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Research Articles

Effect of Crack Cocaine on the Histology of the Kidney of Wistar Rats

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Abstract

Crack cocaine is highly addictive and is produced by the conversion of cocaine, a fine white crystallized powder substance, into a smokable form that could be sold in smaller portions but distributed to more people. The name crack is attributed to the crackling noise that is made when the substance is smoked. The aim of this study is to determine the histological effect of crack cocaine on the kidney of adult albino Wistar rat. A total of forty (40) adult Albino Wistar rats of comparable sizes were used for this study. They were divided into four equal groups (A – D) with ten (10) rats each. Group A served as the control and the rats were given distilled water and feed only. In addition to feed and water, groups B rats were given 0.5 ml *crack cocaine extract* and *crack cocaine extract*, group C rats were given 2 ml *crack cocaine extract*, and group D rats were given 5 ml *crack cocaine extract* respectively. The drug administration was given daily for 14 days (2 weeks) and the weights of both the test and control animals was monitored before and after administration of *crack cocaine extract*. The administration of the*crack cocaine extract* was given orally. The results of this study show no significant ($p \geq 0.05$) alterations in the kidney histology of test wistar rats administered with crack cocaine when compared with the non-cocaine administered group. In conclusion, despite any perceived absence of immediate side effects, the use of cocaine can have insidious long-term consequences on kidney health. The drug's vasoconstrictive properties, potential for hypertension, disruption of blood flow, and induction of oxidative stress can collectively contribute to histological changes within kidney tissues.

1. Introduction

Crack cocaine is highly addictive and is produced by the conversion of cocaine, a fine white crystallized powder substance, into a smokable form that could be sold in smaller portions but distributed to more people. The name *crack* is attributed to the crackling noise that is made when the substance is smoked. Crack began to be produced in the early 1980s. The method is to dissolve cocaine hydrochloride into water

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with sodium bicarbonate (baking soda), which precipitates solid masses of cocaine crystals. Unlike powder cocaine, crack was easier to develop, more cost efficient to produce, and cheaper to buy, which made it more economically accessible. Crack sold for anywhere between $5 and $20 per vial (a small capsule that contains pebble-size pieces of crack that were approximately one tenth of a gram of powdered cocaine).

Crack cocaine was noted for its instantaneous and intense high, which kept users craving more, thus causing an upsurge in crack cocaine addictions. Between 1982 and 1985, the number of cocaine users increased by 1.6 million people [1].

Crack cocaine causes weight loss, high blood pressure, hallucinations, seizures, and paranoia. Emergency room visits due to cocaine incidents such as overdoses, unexpected reactions, suicide attempts, chronic effects, and detoxification increased fourfold between 1984 and 1987 [2].

Cocaine, one of the most frequently consumed recreational drugs, can cause irreversible structural damage to the heart, accelerate cardiovascular disease processes, and trigger arrhythmias and other cardiovascular conditions. In fact, cocaine is the main cause for drug-related visits to the emergency room, and most of these are for cardiovascular problems. Cocaine-associated cardiovascular complications may be further exacerbated by concomitant use of other drugs with cocaine and long-term cocaine use. In a survey on 94 long-term cocaine users (mean regular cocaine use 13.9 $\pm$ 9 years), cardiovascular magnetic resonance imaging found that 71% had some form of cardiovascular disease [3]. Cocaine can be smoked (crack cocaine), injected intravenously, insufflated or "snorted," as well as taken orally or rectally. Since both smoking and intravenous administration have similar pharmacological profiles, smoking a cheap form of "crack" cocaine is particularly popular. Snorting cocaine reduces the drug's bioavailability by more than half because it causes vasoconstriction of the nasal mucus membranes, but snorting is preferred by some users because of the extremely rapid onset of action [3].

In recent decades, substance abuse has emerged as a major public health concern, affecting individuals of all ages and backgrounds. Among the various illicit drugs, crack cocaine, a potent and highly addictive form of cocaine, has gained notoriety for its devastating impact on physical and mental health. As researchers and medical professionals strive to understand the full extent of crack cocaine's detrimental effects, studies focusing on specific physiological systems are crucial to unraveling the complexities of its consequences [4]. Preliminary studies have indicated that cocaine abuse can lead to severe kidney complications, such as nephritis. However, there remains a paucity of research specifically investigating how crack cocaine affects the kidney in the context of an albino Wistar rat model [5].

Crack cocaine abuse has been associated with a myriad of renal complications in humans, ranging from glomerulonephritis and haematuria to Diabetic Nephropathy and sudden kidney failure. However, the mechanisms underlying these adverse kidney effects remain poorly understood. By studying the impact of crack cocaine on the kidney of adult albino Wistar rats, we can elucidate the cellular and molecular changes within the renal tissue, offering valuable insights into the pathophysiological processes that contribute to drug-induced cardiac toxicity. By uncovering the intricate relationship between crack cocaine and the kidney, we can identify novel therapeutic targets and interventions aimed at mitigating the detrimental effects of drug abuse on renal function.

2. Materials and Methods

2.1. Study Area

This study was carried out in Ekpoma, the administrative headquarters of Esan West Local Government Area of Edo State, Nigeria. The area proper lies between latitude 6°45 North of Equator and longitudes 6°5' and 6° 8' East of the Greenwich Meridian. Ekpoma area falls within the rain forest/savannah transitional zone of south western Nigeria. Ekpoma has a population of 172, 400 people. Majority of people in this area are civil servants, traders, business men and women, transporters, farmers, teachers/lecturers and students by occupation. Ekpoma is made up of many quarters, including Eguare, Iruekpen, Emaudo, Ujoelen, Ihumudumu, Illeh, Uke, Uhiele, Ujemen, Ukpenu, Egoro, Emuhi, Igor and Idumebo [6].

2.2. Experimental Animals/Housing Condition

Forty (40) Adult Albino Wistar rats of comparable sizes and weights were procured from the animal house and transferred to the experimental site where they were allowed two (2) weeks of acclimatization. They were housed in well ventilated labeled wooden cages at the site of the experiment. The cages were designed to secure the animals properly especially from wild animals/insects and cleaned daily. During this period of acclimatization, the rats were fed growers' mash and water provided *ad libitum*. Animals were maintained and experimental procedures complied with the guide for care and use of laboratory animals [7].

2.3. Experimental Design

A total of forty (40) adult Albino Wistar rats of comparable sizes were used for this study. They were divided into four equal groups (A – D) with ten (10) rats each. Group A served as the control and the rats were given distilled water and feed only. In addition to feed and water, groups B rats were given 0.5 ml *crack cocaine extract* and *crack cocaine extract*, group C rats were given 2 ml *crack cocaine extract*, and group D rats were given 5 ml *crack cocaine extract*respectively. The drug administration was given daily for 14 days (2 weeks) and the weights of both the test and control animals was monitored before and after administration of *crack cocaine extract*. After the administration, the rats were put under light chloroform anaesthesia and the lungs were obtained. ANOVA was used to analyze the results of the weight and differences was considered significant at $p<0.05$ level of confidence. All data was expressed in table as mean $\pm$ standard deviation (SD).

2.4. Animal Grouping

The experimental animals were separated into four groups (A – D). Group A had ten rats (n = 10) while groups B – D had ten rats (n = 10) each using 4 big cages to house them. Group A served as the control and received only the normal feed (grower's mash) and water with no administration of *crack cocaine extract*, while Group B, C and D received different doses of *crack cocaine extract* and were equally fed with grower's mash and water.

2.5. Study Duration

The preliminary studies, animal acclimatization, drug procurement and preparation, actual animal experiment and evaluation of results, lasted for a period of three months. However, the actual experiment lasted for lasted for four (4) weeks: two weeks of acclimatization and two weeks administration of *crack cocaine extract* to the test animals.

2.6. Collection and Identification of Plant Materials

Fresh prepared aqueous *crack cocaine extract* was collected from a health facility. The aqueous extracts were identified and authenticated by experts.

2.7. Preparation of Plants Extract

The powder *crack cocaine* was weighed using the electric weighing scale and 100 g was dissolved in 1 litre of distilled water and stirred at intervals for 24 hours (1 day). This was later reconstituted to give the required doses of 0.5 ml, 2 ml and 5 ml used in the present study.

2.8. Administration of Substance

Crack cocaine extracts were prepared to prepare the doses of 0.5 ml, 2 ml and 5 ml respectively for the experiment.

The administration of the crack cocaine extracts was given orally as follows:

- **Group A** (Control) received only normal feed (growers' mash) and distilled water daily for 28 days.
- **Group B** received 0.5 ml of crack cocaine extracts, feed and distilled water daily for 28 days.
- **Group C** received 2 ml of crack cocaine extracts, feed and distilled water daily for 28 days.
- **Group D**received 5 ml of crack cocaine extracts, feed and distilled water daily for 28 days.

2.9. Ethical Approval

Ethical approval for the use and collection of samples from laboratory animals was obtained from the Ethics and Review Committee, College of Medical Sciences, Ambrose Alli University, Ekpoma.

2.10. Sample Collection and Analysis

Weight was measured before and after acclimatization. Similar weight measurements were done at the end of the treatment periods and the average weight recorded accordingly. Furthermore, the kidney of each rat was obtained at the end of the experiment under chloroform anaesthesia and fixed in 10% formalin for histological processing.

2.11. Processing Schedule

The tissues were processed according to standard histological procedures. The fixed plastic cassette tissues in 10% formalin were automatically processed by passing them through different grades of alcohol as follows:

70% alcohol	2hrs
80% alcohol	2hrs
90% alcohol	2hrs
90% alcohol	2hrs
95% alcohol	2hrs
Absolute	2hrs
Xylene 1	2hrs
Xylene II	2hrs
Molten paraffin wax 1	2hrs
Molten paraffin Wax II	2hrs

After the last timing, the tissues were removed from their plastic cassettes and placed at the centre of the metallic tissue mould and then filled with molten paraffin wax. They were left to solidify after which they were placed in the refrigerator at 5° C for 15 minutes. After the blocks were cool in the refrigerator for the time stated above, the blocks were removed from the metallic case using a knife and after which the paraffin wax at the side of the blocks were removed. The blocks were trimmed and cut serially at 3 mm on a rotary microtome. The sections were floated in water bath at 55° C and picked up by the use of a clean frosted end slide. The frosted end slides were placed on the hot plate for 40 minutes for adequate attachment of the sections on the slides after which the sections were de-waxed, hydrated, air dried and stored in a slide box ready for staining.

2.12. Staining Procedure

Sections for general tissue structure were stained using Haematoxylin and Eosin staining technique.

1. The sections were de-waxed in 3 changes of xylene 5 minutes
2. The sections were hydrated through descending grades of alcohol (absolute, 95%, 80% and 70%).

3. The sections were stained in Harris haematoxylin 5 minutes
4. The sections were rinsed in running tap-water to remove excess stain
5. The sections were differentiated in 1% acid alcohol 3 seconds
6. The sections were blued in running tap water 10 minutes
7. The sections were counterstained with 1% eosin 1 minute
8. Sections were finally rinsed in water, dehydrated in ascending grades of alcohol (70%, 80, 95% and absolute)
9. The sections were cleared in xylene, air-dried and mounted with dibuthylphthalate propylene xylene (DPX) [8].

The slides were examined under a light microscope at x100 magnification and photomicrographs were taken.

2.13. Data Analysis

All results were expressed as mean ± standard deviation (X ± SD). The obtained data was subjected to statistical analysis using SPSS (version 21). The test groups' values were compared with the values of the control group using One-way analysis of variance (ANOVA) at 95% level of confidence. Values of $P < 0.05$ were considered significant.

3. Results

3.1. Body Weight Changes of Rats at Various Intervals

Table 1 shows the body weight changes of rats in the test and control groups. The results were presented in mean ± standard deviation. At every stage of the weight determinations, the control group (Group A) presented body weight gain at first, second, third and final week after acclimatization, while the test groups (B, C and D) presented body weight loss in the different weeks after acclimatization respectively. Though, the difference in weight didn't show any significant difference ($p > 0.05$) within the test groups, group D was observed to have a higher weight reduction, followed by group C and B respectively. The body weight of control animals (group A) before acclimatization and before sacrificing was 205.50 ± 0.50 g and 245.25 ± 0.50 g. Similarly, the body weight of the test animals in group B before acclimatization and before sacrificing was 215.50 ± 1.00 g and 200.55 ± 2.22 g, group C was 210.40 ± 1.29 g and 195.25 ± 3.24 g, group D was 225.55 ± 1.41 g and 190.25 ± 2.45 g respectively.

Table 1: Body Weight Changes of Rats at Various Intervals

Weight (g)	Control (n = 10)	B (100 mg) (n = 10)	C (200 mg) (n = 10)	D (300 mg) (n 10)
WBA	210.50 ± 0.50	220.50 ± 1.00	215.40 ± 1.29	230.55 ± 1.41
WAA	220.65 ± 0.50	217.75 ± 1.50	210.50 ± 0.42	225.45 ± 1.20
W2WK	225.45 ± 0.50	215.25 ± 1.35	205.85 ± 1.50	215.50 ± 1.84
W3WK	240.15 ± 1.71	210.50 ± 1.50	205.50 ± 1.15	205.35 ± 2.55
FW	250.25 ± 0.50	205.55 ± 2.22	200.25 ± 3.24	195.25 ± 2.45

KEY: WBA: Weight before acclimatization; WAA: Weight after acclimatization
W2WK: Weight at second week of cocaine extracts;
W3WK: Weight at third week of cocaine extracts; FW: Final weight before sacrificing;
Values are mean ± Standard deviation; Wt= weight (Grams); n: Number of sample.

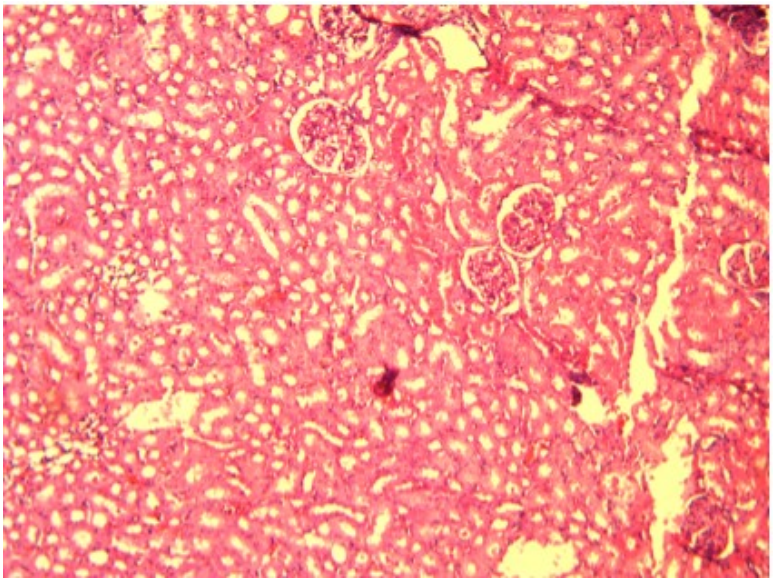

Figure 1: Kidney Control X100

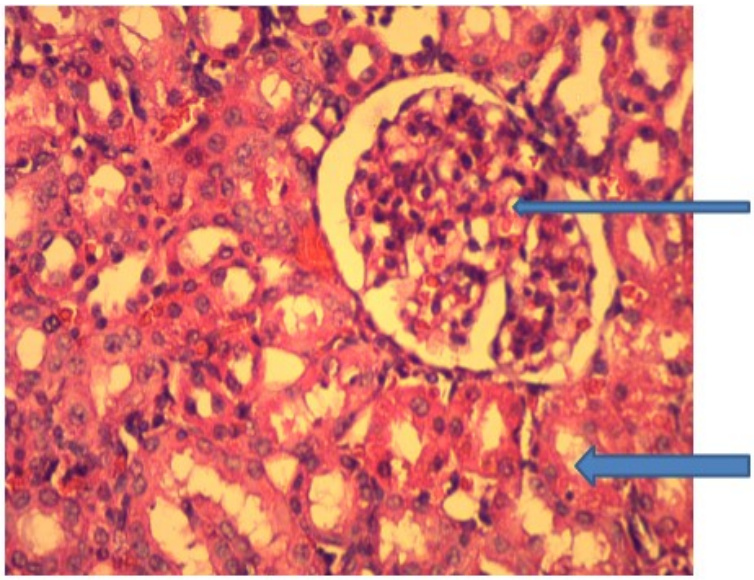

Figure 2: Kidney Control X400: Section Of The Kidney Shows Normal Glomeruli (Thin Arrow) And Normal Tubules (Thin Arrow)

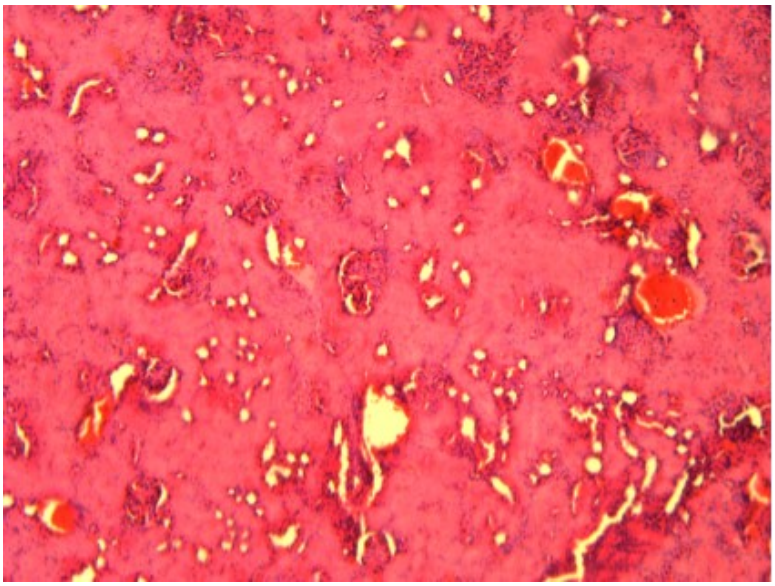

Figure 3: Kidney A X100

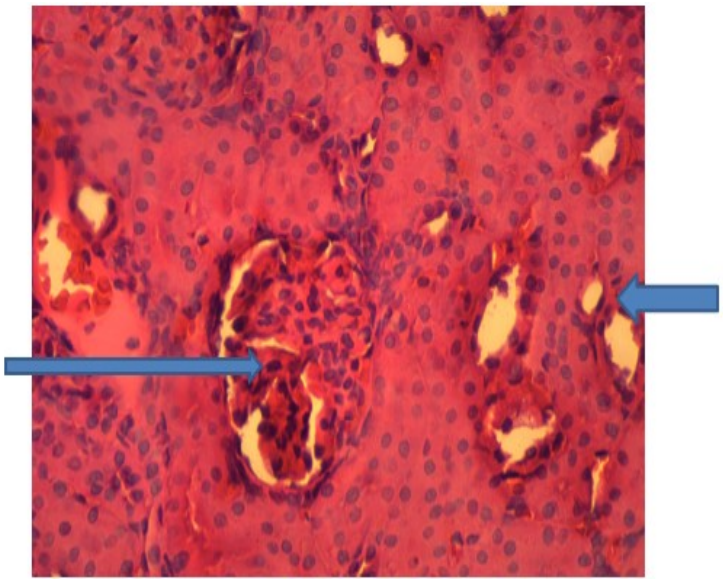

Figure 4: Kidney A X400: Section Of The Kidney Shows Normal Glomerulus (Thin Arrow) And Necrosis Of Tubules (Thick Arrow)

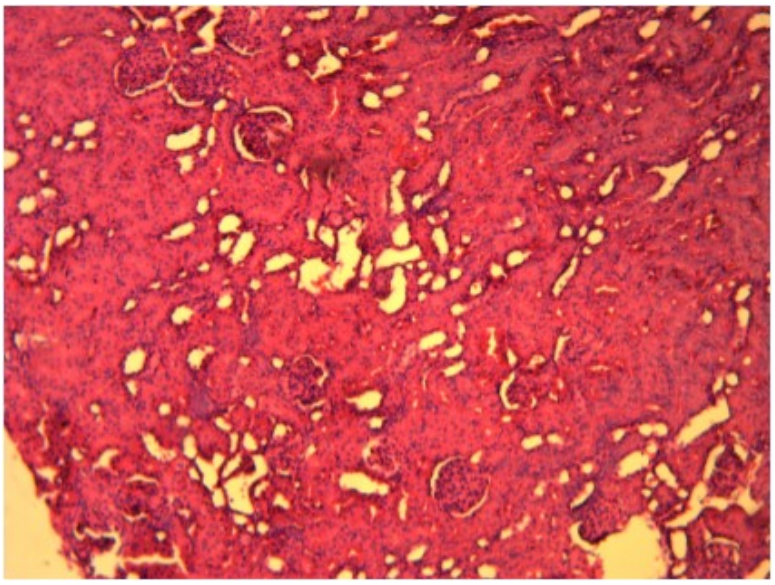

Figure 5: Kidney B X100

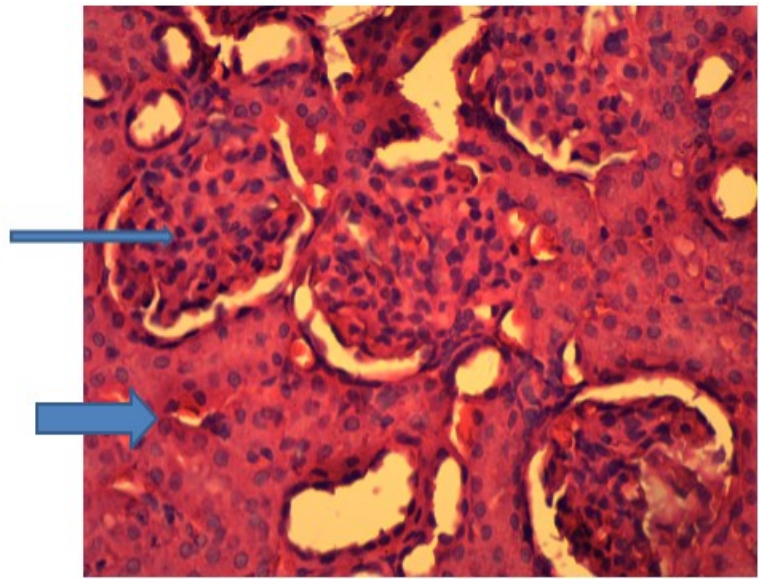

Figure 6: Kidney B X400: Section Of The Kidney Shows Normal Glomeruli (Thin Arrow) And Necrosis Of Tubules (Thick Arrow)

4. Discussion

Cocaine is a tropane alkaloid compound that can be extracted from the leaves of an Andean shrub, Erythroxylon coca, in South America. Cocaine was originally used for local surgeries as an anesthetic agent in the 1880s, but it became a recreational drug in the 1970s. Cocaine use remains a serious public health concern. Although cocaine can adversely affect the function of almost every organ system [9]. According to the most recent World Drug Report, 0.4% of the global population aged 15–64 reported cocaine use in 2019—this corresponds to approximately 20 million people. The latest edition of the European Monitoring Centre for Drug and Drug Addiction (EMCDDA) Drug Report states that it remains the second most abused substance in the European Union, second only to cannabis. Furthermore, despite the global COVID-19 pandemic, European authorities have intercepted at seaports growing amounts of cocaine in 2020. All the while, case reports detailing the harmful consequences of cocaine use abound [10].

Cocaine, a powerful stimulant drug, can have detrimental effects on various organ systems in the body such as including the kidneys. While the primary focus of cocaine's effects by many studies is often on the brain and cardiovascular system, it can also impact kidney histology and function [11].

Cocaine is known to suppress appetite. When individuals use cocaine, they often experience reduced feelings of hunger and may go for extended periods without eating. This appetite-suppressing effect can lead to rapid weight loss over time. This general belief does not resonate with the findings of this study, the findings of this study as observed in table 4.1 observed a non-statistically significant alterations in the test groups administered with varying dosage of cocaine when compared with the control group. The findings of this study contradict the findings of Ersche et al., [12], whose findings on "The skinny on cocaine: insights into eating behavior and body weight in cocaine-dependent men" observed a significant reduced fat mass of cocaine subjects when compared with non-drug using peers and stated that the weight

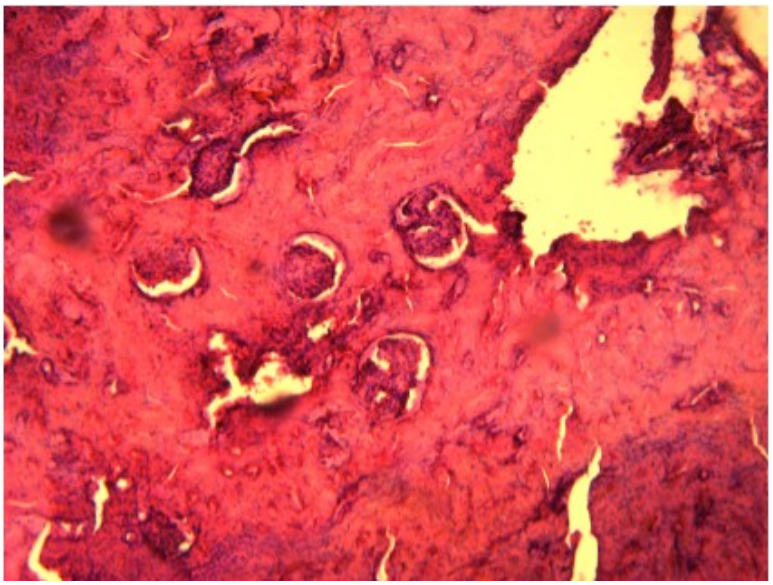

Figure 7: Kidney C X100

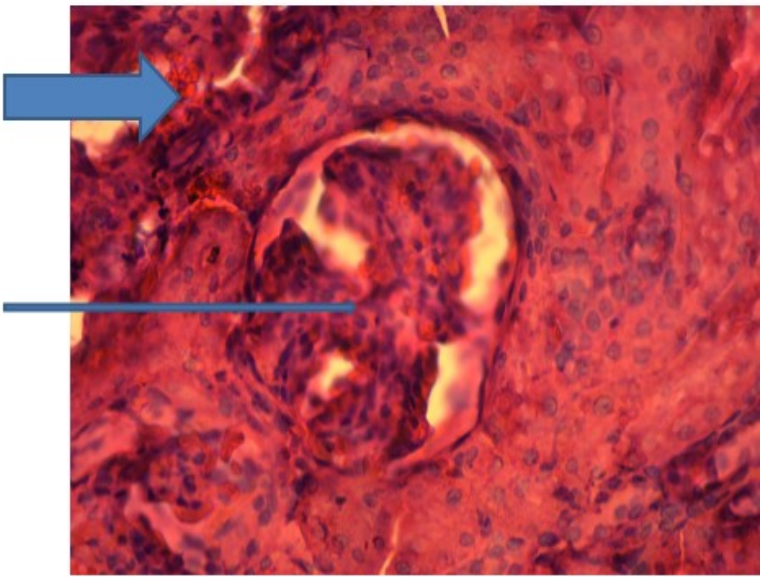

Figure 8: Kidney C X400: Section Of The Kidney Shows Normal Glomeruli (Thin Arrow) And Necrosis Of Tubules (Thick Arrow)

changes in cocaine users reflect fundamental perturbations in fat regulation.

The findings observed in the micrographs of this study shows that the administration of cocaine at varying concentration has no effect on the kidney histology of test wistar rats. The aforementioned findings of this study contradict the findings of Padilha et al., [13] whose study believes that Cocaine use can lead to widespread vasoconstriction, which is the narrowing of blood vessels. This includes the renal arteries that supply blood to the kidneys. Prolonged vasoconstriction can reduce blood flow to the kidneys, potentially leading to ischemia (reduced blood supply) and tissue damage. Other studies also believe Cocaine use can lead to widespread vasoconstriction, which is the narrowing of blood vessels. This includes the renal arteries that supply blood to the kidneys. Prolonged vasoconstriction can reduce blood flow to the kidneys, potentially leading to ischemia (reduced blood supply) and tissue damage [14]. Also, Cocaine's effects on blood pressure can contribute to the development of hypertension (high blood pressure). Hypertension can strain the delicate blood vessels within the kidneys, potentially leading to damage to the blood vessels and other renal structures [15]. The alteration observed in Padilha et al., [13] study could be due to the high concentration used in synthesizing most cocaine consumed.

5. Conclusions

In conclusion, the impact of cocaine on kidney histology is far from benign, and it can lead to a range of detrimental effects even in tissues that may initially appear unaffected. Despite any perceived absence of immediate side effects as observed in this study, the use of cocaine can have insidious long-term consequences on kidney health. The drug's vasoconstrictive properties, potential for hypertension, disruption of blood flow, and induction of oxidative stress can collectively contribute to histological changes within kidney tissues.

While some individuals might not experience immediate symptoms, this should not be misconstrued as an absence of harm. Cocaine's influence on kidney histology can gradually lead to functional impairments, such as reduced filtration efficiency, compromised waste

elimination, and inflammation. Over time, these subtle changes can accumulate and escalate into more severe kidney complications, including acute kidney injury and chronic kidney disease.

It is important to recognize that the damage caused by cocaine at the histological level can occur even before overt clinical symptoms manifest. Therefore, the apparent absence of immediate side effects should not be interpreted as an indication of safety. Understanding the insidious nature of cocaine's impact on kidney histology reinforces the urgency of avoiding its use altogether.

- Patients should abstain from cocaine usage as it can cause addiction
- Understanding the potential consequences of cocaine use on kidney health can be a powerful motivator to avoid the drug. Individuals are advised to be educated about the risks associated with cocaine abuse and make informed decisions to prioritize your well-being.
- Individuals should adopt a healthy lifestyle that includes regular physical activity, a balanced diet, and stress reduction techniques can contribute to overall well-being, potentially minimizing the impact of substance abuse on the body.
- Individuals struggling with cocaine use should seek professional assistance.

Article Information

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Disclaimer (Artificial Intelligence): The author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.), and text-to-image generators have been used during writing or editing of manuscripts.

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