eco-friendly solutions to protect their crops. By harnessing the natural powers of B. pinnatum, we can create a more sustainable and healthier food system for everyone.

2.2 ORGAN OF STUDY-KIDNEY



2.2.1 Position

The bean-shaped kidneys are retroperitoneal in the posterior abdominal region. They lie in the extraperitoneal connective tissue immediately lateral to the vertebral column. In the supine position, the kidneys extend from approximately vertebra T12 superiorly to vertebra L3 inferiorly, with the right kidney somewhat lower than the left because of its relationship with the liver. (Drake*et al*, 2015).

2.2.2 Renal fat and fascia

The kidneys are enclosed in and associated with a unique arrangement of fascia and fat. Immediately outside the renal capsule, there is an accumulation of extraperitoneal fat-the perinephric fat (perirenal fat), which completely surrounds the kidney (diagram above). Enclosing the perinephric fat is a membranous condensation of the extraperitoneal fascia (the renal fascia). The suprarenal glands are also enclosed in this fascial compartment, usually separated from the kidneys by a thin septum. At the lateral margins of each kidney, the anterior and posterior layers of the renal fascia fuse(diagram above). This fused layer may connect with the transversalis fascia on the lateral abdominal wall. Above each suprarenal gland, the anterior and posterior layers of the renal fascia fuse and blend with the fascia that covers the diaphragm.

Medially, the anterior layer of the renal fascia continues over the vessels in the hilum and fuses with the connective tissue associated with the abdominal aorta and the inferior vena cava. The posterior layer of the renal fascia passes medially between the kidney and the fascia covering the quadratus lumborum muscle to fuse with the fascia covering the psoas major muscle. Inferiorly, the anterior and posterior layers of the renal fascia enclose the ureters.

In addition to perinephric fat and the renal fascia, a final layer of paranephric fat (pararenal fat) completes the fat and fasciae associated with the kidney (diagram above). This fat accumulates posterior and posterolateral to each kidney. (Drake *et al*, 2015).

2.2.3 Gross Anatomy of the Kidneys

Each kidney has a smooth anterior and posterior surface covered by a fibrous capsule, which is easily removable except during disease. On the medial margin of each kidney is the hilum of kidney, which is a deep vertical slit through which renal vessels, lymphatics, and nerves enter and leave the substance of the kidney (Diagram below). Internally, the hilum is continuous with the renal sinus, a space within the kidney occupied by the renal pelvis, calices, vessels, and nerves, and a variable amount of fat. Perinephric fat continues into the hilum and sinus and surrounds all structures (Moore *et al*, 2014; Drake *et al*, 2015).

Internally, each kidney consists of an outer renal cortex and an inner renal medulla. The renal cortex is a continuous band of pale tissue that completely surrounds the renal medulla. Extensions of the renal cortex (the renal columns) project into the inner aspect of the kidney, dividing the renal medulla into discontinuous aggregations of triangular-shaped tissue (the renal pyramids). The bases of the renal pyramids are directed outward, toward the renal cortex, while the apex of each renal pyramid projects inward, toward the renal sinus.

The apical projection (renal papilla) is surrounded by a minor calyx.

The minor calices receive urine and represent the proximal parts of the tube that will eventually form the ureter. In the renal sinus, several minor calices unite to form a major calyx, and two or three major calices unite to form the renal pelvis, which is the funnel-shaped superior end of the ureters. (Drake *et al*,2015)

2.2.4 Renal Vasculature

A single large renal artery, a lateral branch of the abdominal aorta, supplies each kidney. These vessels usually arise just inferior to the origin of the superior mesenteric artery between vertebrae LI and LII. The left renal artery usually arises a little higher than the right, and the right renal artery is longer and passes posterior to the inferior vena cava. As each renal artery approaches the renal hilum, it divides into anterior and posterior branches, which supply corresponding portions of the renal parenchyma. Accessory renal arteries are common. They originate from the lateral aspect of the abdominal aorta, either above or below the primary renal arteries, enter the hilum with the primary arteries or pass directly into the kidney at some other level, and are commonly called extra hilar arteries. (Drake *et al,* 2015).

2.2.5 Functional Anatomy Of The Kidneys

From a functional point of view, the kidney may be regarded as a collection of numerous uriniferous tubules specialized for the excretion of urine. Each uriniferous tubule consists of an excretory part called the nephron and of a collecting tubule. The collecting tubules draining different nephrons join to form larger tubules called the papillary ducts of each of which opens into a minor calyx at the apex of a renal papilla. Urinary tubules are held together by scanty connective tissue. Blood vessels, lymphatics and nerves lie in this connective tissue. (Singh, 2011)

2.2.5.1 Nephron

Nephron is defined as the structural and functional unit of kidney. Each kidney consists of 1 to 1.3millions of nephrons which in turn is made up of a blind end called renal corpuscle or Malpighian corpuscle A tubular portion called renal tubule (Sembuligam 2012).

2.2.5.2 Renal corpuscle

Renal corpuscle or Malpighian corpuscle is a spheroidal and slightly flattened structure with a diameter of about 200 μ. Function of the renal corpuscle is the filtration of blood which forms the first phase of urine formation. It is situated in the cortex of the kidney either near the periphery or near the medulla. The renal corpuscle is formed by two portions: Glomerulus and a cup shaped Bowmans capsule. (Sembuligam 2012).

2.2.5.3 Glomerulus

Glomerulus is a tuft of capillaries enclosed by Bowman capsule. It consists of glomerular capillaries interposed between afferent arteriole on one end and efferent arteriole on the other end. Thus, the vascular system in the glomerulus is purely arterial (Fig. 49.3). Glomerular capillaries arise from the afferent arteriole. After entering the Bowman capsule, the afferent arteriole divides into 4 or 5 large capillaries. Each large capillary subdivides into many small capillaries. These small capillaries are arranged in irregular loops and form anastomosis. All the smaller capillaries finally reunite to form the efferent arteriole, which leaves the Bowman capsule. Diameter of the efferent arteriole is less than that of afferent arteriole. This difference in diameter has got functional significance(K, P Sembuligam 2012).

2.2.5.4 Bowman Capsule

Bowman capsule is a capsular structure, which encloses the glomerulus. It is formed by two layers:an inner visceral layer and an outer parietal layer. The visceral layer covers the glomerular capillaries. It is continued as the parietal layer at the visceral pole. Parietal layer is continued with the wall of the tubular portion of nephron. The cleft-like space between the visceral and parietal layers is continued as the lumen of the tubular portion. Functional anatomy of Bowman capsule resembles a funnel with filter paper. Diameter of Bowman capsule is 200 μ (Sembuligam 2012).

2.2.5.5 Collecting Duct

The lower part of the collecting duct lies in medulla. Seven to ten initial collecting ducts unite to form the straight collecting duc, which passes through medulla. Length of the collecting duct is20 to 22 mm and its diameter varies between 40 and 200 μ. Collecting duct is formed by cuboidalor columnar epithelial cells (Sembuligam, 2012)

2.2.6 Histology of the Kidneys

2.2.6.1 The Renal Corpuscle

Glomerulus

The glomerulus is a rounded tuft of anastosing capillaries. Blood enters the tuft through an afferent arteriole and leaves it through an efferent arteriole. The afferent and efferent arterioles lie close together at a point that is referred to as the vascular pole of the renal corpuscle (Singh, 2011).

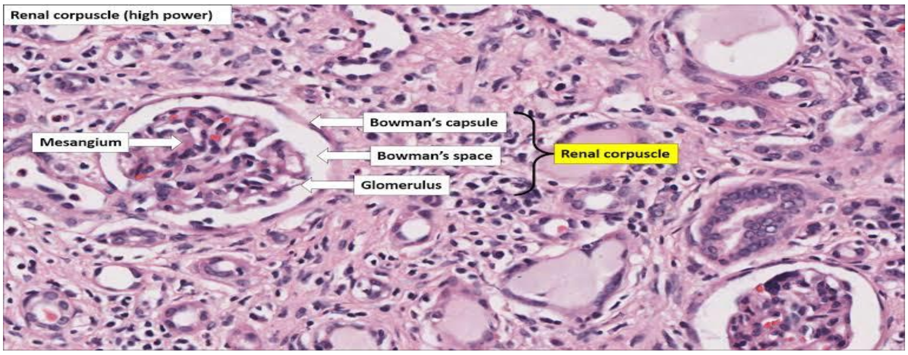
Fig. 2.1: Showing the histology of the Kidney (Singh, 2011).

Bowman's capsule

Also known as the glomerular capsule, it is a double layered-cup, the two layers of which are separated by the urinary space. The outer layer is lined by squamous cells. With the light microscope the inner wall also appears to be lined by simple squamous cells, but the EM shows that these cells, called podocytes, have a highly specialized structure. The urinary space becomes continuous with the lumen of the renal tubule at the urinary pole of the renal corpuscle. This pole lies diametrically opposite the vascular pole (Singh, 2011).

2.2.6.2 The Renal Tubule

As mentioned earlier, the renal tubule is made up (in proximo-distal sequence) of the proximal convoluted tubule, the loop of Henle, and the distal convoluted tubule. The distal convoluted tubule ends by opening into a collectng



tubule. Along its entire length the renal tubule is lined by a single layer of epithelial cells that are supported on a basal lamina (Singh, 2011).

2.2.6.3 Proximal convoluted tubule

The junction of the proximal convoluted tubule with the glomerular capsule is narrow and is referred to as the neck. The proximal convoluted tubule is made up of an initial part having many convolutions (lying in the cotex), and of a terminal straight part that descends into the medulla to become continuous with the descending limb of the loop of Henle. The neck is lined by simple squamous epithelium continuous with that of the glomerular capsule.

The proximal convoluted tubules are 40-60 um in diameter. They have a relatively small lumen. They are lined by cuboidal (or columnar) cells having a prominent brush border. The nuclei are central and euchromatic. The cytoplasm stains pink (with haematoxylin and eosin). The basal part of the cell shows a vertical striation.

2.2.6.4 Loop of Henle

The descending limb, the loop itself, and part of the ascending limb of the loop of Henle are narrow and thin walled. They constitute the thin segment of the loop. The upper part of the ascending limb has a larger diameter and thicker wall and is called the thick segment. The thin segment of the loop of Henle is about 15-30 μm in diameter. It is lined by low cuboidal or squamous cells. The thick segment of the loop is lined by cuboidal cells. With the EM the flat cells lining the thin segment of the loop of Henle show very few organelles indicating that the cells play only a passive role in ionic movements across them. In some areas the lining epithelium may show short microvilli, and some basal and lateral infoldings. The length of the thin segment of the loop of Henle is variable. The loops of nephrons having glomeruli lying deep in the cortex (juxtamedullary glomeruli) pass deep into the medulla. Those associated with glomeruli lying in the middle of the cortical thickness extend into the medulla to a lesser degree, so that part of the loop of Henle lies in the cortex. Some loops (associated with glomeruli placed in the superficial part of the cortex) may lie entirely within the cortex (Singh,2011)

2.2.6.4 Distal convoluted tubule

The distal convoluted tubule has a straight part continuous with the ascending limb of the loop of Henle, and a convoluted part lying in the cortex. At the junction between the two parts, the distal tubule lies very close to the renal corpuscle of the nephron to which it belongs. The distal convoluted tubules are 20-50 pm in diameter. They can be distinguished(in sections)from the proximal tubules by their much larger lumen and the lack of brush border on the cuboida cells lining them. They also stain less intensely pink (with cosin).

2.2.6.5 Collecting Tubule

The terminal part of the distal convoluted tubule is again straight. This part is called the junctional tubule or connecting tubule, and ends by joining a collecting duct. The smallest collecting tubules are 40-50 µm in diameter, and the largest as much as 200 µm. They are lined by a simple cuboidal, or columnar, epithelium. Collecting tubules can be easily distinguished from convoluted tubules by their larger lumina which in transverse sections are circular in contrast to the irregular shapes of convoluted tubules. Also the nature of their lining cells are markedly different. With those of the collecting tubules having clear, lightly staining cytoplasm and usually distinct cell outlines They do not have a brush border

2.2.6.6 Juxtaglomerular Apparatus

Juxtaglomerular apparatus is a specialized organ situated near the a structures: Juxtaglomerular cells, macula densa, and lacis cells (K,P Sembuligam 2012).

2.3 CADMIUM

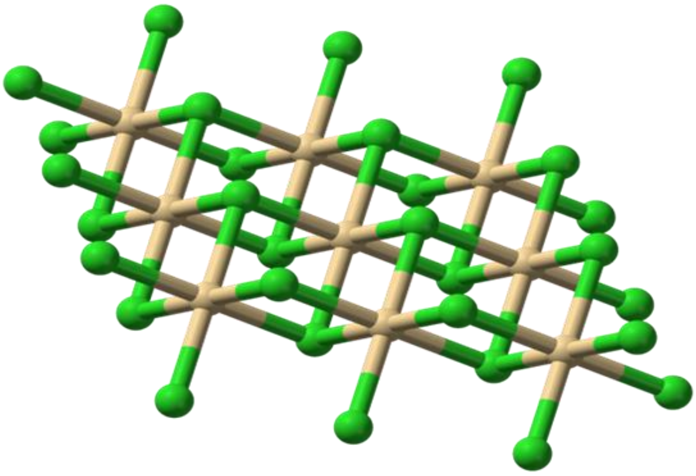
https://m.indiamart.com/proddetail/cadmium-chloride-powder-2854068214955.html

2.3.1 DEFINITION

The chemical element cadmium has an atomic number of 48 and the symbol Cd. The two other stable metals in group 12—mercury and zinc—have chemical properties that are comparable to this delicate, silvery-white metal. Similar to zinc, it exhibits oxidation state +2 in the majority of its compounds, and it melts more slowly than the transition metals in groups 3 through 11. Since group 12's cadmium and its congeners lack partially filled d or f electron shells in either their elemental or common oxidation states, they are frequently not regarded as transition metals. The Earth's crust contains between 0.1 and 0.5 parts per million (ppm) of cadmium on average (Meija,*et al*,, 2016).

It was discovered in 1817 as a zinc carbonate impurity by German scientists Stromeyer and Hermann at the same time.

Most zinc ores include trace amounts of cadmium, which is a byproduct of the zinc production. Long employed as a corrosion-resistant coating for steel, cadmium compounds are also used to color glass, stabilize plastic, and make red, orange, and yellow pigments. Because cadmium is hazardous, its use is typically declining (Morrow, 2010), and lithium-ion and nickel-metal hydride batteries have taken the place of nickel-cadmium batteries. Solar panels made of cadmium telluride are one of its few new applications. Although cadmium is not known to have any biological purpose in higher species, marine diatoms have been found to contain a cadmium-dependent carbonic anhydrase (Meija,*et al*,, 2016).



https://en.m.wikipedia.org/wiki/Cadmium_chloride

Structural formula

2.3.2 CHARACTERISTICS

2.3.2.1 Physical properties

Silvery-white, divalent cadmium is a soft, pliable, ductile metal. It creates complicated compounds but is similar to zinc in many ways (Holleman *et al*., 1985). Cadmium is employed as a protective plate on other metals because it is resistant to corrosion, unlike the majority of other metals (NCBI, 2021). Cadmium is not flammable and insoluble in water when it is in its bulk form, but it can burn and emit hazardous fumes when it is in powder form (Sharma, 2015).

2.3.2.2 Chemical properties

Despite often having an oxidation state of +2, cadmium can also exist in the +1 state. Due to the fact that they lack partially filled d or f electron shells in their elemental or common oxidation states, cadmium and its congeners are not always regarded as transition metals (Cotton, 1999). When cadmium burns in air, it produces brown amorphous cadmium oxide (CdO). The compound also exists in crystalline form, which is a dark red substance that changes color when heated, much like zinc oxide. Cadmium is dissolved by hydrochloric, sulphuric, and nitric acids by producing cadmium chloride (CdCl2), cadmium sulphate (CdSO4), or cadmium nitrate (Cd(NO3)2). The Cd2 2+ cation, which is comparable to the Hg2 2+ cation in mercury (I) chloride, can be created by dissolving cadmium in a solution of cadmium chloride and aluminum chloride (Holleman *et al*., 1985). This produces the oxidation state +1 (Morrow, 2010). The structures of several cadmium complexes with nucleobases, amino acids, and vitamins have been identified (Cd + CdCl2 + 2 AlCl3 → Cd2 (AlCl4)2). (Carballo *et al*., 2013)

2.3.2.3 Biological role and research

Cadmium serves no known purpose in organisms and is acknowledged as a toxic substance (Hogan, 2010). It is considered an environmental pollutant that poses health risks to living organisms (Xu *et al*., 2020). When exposed to cells, cadmium induces oxidative stress and prompts cells to increase their production of antioxidants to protect against potential damage to large molecules (Muthukumar, 2010).

However, despite its general toxicity, certain marine diatoms have been found to have a cadmium-dependent carbonic anhydrase. These diatoms thrive in environments with very low zinc levels, and research indicates that cadmium assumes roles typically carried out by zinc in other anhydrases. This discovery was made using X-ray absorption near-edge structure (XANES) spectroscopy (Lane *et al*., 2005; Lane *et al*., 2000).

In humans, cadmium is preferentially absorbed by the kidneys, and individuals may inhale up to approximately 30 mg of cadmium during childhood and adolescence (Lane *et al*., 2000). As a result, significant research has been conducted to study the toxicity of cadmium in humans, as it is linked to an increased risk of cancer, heart disease, and osteoporosis (Luevano & Damodaran, 2014; Rahim *et al*., 2013; Tellez-Plaza *et al*., 2010; James & Meliker, 2013).

2.3.3 USES OF CADMIUM

It can be used for the following:

Batteries (Krisgnamurthy, 2013)

Electroplating (Scoullous *et al*., 2001)

Nuclear fission (Scoullous *et al*., 2001)

Anticancer drugs (Abyae *et al*., 2019)

Televisions (Kwonspongsagoon, 2006).

Cadmium Toxicity: A Growing Environmental and Health Concern

2.3.3.1 Sources of Cadmium Exposure

Cadmium is released into the environment through various human activities, including mining, smelting, and refining of metals, as well as the production and disposal of batteries, plastics, and other consumer products (Morrow, 2010). Industrial processes, such as electroplating and pigment manufacturing, also contribute to cadmium emissions. Furthermore, cadmium can contaminate food chains through the uptake of polluted soil and water by plants and animals (Xu et al., 2020).

2.3.3.2 Mechanisms of Cadmium Toxicity

Cadmium toxicity occurs through multiple mechanisms, including oxidative stress, inflammation, and disruption of cellular homeostasis (Luevano & Damodaran, 2014). Cadmium ions can bind to proteins, lipids, and DNA, leading to structural and functional changes that impair cellular function. Additionally, cadmium can induce the production of reactive oxygen species (ROS), which can damage cellular components and contribute to the development of various diseases.

2.3.3.4 Health Effects of Cadmium Toxicity

Exposure to cadmium has been linked to a range of health effects, including kidney damage, bone disease, and various types of cancer (James & Meliker, 2013; Tellez-Plaza et al., 2010). Cadmium can accumulate in the kidneys, leading to nephrotoxicity and impaired renal function. Additionally, cadmium exposure has been associated with an increased risk of osteoporosis, fractures, and cardiovascular disease.

2.3.3.5 Prevention and Mitigation Strategies

Preventing cadmium exposure is crucial to minimizing its toxic effects. Strategies for prevention include reducing industrial emissions, implementing proper waste disposal practices, and promoting the use of cadmium-free products (Morrow, 2010). Additionally, individuals can reduce their exposure to cadmium by avoiding smoking, limiting consumption of contaminated foods, and using protective equipment when working with cadmium-containing materials.

CHAPTER THREE

MATERIALS AND METHOD

3.1 MATERIALS

Animals:30 Adult wistar rats; Feed: Growers mash; Instruments: Plastic cages, ceramic plates, Waltman filter paper, funnel, conical flask, surgical blade, forceps, 5ml syringe, laptop, weighing balance, microtome, slide tray, tissue embedding station, microscope, specimen bottles, cotton wool, orogastric tube, disposable gloves, measuring cylinder, pestle and mortar; Reagents:10% formal saline, chloroform, distilled water, eosin, hematoxylin, paraffin wax, xylene.

3.2 Purchase of Cadmium

cadmium were purchased at Emmytex Biomedical store at 47 new Lagos Road opposite UBTH Benin city, Edo state And *Bryophyllum pinnatum* was purchased from department of Agriculture University of Benin, Benin City, Edo state.

3.3 METHOD

3.3.1 EXPERIMENTAL ANIMAL

Animal Care and management

Thirty adult Wistar rats were used as experimental animals in this study. Their weight ranged between 160g and 220g.The rats were purchased and maintained at the animal House in the Department of Anatomy, School of Basic Medical Sciences, College of Medical Sciences, University of Benin, Edo State. The rats were then put in their cages. Before transferring the rats into their cages, cages were cleaned and disinfected. The rats were left to acclimatize for a period of two weeks in their cages. They were fed with livestock's growers marsh manufactured by Top Feed limited, Sapele, Delta State, Nigeria throughout the acclimatization period as much as they were allowed access to water. The cages were made of plastic and wire gauze at the top to allow proper ventilation and the cages were cleaned daily and disinfected at intervals.

Each animal procedure was carried out in accord with approved protocols and in compliance with the recommendation for the proper management and utilization of laboratory animals used for research (Buzek and Chastel, 2010).

3.3.2 EXPERIMENTAL DESIGN

In this study, the animals were divided into six groups; A, B, C, D, E, and F with each group having five Wistar rats which were all weighed prior to the administration. The experimental period spanned for 28 days. The rats were administered with Cadmium for 28 days and *Bryophyllum pinnatum* for 28 days totaling 28 days. Thirty (30) adult Wistar rats weighing between 160g and 220g were separated into six (6) groups of randomized patterns with five (5) rats in each group. All experimental animals were allowed free access to normal animal feed and water.

TABLE 1.0: Experimental design

GROUPS	DOSAGE
Group A	Served as control and were administered with 1ml of distilled water.
Group B	Received 10mg/kg of cadmium for 28 days.
Group C	Received low dose (200mg/kg) of Bryophyllum pinnatum for 28 days.
Group D	Received high dose (400mg/kg) of

	Bryophyllum pinnatum for 28 days.
Group E	Received 10mg/kg of cadmium for 14 days and was treated with low dose (200mg/kg) of *Bryophyllum pinnatum* for 28 days
Group F	Received 10mg/kg of cadmium for 14 days and was treated with high dose (400mg/kg) of *Bryophyllum pinnatum* for 28 days

3.3.3 RENAL TOXICITY INDUCTION

Renal toxicity toxicity was induced by following a modification of binge-drinking model designed by Carson and Pruett (Carson at al., 1966).

3.3.4 METHOD OF SACRIFICE AND TISSUE COLLECTION

At the end of 29 days treatment, the rats were weighed using a weighing scale. Then animals were anesthetized with chloroform for about two minutes and sacrificed. In sacrificing, a midline incision was made through the ventral abdominal wall of each rat. The liver of each rat was harvested immediately, and blotted dry on a filter paper. The rats were weighed and their standard weights calculated using the following formula: Standard weight = {organ weight/(g)/body weight (g)} × 100. The kidney tissues were then fixed for about 24 hours in 10% buffered formalin for routine hematoxylin and eosin histological processing. Blood was directly collected from the abdominal aorta and heart. The samples were put into heparin bottles for renal function analysis. Both the harvested organ (kidney) and blood samples were then taken to the Histopathology laboratory of University of Benin Teaching Hospital (UBTH) for tissue processing and functional analysis respectively.

3.4 HISTOLOGICAL TECHNIQUE

3.4.1 Paraffin Embedding

The kidney was excised and promptly transferred into 10% formal saline for fixation. Dehydration was carried out by passing the tissue through ascending grades of alcohol {70%, 90%, 95%, and 100% (absolute alcohol)} respectively for one hour. The tissue stayed in 70% alcohol for two hours, 90% alcohol for 18 hours (overnight) and 100% alcohol which was changed twice for two hours each. Clearing was carried out using xylene. The tissue was immersed in xylene for one hour so that alcohol will be completely removed. Infiltration of the tissue was carried out in an oven using molten paraffin wax at a temperature range of 30°C to 60°C for one hour. Three changes each at 15 minutes (twice) and 30 minutes (once) were carried out. Embedding was carried out using an embedding mould. The molten paraffin wax was poured into the embedding moulds and the infiltrated tissues were placed in it. The orientation of the tissue was such that both longitudinal and transverse sections were cut. The tissue block was formed by allowing the molten paraffin wax to cool. Before sectioning, the tissue blocks were trimmed and placed on a wooden block holder. Sectioning was carried out a rotatory microtome. The tissue was clipped to the microtome and sectioned at the thickness of five microns. Sections came out as ribbon and we're placed in 20% alcohol for spreading of the tissue. In a 30%-temperature water bath, the ribbons were sliced and floated. The sectioned tissue was placed in xylene for 5 minutes to remove paraffin wax from the tissue. Hydration was carried out by passing the tissues through descending grades of alcohol (100%,95%,100%, and 70%) for 5 minutes each.

3.4.2 STAINING

Hematoxylin and Eosin staining method

The dyes utilized for staining were hematoxylin and eosin. The tissues were stained in hematoxylin for 30 minutes and washed in water for 10 minutes. They were differentiated in

1% acid alcohol briefly and then washed in water. They were subsequently counterstained in Eosin for 2 to 3 minutes, and then rinsed in 90% alcohol

Dehydration was done with the sections passed through ascending grades of alcohol 70%, 90%, 95% for 30 seconds and in absolute alcohol for 2 seconds. The sections were immersed in xylene for 1 minutes. They were mounted in Discrete Plasticizer and Xylene (DPX), covered with coverslip using Canada balsam. Sections were viewed under a microscope.

3.5 PHOTOMICROGRAPHY

The sections of the kidney were obtained and examined under Leica DM750 research microscope with a digital camera (Leica ICC50) attached and connected to a Hewlett-Packard laptop. Digital photomicrographs of the tissue were taken at X40, X100 and X400 objective magnifications. The photomicrographs were then analyzed.

3.6 STATISTICAL ANALYSIS

All collected disks were subjected to statistical analysis using IBM SPSS statistics software (Statistical package for social science) (version 25) and relevant statistical values were obtained. One-way analysis of variance (ANOVA) was carried out and data presented as mean ±SEM LSD post-hoc test was used. Values of $P<0.05$ were considered significant. The statistical values obtained were converted into graphical representations in form of bar charts

CHAPTER FOUR

Results

4.1 Weight

Table 4.1 showing in…… of experimental animals across all groups after administration

Groups/Test	Control	10mg/kg of Cadmium	150mg/kg 200mg/kg *Bryphyllum pinnatum*	300mg/kg of *Bryphyllum pinnatum*	150mg/kg of *Bryphyllum pinnatum* + 10mg/kg of Cadmium	150mg/kg of *Bryphyllum pinnatum* + 10mg/kg of Cadmium	P-value

Initial Weight	149±9.21	156±10.4	149±6.64	178±5.86	153±6.08	141±2.03	0.0548
Final Weight	175±10.3*	140±11.9*	154±7.06	185±6.66	158±4.91	162±2.19*	0.0224
Weight Change	25.7±1.20	-19.7±3.84	5.00±1.53*	7.00±1.15*	5.33±1.20$^{\#}$	21.0±1.53$^{\#}$	<0.0001
Kidney Weight	0.81±0.04	0.98±0.05	0.92±0.05	0.97±0.20	0.96±0.10	0.81±0.08	0.3220
Reno-somatic index	0.45±0.03	0.70±0.02*	0.59±0.02	0.53±0.03	0.60±0.05	0.50±0.05$^{\#}$	0.0026

Body and kidney weight after 28 days. Values are given as mean ± SEM. $^{*}p<0.05$ compared with the initial weight and 100mg/kg of Cadmium only; $^{\#}p<0.05$ compared with the Cadmium alone group.

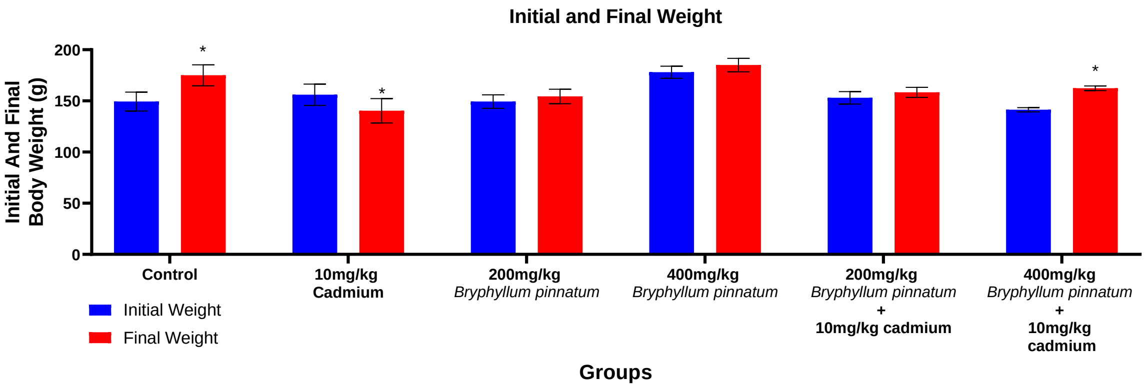


Chart 1: Initial and Final weight after 28 days of administration Values are given as mean ± SEM. $^{*}p<0.05$ compared with the control group.

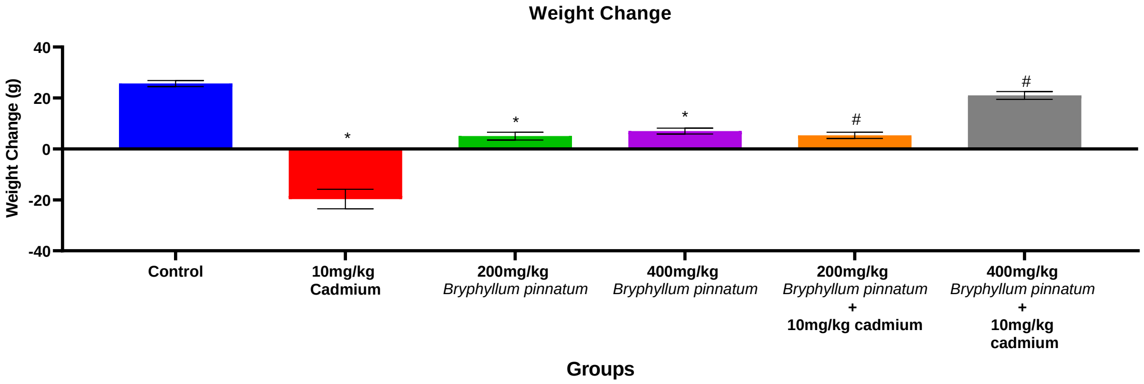


Chart 2: weight change after 28 days of administration Values are given as mean ± SEM. * $p < 0.05$ compared with the control group; $^{\#}$ $p < 0.05$ compared with the Cadmium alone group.

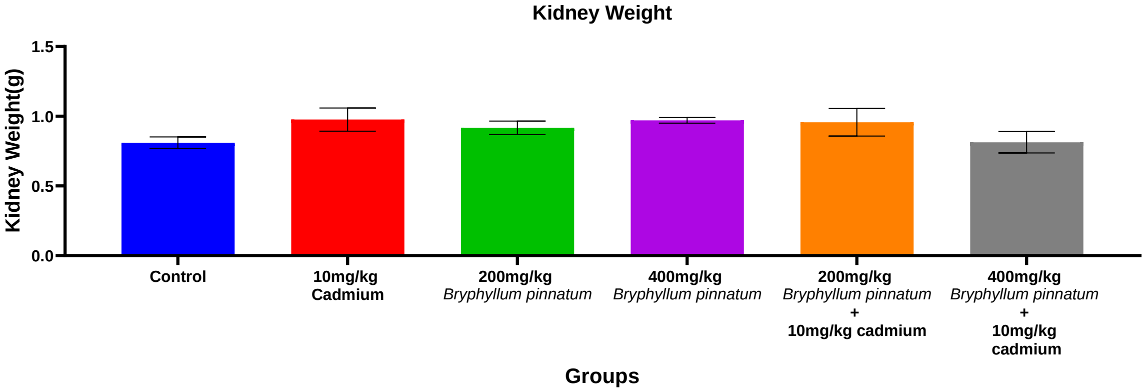


Chart 3: Kidney weight after 28 days of administration Values are given as mean ± SEM.

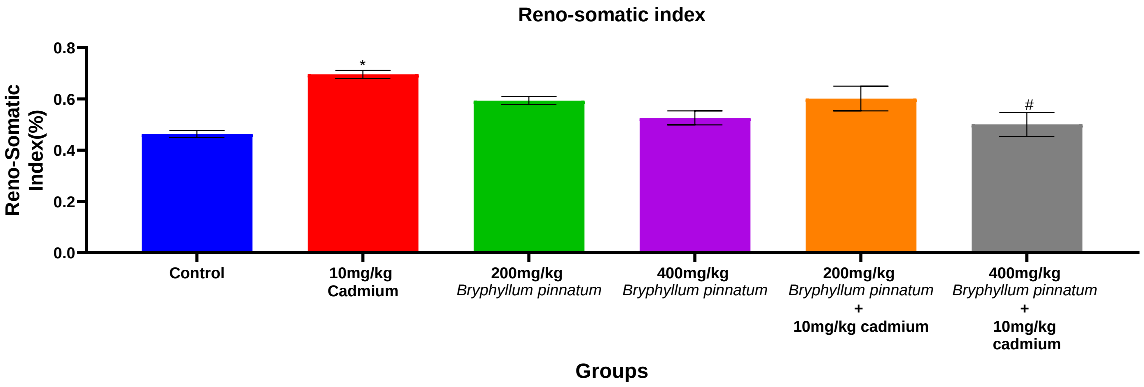


Chart 4: Reno-somatic index after 28 days of administration Values are given as mean ± SEM. $^{*}p < 0.05$ compared with the control group; $^{\#}p < 0.05$ compared with the Cadmium alone group.

4.2 Urea and Creatinine

Table 4.2 showing in…… of experimental animals across all groups after administration

Groups/Test	Control	10mg/kg of Cadmium	150mg/kg 200mg/kg *Bryphyllum pinnatum*	300mg/kg of *Bryphyllum pinnatum*	150mg/kg of *Bryphyllum pinnatum* + 10mg/kg of Cadmium	150mg/kg of *Bryphyllum pinnatum* + 10mg/kg of Cadmium	P-value
Urea	30.3±2.79	109±10.5*	34.0±1.35	34.9±0.53	41.9±2.09$^{\#}$	39.8±3.08$^{\#}$	<0.0001

Creatinine	0.68±0.09	11.6±1.95*	0.81±0.06	0.91±0.24	$0.87\pm0.03^{\#}$	$1.58\pm0.17^{\#}$	<0.0001

Urea and Creatinine levels in the kidney after 28 days. Values are given as mean ± SEM. $^{*}p<$ 0.05 compared with the control group; $^{\#}p<$ 0.05 compared with the Cadmium alone group

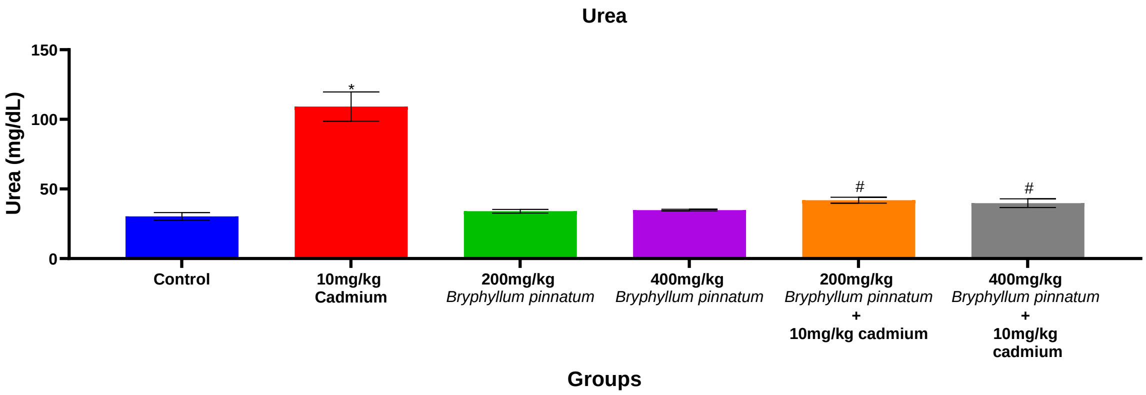


Chart 5: Urea activity in the kidney after 28 days. Values are given as mean ± SEM. $^{*}p<$ 0.05 compared with the control group; $^{\#}p<$ 0.05 compared with the Cadmium alone group.

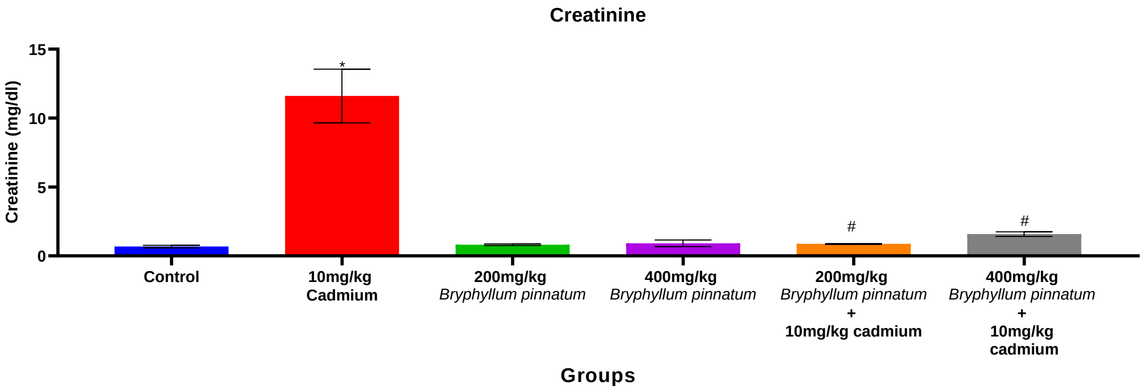


Chart 6: Creatinine activity in the kidney after 28 days. Values are given as mean ± SEM. $^{*}p<$ 0.05 compared with the control group; $^{\#}p<$ 0.05 compared with the Cadmium alone group.

4.3 Oxidative stress

Table 4.3 showing in…… of experimental animals across all groups after administration

Groups/Test	Control	10mg/kg of Cadmium	150mg/kg 200mg/kg *Bryphyllum pinnatum*	300mg/kg of *Bryphyllum pinnatum*	150mg/kg of *Bryphyllum pinnatum* + 10mg/kg	150mg/kg of *Bryphyllum pinnatum* + 10mg/kg	P-value

					of Cadmium	of Cadmium	
Total Protein	1.91±0.04	1.07±0.02*	1.82±0.03	1.91±0.04	1.87±0.06#	1.78±0.08#	<0.0001
Superoxide Dismutase	1.86±0.06	1.32±0.02*	1.76±0.02	2.01±0.05	1.92±0.04#	1.93±0.04#	<0.0001
Catalase	0.85±0.03	0.25±0.03	0.77±0.08	0.74±0.05	0.71±0.07#	0.67±0.04#	<0.0001
Glutathione Peroxidase	2.63±0.10	2.03±0.01*	2.81±0.04	2.51±0.09	2.59±0.09#	2.68±0.04#	<0.0001
Malondialdehyde	0.95±0.09	1.74±0.06*	0.89±0.02	0.91±0.05	0.61±0.10#	0.45±0.02#	<0.0001

Oxidative stress parameters in the kidney after 28 days. Values are given as mean ± SEM. * $p< 0.05$ compared with the control group; $^\#$ $p< 0.05$ compared with Cadmium-alone group.

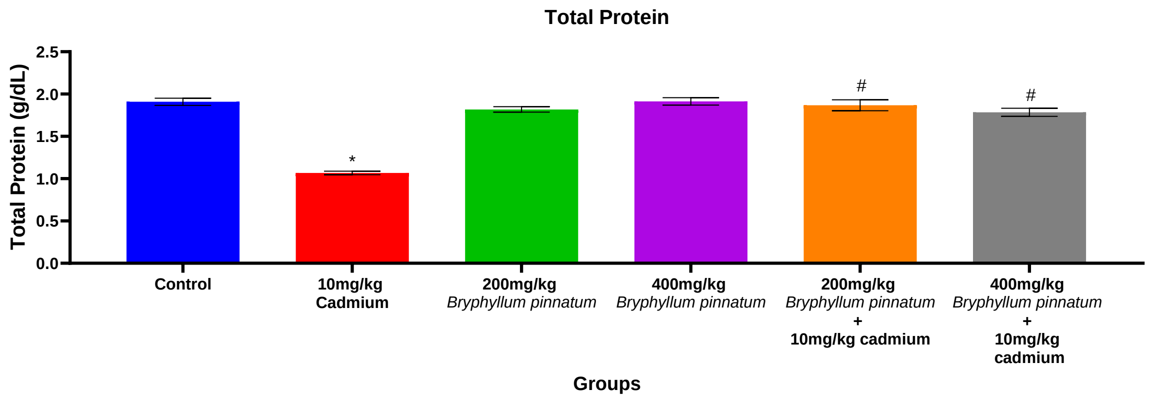


Chart 7: Activity of total protein in the Kidney of control and treatment groups

after 28 days. Values are given as mean ± SEM; * $p< 0.05$ compared with the control group; $^{\#}$ $p< 0.05$ compared with Cadmium-alone group.

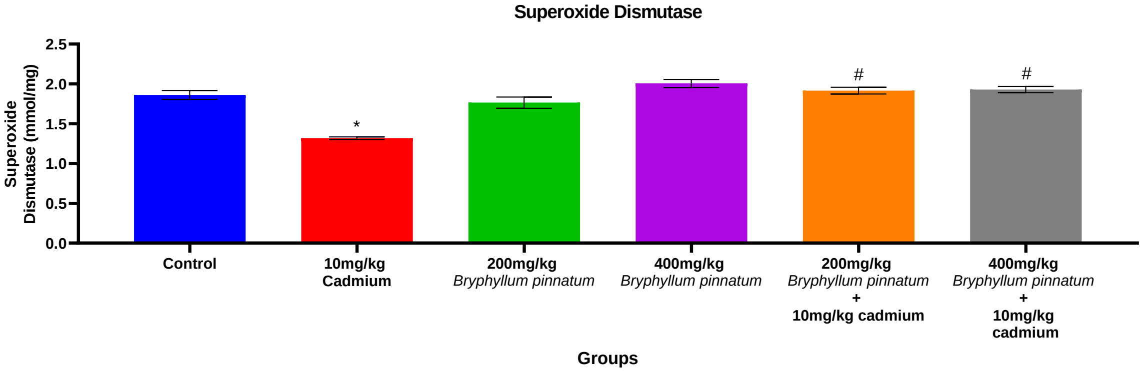


Chart 8: Superoxide dismutase activity in the Kidney of control and treatment groups after 28 days. Values are given as mean ± SEM; * $p< 0.05$ compared with the control group; $^{\#}$ $p< 0.05$ compared with Cadmium-alone group.

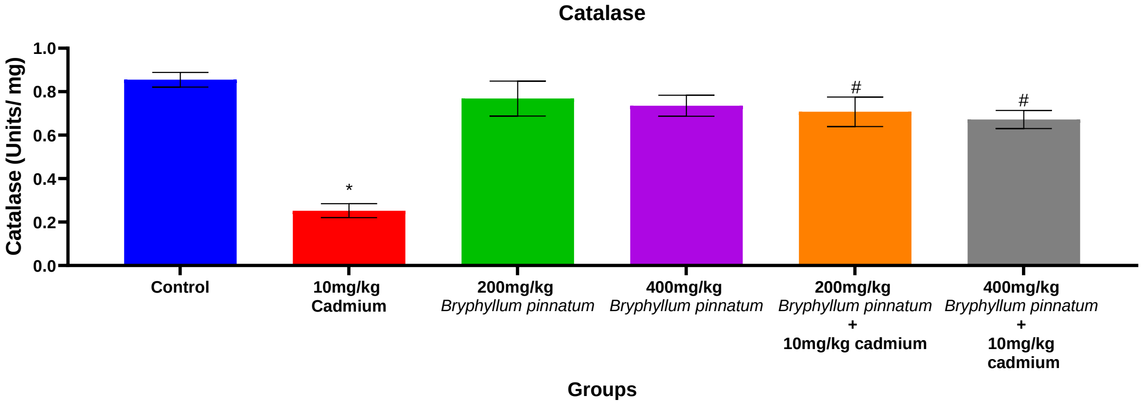


Chart 9: Catalase activity in the Kidney of control and treatment groups after 28 days. Values are given as mean ± SEM; * $p< 0.05$ compared with the control group; $^{\#}$ $p< 0.05$ compared with Cadmium-alone group.

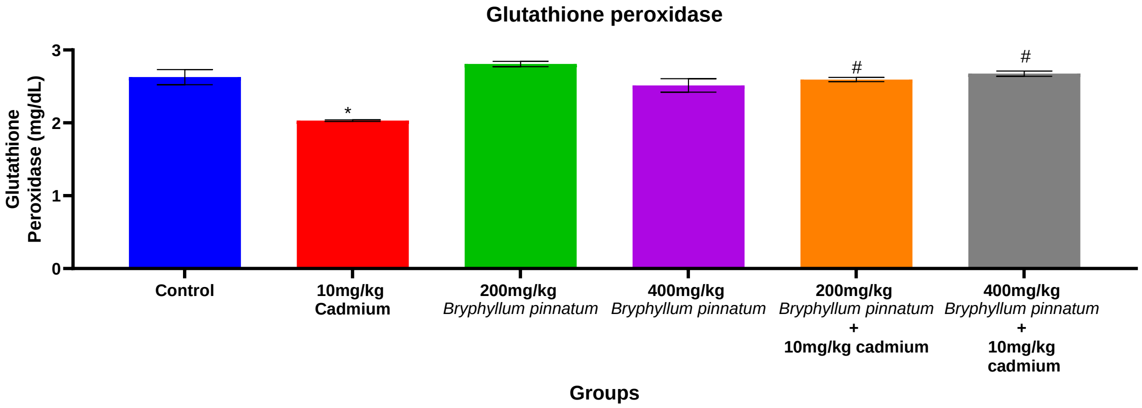


Chart 10: Glutathione Peroxidase activity in the Kidney of control and treatment groups after 28 days. Values are given as mean ± SEM; * $p< 0.05$ compared with the control group; $^{\#}$ $p< 0.05$ compared with Cadmium-alone group.

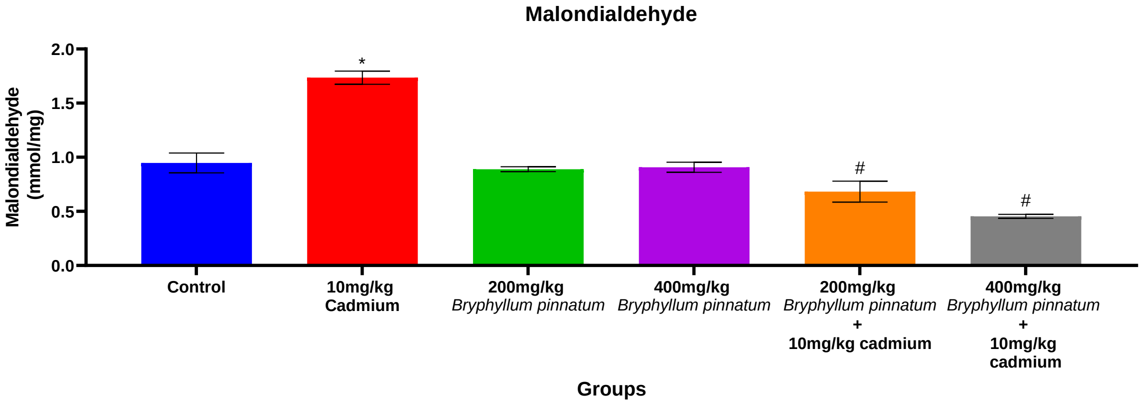


Chart 11: Lipid peroxidation activity in the Kidney of control and treatment groups after 28 days. Values are given as mean ± SEM. * $p< 0.05$ compared with the control group; $^{\#}$ $p< 0.05$ compared with Cadmium-alone group.

4.4 Histology

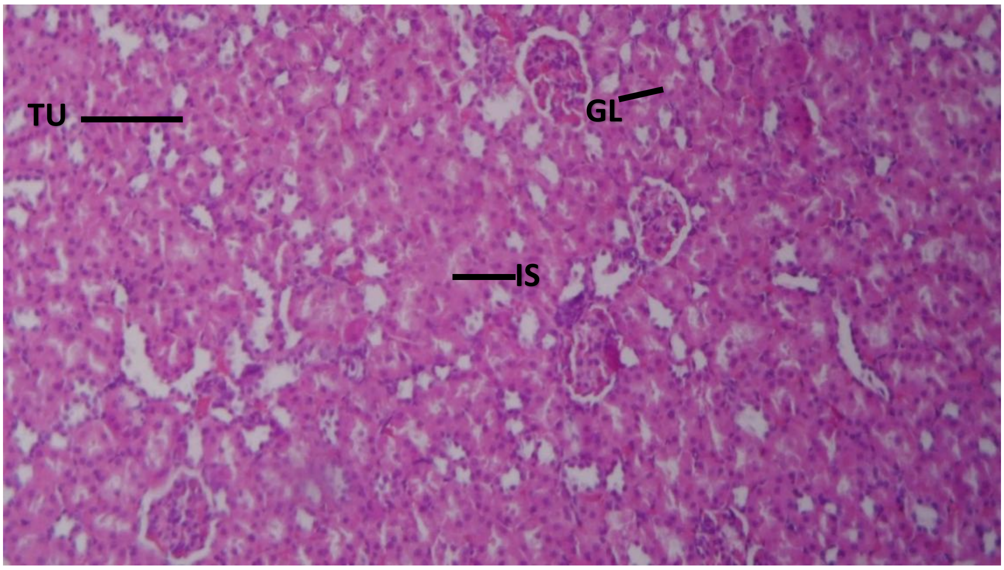


Plate 1. Rat kidneys, control, show: normal tissue architecture: tubules (TU), space (IS) and glomeruli (GL): H&E 100 X

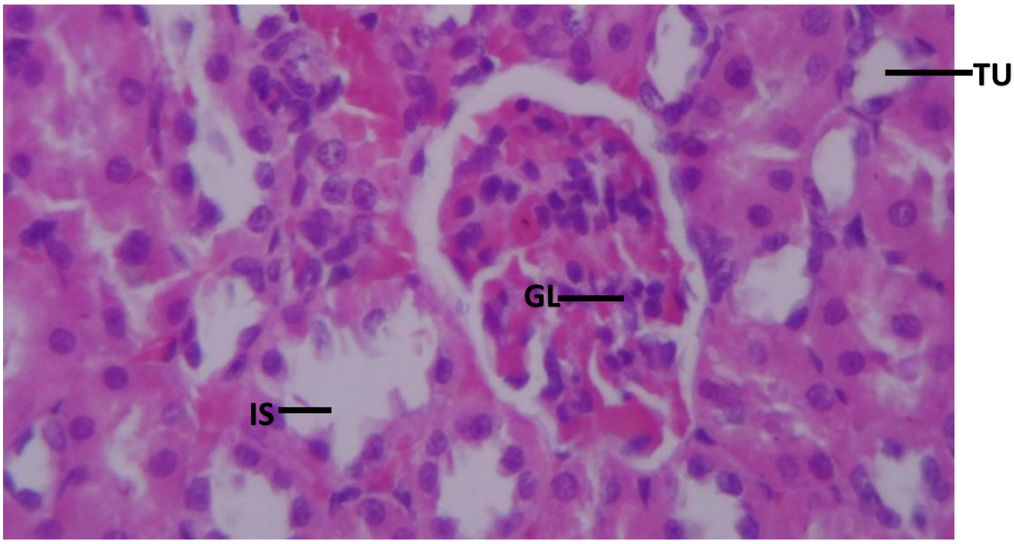


Plate 2. Rat kidneys, control, show: normal tissue architecture: tubules (TU), space (IS) and glomeruli (GL) : H&E 400 X

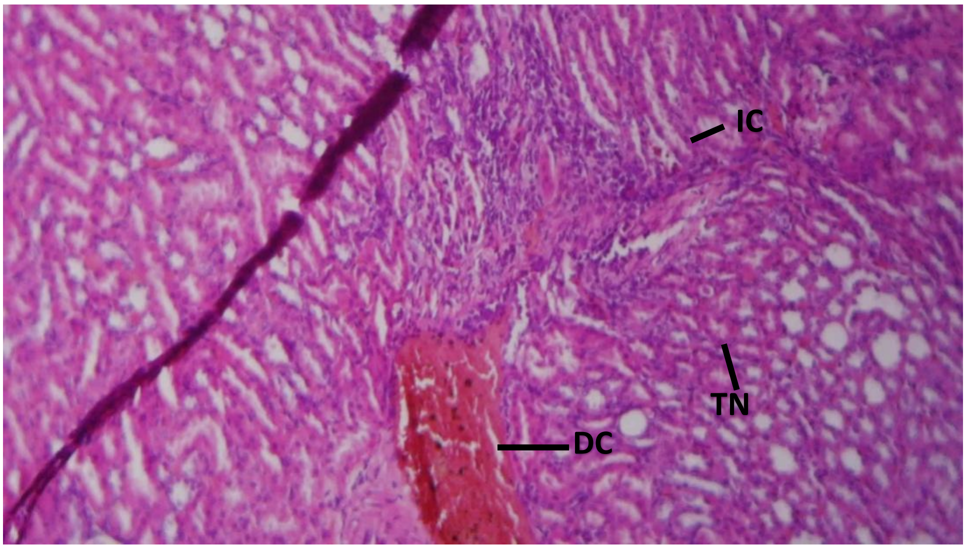


Plate 3. Rat kidneys given Cadmium only show: severe vasodilatation and congestion (DC), heavy interstitial infiltrates of inflammatory cells (IC) and focal tubular necrosis (TN): H&E 100 X

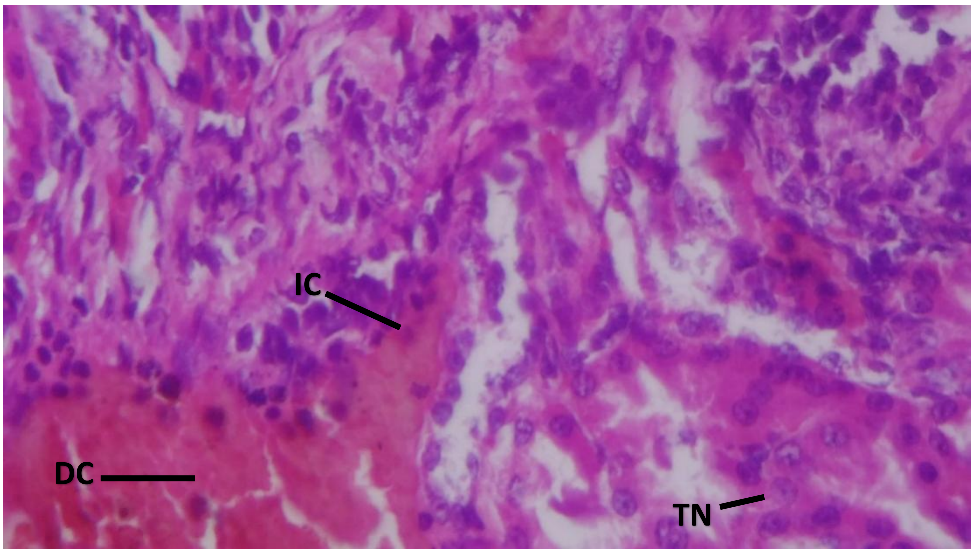


Plate 4. Rat kidneys given Cadmium only show: severe vasodilatation and congestion (DC), heavy interstitial infiltrates of inflammatory cells (IC) and focal tubular necrosis (TN) : H&E 400 X

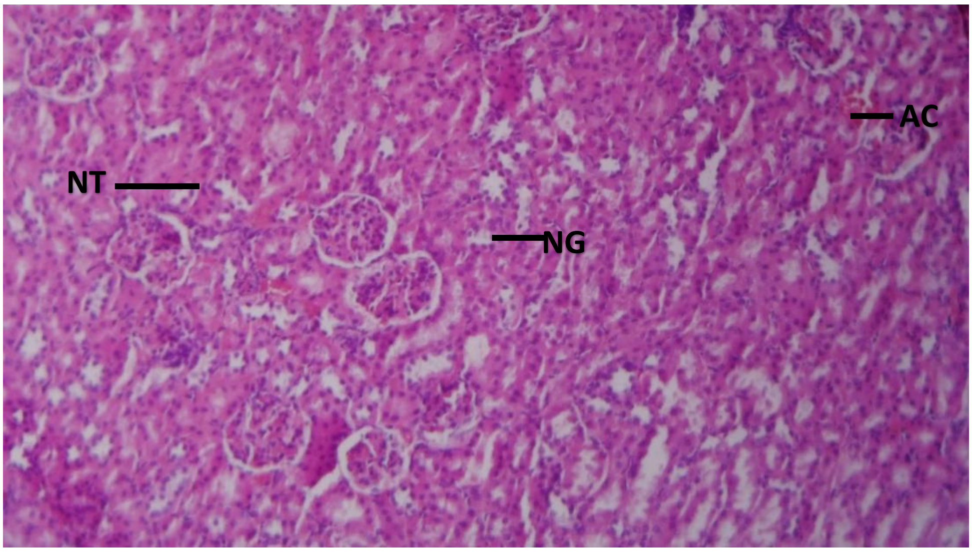


Plate 5. Rat kidneys given 200mg Extract only show: normal tubules (NT) and glomeruli (NG) and active interstitial congestion (AC): H&E 100 X

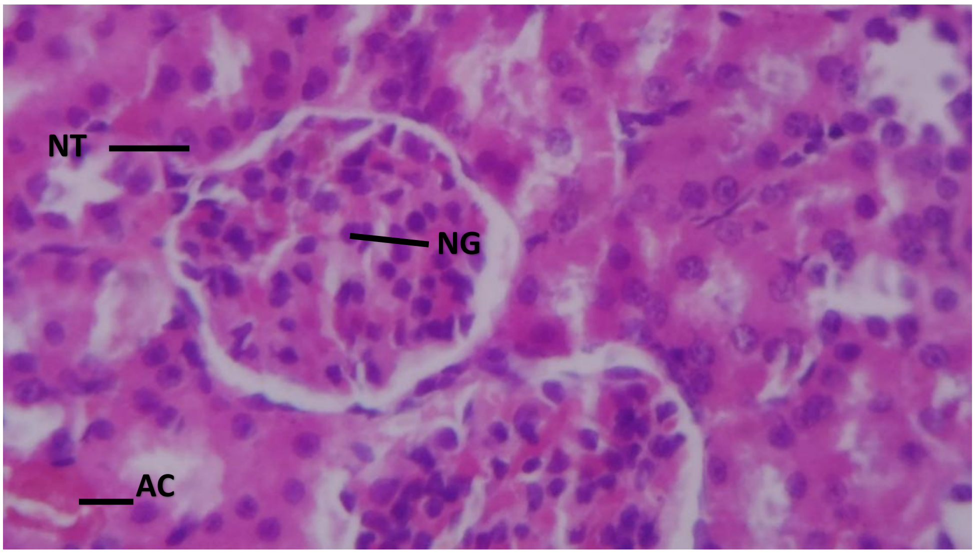


Plate 6. Rat kidneys given 200mg Extract only show: normal tubules (NT) and glomeruli (NG) and active interstitial congestion (AC) : H&E 400 X

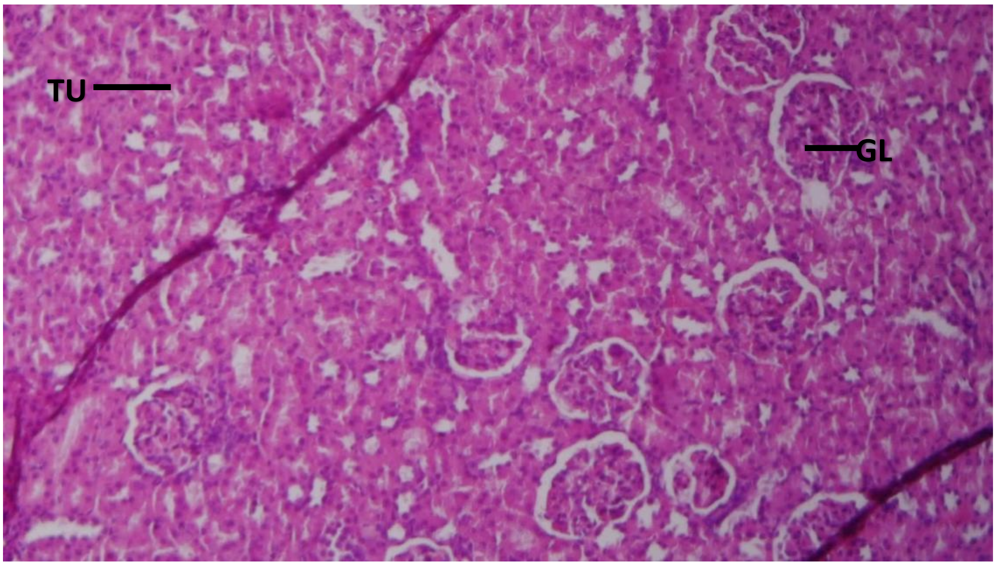


Plate 7. Rat kidneys given 400mg extract only show: tubules (TU) and glomeruli (GL), all normal: H&E 100 X

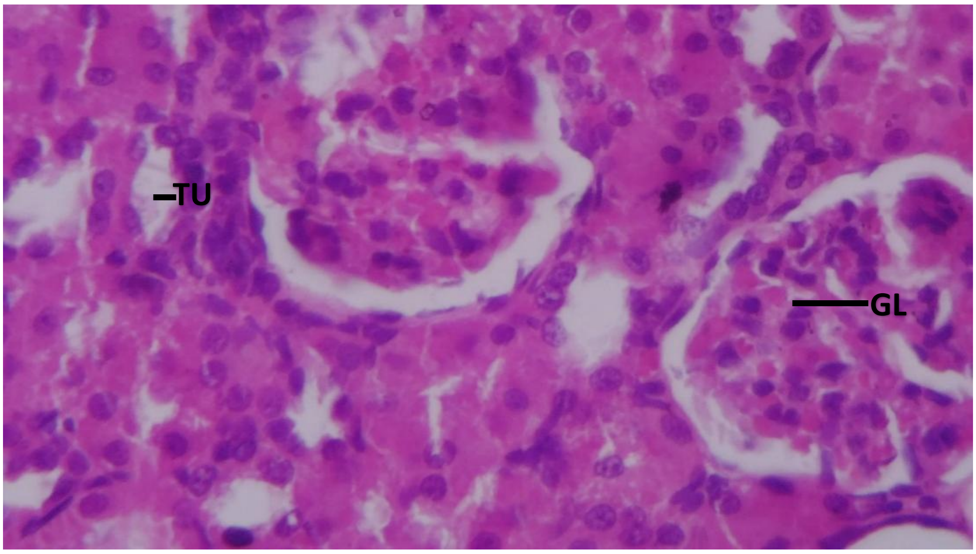


Plate 8. Rat kidneys given 400mg extract only show: tubules (TU) and glomeruli (GL), all normal : H&E 400 X

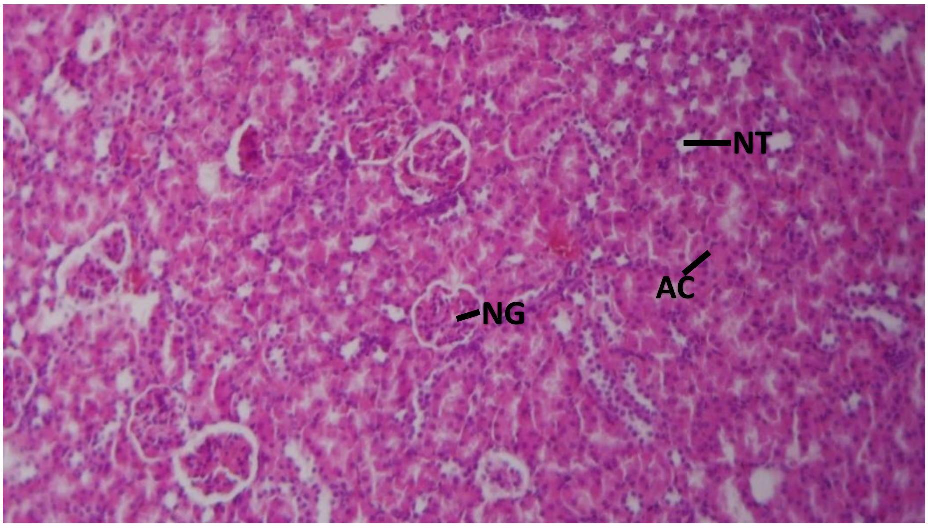


Plate 9. Rat kidney given 200mg Extract followed with Cadmium show: normal tubules (NT) and glomeruli (NG) and active interstitial congestion (AC): H&E 100 X

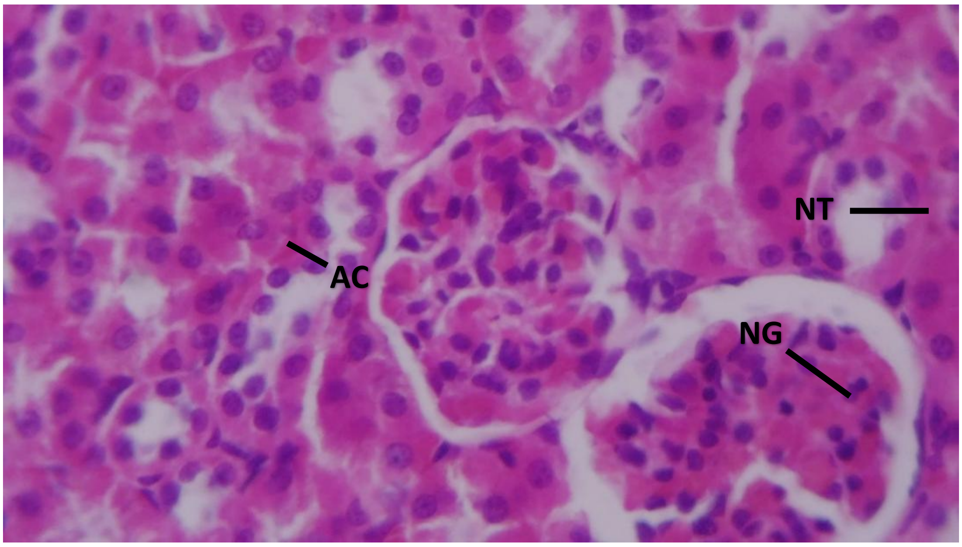


Plate 10. Rat kidney given 200mg Extract followed with Cadmium show: normal tubules (NT) and glomeruli (NG) and active interstitial congestion (AC) : H&E 400 X

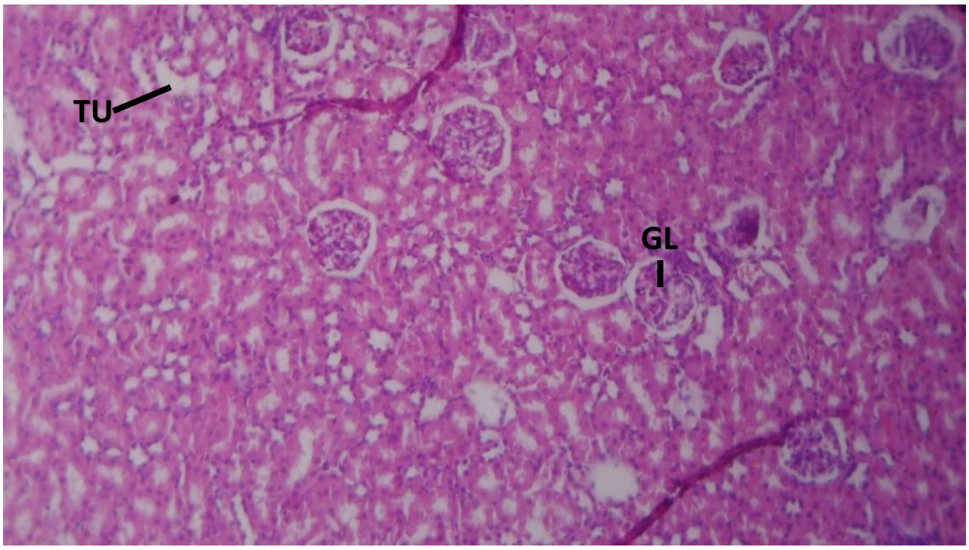


Plate 11. Rat kidney given 400mg Extract followed with Cadmium show: normal tissue architecture: tubules (TU) and glomeruli (GL): H&E 100 X

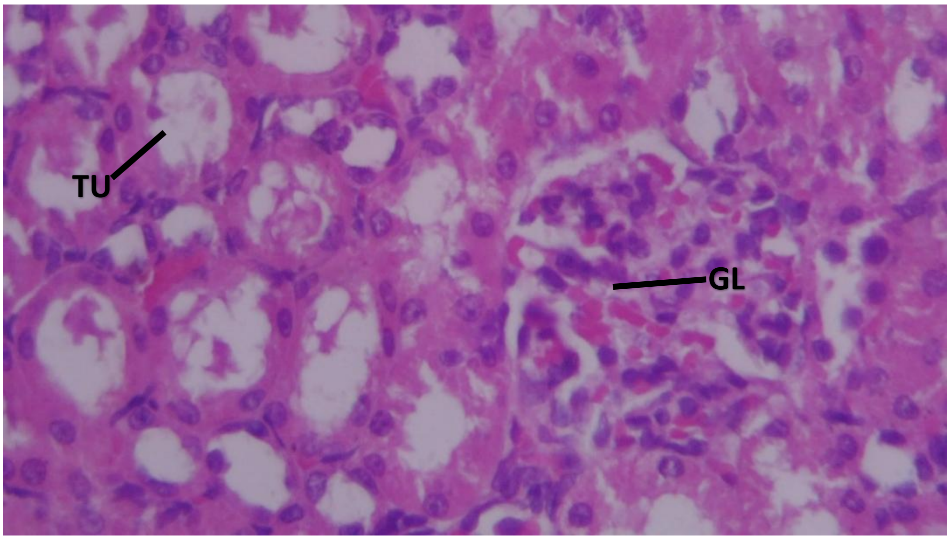


Plate 12. Rat kidney given 400mg Extract followed with Cadmium show: tissue Reference

CHAPTER FIVE

5.0 DISCUSSION, CONCLUSSION AND RECOMMENDATION

5.1 Discussion

The study evaluates the effects of *Bryophyllum pinnatum* in mitigating cadmium-induced nephrotoxicity, with significant implications for understanding both the pathophysiology of cadmium toxicity and potential therapeutic interventions. Cadmium, a known nephrotoxin, caused marked weight reduction, renal impairment, and oxidative stress in the test groups. These effects were evident in parameters such as final body weight, kidney weight, urea, creatinine levels, and oxidative stress markers, indicating renal damage and systemic effects.

Animals exposed to cadmium alone exhibited substantial weight loss, a significant rise in the reno-somatic index, and increased urea and creatinine levels, correlating with renal dysfunction. Histological assessments confirmed these findings, revealing severe tubular necrosis, interstitial inflammation, and congestion. These results align with previous studies highlighting cadmium's nephrotoxic effects through oxidative stress and apoptosis pathways (Bernard, 2008). The increased malondialdehyde (MDA) levels further supported the lipid peroxidation caused by cadmium-induced oxidative stress, consistent with other studies emphasizing MDA as a marker of oxidative injury (Johri *et al*., 2010).

Treatment with *Bryophyllum pinnatum*, particularly at higher doses (200–300 mg/kg), mitigated these effects significantly. Parameters such as weight gain, normalized urea, and creatinine levels, and reduced reno-somatic indices reflected renal protection. Histological analysis demonstrated a preservation of normal kidney architecture, suggesting a potent nephroprotective role of the plant extract. These findings corroborate the antioxidant potential of Bryophyllum pinnatum observed in earlier research, which attributed its efficacy to flavonoids and polyphenols that scavenge free radicals and reduce oxidative damage (Mabberley, 2017).

The antioxidative defense parameters—superoxide dismutase (SOD), catalase, and glutathione peroxidase—further substantiated the protective effects of *Bryophyllum pinnatum.* Cadmium-exposed groups showed diminished activity of these enzymes, confirming oxidative stress. Conversely, *Bryophyllum pinnatum* administration restored these enzyme activities, highlighting its role in maintaining redox homeostasis. This aligns with studies on plant-derived antioxidants demonstrating similar effects (Akinmoladun *et al*., 2010). Interestingly, the combined treatment groups (cadmium + Bryophyllum pinnatum) showed a dose-dependent protective effect, underscoring the potential therapeutic value of the plant extract in combating cadmium toxicity.

While cadmium alone increased MDA levels, *Bryophyllum pinnatum* treatment reduced lipid peroxidation, further affirming its antioxidative capacity. Lower MDA levels in the high-dose groups emphasize the efficacy of *Bryophyllum pinnatum* in mitigating oxidative damage, as supported by histological evidence showing reduced necrosis and inflammation in kidney tissues. These results resonate with the findings of Acharya *et al*. (2019), who documented similar protective effects of plant-based antioxidants in experimental nephrotoxicity models.

The study's implications are profound, suggesting *Bryophyllum pinnatum* as a viable intervention for cadmium-induced nephrotoxicity. By counteracting oxidative stress and preserving renal function, it offers a promising natural alternative to conventional therapies. Future research could expand on these findings by exploring the molecular mechanisms underlying its protective effects and evaluating its efficacy in clinical settings.

Histological examination provided crucial evidence supporting these biochemical findings. In the control group, kidney tissue exhibited normal architecture, with intact glomeruli and tubules. Cadmium exposure, however, resulted in severe histopathological changes, including tubular necrosis, glomerular damage, interstitial congestion, and heavy inflammatory cell infiltration. These observations are consistent with known cadmium-induced renal damage characterized by necrosis and inflammation (Johri *et al*., 2010). The groups treated with *Bryophyllum pinnatum* extract, particularly at 200 mg/kg and 300 mg/kg doses, displayed marked improvements in histological architecture. The tubules and glomeruli appeared normal, with reduced necrosis and inflammation. Even in the combined treatment groups (cadmium + extract), the kidney tissues showed near-normal histology, with minimal congestion and preserved tubular structures. This suggests that *Bryophyllum pinnatum* effectively mitigates cadmium-induced histopathological damage.

Comparing the high-dose treatment (300 mg/kg) to prior studies, the extract demonstrated effects comparable to synthetic antioxidants, further validating its efficacy as a nephroprotective agent. Histological findings revealed a reduction in inflammatory responses and preservation of renal architecture, supporting its role in attenuating cadmium toxicity. This is likely attributable to the extract's rich phytochemical content, which includes flavonoids and phenolics with known anti-inflammatory and antioxidative properties (Mabberley, 2017).

The study's integration of biochemical, physiological, and histological findings underscores the robust nephroprotective effects of *Bryophyllum pinnatum*. By counteracting oxidative stress, preserving renal function, and maintaining structural integrity, it presents a promising natural intervention for cadmium-induced nephrotoxicity. Future research should explore the molecular mechanisms underlying these effects and assess the clinical applicability of *Bryophyllum pinnatum* in human populations affected by environmental toxins.

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