

## Evaluation of the Histological Effects of Allium Cepa Administration on the Prostate Histology and Prostate Specific Antigen of Male Albino Rats Induced with Ciprofloxacin

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### ABSTRACT

The primary objective of this study is to assess the histological impact of Allium cepa administration on prostate histology and prostate-specific antigen (PSA) levels in male albino rats that were induced with ciprofloxacin. A total of 100 albino rats, each weighing between 150–250g, were used in the experiment. The experimental group was further divided into four subgroups, each containing 10 rats, labeled as Groups A, B, C, D, and E. Group A served as the control, while Group B received only ciprofloxacin. Group C was administered ciprofloxacin along with 100mg of Allium cepa extract, whereas Group D received ciprofloxacin and 200mg of Allium cepa extract. Group E was treated solely with Allium cepa extract. Groups B, C, and D were given 22.86 mg/kg of oral ciprofloxacin (500 mg/tablet), manufactured by Fidson Health Care Ltd. The ciprofloxacin was obtained from a reputable pharmaceutical store in Ekpoma, Edo State, and administered via gavage. The control group was provided with only water and food. The PSA levels in control and test subjects were recorded as Mean ± SEM. For the control group, the PSA level was 0.6250 ± 0.085 ng/ml. The PSA levels for test groups B, C, D, and E were 1.575 ± 0.417 ng/ml, 1.200 ± 0.123 ng/ml, 1.125 ± 0.048 ng/ml, and 3.300 ± 0.835 ng/ml, respectively. Notably, only Group E exhibited a significant increase (P<0.05) in PSA levels when compared to the control group. In conclusion, this study indicates that exposure to ciprofloxacin and Allium cepa at mild or moderate doses can lead to severe histopathological changes in the testis, prostate, and epididymis, with the exception of the brain

## **INTRODUCTION**

Onion (*Allium cepa*) is a common ingredient found in most households. The purple-skinned variety not only enhances the flavor of dishes but also provides several health benefits. Additionally, it is frequently incorporated into natural remedies and beauty treatments. Although it is not typically used as a dedicated medicinal herb, onion offers a wide range of positive effects on the body. Regular consumption, especially in its raw form, can support overall health and enhance vitality (1).

## **LITERATURE REVIEW**

Ciprofloxacin is an antibiotic classified under the fluoroquinolone family and is commonly prescribed to treat bacterial infections. It is also used in cases of anthrax exposure and certain types of plague (2). Despite its effectiveness, fluoroquinolone antibiotics have been associated with severe and potentially irreversible side effects. Ciprofloxacin, a widely used fluoroquinolone, is generally well-tolerated, but there have been rare reports of adverse reactions. A study conducted by Peirouvi et al. (2011) revealed that administering ciprofloxacin to male Wistar rats caused significant necrosis of the germinal epithelium within the seminiferous tubules, leading to impaired spermatogenesis. Additionally, ciprofloxacin was found to damage the basement membrane of some seminiferous tubules, resulting in lumen enlargement due to the accumulation of shed germinal cells (3).

Onions, known for their nutritional and medicinal properties, are cultivated and consumed worldwide. They contain phenolics and flavonoids, which exhibit beneficial properties such as anti-inflammatory, cholesterol-lowering, anticancer, and antioxidant effects. Onions are composed of approximately 89% water, 1.5% protein, and essential vitamins like B1, B2, and C. They also contain important minerals such as potassium and selenium (1).

The prostate gland weighs approximately 20 grams and has a funnel-like shape, measuring about 4 centimeters in length, 3 centimeters in width, and 2 centimeters in depth. It is located within the true pelvis, extending from the base of the bladder neck to the urogenital diaphragm and levator ani muscle at its apex. The apex of the prostate contains muscle fibers derived from the urogenital diaphragm. The seminal vesicles extend from the posterior aspect of the prostate gland to the back surface of the bladder.

The impact of onions on PSA levels in Wistar rats was first examined by Orçun et al. (2005). Their study found that administering onion extracts resulted in a significant reduction in PSA levels compared to the control group. This effect may be due to the enhanced interaction of antioxidants. These findings are consistent with research conducted by Freedland et al. (2003), which demonstrated a dose-dependent decrease in PSA levels following onion extract consumption. The highest concentration of onion extract had the most pronounced effect in lowering PSA levels. Several factors, including lifestyle choices, can influence PSA levels, suggesting that onion extracts might have properties that inhibit 5 $\alpha$ -reductase, an enzyme linked to the development of benign prostatic hyperplasia. PSA is a substance produced by the prostate gland (4), which can be generated by both normal and cancerous prostate cells. The PSA

test measures the concentration of PSA in the bloodstream of adult males. The observed decrease in PSA levels among the onion extract-treated groups indicates that onions may have therapeutic potential against prostate cancer. Elevated PSA levels are commonly detected in adult males diagnosed with prostate cancer (5).

## **METHODOLOGY**

### **Experimental Animals**

A total of 100 albino rats (150–250g) were used, receiving proper care per laboratory standards. They were divided into control and experimental groups, with the latter further split into five subgroups (A–E, 10 rats each). Group A was the control, while Groups B, C, and D received ciprofloxacin (22.86 mg/kg), with C and D also receiving *Allium cepa* extract (100mg and 200mg, respectively). Group E received only *Allium cepa* extract. Ciprofloxacin (500 mg/tablet) was obtained from Rehoboth Pharmacy Ltd. and administered via gavage. The control group received only food and water.

### **Materials**

A total of 100 adult male albino rats were obtained from the Animal House at Ambrose Alli University, Ekpoma. Ciprofloxacin tablets (500 mg/tablet) from Fidson Health Care Ltd. were purchased from Rehoboth Pharmacy Ltd., Ekpoma. Additionally, 20 mature *Allium cepa* bulbs (Sokoto local variety, ~200g) were sourced from a local market and authenticated at the Department of Botany, Ambrose Alli University.

### **Preparation and Experimental Procedures**

The *Allium cepa* extract was prepared following Azu et al. (2007). Fresh onion bulbs were washed, blended, and left undisturbed for 24 hours to release active compounds. The extract was filtered through a cloth mesh and stored at 4°C for use. Ciprofloxacin extract was prepared by dissolving a 500mg Ciprotab tablet in 100ml of distilled water, with measured doses administered to designated groups.

A total of 100 eight-week-old male rats were randomly assigned to five groups (A–E), each containing 20 rats. Group A served as the control, receiving only distilled water. Group B was given ciprofloxacin (22.86 mg/kg bw), while Groups C and D received ciprofloxacin combined with onion extract (100 mg/kg bw and 200 mg/kg bw, respectively). Group E received only onion extract (100 mg/kg bw) Azu et al., (2007).

### **Sample Collection**

#### **Determination of PSA Levels (Butt and Blunt, 1988)**

The PSA test uses an enzyme immunoassay sandwich method with fluorescent detection (ELFA). It employs a solid-phase receptacle (SPR) that functions as both the solid phase and pipetting device. Pre-packaged reagents are provided in sealed strips, and the instrument automates all assay steps. The reaction medium is cycled through the SPR, where the sample is mixed with an alkaline phosphate-labeled anti-testosterone conjugate for analysis.

### Histological Processing

The tissues were processed using automatic tissue processor according to the processing schedule used in histopathology laboratory of Ambrose Alli University, Ekpoma, Edo State, Nigeria.

### Statistical Analysis

Data obtained was analyzed using SPSS version 22 statistical software package. Results generated was expressed as mean  $\pm$  SD and a P-value of  $<0.05$  was considered significant

### RESULT

The results shows the body weight of control and test groups at baseline weight, acclimatization weight and weight after administration. It also shows biochemical parameters like Prostatic Specific Antigen. It also shows micrographs of sperm cells, Brain tissue, Testis tissue, Epididymis and Prostate tissue. Figure 4.1 indicates the levels of PSA among different groups (control and test subjects), PSA for test subjects were  $1.575 \pm 0.417$ ,  $1.200 \pm 0.123$ ,  $1.125 \pm 0.048$  and  $3.300 \pm 0.835$  for group B,C,D and E respectively in which only group E was found to significantly increase ( $p < 0.05$ ) when compared with control of  $1.300 \pm 0.108$

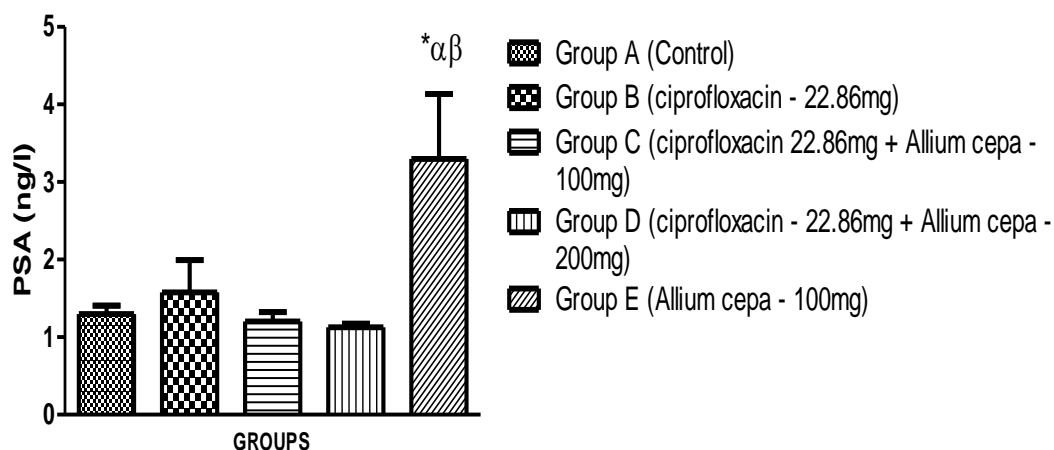


Figure 1. The Level of PSA Among the Different Groups of Wister Rats

\* mean significant  $p \leq 0.05$  when compared with control;  
 $\alpha$  mean significant  $p \leq 0.05$  when compared with group C  
 $\beta$  mean significant  $p \leq 0.05$  when compared with group D

**Prostate Gland**

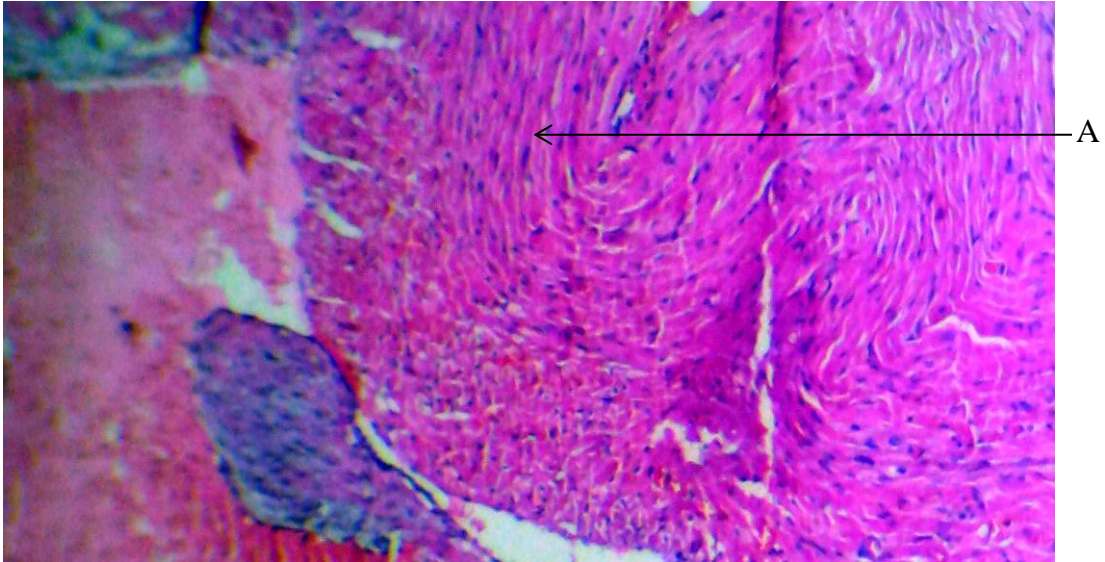


Plate 1. Photomicrograph of Prostate of Experimental Animal (Group A) Showing Normal Histomorphology with Fibromuscular Stroma (A) (H and E X400)

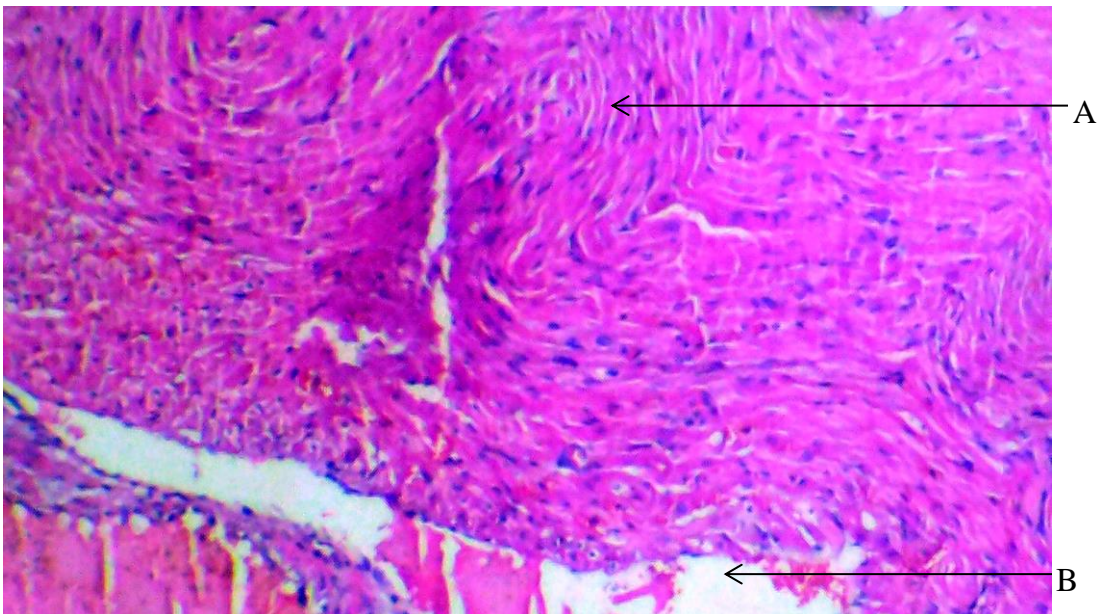


Plate 2. Photomicrograph of Prostate of Experimental Animal (Group B) Showing Normal Histomorphology with Fibromuscular Stroma (A) and Gland (B) (H and E X400)

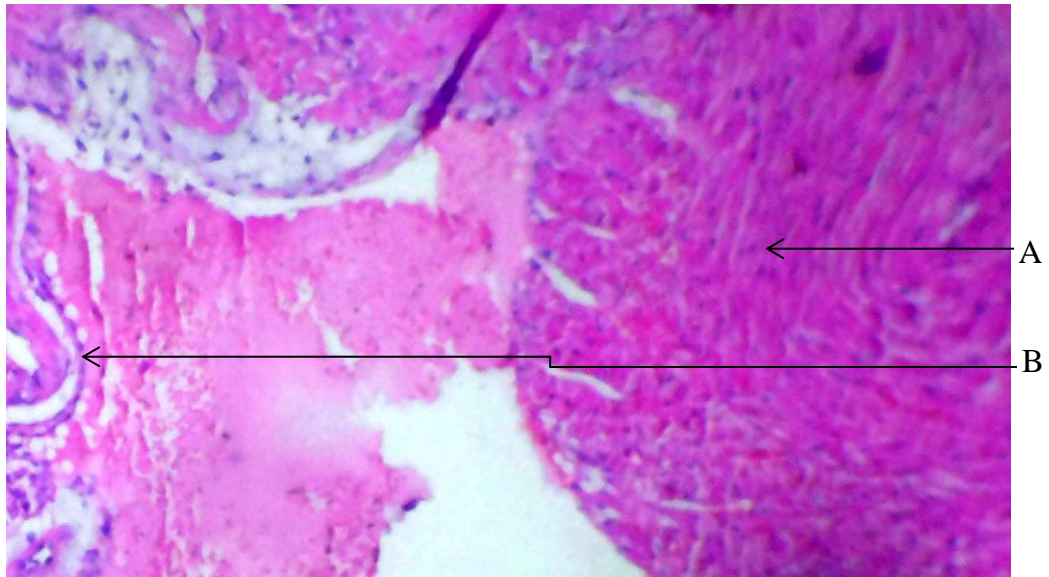


Plate 3. Photomicrograph of Prostate of Experimental Animal (Group C) Showing Histomorphology with Fibromuscular Stroma (A) and Lumen (B) (H and E X400)

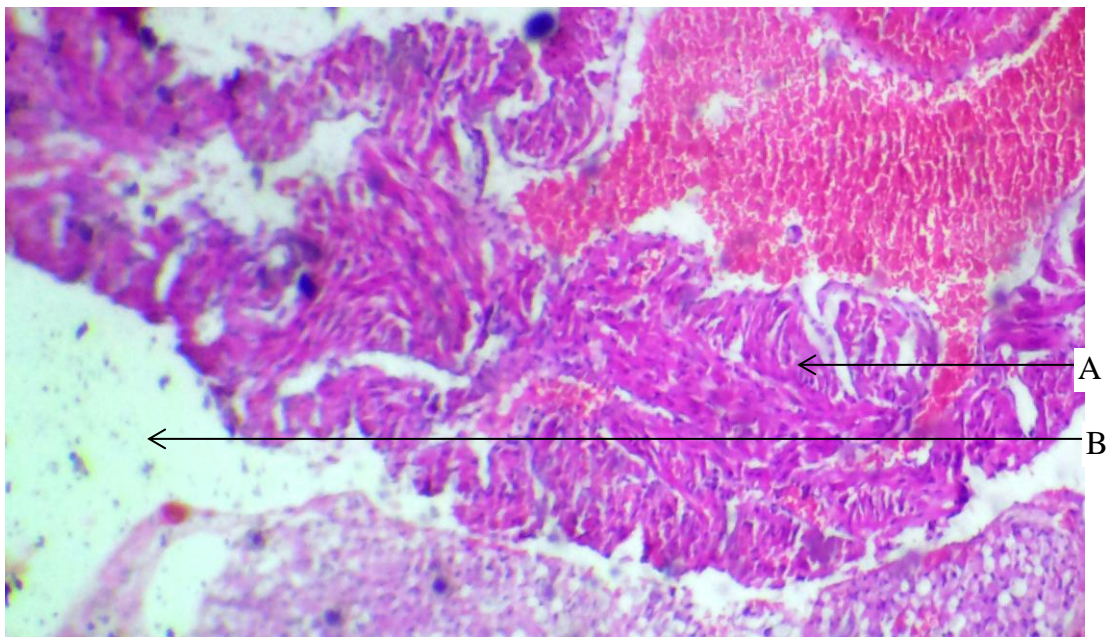


Plate 4. Photomicrograph of Prostate of Experimental Animal (Group D) Showing Histomorphology with Fibromuscular Stroma (A) and Glandular Lumen (B) (H and E X400)

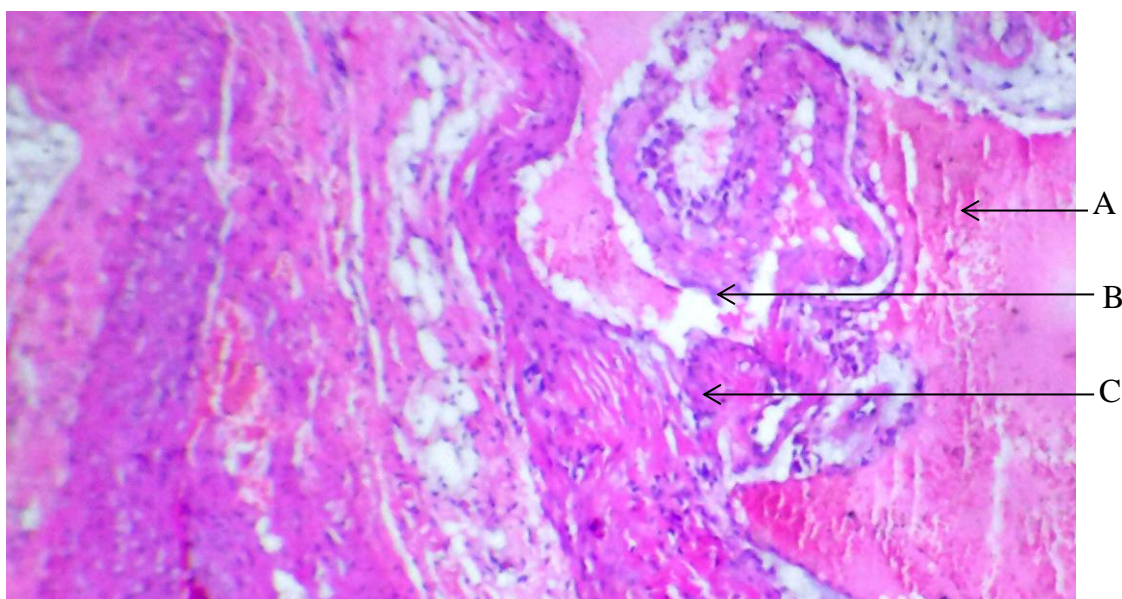


Plate 5. Photomicrograph of Prostate of Experimental Animal (Group E) Showing Fibromuscular Stroma (B) and Gland (A) and Fibromuscular Stroma (C) (H and E X400)

## DISCUSSION

The PSA levels were measured in both the control and test groups. The control group had an average PSA level of  $1.300 \pm 0.108$  ng/ml, while the test groups recorded  $1.575 \pm 0.417$  ng/ml,  $1.200 \pm 0.123$  ng/ml,  $1.125 \pm 0.048$  ng/ml, and  $3.300 \pm 0.835$  ng/ml, respectively. Significant variations in PSA levels were observed across all groups, with some experiencing an increase while others showed a decrease. A statistically significant difference ( $P \leq 0.05$ ) was noted.

Group E, which received *Allium cepa* extract (100 mg), exhibited a significant increase ( $P \leq 0.05$ ) in PSA levels compared to the control. This result aligns with the findings of Nnodim et al. (2020), who also observed an increase in PSA concentration in rats treated with onion extracts. This increase may be linked to enhanced antioxidant interactions, as proposed by Nnodim et al. (2020) (6). Elevated PSA levels are often associated with prostate cancer in adult males. Previous studies suggest that onion extracts may have an inhibitory effect on  $5\alpha$ -reductase, an enzyme involved in the development of benign prostatic hyperplasia, as reported by Lilja (2003) (4).

No statistically significant ( $P \geq 0.05$ ) differences were observed in Groups B (Ciprofloxacin - 22.86 mg), C (Ciprofloxacin - 22.86 mg + Onion extract - 100 mg), and D (Ciprofloxacin - 22.86 mg + Onion extract - 200 mg) when compared to the control group. The micrographs of the control group and Group B showed the prostate gland with its glandular epithelium (GE) and fibromuscular stroma (FMS). However, no significant histological differences were noted between these groups following ciprofloxacin administration.

In Group C, where rats were treated with Ciprofloxacin (22.86 mg) and Onion extract (100 mg) for 14 days, the photomicrograph displayed regions with

dispersed cells. This may be due to increased cellular growth in the prostate, leading to glandular enlargement. These findings are consistent with those of Deters et al. (2021), who suggested that a combination of synthetic and natural antibiotics can lead to chronic bladder outlet obstruction (7).

The photomicrograph of Group D (Ciprofloxacin - 22.86 mg + Onion extract - 200 mg) revealed the presence of adipocytes. This condition may be influenced by genetic predisposition and exposure to environmental pollutants, including chemicals such as ciprofloxacin and *Allium cepa*. The results of this study align with Christina (2019), who observed prostate adenocarcinoma following the administration of chemical drug agents. These agents were found to induce DNA mutations, leading to the proliferation of cancerous cells (8).

In the photomicrograph of Group E, the prostate gland cluster exhibited fibrosis, possibly resulting from abnormal epithelial cell proliferation within previously noncancerous acini or ducts. This may be due to the toxic effects of *Allium cepa* extract. Similar observations were reported by Kim et al. (2005), who suggested that this phenomenon might be attributed to cells with genetic and molecular characteristics resembling those of cancer cells (9).

## CONCLUSIONS AND RECOMMENDATIONS

Among the test groups, a notable increase ( $P \leq 0.05$ ) in PSA (prostate-specific antigen) levels was observed only in Group E when compared to the control group. The findings of this study suggest that exposure to ciprofloxacin and *Allium cepa* at mild to moderate doses may cause considerable histopathological changes in the prostate. Furthermore, onion toxicity has the potential to induce significant biochemical and histological alterations.

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