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# THERAPEUTIC PROPERTIES OF FICUS EXASPERATA EXTREACT ON GENTAMICIN INDUCED KIDNEY DAMAGE

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## ABSTRACT

**Background/Introduction:** Drug induced kidney toxicity is on the increase globally and account for high mortality rate resulting from kidney failure. This study was designed to ascertain the therapeutic properties of *ficus exasperata* on gentamicin mediated renal damage of adult male wistar rats. **Methods and Materials**: Twenty five (25) wistar rats weighing (140-230g) were randomly divided into five groups of five rats each. Group I received distilled water, group II was administered with gentamicin intraperitoneally for 14 days. Rats in group III was administered daily with aqueous extract of ficus exasperata (100 mg/kg) for 14 days. Rats in group V and VI were administered with 50mg/kg of gentamicin for 7 days and aqueous extract of ficus exasperata (100mg/kg and 200 mg/kg respectively) for next 7 days. The animals were weighed and sacrificed a day after the last administration, the kidney was isolated and fixed for histological examination. Blood samples was collected for biochemical analysis of Serum Urea and Creatinine Level. Data obtained from this study were analyzed using SPSS with one way ANOVA and P value less than 0.05 was considered statistically significant. **Result:** There was significant loss in body weight of wistar rats in group B administered with gentamicin when compared to normal control (group A) and groups administered with the extract. There was significant increase in the serum creatinine and urea levels in group administered with only gentamicin, this was however attenuated by administration of ficus exasperata. The microanatomy of the kidney administered with gentamicin was characterized by mild focal tubulointerstitial lymphocytic inflammation and destruction of renal tubules, the normal control and the group administered with ficus exasperata showed a normal histology of the kidney with normal glomeruli (arrows) surrounded by renal tubules and a well distinct basal membrane. **Conclusion:** Our findings indicates that *Ficus exasperata* reduces the amount of gentamicin that builds up in kidney tissue and mitigates the negative impact that gentamicin has on renal tubular function.**.** This suggest that *ficus exasperata* contain therapeutic properties against gentamicin induced kidney toxicity, which may be due to it's anti-oxidative proprieties.

**KEYWORDS:** *Gentamicin, Ficus exasperata, Nephrotoxicity, Serum creatinine and Urea levels.*

## 1. INTRODUCTION

Nephrotoxins are harmful substances like drugs, chemicals that can cause toxicity to the structure of the kidney.[1] The kidney is principally involved in removing waste products and drugs from the body and as such it is a primary target for drug induced nephrotoxicity.[2,3] Kidney damage has become a major health challenge globally and it is increasingly becoming a major occurrence in Africa and Nigeria in particular.[4,5] The exposure of the kidney to harmful substances, toxins and drugs results in impaired kidney-specific detoxification and excretion.[6] Numerous prescription and over-the-counter drugs are administered to patients. Sadly, both acute and chronic kidney injury are still frequently brought on by drug use.[7] These medications can cause a variety of kidney lesions, most notably tubular-limited dysfunction, glomerular injury with proteinuria, fully developed acute kidney injury, and long-term chronic kidney injury.[8]

Drugs cause about 20% of nephrotoxicity, but as the average life expectancy rises, elderly patients' medication causes up to 66% more nephrotoxicity. Nephrotoxicity has limited the use of chemotherapy and anticancer drugs.[9-11] For the treatment of severe gram-positive and gram-negative bacterial infections, gentamicin (GNT), an

aminoglycoside antibiotic, is used. The nephrotoxic side effect is one of the main therapeutic restrictions, despite the drug's potent antibacterial properties.[12] The nephrotoxicity brought on by Gentamicin is a complex issue involving numerous pathways, including the decrease in renal blood flow, oxidative stress, inflammation, lipid peroxidation, apoptosis, and more.[13]

Due to the challenges and high cost of treating and managing kidney damage related health conditions, there is a great need to study the efficacy of medicinal plant in mitigating against adverse effect of drugs and related chemicals on the kidney. Ficus exasperata commonly called sand paper leaf is a plant belonging to the fig family and found in most tropical regions across Africa and commonly used in managing various diseases in Nigeria. In traditional medicine different parts of *Ficus exasperata* are used as analgesic, anti-arthritic, diuretic, wound healing, anti-parasitic, vermifuge and for treatment of hemorrhoids and venereal diseases and this is attributed to high alkaloids properties. Aqueous extract of Fiscus exasperata leaf has been reported to exhibit high anti-oxidant effect, which is attributed to its high level of alkaloids content.[14-15] This work was designed to study the therapeutics proprieties of ficus exasperata on gentamicin induced nephrotoxicity using Wistar rats.

## 2.1 MATERIALS AND METHODOLOGY

### 2.2. PLANT COLLECTION

*ficus exasperata leaves* were obtained from University of Nigeria Enugu Environs and taken to the Department of Plant Science and Biotechnology, University of Nigeria, Nsukka for identification.

### 2.3. FICUS EXASPERATA EXTRACTION

Ficus exasperata leaves were rinsed in clean water and allowed to air dry in the laboratory at room temperature. The air-dried leaves were then chopped into a fine powder in an electric blender. The fine powder was subsequently immersed in 2 liters of distilled water for 24 hours, filtered through Whatman No. 1 filter paper (150 mm), and evaporated at 50 degrees Celsius to derive a crude extract of Ficus exasperate. Crude extract residue was measured and dissolved in distilled water for use on every single day of the experiment; 10g of crude extract was dissolved in 100ml of normal saline in order to produce the stock solution used for daily administration.

### 2.4. ANIMAL PROCUREMENT

Twenty five (25) adult male wistar rats weighing 140g-230g were purchased from the animal house of the department of Pharmacology and Toxicology, University of Nigeria, Nsukka. The rats were housed in aluminum cage, placed in a well-ventilated environment in the animal house of the Department of Anatomy, University of Nigeria, Enugu campus. The animals were acclimatized for two weeks before the commencement of the experiment and they were allowed free access to clean water and standard livestock pellets. This work was carried out in accordance with the principles of laboratory animal care and standard procedure for experiment.

### 2.5. CHEMICAL AND DRUGS

Laboratory reagents and Gentamicin, all of analytical standard were purchased from pharmacy and chemical outlet located in Enugu State, Nigeria.

### 2.6. ETHICAL CONSIDERATION

The U.S. National Institutes of Health's (NIH) Institutional Animal Ethics Committee (IAEC) rules for the care and use of laboratory animals were followed in the study, which was approved by the committee. The study was conducted at the University of Nigeria, Enugu Campus and was approved by the college of medicine research ethics committee.

### 2.7. EXERIMENTAL DESIGN

The wistar rats were randomly divided into five groups of five (5) rats each. The rats in group (I) served as control group and received normal saline for 14 days, Group II was administered gentamicin (100mg/kg) intraperitoneally for 14 day; Group III was administered daily with aqueous extract of ficus exasperata orally for 14 days (100mg/kg) Group V and VI wistar rats received Gentamicin (100mg/kg) intraperitoneally for 7 days and aqueous extract of ficus exasperata (100mg/kg and 200mg/kg) for the next 7 days.

**Table 1: Showing Experimental Grouping And Administration.**

| GROUP | ADMINISTRATION |
|---|---|
| I | 0.5ml Normal saline for 14 days |
| II | 100mg/kg of Gentamicin for 14days |
| III | Administration of 100mg/Kg of FEE for 14days |
| IV | Administration with 100mg/kg of Gentamicin for 7 days and 100mg/kg of FEE for the next 7 days |
| V | Administration with 100mg/kg of Gentamicin for 7 days and 200mg/kg of FEE for the next 7 days |

*FEE- *Ficus exasperata*

### 2.8. BODY WEIGHT MEASUREMENT

Using a digital weighing scale, the rat's initial body weight was measured and recorded to the nearest gram on Day one (1) and Day fifteen (15).

### 2.9. ANIMAL SACRIFICE

On day 15, after completion of administration period. The rats were sacrificed by cervical dislocation. The kidney was isolated, fixed in 10% formaldehyde solution and taken to laboratory for routine histological investigation. Blood was collected through cardiac puncture and emptied into a tube. The collected blood sample was allowed to clot for about 2 hours and there after centrifuge for 10 minutes to separate the serum from the blood cells. Serum samples were taken to a

standard lab for laboratory analysis to determine the serum creatinine and urea level and measurement recorded in mg/dl.

**2.10. HISTOLOGICAL EXAMINATION**

Histological examinations of the kidney were carried out according to routine histological method. Kidney tissues from all groups were fixed in a 10% formaldehyde solution in phosphate buffer before being processed with paraffin wax embedding medium. Rotator microtomes were used to slice tissue blocks into sections, which were then stained with routine H&E stain for histological analysis.

**2.11. DATA ANALYSIS**

Data obtained from this study was analyzed using SPSS (v20) and value expressed as mean ±Standard Deviation of mean. Statistical difference in mean between groups was analyzed using one way ANOVA (Analysis of variance) and P-value less than 0.05 was considered as statistically significant.

**3.0. RESULT**

**Table 2: Mean And Standard Deviation Of Body Weight And Change In Body Weight.**

| GROUPS | MEAN WEIGHT DAY ONE | MEAN WEIGHT AT DAY FOURTEEN | MEAN DIFFERENCE ± STANDARD DEVIATION |
|---|---|---|---|
| **I** | 144.6 | 181.1 | 36.4 ± 18.1 |
| **II** | 189.8 | 163.2 | -26.6 ± 28.2a |
| **III** | 170.4 | 197.1 | 26.6 ± 3.7[ab] |
| **IV** | 167.6 | 167.9 | -0.4 ± 14.5[ab] |
| **V** | 174.8 | 178.4 | 3.6 ± 4.2[ab] |

Values expressed as mean ±SD, n=4, P value ≤ 0.05
a- Significant when compared with normal control.
b-Significant when compared with negative control.

As shown in table 2, there was significant increase in weight (36.4± 18.1) in the normal control group (I) while group (II) treated with only 100mg/kg of gentamicin showed significant reduction in weight with -26.6±28. Group III that received aqueous extract of ficus exasperata showed a significant increase in weight.

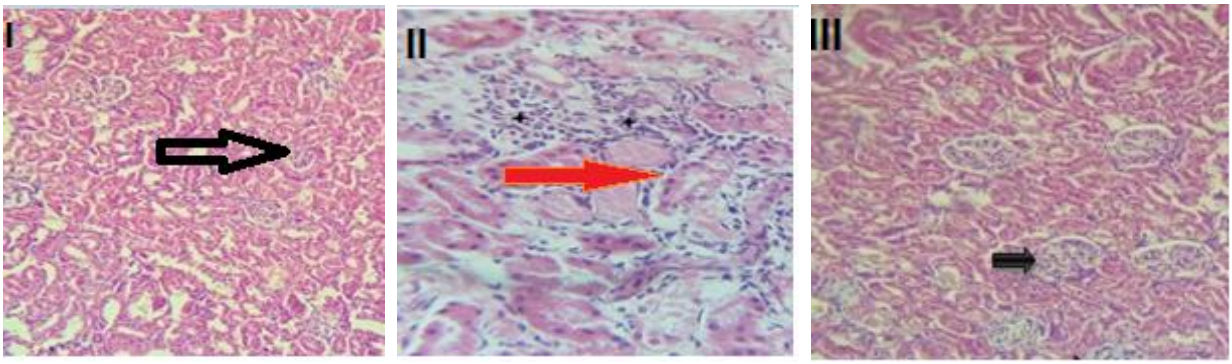
**RESULT OF BIOCHEMICAL ANALYSIS**

**Table 3: Showing Mean Value for Serum Creatinine, Urea Level.**

| GROUPS | SERUM CREATNINE LEVEL | UREA LEVEL |
|---|---|---|
| I | 1.5±0.1[b] | 18.0±2.5[b] |
| II | 2.7±0.2 [a] | 124.4±9.6[a] |
| III | 1.5±0.1 [b] | 19.8±8.5[b] |
| IV | 2.1±0.2[ab] | 54.8±25.3[ab] |
| V | 1.4±0.2 [b] | 54.0±46.7[ab] |

Values expressed as mean ± SD, P value ≤ 0.05
a- Significant when compared with normal control.
b- Significant when compared with negative control.

**3.1: HISTOLOGICAL RESULT.**



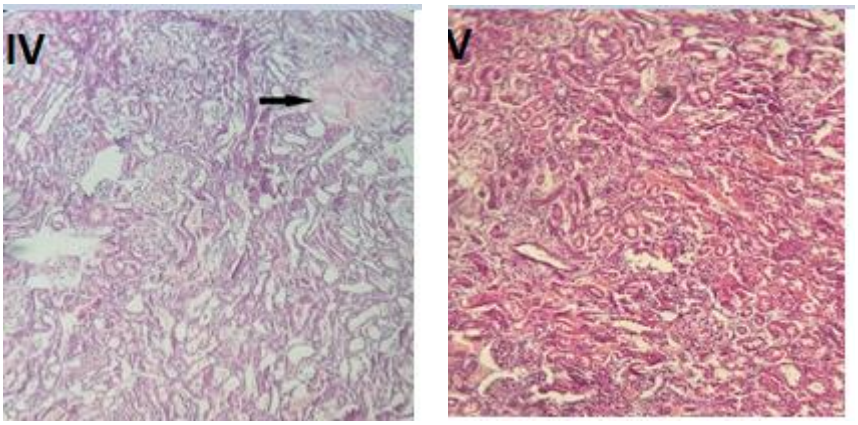



**Figure 1: Photomicrograph of kidney of Wistar rat in group I-V.**

**Stain: H& E**

**I:** showing normal kidney with normal glomeruli (Black arrow). **II**: showing mild focal tubulointerstitial lymphocytic inflammation and destruction of renal tubules. (red arrow**) III:** showing Normal kidney with normal glomeruli (arrows) surrounded by renal tubules and interstitium and a well distinct basal membrane. **IV:** showing focus of tubular necrosis (arrow) and Normal glomerulus**. V:** showing normal kidney with normal glomeruli surrounded by renal tubules and interstitium Mg×100.

## 4.0. DISCUSSION

The aim of this study is to determine the therapeutics effect of ficus exasperata extract on gentamicin induced kidney damage. Medicinal plant and herbs provide an affordable and readily available alternate source of remedy in healthcare management. *Ficus exasperata* have very rich alkaloids content and have been documented to have properties capable of ameliorating oxidative stress induced tissue injury.[14,15] Nephrotoxicity is defined as a sharp decline in kidney function due to the toxic effects of drugs and chemicals.[1]

Most drug induced nephrotoxicity occur as a result of several mechanisms, including renal tubular toxicity, inflammation, glomerular damage, crystal nephropathy, and thrombotic microangiopathy. From the result of body weight, it was noted that gentamicin significantly reduced the body weight of wistar rats in the group administered gentamicin only when compared to the normal control group. This is similar to reported studies by.[16-17] However there was a significant weight gain in the groups that received extract only. This showed that aqueous extract of *Ficus exasperata* have no negative effect on body weight of wistar rats. This findings is similar with the study by[18] which reported that administration of ethanol extract of *Ficus exasperata* resulted in an increase in body weight. There was little loss of weight in group IV exposed to gentamicin and treated with 100mg/kg of the extract, and in the high dose of 200mg/kg there was slight right gain, showing that at high dose of the extract may cause a positive impact on weight gain.

Blood urea and serum creatinine are the traditional markers to test for nephrotoxicity and renal dysfunction.[1,19] In our study, serum urea and creatinine levels in the Gentamicin-treated rats increased abnormally and significantly ($P < .05$) compared to the normal control group.

The kidneys actively secrete creatinine, a by-product of muscle metabolism, which is then excreted unchanged. If kidney filtration capacity is inadequate, its blood level rises, indicating significant nephron damage. Our results regarding creatinine levels corroborate prior research that demonstrated a link between elevated creatinine concentration and gentamicin toxicity. As a waste product of protein metabolism, urea is produced by the liver during the urea cycle and is then transported and eliminated by the kidney as a component of urine. It serves as a sensitive biomarker for evaluating renal tissue damage.[21] As a result, urea is retained in renal tissue injury. Nephritis, renal ischemia, urinary tract obstruction, and extrarenal diseases are all linked to increased urea levels. The results of this study show that the gentamicin-induced rise in serum urea and creatinine levels is consistent with the results of.[21, 22, 23]

Rats administered with Ficus *exasperata* (100 mg/kg and 2000 mg/kg) after receiving gentamicin showed reduced nephrotoxicity injury as evidenced by decreasing serum urea and creatinine levels. Oxidative stress and tissue damage as result of oxidative stress have been implicated as one of the mechanism by which gentamicin induced kidney injury characterized by tubular necrosis. Creatinine and urea level reduction by *Ficus exasperata* might be attributed it's high antioxidant properties.

The Histological examination of the kidney showed normal histology of the kidney in the normal control group, with kidney microanatomy showing normal glomeruli, proper distinct basal membrane, renal tubules clearly seen and appear to be normal. However in the gentamicin only treated rats, the microanatomy showed an abnormal histology of the kidney characterized by mild focal tubulointerstitial lymphocytic inflammation and destruction of glomeruli and destruction of renal tubules. This findings as previously reported by.[20, 21, 23]

Which reported that gentamicin is capable of destroying the of the kidney histoarchitecture via inflammation and redox pathways.

The histology of the kidney in the groups administered with ficus *exasperata* extract only (III) and group (IV and V) co-treated with ficus *exasperata* extract after gentamicin exposure, the kidney histology showed a normal kidney with normal glomeruli surrounded by renal tubules and interstitium and a well distinct basal membrane. However there as mild sign of tubular necrosis and normal glomeruli seen in the group (IV) that was administered with 100mg/kg of ficus *exasperata* extract after gentamicin exposure, while there was a noticeable improvement in the microanatomy of the kidney in group (V) treated with 200mg/kg of ficus *exasperata* extract compard with the 100mg/kg treated group. This implies that higher dose of extract possess curative ability on the histology of kidney toxicity, this curative abilities of the extract can be attributed to the high antioxidant effect and also the higher concentration of alkaloids that help restore the kidney histology to normal as reported by.[24,25]

## 5.0. CONCLUSION

In conclusion ficus *exasperata* exhibited therapeutic role against renal damage induced by gentamicin, as seen by the improvement of body weight, reduction of creatinine, urea level and improvement of the histology of the kidney.

**CONFLICT OF INTEREST**: Authors declare no conflict of interests.

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