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Evaluation of the Effect of Ginger Zingiber Officinale Extract on Kidney of Albino Rat Administered with Graded Doses of Piroxicam

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A R T I C L E I N F O

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A B S T R A C T

Ginger or ginger root is the rhizome of the plant Zingiber officinale, commonly consumed as a delicacy, medicine, or spice. It is named after its genus and belongs to the Zingiberaceae family. Ginger is native to southern China and later spread to the Spice Islands, other parts of Asia, West Africa, and the Caribbean. This study aims to evaluate the effects of ginger Zingiber officinale extracts on the kidney when administered alongside graded doses of piroxicam. Fifty albino rats were used, divided into five (5) equal groups (A to E) of ten (10) rats each. Group A served as the control, while Group B received 2.7mg/kg of piroxicam. Group C was administered 400mg/kg of ginger, Group D received 2.7mg/kg of piroxicam and 100mg/kg of ginger, and Group E received 2.7mg/kg of piroxicam along with 400mg/kg of gingerData on weight changes were analyzed using ANOVA, with statistical significance set at $P < 0.05$. All results were expressed as Mean ± Standard Error of Mean (SEM) and presented in tables for statistical comparison. However, Group B (administered 2.7mg/kg of piroxicam) displayed signs of renal distortion, while Group C (administered 400mg/kg of ginger) showed adipose tissue formation. Groups D and E, which received both piroxicam and ginger at different doses, exhibited normal histological features. Further research is recommended to determine the precise effects of mild, moderate, and high doses of Zingiber officinale (ginger) on kidneys affected by varying levels of piroxicam

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INTRODUCTION

Ginger, scientifically known as Zingiber officinale, is the rhizome of a flowering plant widely utilized as a spice, culinary ingredient, and traditional medicine. It gives its name to the Zingiberaceae family, which also includes other notable spices such as turmeric, cardamom, and galangal. Despite sharing aromatic properties, ginger is not closely related to the plants commonly referred to as wild ginger (Asarum species); these are dicots in the Aristolochiaceae family and contain compounds like aristolochic acid, which can be harmful. (Ede et al., 2014). Native to southern China, ginger spread to the Spice Islands and other parts of Asia, eventually reaching West Africa and the Caribbean. It was introduced to Europe via India in the 1st century CE through the spice trade. The plant Ginger develops clusters of white and pink buds that open into yellow flowers. Valued for its beauty and ability to thrive in warm climates, it is commonly used in subtropical landscaping. This perennial plant grows up to a meter (3–4 feet) tall, with leafy stems that regenerate annually. Traditionally, its rhizome is harvested after the stalk withers, then processed by scalding or scraping to prevent sprouting. In some cultures, the aromatic perisperm of certain Zingiberaceae species is also utilized as a sweet treat, condiment, and sialogogue (Breyer-Brandwijk, 2002).

The kidneys are responsible for eliminating various waste products generated by metabolism, including nitrogenous wastes such as urea, which results from protein breakdown, and uric acid, a byproduct of nucleic acid metabolism. The kidneys also perform the function of urine formation. In mammals and certain birds, urine concentration is controlled by a countercurrent multiplication system. This mechanism relies on key nephron structures, including the hairpin-shaped tubules, water and ion permeability in the descending limb, water impermeability in the ascending limb, and active ion transport along most of the ascending limb. Additionally, countercurrent exchange through the blood vessels supplying the nephron is crucial for this process. Under normal plasma conditions, glucose is fully reabsorbed in the proximal tubule through the Na^+/glucose co-transporter. However, when plasma glucose exceeds 350 mg/dL, these transporters become saturated, leading to glucose excretion in the urine. Glucosuria can occur at plasma glucose levels around 160 mg/dL, serving as a key indicator of diabetes mellitus. Similarly, amino acids are reabsorbed in the proximal tubule through sodium-dependent transporters. Hartnup's disease, which is characterized by a deficiency in the tryptophan transporter, leads to pellagra (Ede et al., 2014).

LITERATURE RIVIEW

Ginger has been utilized for centuries for its anti-inflammatory properties and antioxidant effects (Terry et al., 2011). Toxic chemicals contribute to kidney damage through oxidative stress. Carbon tetrachloride (CCL4) is a widely recognized compound used to induce chemical injury (Brattin et al., 2005). In this study, we examined the impact of ginger aqueous extract, as it has been reported to enhance glomerular damage. The protective effect of ginger against oxidative stress in mice can be attributed to its antioxidant properties. Ginger is rich in vitamins A, B, C, and E, as well as magnesium and other trace elements, which function as antioxidants and help prevent tissue damage caused by toxicants (Terry et al., 2011). This research aimed to assess the effects of ginger (Zingiber officinale) extracts on the kidneys in mice treated with varying doses of piroxicam.

METHODOLOGY

Research Design

Fifty albino rats were divided into five groups, with one serving as a control and the others receiving different doses of piroxicam and ginger for 21 days. Weight changes were tracked, and after treatment, the rats were anesthetized for kidney collection and immunohistochemistry analysis. Data were analyzed using ANOVA ($P < 0.05$), with results expressed as Mean ± SEM in tables.

Geographical Description of the Study Area

The study was carried out at the Department of Histopathology, Ambrose Alli University, and the Irrua Specialist Teaching Hospital in Edo State, Nigeria. Edo State, situated in the south-south geopolitical zone, spans 17,450 sq. km with a population of 3.1 million and is located between longitude 06°04'E–06°43'E and latitude 05°44'N–07°34'N.

Experimental Animals/Housing Condition

Fifty adult albino rats (90g–130g) were obtained from the Animal Farm, Histopathology, Ekpoma, Edo State, and acclimated for two weeks in the experimental lab. They were housed in wire mesh cages with tripods to prevent fecal contamination and were given Growers' mash and water ad libitum. The study adhered to standard guidelines for laboratory animal care and use.

Animal Grouping and Study Duration

The animals were divided into five groups (A–E) of ten rats each and housed in five large cages. Group A served as the control, while Groups B–E were test groups. The entire study, including preliminary research, acclimatization, substance preparation, experimentation, and result evaluation, spanned five months.

Substance Administration

Group A (Control) received only normal feed (Growers' mash) and water. Group B was given 2.7mg/kg of piroxicam, while Group C received 400mg/kg of ginger. Group D was administered 2.7mg/kg of piroxicam along with 100mg/kg of ginger, and Group E received 2.7mg/kg of piroxicam combined with 400mg/kg of ginger.

Sample Collection and Analysis

Weights were recorded before and after acclimatization, then weekly, with averages documented. The kidney was collected under chloroform anesthesia and preserved in 10% formalin for immunohistochemical analysis. Growth performance and feed utilization were evaluated at the study's conclusion using the method described by Dada and Ikuerowo (2009).

Histological Processing and Staining Procedure

Tissues were processed using an automatic tissue processor according to standard protocols at Irrua Specialist Teaching Hospital. Samples fixed in 10% formalin were dehydrated with graded alcohols, cleared with xylene, and embedded in paraffin wax. Once solidified, they were sectioned at 5 nm using a rotary microtome. Sections were floated in a 55°C water bath, mounted on frosted slides, and attached using a hot plate. For staining, sections were deparaffinized, rehydrated through decreasing alcohol concentrations, and stained with hematoxylin (3–5 minutes). After differentiation in 1% acid alcohol and washing, eosin staining (10 minutes) was applied, followed by dehydration, clearing with xylene, and mounting. Prepared slides were examined under a light microscope, and photomicrographs were captured

RESULT AND DISCUSSION

Table 4.1 presents the baseline weight, post-acclimatization weight, and pre-sacrifice weight of both control and test subjects. The Mean ± SEM values for the control group were 247.00 ± 3.35 at baseline, 219 ± 9.36 after acclimatization, and 219 ± 6.40 before sacrifice. Statistical analysis showed no significant difference ($p < 0.05$) between any test group and the control.

Table 1. Comparison of Mean ± S.E of Different Stages of Weight Measurement in Groups and Control Group Using ANOVA.

Weight	**Group A (Control) (N=10)**	**Test group**				**F Valu**	**P valu**
		Group B (N=10)	**Group C (N=10)**	**Group D (N=10)**	**Group E (N=10)**		
Baseline Weight(gram)	247.00 ±3.35	244.00 ±1.63	244.00 ±1.63	241.00 ±1.80	241.00 ±1.80	1.370	0.2596
After Acclimatization(gram)	249.00 ±9.36	236.70 ±4.41	226.70 ±8.03	240.00 ±4.47	241.00 ±2.33	2.300	0.0782
Before Sacrifice(gram)	248.00 ±6.40	221.10 ±10.20	221.70 ±10.14	240.00 ±4.47	205.00 ±13.76	1.172	0.3399

*Means Statistically Significant (P<0.05)

H And E Staining Micrographs

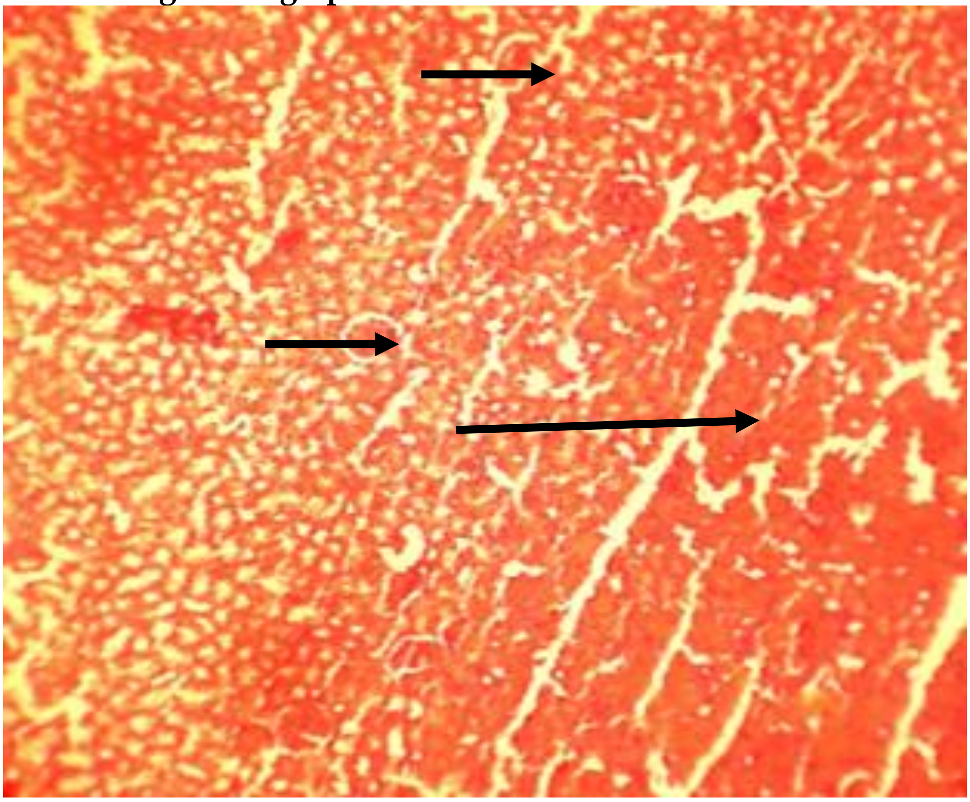

Fig 1. Group A (Control) Received Only Normal Feed (Growers' Mash) and Water Daily

Photomicrograph of Sections of the kidney of experimental animal showing normal renal corpuscle (long arrow) interstitial and tubules (short arrow). H &EX400 magnification

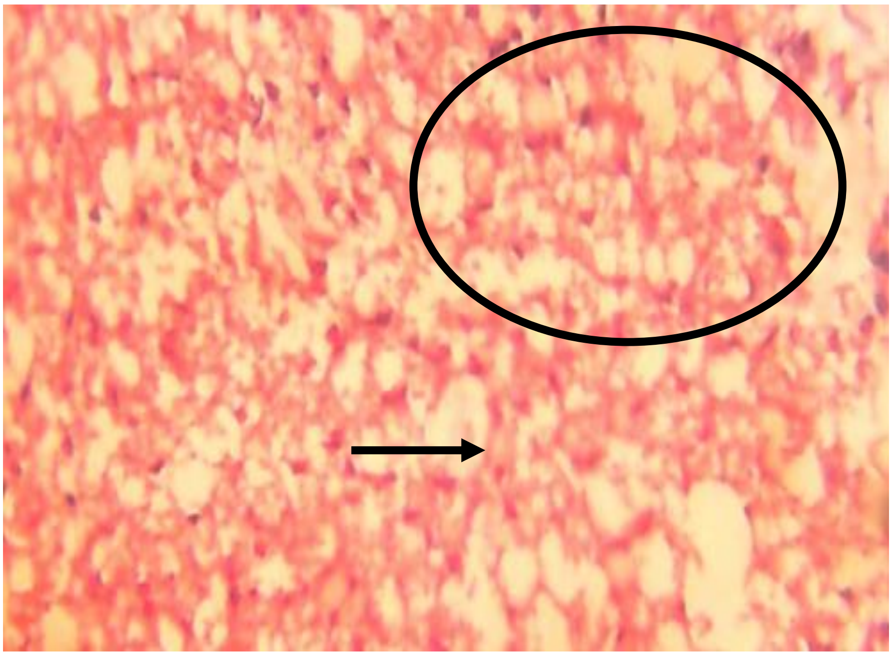

Fig 2. Group B were Administered 2.7mg/Kg of Peroxicam

Photomicrograph of Sections of the kidney of experimental animal showing renal tubules (short arrow) and renal distortion (circle) H &EX400 magnification

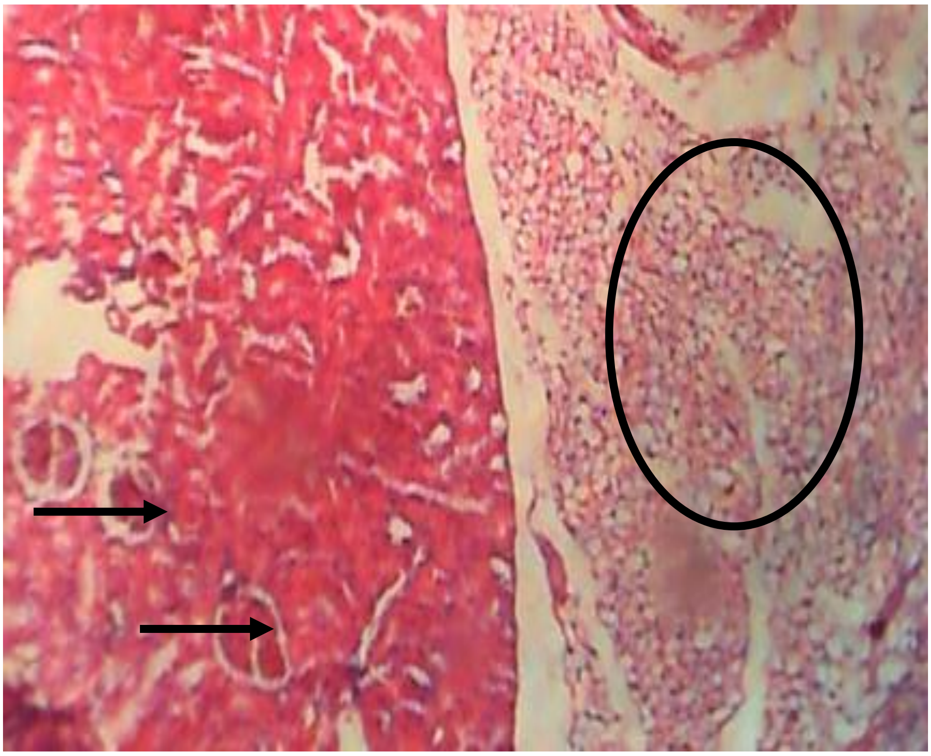

Fig 3. Group C were Administered 400mg/Kg of Ginger

Photomicrograph of Sections of the kidney of experimental animal showing renal tubules (short arrow) and adipose tissue Formation (circle) H &EX400 magnification

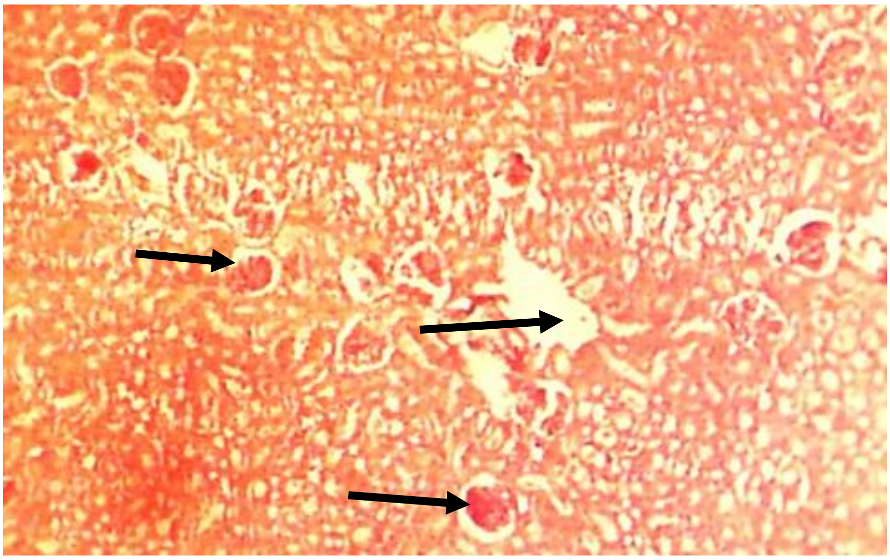

Fig 4. Group D were Administered 2.7mg/Kg of Peroxicam and 100mg/Kg Ginger

Photomicrograph of Sections of the kidney of experimental animal showing normal renal corpuscle (long arrow) normal interstitial and tubules (short arrow). H &EX400 magnification

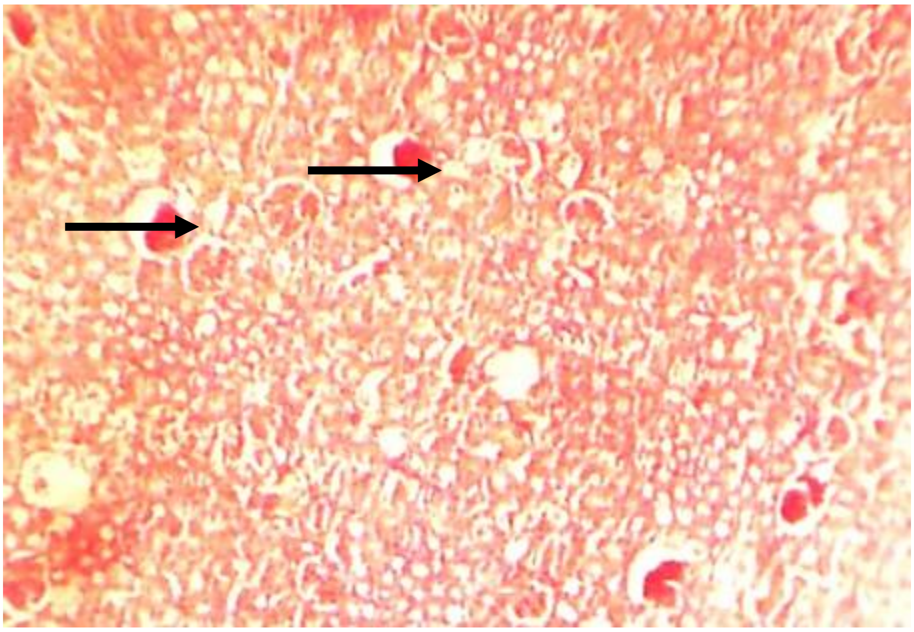

Fig 5. Group E were Administered 2.7mg/Kg of Peroxicam and 400mg/Kg Of Ginger.

Photomicrograph of Sections of the kidney of experimental animal showing normal interstitial and tubules (short arrow). H &EX400 magnification.

Ginger kidney protective effect has been of limited value as previous studies was not randomized with common drug toxicity. Piroxicam on the other hand, has a powerful prostaglandin inhibitor, it is effective and well-tolerated for treating primary dysmenorrhea. (Gabr et al., 2019). The aim of this study was to evaluate the effect of ginger (zingiber officinale) extracts on kidney administered with graded doses of piroxicam. The results of this study shows that there was no significant ($p<0.05$) difference in the body weight across all the groups. Therefore, the change in the body weight was not due to the administration of the substance but due the feed intake.

The result of Group A (Control) fed with only normal feed (growers' mash) and water daily showed a normal histological feature. Group B (administered 2.7mg/kg of peroxicam) showed evidence of renal distortion. These changes may have occurred because the concentration of the drug in the blood is influenced by capillary constriction, which reduces the glomerular filtration of the drug, thereby diminishing its effect and offering protection to the tubular cells (Stevens & Lowe, 2007). This may result in glomerular shrinkage and atrophy. At the same time, mesangial cell processes might retract due to filament contraction, possibly triggered by angiotensin II within these cells (El-Banhawy et al., 2004).

This could also be attributed to the edema in the proximal convoluted tubules, resulting in to their expansion and withdrawal of most microvilli, with some being destroyed. This may result from reducing the uptake of glomerular filtrate, which helps counteract the harmful effects of the drug. These findings align with those of Jackson and Lawrence (2008), who observed that administering either indomethacin or phenylbutazone resulted in papillary necrosis, tubular degeneration, and infiltration of inflammatory cells.

This result was in similarity with El-Banhawy et al., (2004), which showed tubular lesions were accompanied by inflammatory cell infiltration into the intertubular tissues. in an attempt to reduce the damage caused by piroxicam toxicity. Some of these external stressors likely contributed to the tubular lesions. In the current study, the various segments of the loop of Henle were less impacted by the piroxicam dose, indicating that the primary target of the drug may be the convoluted and collecting tubules. Similar findings were reported by El-Banhawy, et al., (2004).

Also in a similar report, Abrahams and Levinson observed damage to the epithelial lining of the collecting tubules in the kidneys of rats given excessive amounts of an analgesic mixture containing aspirin, phenacetin, and caffeine. Additionally, El-Banhawy et al. (2004) found significant damage to kidney cells and tissues in rats treated with the analgesic narcotic flunitrazepam. Numerous studies have reported significant changes within the ultrastructure of the cellular components of the proximal convoluted tubules due to treatment with various toxic substances (Trump & Bulger, 2008). After four weeks of treatment, hepatocytes appeared to be nearly normal.

Group C (administered 400mg/kg of ginger) showed evidence of adipose tissue formation and this was in contrast with Altman & Marcussen, (2001) as they found that ginger extract and ginger juice have anti-emetic properties that help reduce chemotherapy-induced nausea and vomiting in experimental animals. This aligns with the study by Haniadka et al. (2013), which reported that ginger functions as a free radical scavenger and antioxidant, preventing lipid peroxidation, and that these properties may contribute to its well-known gastroprotective effects. The changes observed in the current study may have been a result of enhanced effects due to prolonged administration of the dose.

The retention of water within hepatocytes led to edema, which may have resulted from a reduction in the energy required for regulating cellular ion concentration, as indicated by Yukiko et al. NSAIDs are widely recognized for their potential to induce hepatic injury (Lapeyre-Mestre et al., 2006; Hargus et al., 2005). Furthermore, the disease-related changes may impair liver function, disrupting the secretion of plasma proteins (Lapeyre-Mestre et al., 2006). This leads to a reduction in blood osmotic pressure, leading to reduced removal of tissue fluids, which accounts for the edema and blockage noted in various tissues (Zhang & Wang, 2004).

Also, Group D (administered 2.7mg/kg of peroxicam and 100mg/kg ginger) and Group E (administered 2.7mg/kg of peroxicam and 400mg/kg of ginger) also all showed normal histological features. This could be due to the fact that on combination of this drugs, reduced to side effects of each of the substances.

CONCLUSIONS AND RECOMMENDATIONS

This study found that while piroxicam alone caused renal damage, combining it with ginger helped preserve normal kidney structure. No significant weight changes were observed, indicating that feed intake, not drug administration, influenced body weight. The results suggest that ginger may have a protective effect against piroxicam-induced kidney toxicity, highlighting its potential as a natural therapeutic agent for reducing NSAID-related side effects.

Based on the Histological Findings Observed in the Current Study, it may be Concluded that;

- There is need for further study to determine accurately the effect of introduction of mild, moderate and high dosage of Zingiber officinale (ginger) on kidney already induced with varying doses of Piroxicam.

FURTHER STUDY

This study still has a delay, so it is necessary to conduct further research on the topic of Evaluation of the Effect of Ginger Zingiber Officinale Extract on Kidney of Albino Rat Administered with Graded Doses of Piroxicam to improve this study and add insight for readers

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