INVESTIGATING THE EFFECT OF *DENDROPANAX TRIFIDUS (MAKINO)* EXTRACT ON THE KIDNEY OF A WISTAR RAT

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BEING A PROJECT WORK SUBMITTED TO THE DEPARTMENT OF ANATOMY, SCHOOL OF BASIC MEDICAL SCIENCE, UNIVERSITY OF BENIN, BENIN CITY.

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CERTIFICATION

This is to certify that the project work titled: "**INVESTIGATING THE EFFECT OF AQUEOUS EXTRACT OF *Dendropanax trifidus* (THUNB) ON THE KIDNEY OF ADULT WISTAR RATS"** was carried out by me **TESTIMONY BASIL ADANNA** with matriculation number **BMS2004945** and it meets the regulations governing the award of *Bachelor of Science Degree in Anatomy*, School of Basic Medical Sciences, University of Benin, Benin City, Nigeria.

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(EXTERNAL EXAMINER)

CERTIFICATION OF PROJECT ON PLAGIARISM

We the undersigned attest and declare that the project undertaken by **TESTIMONY BASIL ADANNA** with matric no BMS2004945

TITLED:

INVESTIGATING THE EFFECT OF DENDROPANAX TRIFIDUS (MAKINO) EXTRACT ON THE KIDNEY OF A WISTAR RAT

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DR E.E IGAHLO *DATE*
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HEAD OF DEPARTMENT

DEDICATION

I dedicate this project to God Almighty for his Grace and favour throughout my undergraduate studies and to my parents Mr and Mrs Basil,my siblings and my uncles and everyone who contributed to the success of this project.

ACKNOWLEGEMENT

My infinite gratitude goes to the LORD ALMIGHTY for his faithfulness and benevolences towards my academic pursuit.

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My greatest gratitude to my parents, MR and MRS BASIL for all the help you provided me with all through my time as a student, may God bless you.

Special thanks to the head of department, DR ADAZE B. ENOGIERU, for his fatherly concerns, guidance and diligence towards seeing us attain value in life.

To my friends who influenced the success of this study, I am grateful.

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ABSTRACT

This study investigates the effects of *Dendropanax trifidus*, a traditional medicinal plant, on kidney function and morphology in Wistar rats. The aim is to evaluate the potential nephroprotective and therapeutic properties of *Dendropanax trifidus* extract through a series of experimental assays. Wistar rats were divided into control and treatment groups, receiving varying doses of *Dendropanax trifidus* extract over a predetermined period.

Biochemical analyses were conducted to assess kidney function, including serum levels of creatinine, urea and electrolytes. Histological examinations of kidney tissues were performed to evaluate morphological changes and structural integrity. Results demonstrated that administration of *Dendropanax trifidus* significantly improvedrenal function markers in a dose-dependent manner, suggesting its potential nephroprotective effects. Histological analysis revealed a reduction in tubular injury and preserved glomerular architecture in treated rats compared to controls.

These findings indicate that *Dendropanax trifidus* may possess beneficial effects on kidney health, potential offering a natural therapeutic option for the management of renal disorders. Further studies are warranted to elucidate the underlying mechanisms of action and to explore possible clinical applications in nephrology.

CHAPTER ONE

BACKGROUND OF STUDY

Since its inception, herbal extracts have been used as natural remedies to treat a variety of aliment [punit kumar et 2019]. The use of medicinal plant has been practiced since ancient times and has been recommended as source of modern medicine[kumar shalimi et al 2021]. In recent years, herbal medicine has attracted attention to the alternative medicine for preventing related diseases.

Dendropanax trifidus [makino] is a shrub or a small tree. The leaves are typically glossy and compound with a distinctive triofoliate structure [3 leaflets]; it's a valuable plant with diverse phytochemical constituents and has been proven biological activities. Natural products continue to make extensive contribution to human health alongside modern medicine and in drug discovery. According to report of WHO universally 80 per cent of people still trust natural medicine at present for remedies especially the eastern part or Asia. The common name for DT is known as SILO TREE OR THUNB.

KIDNEY

The kidney is a bilateral organ placed retroperitoneal in the upper left and right abdominal quadrant and the part of urinary system. It is a bean shaped organ reddish brown in colour and located in the posterior abdomen. Their main function is to filter and excrete waste product from the blood, they are responsible for water and electrolyte balance in the body

AIMS OF STUDY

The aim of this study is to investigate the effects of aqueous extract of dendropanax trifidus on the kidney of adult wistar rat

SPECIFIC OBJECTIVES OF THE STUDY

The specific objectives of this study includes investigating the effects of aqueous extract of Dendropanax trifidus on

Body weight of the wistar rat

Weight of the organ [kidney]

Organ-somatic index

Histology of the kidney

Hematological parameter

Active phytochemical constituents on dendropanax trifidus extract.

This study will show if the extract is beneficial to the organ. If toxic, the study would investigate the dosage at which the extract becomes toxic to the organ of the wistar rat.

SIGNIFICANCE STUDY

Medicinal plants are considered an important source of new chemical with potential therapeutic effects. Herbals remedies have recently attracted a lot of attention as useful alternative medicine to treat or prevent lifestyle disorder. The significance of dendropanax trifidus and its effects is multifaceted encompassing such as pharmacology, toxicology and traditional medicine.

Its studies can validate or refute these traditional uses providing a bridge between folk medicine and modern biochemical science. This results could lead to ***ACI OR CKD***.

CHAPTER TWO
LITERATURE REVIEW

2.1 PLANT OF STUDY

The dendropanax trifidus genus belong to the Araliceae family and is found throughout the south west region of east asia , korea and Japan furthermore it is considered a neutropical genus containing approx 91 to 95 species distributed from the malay peninsula and central south American [9,10,11]. Dendopanax trifidus is a valuable plant with diverse phytochemical constituent and proven biological activities, It's from a Greek word *'Dendro'* meaning *'tree'* and *'panax'*

meaning *'all healing'* and *'TRIFIDUS'* meaning *'three parted leaf'* the names are from Latin and Greek roots. Popularly, it's called ***SILO TREE***.

2.1.1 TAXONOMY OF Dendropanax trifidus

Kingdom Plantae

Family: Araliaceae

Genus: Dendropanax -

Species: Dendropanax trifidus

2:1:2 BOTANICAL DESCRIPTIONS

Dendropanax trifidus can grow as a shrub or small tree, typically reaching heights of 4 to 10 meters (13 to 33 feet). It has a dense canopy and a branching structure that creates an appealing visual aspect in forest environments. The leaves are usually large, broad, and palmately lobed, often giving the plant a robust appearance and glossy, while the underside may be paler and slightly hairy. Dendropanax trifidus thrives in subtropical and tropical forest ecosystems, often found in shaded understory areas with moist, well-drained, and fertile.

2:1:3 ORIGIN AND DISTRIBUTION

Dendropanax trifidus is primarily native to East Asia, particularly within subtropical and tropical forest ecosystems. It has evolved in regions characterized by high humidity and ample rainfall, contributing to its adaptation to the forest undergrowth where it can thrive in shaded conditions.

Geographical Distribution: Dendropanax trifidus can be found in several countries across East Asia, including:

Taiwan: It is commonly found in the mountainous and hilly regions, often at elevations ranging from 1,000 to 2,500 meters (approximately 3,280 to 8,202 feet). [Huang Y.M and Chen C.S 1993]

Japan: Particularly on the southern islands such as Kyushu and Shikoku, Dendropanax trifidus can be located in subtropical forests.

China: The species is found in provinces such as Fujian, Guangdong, and Hunan, where it grows in moist, shaded environments.

Okinawa Islands: This plant also occurs in the Okinawa region, which has a subtropical climate conducive to its growth.

Other Southeast Asian Countries: While less common, Dendropanax trifidus may be present in areas of Vietnam and in the broader Southeast Asian region, depending on local conditions. [Li,C.H and Wang H.S 2002].

Dendropanax trifidus originates from East Asia, with its distribution primarily centered in Taiwan, Japan, and southeastern regions of China. Its preference for subtropical forest habitats at higher elevations highlights its ecological importance and the need for conservation efforts in its native environments [Hwang,S.Y and Lee, T.Y 2015].

.*2:1:4 PHYTOCHEMICAL ANALYSIS*

Phytochemicals are bioactive phytochemicals that may provide beneficial health beyond nutrition to reduce the risk of major diseases. Example of phytochemical includes-

Flavonoids, phenolic acids, saponins and triterpenes.

Dendropanax trifidus have been particularly noted for their potent antioxidant properties which help in neutralizing free radical and protecting cells from oxidative stress. This activity is beneficial in preventing and treating conditions associated with cellular damage such as Saponins present in Dendropanax trifidus are known for their immune-boosting properties. These ***compounds can stimulate immune responses and enhance the activity of certain immune cells,*** making them valuable in traditional medicine practices aimed at enhancing general health and resilience to infections (Raven et al., 2012). Terpenoids,

another group of phytochemicals in this plant, exhibit anti-inflammatory effects by inhibiting the release of pro-inflammatory cytokines and modulating pathways that cause inflammation in the body (Judd et al., 2016).

Cardiovascular diseases and certain cancer [Lee t al 2023] especially flavonoids.

Phenolic acid which are also found in significant quantities contribute to the plant antioxidant effect by modulating various pathway [Zhang et al 2018].

Essential oils derived from the plant exhibit antimicrobial effect making dendropanax trifidus a valuable natural remedy for microbial infections. Bioactive compound was isolated through extraction and fractionation and their quality and quantity were determined.

FLAVONOID-16%

TANINS-08%

SAPONIN-03%

LIGNIN-01%

ALKALOIDS-12%

2:15 MEDICINAL AND THERAPEUTIC BENEFITS

Dendropanax trifidus has various medicinal benefits. The plant contains various bioactive compounds that contribute to its therapeutic properties including antioxidant, anti-inflammatory, antimicrobial and hepatoprotective effects [***Kim et 2014***].

The dendropanax trifidus is used to treat various medical conditions like chronic inflammation which can negativity impact kidney function.

Diuretic effects help in promoting urine production and aiding in the elimination of toxins. Renoprotective effects has preliminary studies on related phytochemical that may help protect AKI [Acute kidney injury] and improve renal function.

The terpenoid in dendropanax trifidus compound have been shown to inhibit proinflammatory cytokines and enzymes reducing inflammation. This activity makes it useful in the treatment of [Zhang et al 2018]. Comorboid conditions like Diabetes, hypertension which are common risk factors for kidney diseases.

2.15 TOXICITY OF DENDROPANAX TRIFIDUS

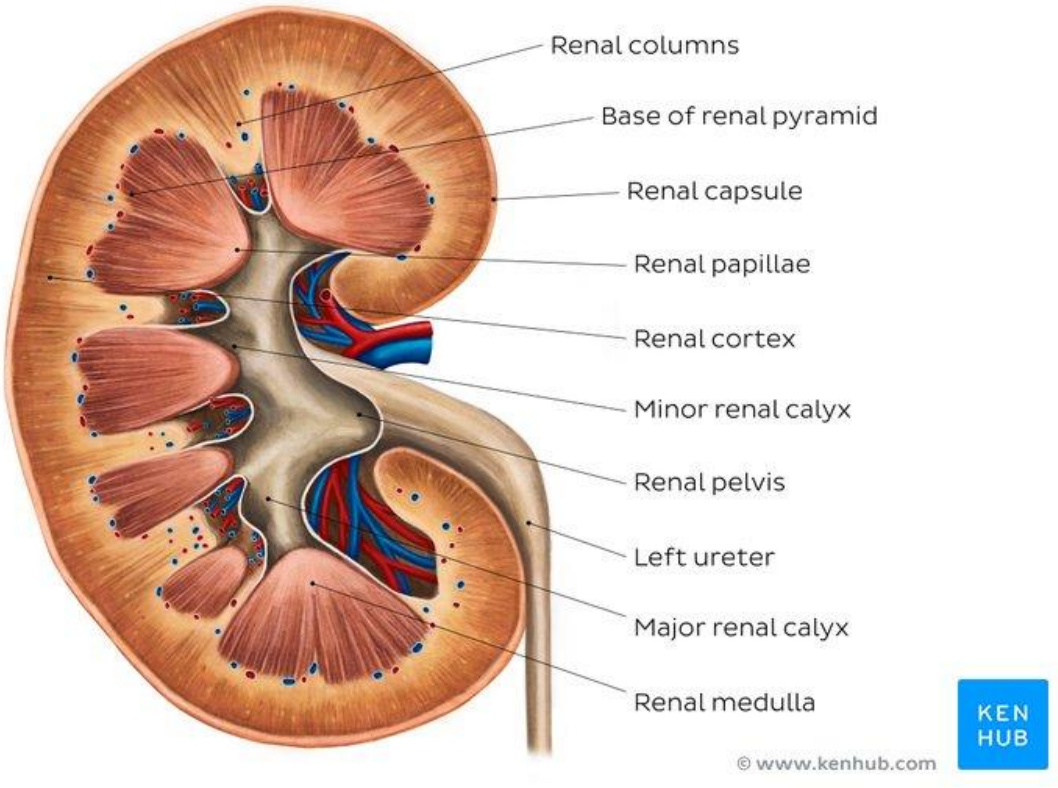
The dendropanax trifidus [Makino Hara] is a plant that has garnered interest for its potential medicinal benefits, especially in traditional medicine. However like many plants, there may be concerns about toxicity or adverse effects associated with its use. Many plants in the Araliaceae family contain saponins, which can have toxic effects at high doses. If present in Dendropanax trifidus, they could lead to gastrointestinal distress or other systemic effects. Like dendropanax trifidus may interact with certain medications, potentially altering their effects or causing adverse reactions on kidney, liver, or other metabolic processes.

DETERMINATION OF ISOLATE

Potential nephroprotect research may indicate whether Dendropanax trifidus has nephroprotective properties that can help prevent kidney damage from various stressors (e.g,toxins,high blood sugar levels).While the potential effects of active compounds from dendropanax trifidus on kidney health appear promising ,further research is needed to elucidate specific mechanisms ,optimal dosages and any possible side effects of interactions.

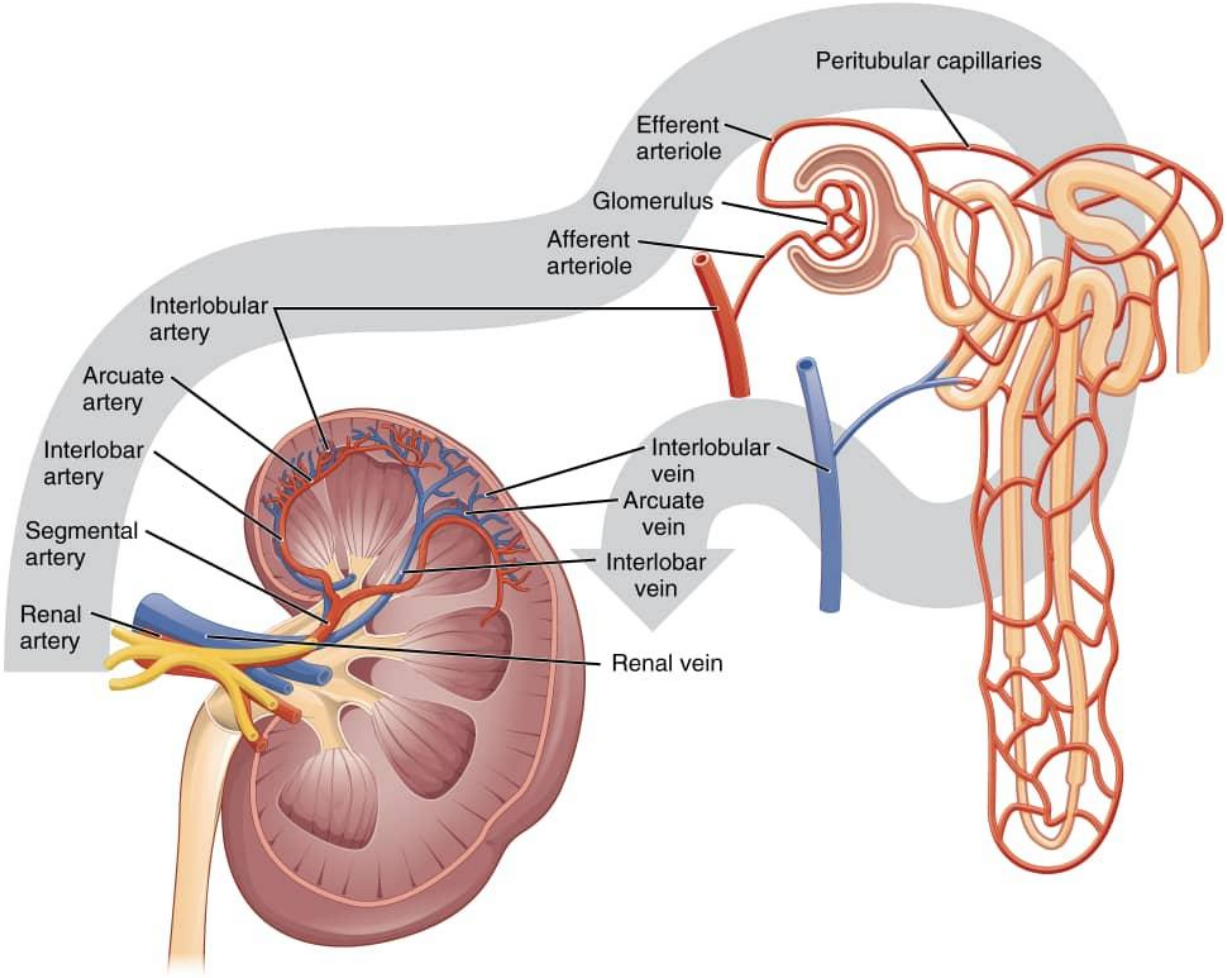
Animal a clinical study will be essential to confirm these effects and translate findings into therapeutic applications for kidney health.

2.2 ORGAN OF STUDY



The kidneys is bilateral organs placed retroperitoneally in the upper left and right abdominal quadrant and are part of the urinary system, it is a two bean shaped organs, where we can describe the superior and inferior poles as well as the major convexity pointed laterally and the minor concavity pointed medially. The kidney is reddish brown in colour and located in the posterior abdomen. Their main function is to filter and excrete waste product from the blood. They are also responsible for water and electrolyte balance in the body. Metabolic waste and excess electrolyte are excreted by the kidneys to form urine. Urine is transported from the kidneys to the bladder by the ureters. About one third of all blood leaving the heart passes into the kidneys for filtration before being pumped to the cells and tissues of the body. When the kidney malfunction, it may lead to various complication such as fluid retention that can lead to edema or swelling of the extremities, pulmonary edema or fluid in the lung.

2.2.1 *GROSS ANATOMY OF THE KIDNEY The kidney*



Have their anterior and posterior surfaces. The anterior surface faces towards the anterior abdominal wall, whereas the posterior surface is facing the posterior abdominal wall. These surfaces is separated by the edges of the kidney which are the major concavity laterally and the minor concavity medially. The center of the minor concavity is marked as the hilum of the kidney where the renal artery enters the kidney and the renal vein and ureter leaves the kidney. The kidney is positioned retroperitoneally meaning that they are not wrapped with the peritoneal organs but rather are placed behind it External anatom. The kidneys are located between the transverse processes of T12-L3 vertebrate with the left kidney typically positioned slightly more superiorly than the right. This is because the liver and the stomach offset the symmetry of the abdomen with the liver forcing the right kidney a bit down and the stomach forcing the left kidney a bit up. The superior poles [extremities] [T12]of both kidneys are more medially pointed towards the spine than the inferior poles [extremities][L3]. The hilium of the kidney usually project at the level of the L12 vertebra. The ureter is seen paravertebrally starting from the L2 and going downwards. The most superior vessel is the renal vein which exit the kidney just under is the renal artery that enters in and under the artery is the exiting ureter.

PATTERNS OF THE KIDNEY RENAL VEIN-RENAL ARTERY-URETER

The kidney tissue is protected by the three layers that entirely surround the kidney. The fibrous capsule [capsule] the perirenal fat body [perinephric fat] The renal fascia which besides the kidney also encloses the suprarenal gland and its surrounding fat.

RELATION

The highest portion of the superior pole is covered with the right suprarenal gland. The superior one half of the anterior surface is in contact with the layer of peritoneum that separates it from the liver. This potential space that separates the liver from the right kidney is called the HEPATORENAL POUCH OF MORISON, POSTERIOR SURFACE OF THE KIDNEY. The posterior surfaces of both kidneys are related to certain neurovascular structures and muscles.

1) Artery-subcostal artery 2Bones-11th and 12th ribs
2) Nerves-iliohypogastric and ilioinguinal nerves.
3) Muscles-diaphragm, psoas major, quadratus lumborum, transversus abdominis.

INTENAL ANATOMY: The parenchyma of the kidney consists of the outer renal cortex and the inner renal medulla. The main unit of the medulla is the renal pyramid .there are 8-18 renal pyramids in each kidney that on the coronal section look like triangles lined next to each other with their bases directed towards the cortex and the apex to the hilium. The apex of the pyramid projects medially towards the renal sinus. This apical projection is called the renal papilla and its opens to a minor calix which unite with several minor calyxes to form major calix. The pyramids are separated by extension of the cortex called the RENAL COLUMNS. The pyramids contain the functional units of the kidney, the nephron which filters blood in order to produce urine which then is transported through a system of the structure called the CALICES. Internally, the kidneys have an intricate and unique structure .The renal parenchyma can be divided into two main areas- the outer cortex and inner medulla. The cortex extends into the medulla, dividing it into triangular shapes-these are known as renal pyramids. The apex of a renal pyramid is called a renal papilla. Each renal papilla is associated with structure known as minor calyx, which collects urine from the pyramids. Several minor calices merge to form a major calyx. Urine passes through the major calices into renal pelvis, a flattened and funnel-shaped structure. From the renal pelvis, urine drains into the ureter, which transports it to the bladder for storage. The medial margin of each kidney is marked by a deep fissure known as the renal hilum. This acts as a gateway to the kidney-normally the renal vessels and ureter enter/exit the kidney via this structure [TM ltd 2022].

ANATOMICAL RELATIONS: The kidneys sit in close proximity to many other abdominal structures which are important to be aware of clinically.

RIGHT KIDNEY SUPERIORLY-the right adrenal gland

ANTERIORLY-The right lobe of the liver, the duodenum and the hepatic flexure of the colon POSTERIORLY-The diaphragm, and muscles of the posterior abdominal wall 11th and 12th rib Psoas major, quadratus lumborum and transversus abdominis Subcostal, iliohypogastric and ilioinguinal nerves.

LEFT KIDNEY SUPERIORLY-The left adrenal gland

ANTERIORLY-The spleen, stomach, pancreas, jejunum and splenic flexure of the colon POSTERIOR-Diaphragm 12th rib Psoas major, muscles of the posterior abdominal wall.

2.2.2 EMBRYOLOGY OF THE KIDNEY: The development of the urinary system involves the transient formation and remodeling of the intermediate mesoderm, being the middle germ layer of the developing embryo. During development, three successive pairs of kidneys appear; the pronephros, the mesonephros and the metanephros. The pronephros appears and subsequently degenerates, the mesonephros becomes temporarily functional before degenerating, and the permanent metanephros ascends from the pelvis to the lumbar region. By week 4, the intermediate mesoderm condenses and recognize into a series of epithelial buds. At the cranial level, these buds form the first pair of kidneys, the pronephros. In humans, the pronephros degenerates as rapidly as it forms providing a glimpse of evolutionary history similar to what is observed in the pharyngeal apparatus. The pronephros is the functional kidney of their early larval life and is crucial for proper systematic osmoregulation. Hence the pronephros is crucial to the development cascade that leads to the formation of the permanent kidney. *MESONEPHROS* during the degeneration of the pronephros, the epithelial buds at the thoracic and lumbar levels forms the second pair of kidneys; the mesonephros degenerates at the thoracic level, but persists at the lumbar level. Simultaneously and also at the lumbar level, 20-30 pairs of mesonephric tubules lengthen from the mesonephric buds. After week 10, the mesonephric system ceases to function and completely regresses in females. Whereas in males, the mesonephric ducts and ductless persist to eventually form important elements of the male genital system, such as the epididymis, the ductus deferens, the seminal vesicles, and the ejaculatory duct. *METANEPHROS* while the mesonephros functions a temporary excretory system, the definitive kidney, the metanephros forms at the sacral level. The formation of the metanephros consists of two structures that are initially separated-the metanephric blastema and the ureteric bud.

RELOCATION OF THE KIDNEY: During week 6 to week 9, the metanephric kidneys relocate themselves by following a path on both sides of the dorsal aorta. This relocation process is characterized by three mechanisms that occur concurrently; ascension, medial, rotation, and revascularization. First the kidneys ascend from the sacral to the lumbar region, second, the hilum of each kidney - initially facing ventrally-rotates medially to face the dorsal aorta. Third, the ascending and medially generating kidney is progressively revascularized by a series of arterial sprouts from the dorsal aorta.

2.2.3 HISTOLOGY OF THE KIDNEY: Now let's take a closer look at the parenchyma layers. The renal cortex is the outer is the outer layer of the kidney tissue. It's darker than its underlying renal medulla because its receives over 90 percent of the kidney blood supply. The cortex has a grainy appearance, as it mostly contains ovoid and coiled parts of the nephrons [renal corpuscles and convoluted tubules]. The renal medulla appears striped, as it contains vertical nephron structures [tubules, collecting ducts]. It consists of renal [medullary] pyramids separated by projection of the renal cortex [renal columns].

2.2.4 BLOOD SUPPLY: The kidneys are supplied with blood via the renal arteries, which arise directly from the abdominal aorta, immediately distal to the origin of the superior mesenteric artery. Due to the anatomical position of the abdominal aorta [slightly to the left of the midline], the right renal artery is longer and crosses the vena cava posteriorly. The renal artery enters the kidney via the renal hilum. At the hilum level, the renal artery forms an anterior and a posterior division, which carry 75 percent and 25 percent of the blood supply to the kidney respectively. The segmental branches of the renal undergo further division to supply the renal parenchyma. Each segmental artery divides to form interlobar arteries. They are situated either side every renal pyramid. These interlobar arteries undergo further division to form the arcuate arteries. At 90 degree to the arcuate arteries, the interlobular arteries arise. The interlobular arteries pass through the cortex, dividing one last time to form afferent arterioles. The afferent arterioles form a capillary network, the glomerulus, where filtration takes place. The capillaries come together to form the efferent arterioles.

2.2.5 INNERVATION: Both the sympathetic and para sympathetic division of the autonomic nervous system are responsible for innervating the kidneys. Thoracolumbar outflow from T10 -L1 provide vasomotor supply through the thoracolumbar splanchnic nerve after synapsing at the renal and coeliac ganglia. Parasympathetic fibers from the vagus nerve as well as fibers from the intermesenteric plexus [S2 to S4] also innervate the kidneys. Afferent fibers conveying pain from the viscera travel along the sympathetic pathway. The afferent fibers that detect pain originating from the kidney stones in the renal pelvis or calices travel through the coeliac plexus to the sympathetic trunk by route of the splanchnic nerves. The associated nausea and vomiting may result from afferent travelling along the vagal route.

2.2.6 LYMPHATICS: Lymph from the kidney drains into the lateral aortic [or para-aortic] lymph nodes, which are located at the origin of the renal arteries.

2.2.7 FUNCTIONS: The kidney have the following function

FORMATION OF URINE: The kidneys form urine which passes through the ureters to the bladder for storage prior to excretion. The composition of urine reflects the activities of the nephrons in the maintenance of homeostasis. Waste products of protein metabolism are excreted; electrolyte balance is maintained by the excretion of hydrogen ions. There are three processes involved in the formation of urine; Simple filtration, Selective reabsorption Secretion

SIMPLE FILTRATION: Filtration takes place through the semi permeable walls of the glomerulus and glomerular capsule. Water and a large number of small molecules pass through, although some are reabsorbed later. Blood cells, plasma proteins and other large molecules are unable to filter through and remain in the capillaries. Filtration is assisted by the differences between, the blood pressure in the glomerulus and the pressure of the filtrate in the glomerular capsule. *CONSTITUENTS OF GLOMERULAR FILTRATE AND GLOMERULAR CAPILLARIES* blood constituents in glomerular filtrate Blood constituents remaining in the glomerulus Water leukocyte Mineral salts erythrocyte Amino acids platelet Ketoacids plasma protein Glucose some drugs Hormones Creatinine Urea Uric acid Toxins

SELECTIVE REABSORPTION: Selective reabsorption is the process by which the composition and volume of the glomerular filtrate are altered during its passage through the convoluted tubules, the medullary loop and the collecting tubules. The general purpose of this process is to reabsorb into the blood those filtrate constituents needed by the body to maintain fluid and electrolyte balance and the PH of the blood. Parathyroid hormone- from the parathyroid glands and calcitonin from the thyroid gland together regulate reabsorption of calcium and phosphate. Antidiuretic hormones- from the posterior lobe of the pituitary gland increase the permeability of the distal convoluted tubules and collecting tubules increasing water reabsorption. Nitrogenous waste products, such as urea and uric acid, are reabsorbed only to a slight extent.

COMPOSITION OF URINE Water Urea Creatinine Ammonia Sodium

CLINICAL CORRELATION DIABETIC KIDNEY: Renal failure is the cause of death in 10 percent of all diabetics and up to 50 percent of cases ò the isulin dependent (type1} diabetes mellitus. There is damage to large and small blood

vessels in many parts of the body, the effects include -acute pyelonephritis with papillary necrosis -nephrotic syndrome.

ACUTE RENAL FAILURE: There is a sudden and severe reduction in the glomerular filtration rate and kidney function that is usually reversible over days or weeks when treated. This occurs as a complication of a variety of conditions not necessarily associated with the kidneys. The causes of acute renal failure are classified as -prerenal: the result of reduced renal blood flow -post renal: obstruction to the outflow of urine e.g. tumour of the bladder, uterus or cervix, large calculus in the renal pelvis.

URINARY INCONTINENCE: There is involuntary passage of urine due to defective voluntary control of the external urethral sphincter

CHAPTER THREE

3.1 MATERIALS AND METHOD

Materials
Animals-30 Adult wistar rat
Extract-Aqueous extract of dendropanax trifidus
Feed-Growers mash.

Instruments-Cotton wool, disposable gloves, specimen bottles, forceps, surgical blade, orogastric tube, 5ml syringe, plastic cages, masking tape, weighing balance, microtome, slide tray, tissue embedding station, microscope .

Reagent-10% formal saline, chloroform, distilled water, eosin, hematoxylin, paraffin wax, xylene.

3.2 EXPERIMENTAL ANIMALS

Twenty-five [25] Adult wistar rat weighing 120-180g were used as experimental animals in this study. The animals were purchased and maintained at the animal house of the department of anatomy, UNIBEN. The cages used to house the rats for the experiment were cleaned and disinfected before the rats were transferred. The rats were allowed to grow and acclimatized for a period of 3 weeks in their cages, they were fed with livestock growers mash manufactured in Edo State.

Acclimization and the experimental period lasted for total of 8 weeks [3 weeks of acclimization and 5 weeks of experimental period]. The cages were made of plastic and wire gazed at the top allowing it for proper ventilation.

3.3 PROCUREMENT AND PREPARATION OF PLANT EXTRACT

Procurement of plant

The leaves of Dendropanax trifidus were harvested in EHEN EDO STATE.

3.4 PREPARATION OF PLANT EXTRACT

A stainless steel tubuar filter with high filtration precusion was used. After maceration, extraction was performed using basic extraction and fractionation procedures to determine the quality and quantity of bioactive compound, ethanol was used for solvent extraction.

Purification of phytochemical was achieved using various chromatographic techniques such as paper chromatography and thin layer chromatography. Finally, uv spectroscopy was used to characterize the compounds. The plants were collectively accurately and timely and their authenticity was confirmed through expert drying and proper grinding.

3.4 EXPERIMENTAL DESIGN

GROUPS	DOSAGE
A(control)	Received feed and water only
B	Received 100mg/0.1ml of DT exact
C	Received 200mg/0.1ml Of DT exact
D	Received 300mg/0.3ml of DT exact
E	Received 0.4mL of DT exact

3.5 METHOD OF SACRIFICE AND TISSUE COLLECTION

At the end of the experimental period, the final weight of the rats were taken using compact electric weighing scale calibrated in grams .Cotton wool were soaked with chloroform of about 50ml in an enclosed container and the rats was placed in the enclosed container containing the chloroform to about 30-50 sec to anesthetize it. After anaesthetization, the rats was placed in a supine position on the dissection table.

Abdomino-thoracic incision was made on the rat to expose the abdominal viscera. Thereafter blood samples were collected through inferior vena cava and through the heart by the process of venous and cardiac puncture respectively .Using 5ml syringes, the blood samples were transferred into an EDTA bottle for haematological analysis. After that the kidney was harvested weighed and fixed in 10% formaline saline in a universal bottle for histological analysis.

3.6 HISTOLOGICAL TECHNIQUES

1. **The kidney were excised and promptly transferred into 10% formal saline for fixation. The tissues were dehydrated by passing through an ascending grade of alcohol.**
2. **The tissue containing alcohol were cleaned using xylene for an hour , to completely remove the alcohol.**

3. **The tissue were infiltrated with molten paraffin wax for 22 hours at a temperature range of 30 -60C**
4. **Embedding of the tissue was carried out with the use of a embedding mould. The molten paraffin wax was poured into embedding mould and then the infiltrated tissue was placed into it in a way in which the sections can be easily cut both longitudinally and then transversely .It was then put in the cold chamber to solidify in a plastic cassette.**
5. **This is allowed to cool and form a block, afterwards it is separated [this is also called D-blocking]. The tissue is ready for sectioning.**
6. **The sectioning was carried out on a rotary microtome and sectioned at a thickness of 5 microns.**
7. **Sections came out in ribbons and were placed in 20% alcohol for spreading of the tissue and it was allowed to float in a water bath at a temperature of 30 C.**
8. **The sectioned tissue were picked from the water bath using a microscope slides and placed on the hot plate to melt excess wax and dry the tissue on the slide.**
9. **The sectioned tissue were placed in xylene for 5minutes to remove paraffin wax from the tissues.**

10. **Hydration was carried out by passing the tissues through descending grade of alcohol [100%,96%,90% and 70%] and water for 5 minutes each.**
11. **Staining was done using haematoxylin and eosin dyes. The tissue were stained in haematoxylin for 10 minutes and raised in water. After that, they were differentiated in 1% acid alcohol briefly and blue to develop the color.**
12. **They were subsequently counterstained with eosin and rinsed in 90% alcohol. Dehydration was done in 90% alcohol and two changes of absolute alcohol at 5 minutes each.**
13. **The sections were there after cleared in xylene for 5 minutes.**
14. **Finally, the slides were mounted with a cover slip, ready to be viewed under a microscope.**

3.7 STATISTICAL ANALYSIS

Results obtained was expressed in mean + standard error of mean [SEM] . Differences among the mean were determined by one way ANOVA. Values were considered to be statistically significant if P value was less than 0.05 [P, <0.05]. Statistical package Graph Pad Prism version 9.0 for windows was used to analyze the data obtained in this study.

CHAPTER FOUR

RESULTS

Statistics

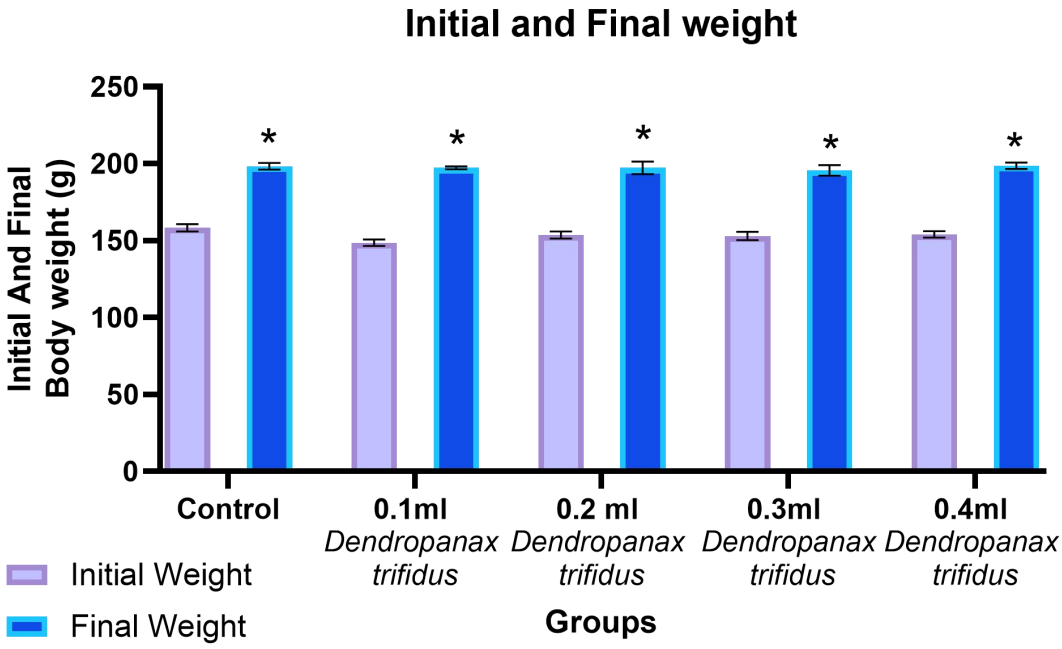


Chart 1: Initial and Final weight after administration Values are given as mean ± SEM. * $p < 0.05$ compared with the initial weight.

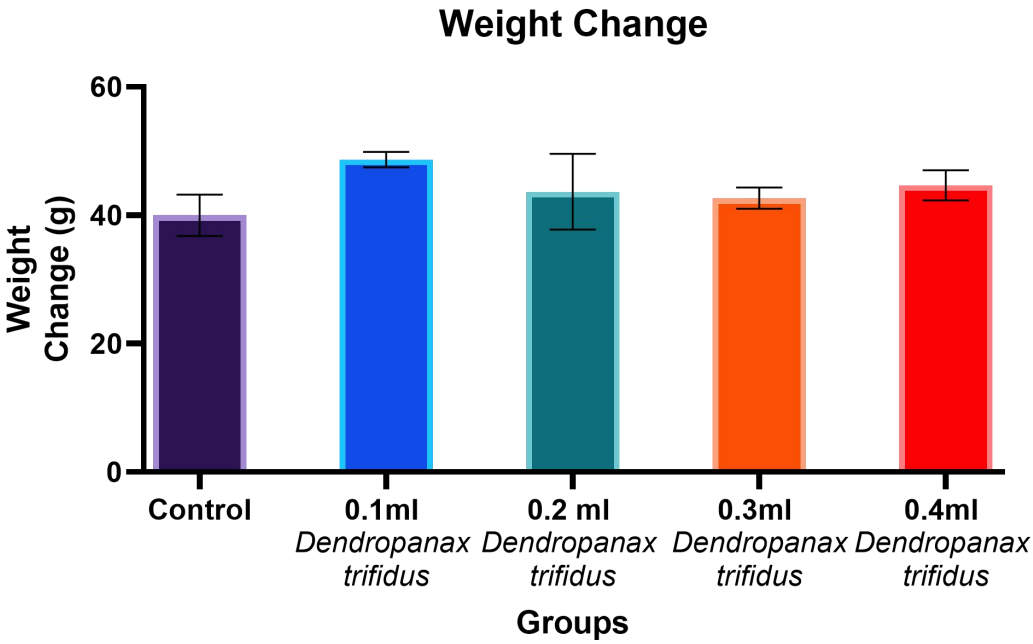


Chart 2: weight change after administration. Values are given as mean ± SEM.

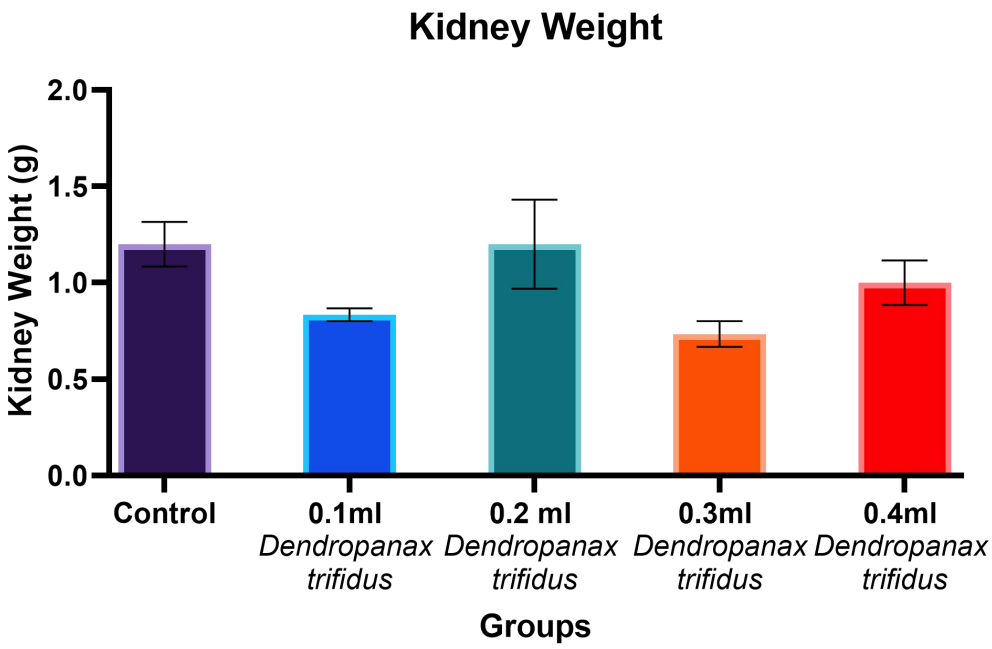


Chart 3: Kidney weight of control and treatment groups after administration. Values are given as mean ± SEM.

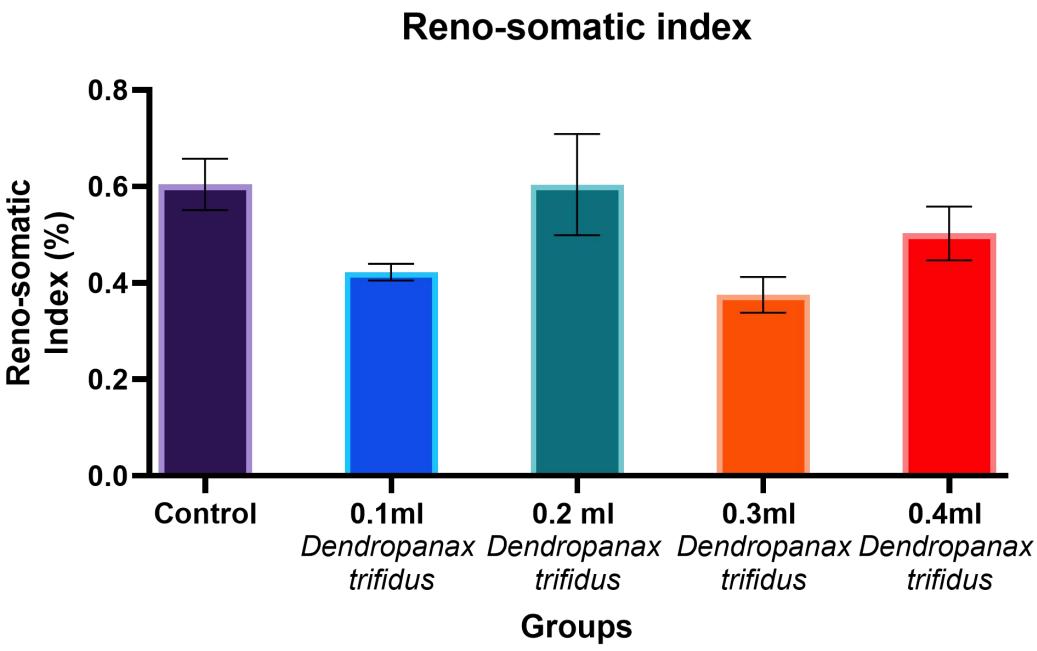


Chart 4: Reno-somatic index of control and treatment groups after administration. Values are given as mean ± SEM.

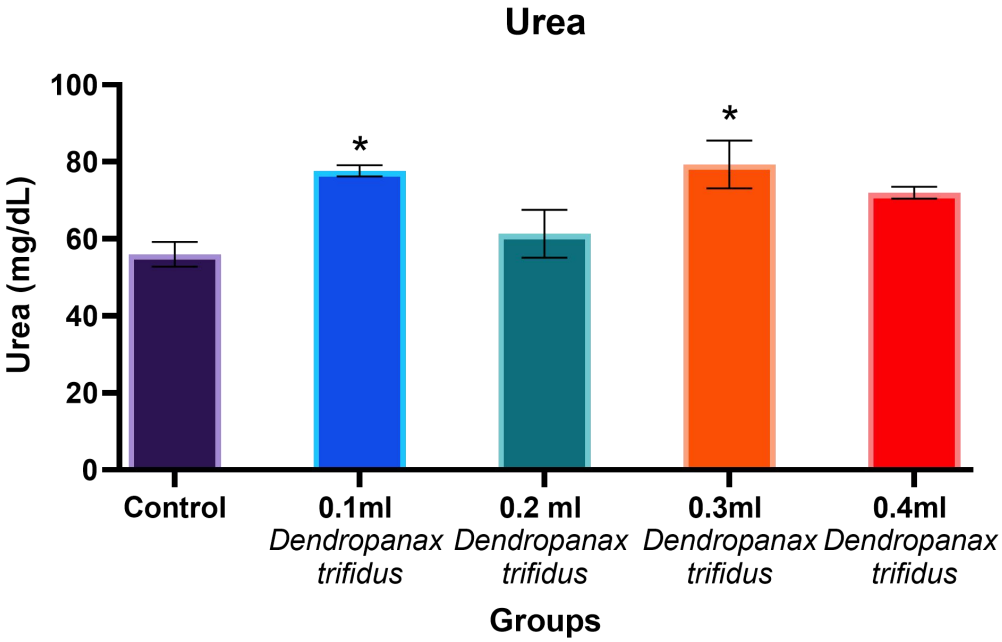


Chart 5: Activity of Urea in the Kidney of control and treatment groups after administration. Values are given as mean ± SEM. * $p< 0.05$ compared with the control group.

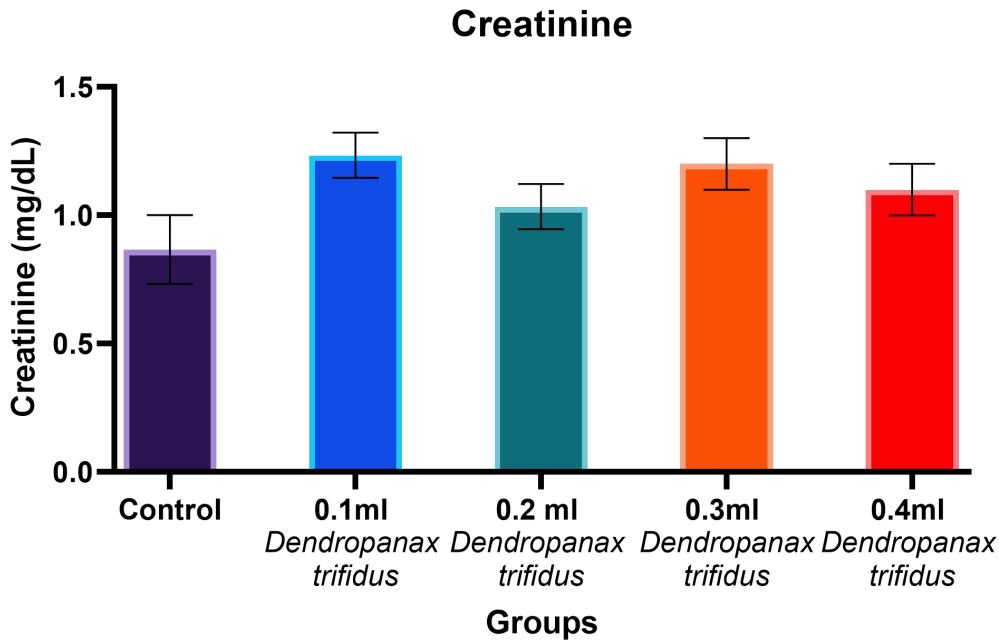


Chart 6: Activity creatinine in the kidney of control and treatment groups after administration. Values are given as mean ± SEM.

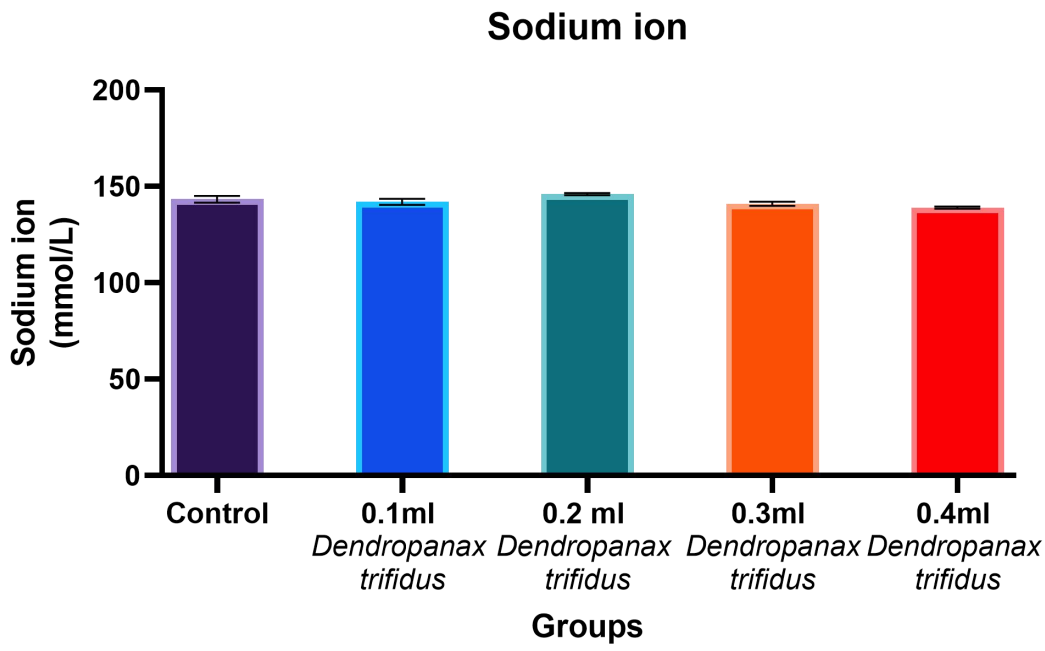


Chart 7: Activity of Sodium ion in the Kidney of control and treatment groups after administration. Values are given as mean ± SEM.

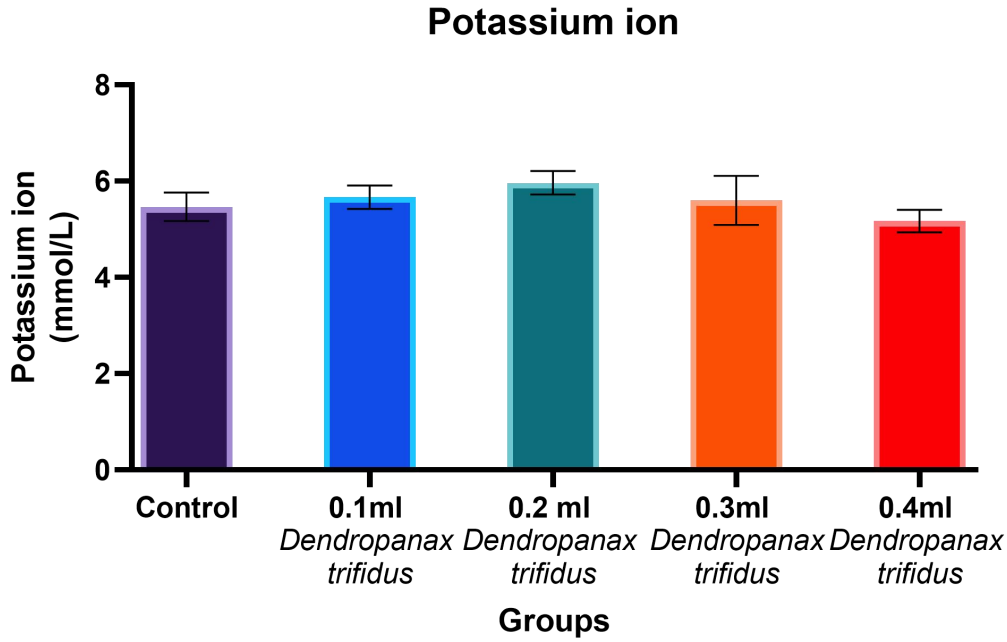


Chart 8: Activity of Potassium in the Kidney of control and treatment groups after administration. Values are given as mean ± SEM.

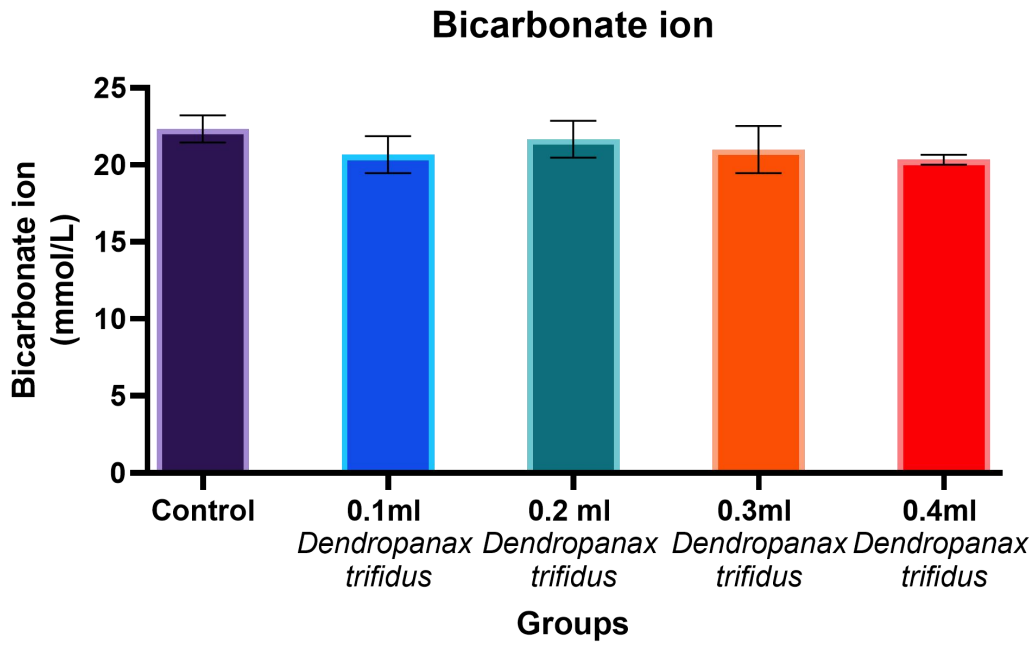


Chart 7: Activity of Bicarbonate ion in the Kidney of control and treatment groups after administration. Values are given as mean ± SEM.

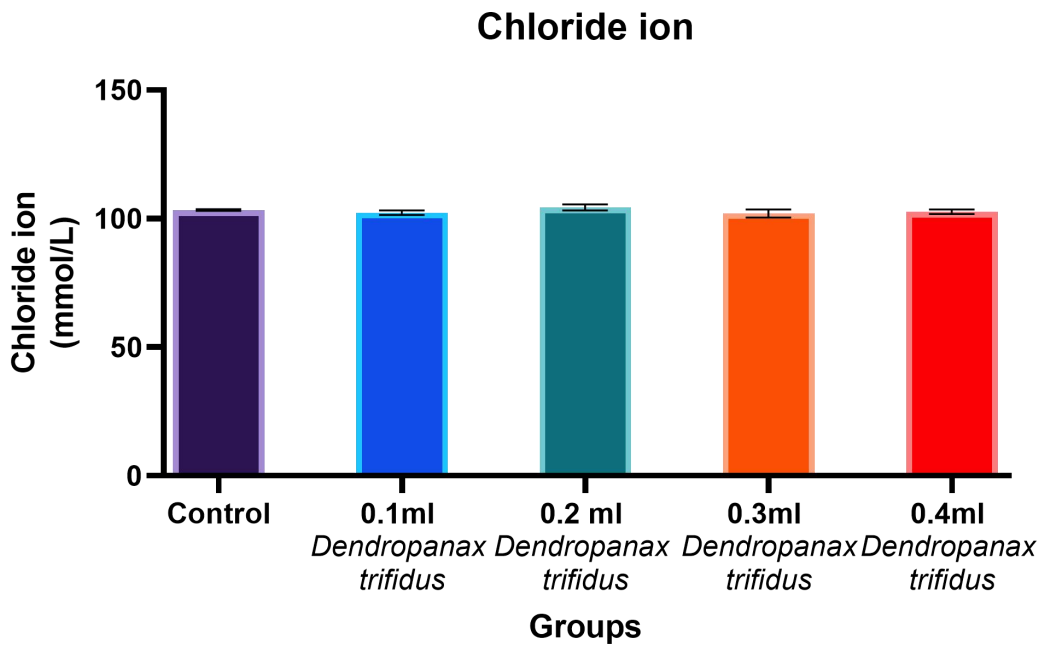


Chart 8: Activity of Chloride ion in the Kidney of control and treatment groups after administration. Values are given as mean ± SEM.

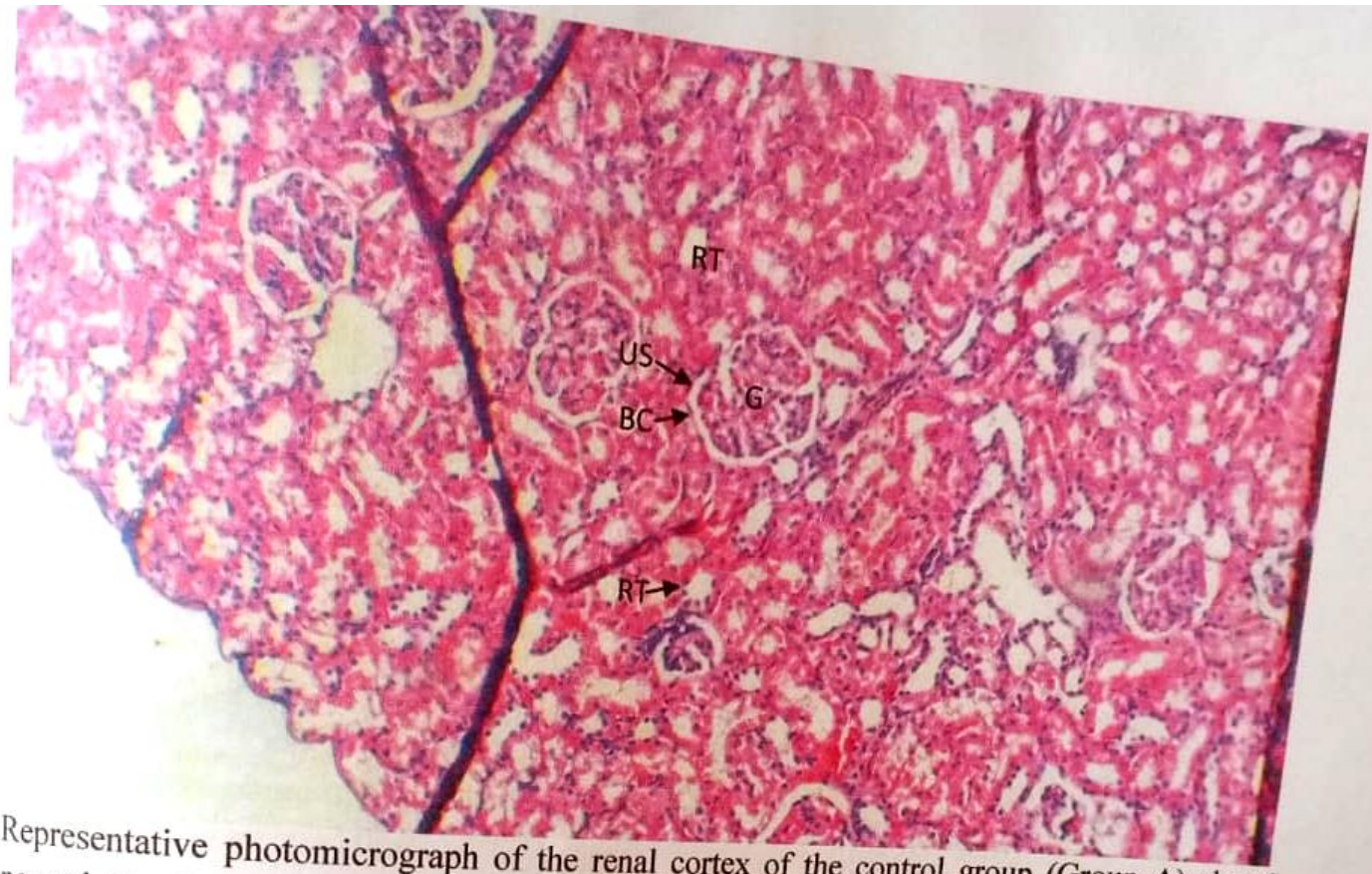
EXPLANATION

Result shows a statistically significant increase in the final weights of rats within each group when compared to their initial weight, thus, the extract significantly improved appetite.

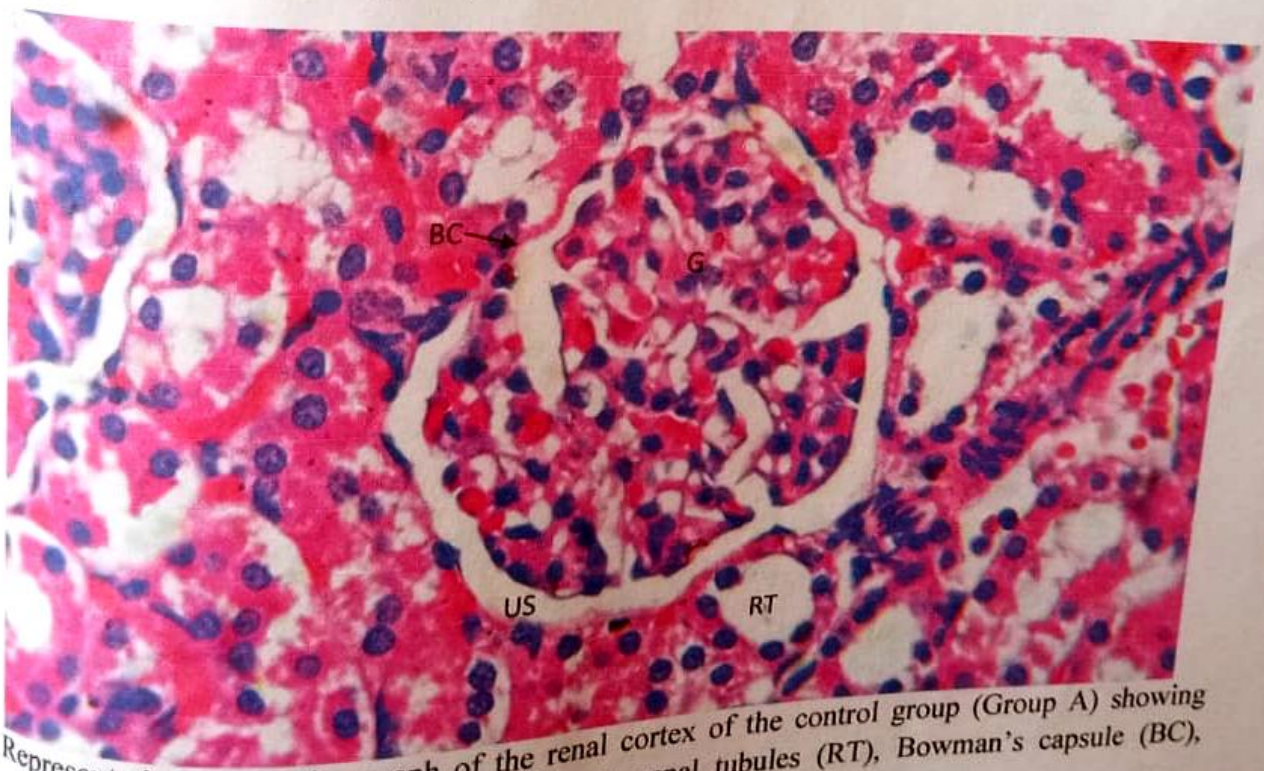
There was a statistically significant increase in urea levels for rats treated with 0.1ml and 0.3ml of *Dendropanax trifidus* when compared with control. Increased level of urea in the blood is considered an anomaly.

CONCLUSION

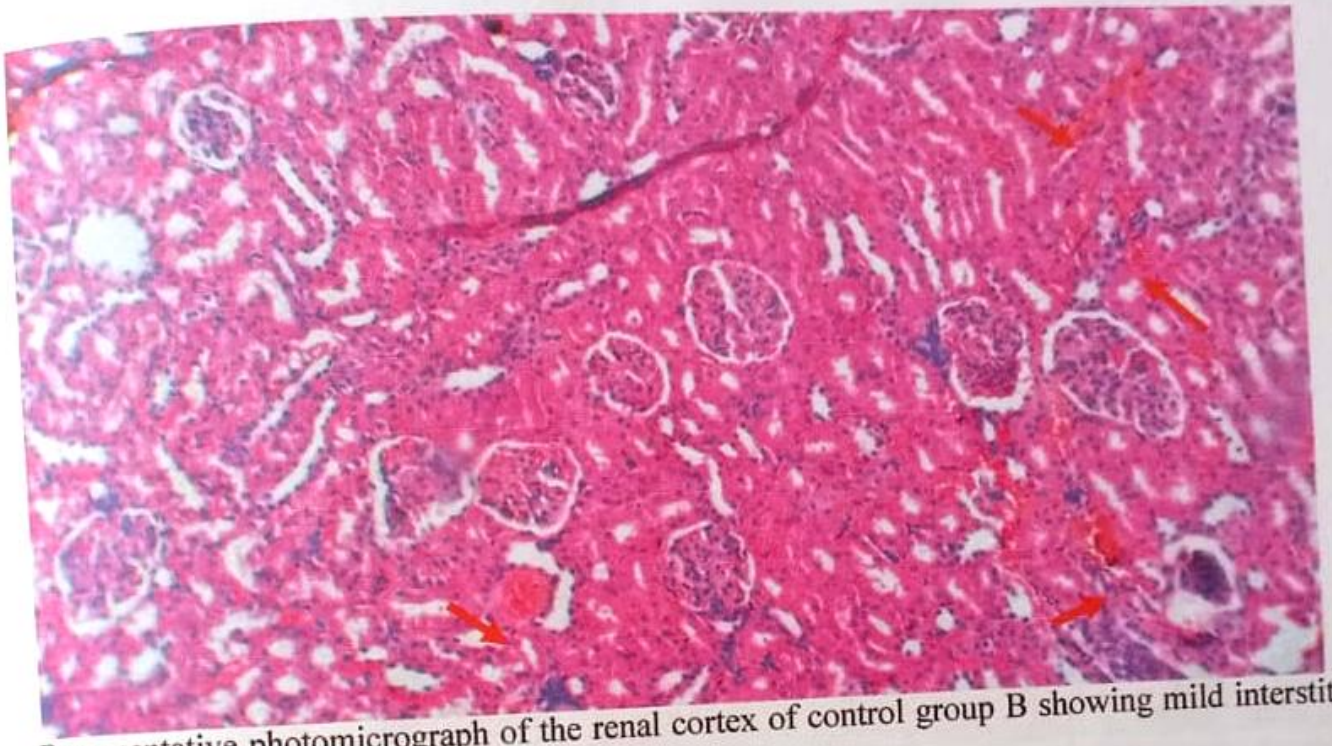
The findings from this study underscore the potential nephroprotective effects of Dendropanax trifidus on kidney function and morphology in Wistar rats. The administration of Dendropanax trifidus extract resulted in significant improvements in serum biomarkers associated with renal health, including reduced levels of creatinine and urea. Furthermore, histological examination is yet to be interpreted for more details or research.



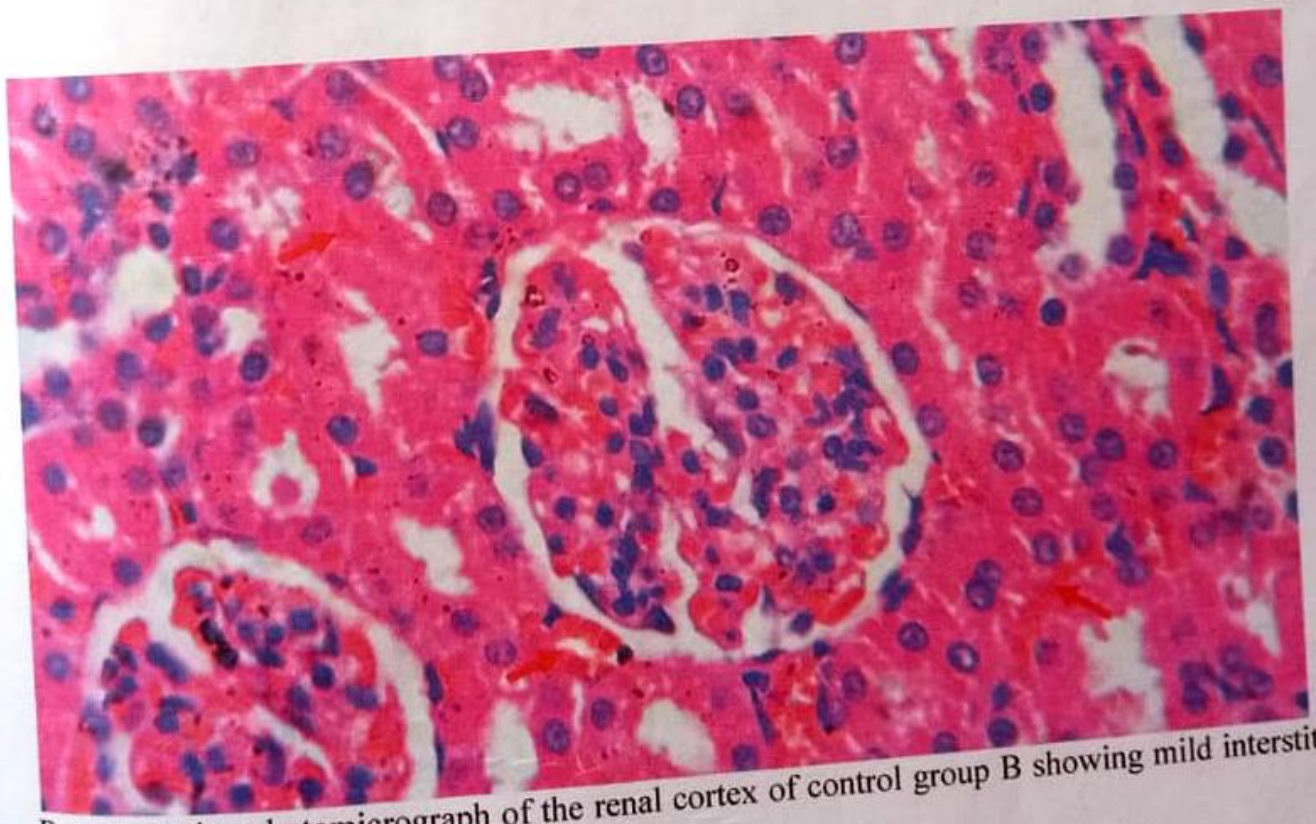
Representative photomicrograph of the renal cortex of the control group (Group A) showing normal histological features; glomerulus (G), renal tubules (RT), Bowman's capsule (BC), urinary space (US) (H&E; 100×)



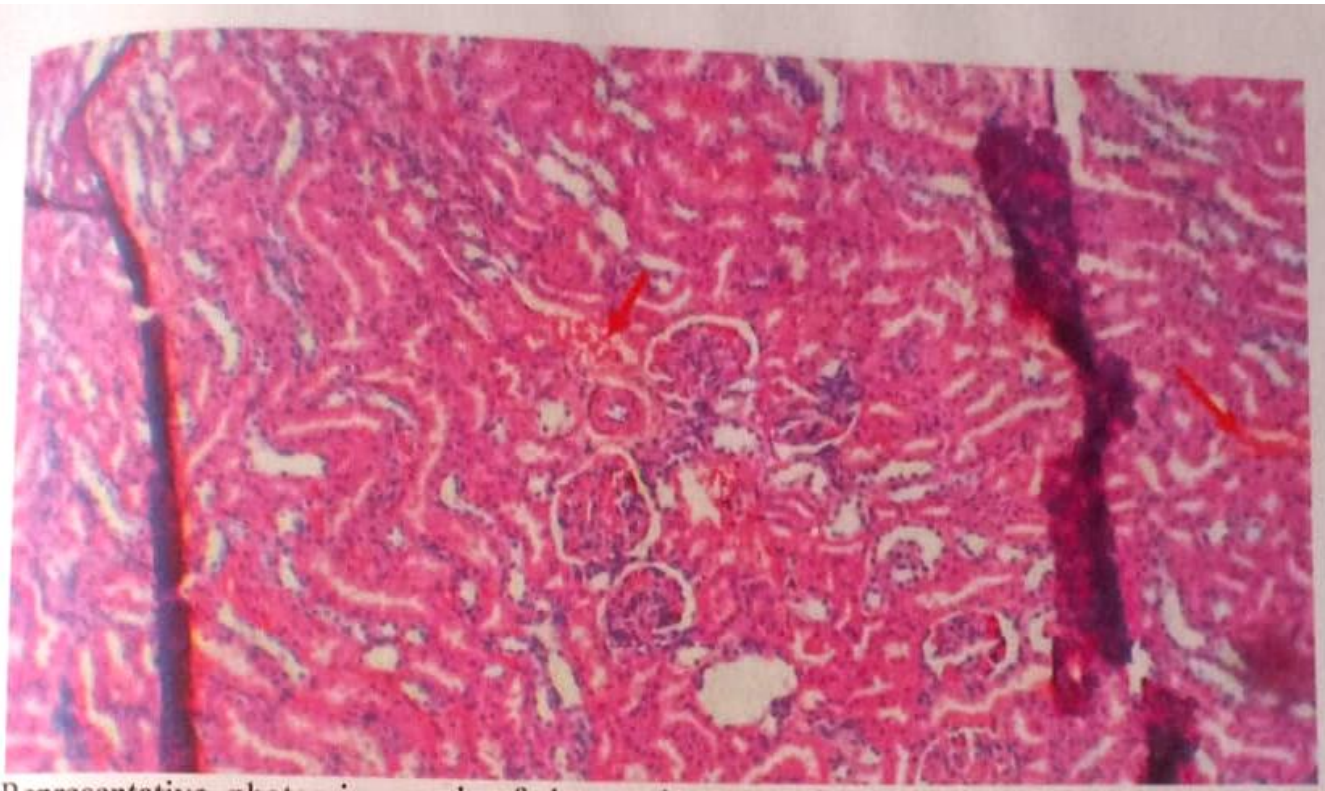
Representative photomicrograph of the renal cortex of the control group (Group A) showing normal histological features; glomerulus (G), renal tubules (RT), Bowman's capsule (BC), urinary space (US) (H&E; 400×)



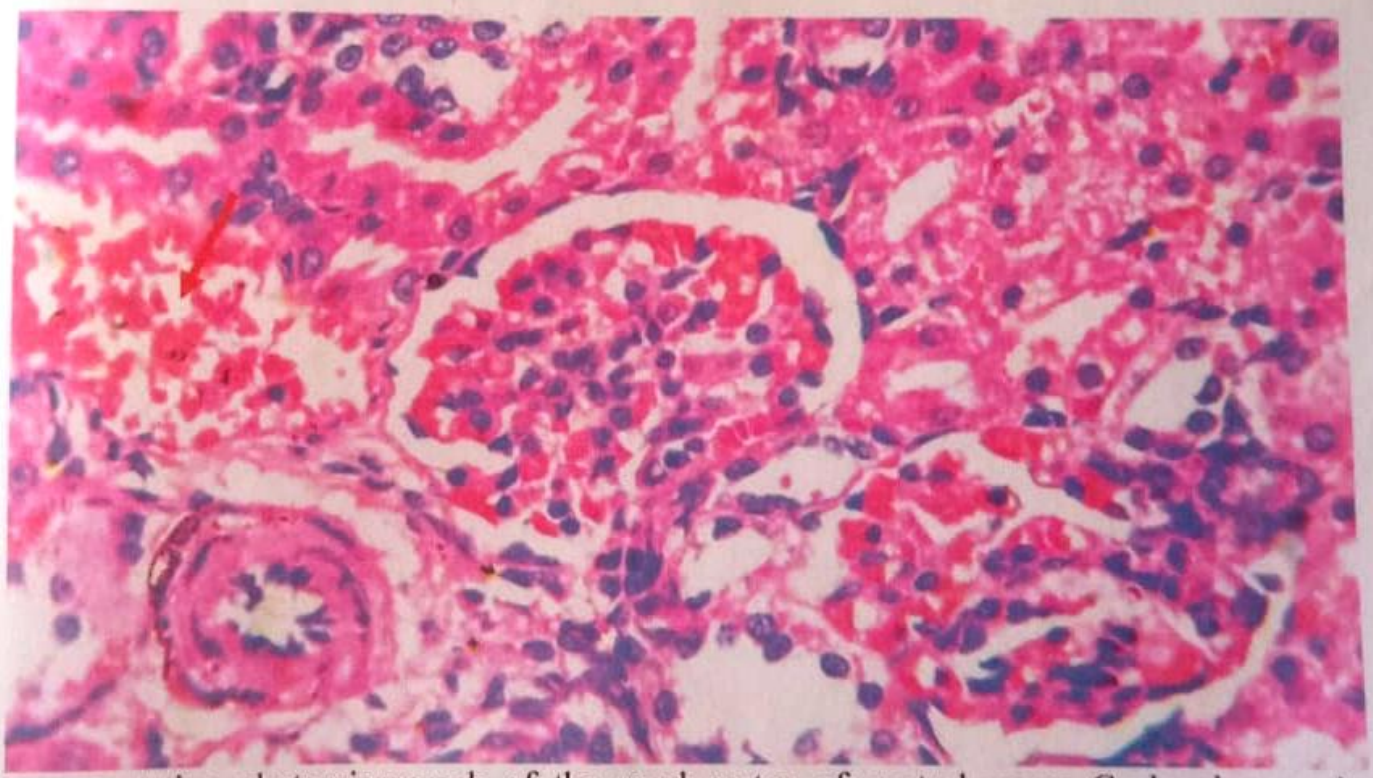
Representative photomicrograph of the renal cortex of control group B showing mild interstitial hyperemia (red arrows) (H&E; 100×)



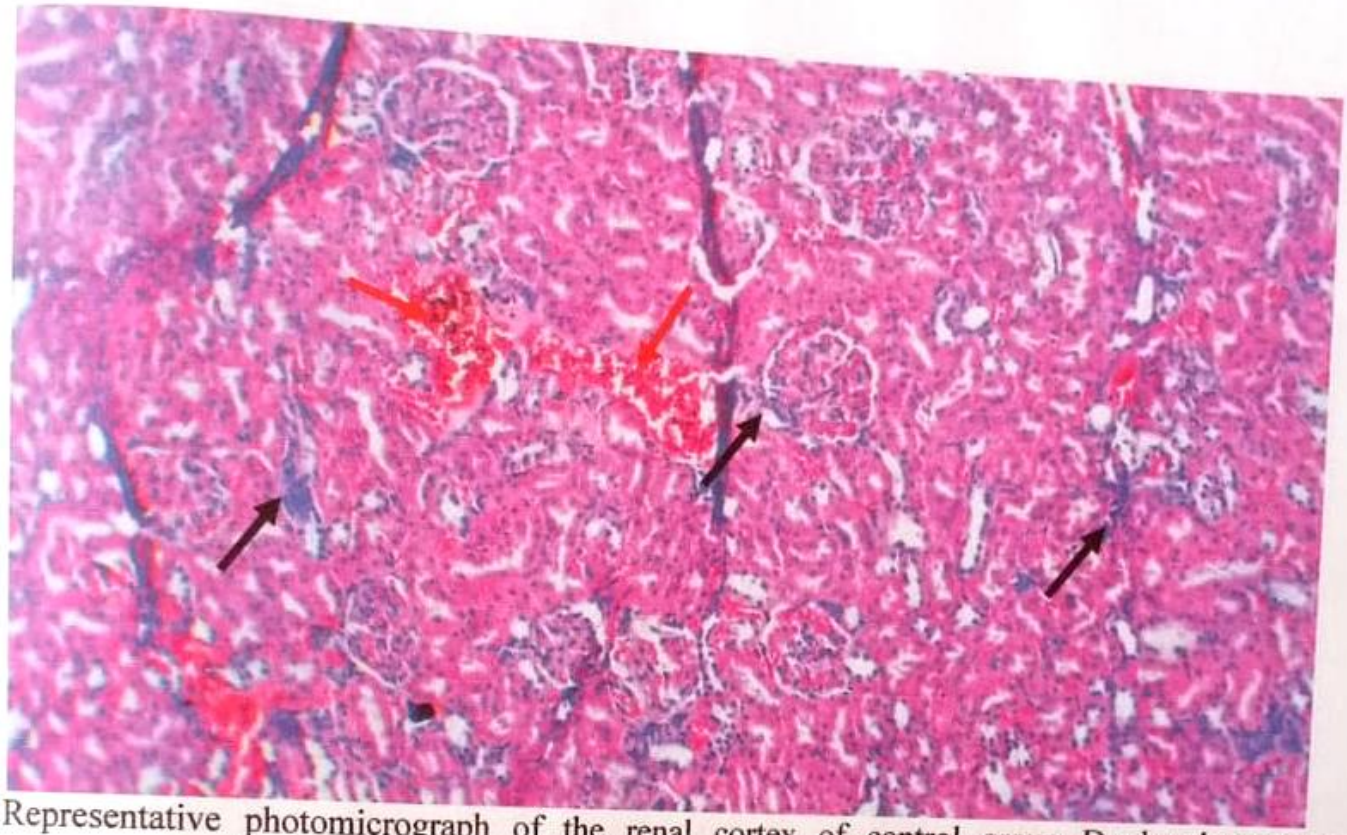
Representative photomicrograph of the renal cortex of control group B showing mild interstitial hyperemia (red arrows) (H&E; 400×)



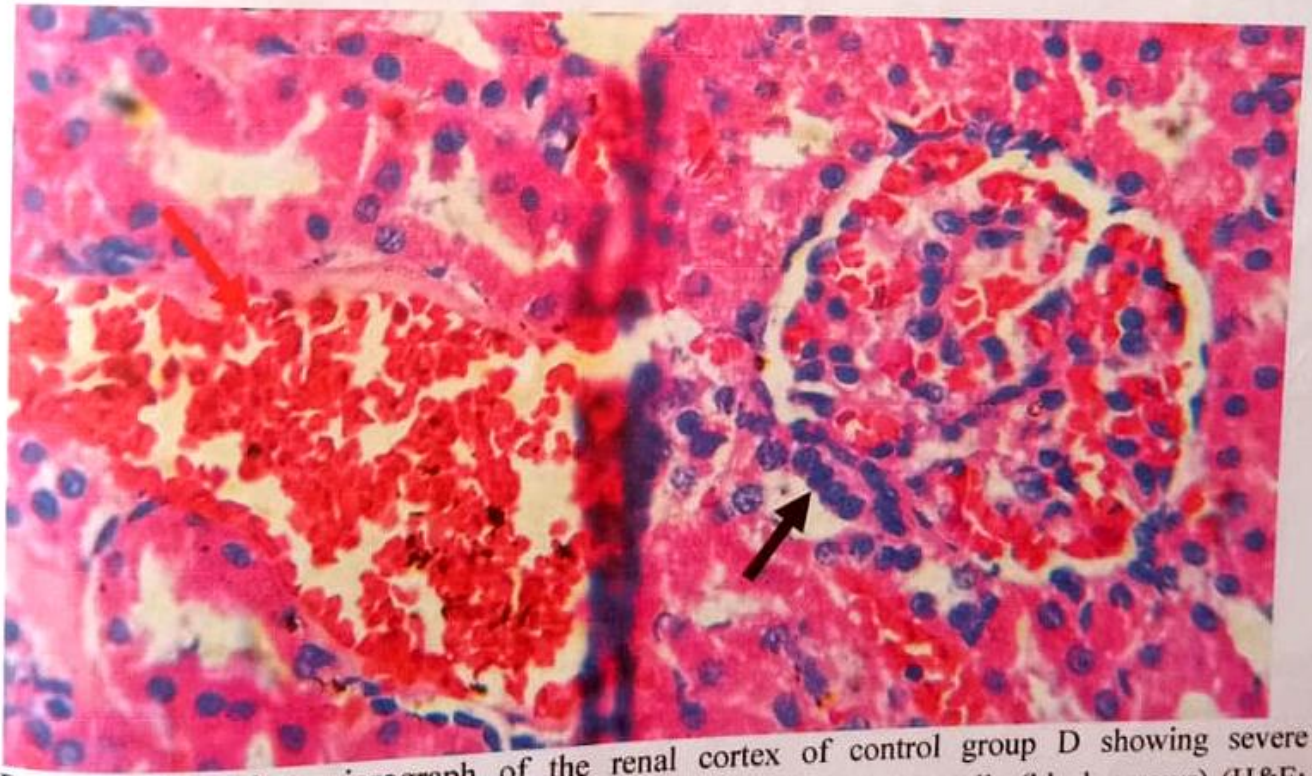
Representative photomicrograph of the renal cortex of control group C showing moderate interstitial hyperemia (red arrows) (H&E; 100×)



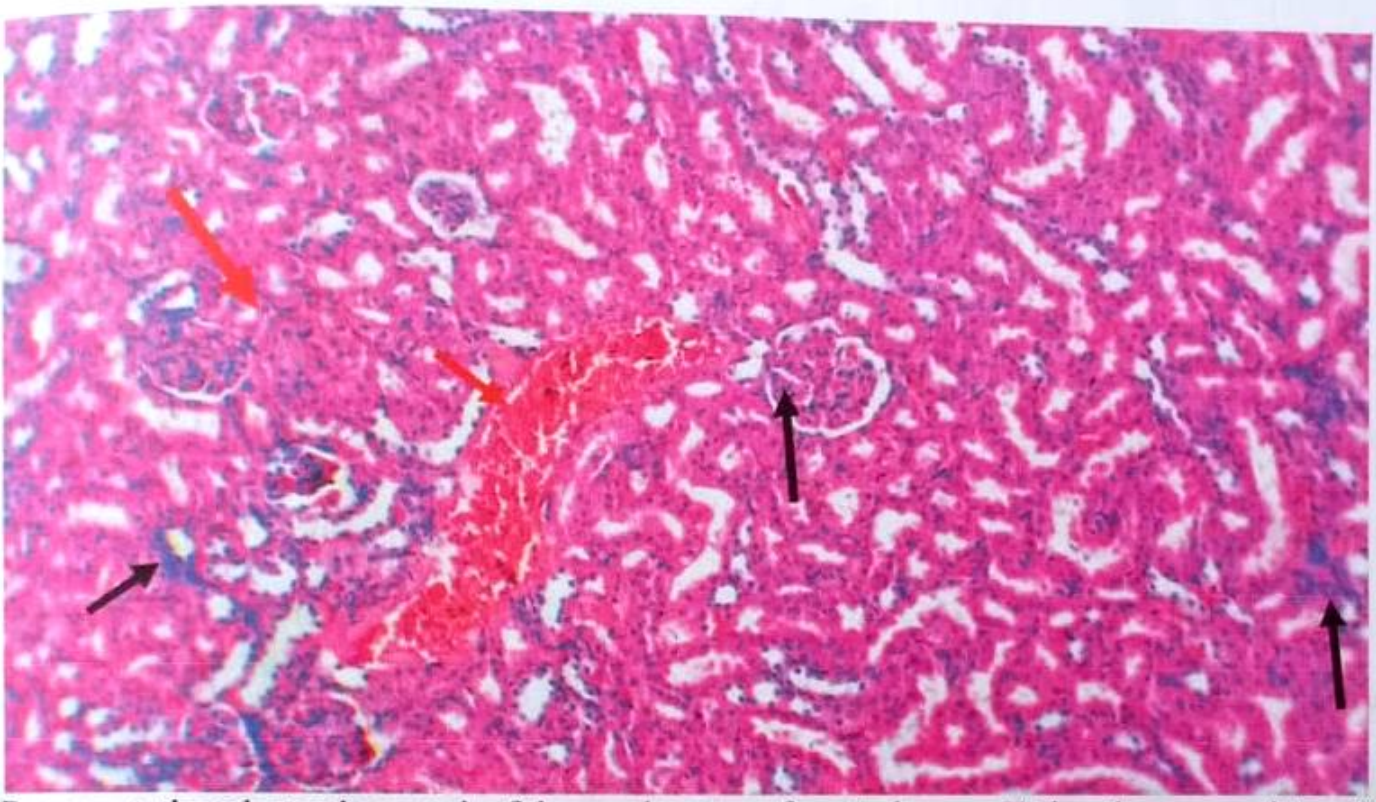
Representative photomicrograph of the renal cortex of control group C showing moderate interstitial hyperemia (red arrows) (H&E; 400×)



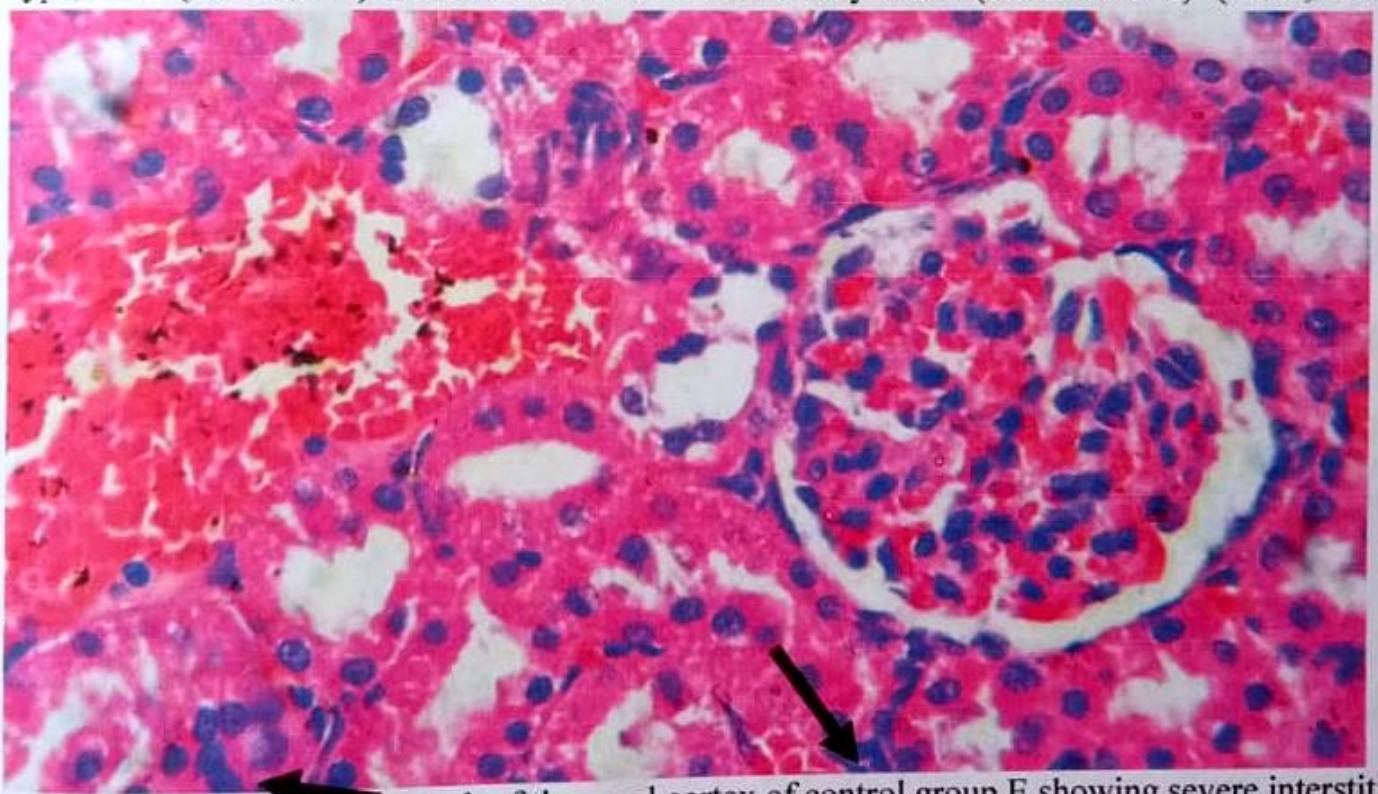
Representative photomicrograph of the renal cortex of control group D showing severe interstitial hyperemia (red arrows) and infiltrates of inflammatory cells (black arrows) (H&E; 100×)



Representative photomicrograph of the renal cortex of control group D showing severe interstitial hyperemia (red arrows) and infiltrates of inflammatory cells (black arrows) (H&E; 400×)



Representative photomicrograph of the renal cortex of control group E showing severe interstitial hyperemia (red arrows) and infiltrates of inflammatory cells (black arrows) (H&E; 100×)



Representative photomicrograph of the renal cortex of control group E showing severe interstitial hyperemia (red arrows) and infiltrates of inflammatory cells (black arrows) (H&E; 400×)

CHAPTER FIVE

DISCUSSION, CONCLUSION AND RECOMMENDATION

5.1 DISCUSSION

The study evaluates the renal effects of Dendropanax trifidus extract by analyzing weight changes, renal function biomarkers, electrolyte balance, and histopathological changes in treated rats. The results indicate a statistically significant increase in the final weights of rats across all treatment groups, suggesting that's the extract improved appetite, potentially due to its bioactive compounds enhancing metabolic activity or stimulating feeing behaviour. Appetite stimulation can be attributed to certain phytochemicals found in plant extracts that influence metabolic pathways, including polyphenols and flavonoids, which have been shown to regulate hunger related hormons such as ghrelin and leptin. Previous research on plant extracts with antioxidants properties support the role of bioactive compounds in appetite stimulation and metabolic enhancement (Boix-Castejo'n et al; 2023). However, excessive weight gain could also indicate fluids retention, which may suggest kidney dysfunction in some cases .When kidney function is impaired; the body may struggle to regulate fluid balance, leading to edema and weight gain due to fluid accumulation in tissues (Jones, 2024). Therefore, while the observed weight gain may suggest improved appetite.

Renal function was assessed through urea and creatinine levels, which are key biomarkers of kidney function and are widely used in clinical and experimental nephrology to determine renal efficiency. Urea, a byproduct of protein metabolism, is excreted by the kidneys through the glomerular filtration process. When kidney function is compromised, urea accumulates in the blood, leading to a condition known as UREMIA. The study observed a statistically significant increase in urea levels in rats treated with 0.1ml and 0.3ml of Dendropanax trifidus extract compared to controls. This increase suggests a reduced ability of the kidneys to filter out metabolic waste, potentially indicating nephrotoxicity or impaired renal function. Elevated urea levels can also be associated with increased protein breakdown or dehydration, further complicating the interpretation of the results. Similarly, creatinine, other crucial renal biomarkers is a waste product formed from muscle metabolism and excreted primarily through the kidneys. Increased creatinine levels in the treatment groups suggest a possible decline in glomerular filtration rate (GFR), indicating that the extract may be adversely affecting renal clearance mechanisms (Rewa and Bagshaw, 2014). These findings contrast with studies that demonstrate nephroprotective effects of other Dendropanax species. For instance, Sachan et al. (2020) found that Dendropanax morbifera extract improved renal function by reducing oxidative stress and inflammation. The discrepancy suggests that the specific phytochemical composition, dosage, or mode of administration plays a crucial role in renal outcomes. Differences in preparation methods, such as aqueous

versus ethanolic extracts,may also influence the bioavailabilty and toxicity profile of the plants active compounds.

Electrolyte balance was also examined, with disruption noted in sodium, potassium, bicarbonate and chloride levels. Electrolyte imbalances are critical indicators of kidney dysfunction as the kidneys play a crucial role in maintaining homeostasis by regulating the excretion and reabsorption of electrolytes. Sodium and potassium are essential for nerve function, muscle contraction, and fluid balance. The study found alternations in these ions, suggesting potential dysfunction in renal tubules, which are responsible for ion exchange and balance. Disruptions in sodium levels can contribute to hypertension and cardiovascular diseases, given that excess sodium retention can increase blood pressure by promoting fluid overload. Potassium homeostasis is equally critical, as hyperkalemia _an excess of potassium in the bloodstream _can lead to severe cardiac arrhythmias, muscle weakness and neuromuscular impairments (Crawford, 2014). The kidneys regulate potassium levels primarily through tubular secretion, and any impairment in this function could explain the observed imbalances. Additionally, changes in bicarbonate and chloride levels indicate potential acid-base disturbance. Bicarbonate is a key component of the body's buffering system, maintaining pH balance and preventing metabolic acidosis, a condition commonly observed in chronic kidney diseases (Nagami and Kraut, 2024). Reduced bicarbonate levels may suggest impaired renal acid-base

regulation, leading to acidosis, which can exacerbate kidney damage. These findings suggest that Dendropanax trifidus extract may interfere with normal electrolyte regulation, potentially increasing the risk of renal and cardiovascular complications.

Histological analysis of kidney tissue revealed progressive interstitial hyperemia and inflammatory infiltrates, particularly in higher -dose treatment groups. Hypermia which refers to increased blood flow to tissues is often associated with inflammation and can indicate early signs of tissue injury. The presence of inflammatory cell infiltrates further supports the possibility of nephrotoxicity, as inflammation is a hallmark of kidney damage caused by toxins, infections, or auto-immune conditions. The severity of histopathological changes appeared to be dose-dependent with higher doses of the extract inducing more pronounced hyperemia and inflammatory cell accumulation. Severe interstitial hyperemia and inflammatory cell infiltration in groups D and E suggest kidney inflammation, possibly indicating early nephrotoxicity.

Chronic inflammation in the renal cortex can contribute to progressive fibrosis, a condition that may lead to irreversible kidney damage over time. Similar histopathological changes have been observed in nephrotoxic models expose to heavy metals and plant toxins (Noguier et al; 2017).

However, previous studies on Dendropanax extracts have reported anti-inflammatory effects in other organ systems, suggesting that specific compounds

or dosages may determine toxicity outcomes (Akram et al;2016;Burhanu et al;2018;Balakrishnan et al; 2020). The discrepancy between anti-inflammatory and nephrotoxic effects in different studies may be due to variations in experimental conditions, including species differences, duration of exposures and bioactive compound interactions.

The observed nephrotoxicity suggests potential therapeutic interventions to mitigate renal damage. Increased hydration may help enhance renal clearance and reduce the accumulation of urea and creatinine (Abdelatif et al; 2010). Hydration is a fundamental approach to supporting kidney function, as it facilitates the excretion of metabolic waste and prevents the buildup of toxic substances (Abdelatif et al; 2010). Nephroprotective agents such as antioxidants like N-acetylcystenine and flavonoids may counteract oxidant stress - induced damage. Several studies have demonstrated that antioxidant supplementation can protect against renal injury by reducing inflammation and improving mitochodrial function (Brzos'ka et al; 2016; Khalaf and Salih, 2023). Dietary modifications, including reduced protein intake, may also help lower urea levels and ease the burden on the kidneys (Kramer, 2019). High protein diets can exacerbate kidney dysfunction by increasing nitrogenous waste production, further impairing renal clearance (Ko et al; 2020). In cases of significant electrolyte imbalances, pharmacological interventions such as diuretics or electrolyte supplement may be required to restore homeostasis. Diuretics can

help regulate sodium and potassium levels preventing fluid overload and reducing the risk of hypertension (Sok-Fun-Khow et al; 2014). Additionally, anti - inflammatory therapies, including corticosteroids or natural compounds like curcumin, could help alleviate renal inflammation and prevent the progression of kidney damage. Curcumin, a polyphenolic compounds derived from tumeric has been shown to modulate inflammatory pathways and protect against kidney fibrosis (Cai et al ; 2022).

5.2 CONCLUSION

This study highlights the potential nephrotoxic effects of Dendropanax trifidus extract at higher doses, as evidenced by increased urea and creatinine levels, electrolyte imbalances and histopathological alternations. While the extract appears to enhance appetite, its adverse effects on kidney function warrant caution. The findings suggest that prolonged or excessive use of the extract may lead to renal impairment.

5.3 RECOMMENDATION.

Further research on optimal dosges and long term effect of dendropanax trifidus on kidney health. Future studies should focus on elucidating the mechanisms underlying its nephrotoxic potential and exploring ways to harness its benefits while minimizing risks. Understanding the pharmacokinetics and toxicology of *Dendropanx trifidus* in detail will be essential for its potential therapeutic application, ensuring that its benefits outweigh its risks.

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