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# Mitigating Marijuana-Induced Nephrotoxicity: The Role of Selected Local Spice Diets in Wistar Rats

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## ABSTRACT

This study investigated the mitigating marijuana-induced nephrotoxicity: the role of selected local spice diets in Wistar rats. A legal permit was obtained from the Office of the NDLEA to purchase the dried leaves of marijuana. Sixty five adult Wistar rats weighing between 150 and 200g were purchased from the Animal House, University of Port Harcourt. The rats were divided into eight groups of five rats per group. Group 1, 2, and 3 served as normal and negative controls respectively. Group 2 and 3 were fed with high dose of marijuana. Group 4-13 were fed wit tumeric and ginger diets for 30 days. The mean creatinine and urea levels of the group 3 was 101.6±41.52mmol/L and 54.27±2.22mmol/L respectively. The mean creatinin levels of group 10-12mmol/L were 77.26±39.4mmol/L, 91.71±9.17mmol/L, and 89.96±17.49mmol/L while the urea levels were 51.51±1.48mmol/L, 49.85±0.29mmol/L, and 45.64±0.09mmol/L, which were significantly different from the negative control values at $p \leq 0.05$. The mean $Na^+$ level of group 2 and 3 were 249.8±29.68mmol/L and 236.67±18.93mmol/L respectively while those of group 6-13 were 242.79±44.26mmol/L, 218.14±39.92mmol/L, 240.38±28.39mmol/L, 252.51±37.04mmol/L, 289.68±88.04mmol/L, 251.8±45.18mmol/L, 234.77±13.32mmol/L, and 250.4±33.24mmol/L respectively, were significantly increased in comparison to those of group 2 and 3. Single and combined tumeric and ginger diets significantly increased in the creatinine and urea levels of rats in group 4-13 in comparison to those of group 2 and 3. Tumeric and ginger diets significantly increased the mean plasma $Na^+$ levels in comparison to those of group 2 and 3, hence mitigated the marijuana- nephrotoxicity in rats.

**Keywords**: Marijuana, tumeric, ginger, nephrotoxicity, creatinine, urea, sodium ion

## INTRODUCTION

Marijuana use has been linked to various health complications, including nephrotoxicity. Research suggests that prolonged marijuana exposure can lead to kidney damage due to its ability to induce oxidative stress, inflammation, and impair the body's natural detoxification processes (Volkow *et al.,* 2014). The kidney's critical role in filtering toxins makes it vulnerable to such damage, leading to an accumulation of harmful metabolites and oxidative stress markers, which contribute to tissue damage (Renard *et al.,* 2017).

The nephrotoxic effects of marijuana are largely attributed to increased oxidative stress and inflammation. Marijuana can lead to oxidative stress by generating reactive oxygen species (ROS) that overwhelm the kidney's antioxidant defenses. This results in lipid peroxidation, protein oxidation, and DNA damage, all of which contribute to tissue injury and impaired kidney function (Adeyemi *et al.,* 2016). Studies also suggest that marijuana use triggers an inflammatory response in kidney tissues, exacerbating tissue damage and fibrosis over time (Renard *et al.,* 2017).

Spices such as ginger, turmeric, and marijuana are known for their potent antioxidant, anti-inflammatory, and nephroprotective effects. Their bioactive components, such as curcumin, allicin, and eugenol, can help reduce oxidative stress and inflammation, making them potential agents for mitigating nephrotoxicity (Prakash *et al.,* 2017; Sharma *et al.,* 2017).

Marijuana exerts its effects primarily through interaction with the endocannabinoid system (ECS), which plays a crucial role in regulating various physiological processes, including pain sensation, mood, appetite, and memory (Maccarrone *et al.,* 2017). THC binds to cannabinoid receptors (CB1 and CB2) in the brain and peripheral tissues, leading to its psychoactive effects, while CBD interacts with the ECS differently, often exhibiting anti-inflammatory and neuroprotective properties (Pertwee, 2015).

Ginger is rich in antioxidants such as gingerols and shogaols, which have demonstrated nephroprotective effects in various models of kidney injury (Prakash *et al.,* 2017). A study by Ali *et al.* (2015) found that ginger supplementation significantly reduced oxidative stress markers and improved kidney function in rats exposed to nephrotoxic drugs. The active compound in turmeric, curcumin, has been extensively studied for its antioxidant and anti-inflammatory properties. Curcumin has been shown to protect against drug-induced nephrotoxicity by scavenging free radicals and inhibiting pro-inflammatory cytokines (Sharma *et al.,* 2017). A study by Singh *et al.* (2015) demonstrated that curcumin effectively reduced renal oxidative stress and inflammation in an animal model of drug-induced kidney damage.

Several studies have explored natural remedies to mitigate drug-induced nephrotoxicity. Local spices, which are rich in bioactive compounds like antioxidants and anti-inflammatory agents, have shown promise in protecting against such damage. This study seeks to the role of selected local spice diets in mitigating marijuana-induced nephrotoxicity Wistar rats.

## MATERIALS AND METHODS

### Nature/Sources of Sample

A legal permit was obtained from the Office of the National Drug Law Enforcement Agency (NDLEA) to purchase the dried leaves of marijuana. Turmeric and Ginger was bought from the local market in Rumuokoro, sun dried and milled to fine powder.

### Collection/Preparation of Samples

The marijuana dried leaves were blended into fine powdered form for feed formulation by blending with other rat standard chow components. The ginger and turmeric samples were washed and cut into tiny sizes and air dried for 1 week, then blended into a fine powdered form. Each samples will be blended with a standard rat chow components.

### Chemicals/Reagents

Chemicals put adopted for the present research were purchased from commercial industries and the manufacturers' standard methods and procedure.

### Research Design

Sixty five (65) adult Wistar rats weighing between 150 and 200g were purchased from the Animal House, University of Port Harcourt, Rivers State. Throughout the experiment, the animals were kept in well-ventilated plastic cages at room temperature with a 12-hour light/dark cycle. They had free access to water and food, which was just regular rat chow. The ethics of animal handling were followed when handling the rats. The National Academy of Science (NAS)-approved "Guide for the Care and Use of Laboratory Animals" specified the humane treatment that the animals received. The rats were equalized as nearly as possible with respect to body weight such that the mean weight of the groups will not differ by more than $\pm$ 3.0g. The rats were divided into 13 groups of five rats per group as shown in the table below.

Table 1 Experimental Design

| Groups | Administration |
|---|---|
| 1. | 100g standard rat chow (SRC) |
| 2. | 90g SRC and 10g marijuana diet |
| 3. | 80g SRC and 20g marijuana diet |
| 4. | 70g SRC and 30g marijuana diet |
| 5. | 85g SRC,10g marijuana and 5g ginger diet |
| 6. | 80g SRC, 10g marijuana and 10g ginger diet |
| 7. | 75g SRC, 10g marijuana and 15g ginger diet |
| 8. | 85g SRC,10g marijuana and 5g turmeric diet |
| 9. | 80g SRC, 10g marijuana and 10g turmeric diet |
| 10. | 75g SRC, 10g marijuana and 15g turmeric diet |
| 11. | 85g SRC,10g marijuana and 2.5g turmeric diet 2.5g ginger diet |
| 12. | 80g SRC, 10g marijuana and 5g turmeric diet 5g ginger diet |
| 13. | 75g SRC, 10g marijuana and 7.5g turmeric diet7.5g ginger diet |

**Biochemical Analysis**

Different biochemical parameters were measured using ELISA and Randox kits in a biochemical analyzer. Kidney homogenate biomarkers determined were sodium ion (Na+), potassium ion (K+), chloride ion (Cl-), bicarbonate ion (HCO3-), creatinine and blood urea nitrogen (BUN). The oxidative stress biomarkers of homogenate determined were malondialdehyde (MDA), glutathione (GSH), glutathione peroxidase (GPx), superoxide dismutase (SOD) and catalase (CAT). Lipid profile parameters determined were total cholesterol, high density lipoprotein cholesterol (HDL), low density lipoprotein cholesterol (LDL), and trglyceride (TG)

**Histological Analyses of Kidney Tissues**

Histopathological examination was carried out based on standard laboratory method. The kidney and liver tissues was fixed in 10% formalin, dehydrated embedded paraffin sectioned and stained with hematoxlin and eosin. The glacial glass slides were viewed under the microscope at x 40 magnification.

**Statistical Analysis**

The data were expressed as means ± standard error of the mean (SEM). The analysis was carried out using the Statistical Package for Social Science (SPSS version 20.0). One-way analysis of variance (ANOVA) was done followed by Tukey's post hoc test was applied to compare means among groups at $p \leq 0.05$ level of significance.

**RESULTS**

Table 2 Ameliorative potential of selected spice diets on plasma kidney biomarkers on marijuana-induced kidney toxicity in rats (n=5)

| Total | Chloride (mmol/L) | Potassium mmol/L | Creatinine mmol/L | Sodium mmol/L | Urea mmol/L |
|---|---|---|---|---|---|
| Grp 1 | 98.4 ± 5.92 | 7.59 ± 0.35 $^{d}$ | 62.44 ± 21.14 $^{a}$ | 251 ± 31.69 | 46.44 ± 1.09 $^{a}$ |
| Grp 2 | 96.12 ± 5.23 | 6.6 ± 1.29 $^{d}$ | 87.84 ± 48.19 $^{ab}$ | 249.8 ± 29.68 | 46.44 ± 0.36 $^{a}$ |
| Grp 3 | 102.25 ± 6.27 | 5.63 ± 0.40 $^{bcd}$ | 101.6 ± 41.52 $^{ab}$ | 236.67 ± 18.93 | 54.27 ± 2.22 $^{ab}$ |
| Grp 4 | 109.5 ± 1.4 | 4.66 ± 0.36 $^{abc}$ | 82.55 ± 22.23 $^{ab}$ | 202.61 ± 29.27 | 60.73 ± 14.83 $^{b}$ |
| Grp 5 | 98.54 ± 1.26 | 3.6 0± 0.18$^{a}$ | 48.68 ± 20.41 $^{a}$ | 245.89 ± 65.27 | 51.17 ± 1.52 $^{ab}$ |
| Grp 6 | 96.58 ± 7.62 | 5.7 ± 0.17 $^{cd}$ | 124.88 ± 78.89 $^{ab}$ | 242.79 ± 44.26 | 53.19 ± 0.28 $^{ab}$ |
| Grp 7 | 95.66 ± 9.47 | 3.65 ± 0.15 $^{a}$ | 50.8 ± 41.28 $^{a}$ | 218.14 ± 39.92 | 59.24 ± 1.73 $^{b}$ |
| Grp 8 | 105.13 ± 10.82 | 4.14 ± 0.19 $^{a}$ | 122.77 ± 13.22 $^{ab}$ | 240.38 ± 28.39 | 51.07 ± 1.5 $^{ab}$ |
| Grp 9 | 98.91 ± 2.53 | 4.17 ± 0.13 $^{ab}$ | 167.77 ± 14.38 $^{b}$ | 252.51 ± 37.04 | 51.85 ± 0.48 $^{ab}$ |
| Grp 10 | 101.84 ± 10.58 | 4.07 ± 0.49 $^{a}$ | 77.26 ± 39.44 $^{ab}$ | 289.68 ± 88.04 | 51.51 ± 1.48 $^{ab}$ |
| Grp 11 | 101.28 ± 17.39 | 4.97 ± 0.35 $^{abc}$ | 91.71 ± 9.17 $^{ab}$ | 251.8 ± 45.18 | 49.85 ± 0.29 $^{ab}$ |
| Grp 12 | 87.34 ± 5.24 | 4.06 ± 0.80 $^{a}$ | 89.96 ± 17.49 $^{ab}$ | 234.77 ± 13.32 | 45.64 ± 0.09 $^{a}$ |
| Grp 13 | 92.45 ± 11.61 | 4.95 ± 0.26 $^{abc}$ | 130.18 ± 116.18 $^{ab}$ | 250.4 ± 33.24 | 95.66 ± 0.59 $^{ab}$ |

Values are expressed as mean ± SD. (n= 4 rats). Means in same column with the same superscript alphabets are not significantly different at p<0.05, while means in same column with different superscript alphabets are significantly different at p<0.05.

Table 3 Ameliorative potential of turmeric and ginger diets on oxidative stress kidney biomarkers on marijuana-induced kidney toxicity in rats (n=5)

| Grps | Nitric oxide (µg/ml) | MDA (µmol/mg protein) | CAT (mmol/min/mg tissue) | SOD (units/mg tissue) | GSH nmol/mg protein | GPx activity (µmol/min/mg tissue) |
|---|---|---|---|---|---|---|
| Grp 1 | 31.29 ± 0.98 | 0.72 ± 0.02 | 2.18 ± 0.07 | 0.24 ± 0.05 $^{c}$ | 5.66 ± 0.41 | 18.44 ± 2.38 $^{ab}$ |
| Grp 2 | 30 ± 1.29 $^{a}$ | 0.73 ± 0.08 | 2.37 ± 0.48 | 0.12 ± 0.01 $^{a}$ | 5.5 ± 0.72 | 19.67 ± 0.91 $^{ab}$ |
| Grp 3 | 30.97 ± 0.98 $^{bc}$ | 1.74 ± 0.14 | 0.89 ± 0.47 | 0.15 ± 0.01 $^{ab}$ | 6.42 ± 0.9 | 19.79 ± 2.43 $^{a}$ |
| Grp 4 | 29.9 ± 1.45 $^{bc}$ | 0.63 ± 0.01 | 0.95 ± 0.00 $^{a}$ | 0.15 ± 0.01 $^{ab}$ | 5.05 ± 0.5 | 21.69 ± 1.5 $^{b}$ |
| Grp 5 | 30.33 ± 1.00 | 0.67 ± 0.15 | 0.47 ± 0.00 $^{a}$ | 0.25 ± 0.05 $^{c}$ | 5.06 ± 0.16 | 21.54 ± 1.94 $^{ab}$ |
| Grp 6 | 29.95 ± 0.51 | 0.73 ± 0.21 | 1.1 ± 0.72 | 0.22 ± 0.01 $^{bc}$ | 4.91 ± 0.25 | 20.13 ± 2.04 $^{ab}$ |
| Grp 7 | 29.57 ± 0.18 | 0.98 ± 0.44 | 1.73 ± 0.54 | 0.25 ± 0.04 $^{c}$ | 5.57 ± 0.63 | 18.61 ± 1.92 $^{ab}$ |
| Grp 8 | 29.95 ± 2.1 | 0.65 ± 0.14 | 1.7 ± 0.92 | 0.24 ± 0.03 $^{c}$ | 5.5 ± 0.18 | 20.18 ± 1.27 $^{ab}$ |
| Grp 9 | 29.36 ± 0.16 $^{bc}$ | 1.1 ± 0.47 | 2.46 ± 1.75 | 0.21 ± 0.01 $^{abc}$ | 5.45 ± 0.65 | 21.18 ± 1.72 $^{ab}$ |
| Grp 10 | 30.32 ± 0.85 | 0.84 ± 0.31 | 2.05 ± 0.28 | 0.24 ± 0.04 $^{c}$ | 5.46 ± 0.64 | 18.41 ± 2.18 $^{ab}$ |
| Grp 11 | 30.92 ± 0.4 | 0.65 ± 0.05 | 2.04 ± 0.53 | 0.25 ± 0.03 $^{c}$ | 4.85 ± 0.61 | 16.44 ± 1.15 $^{a}$ |
| Grp 12 | 31.83 ± 0.74 | 0.88 ± 0.25 | 4.04 ± 4.33 $^{b}$ | 0.27 ± 0.02 $^{c}$ | 5.93 ± 0.91 | 20.05 ± 1.8 $^{ab}$ |
| Grp 13 | 31.02 ± 0.56 | 1.12 ± 0.35 | 2.48 ± 0.43 | 0.27 ± 0.03 $^{c}$ | 5.37 ± 0.61 | 21.41 ± 0.67 $^{ab}$ |

Values are expressed as mean ± SD. (n= 4 rats). Means in same column with the same superscript Alphabets are not significantly different at p<0.05, while means in same column with different superscript alphabets are significantly different at p<0.05

Table 4. Ameliorative effects of selected spices on the lipid profile of marijuana-induced kidney toxicity in Wistar rats (n=5)

| Groups | TG (mg/dl) | T-CHOL (mg/dl) | HDL (mg/dl) | LDL (mg/dl) |
|---|---|---|---|---|
| Grp 1 | 177.46 ± 3.36 $^{ab}$ | 116.56 ± 14.99 $^{c}$ | 40.25 ± 1.19 $^{abc}$ | 40.83 ± 14.96 $^{d}$ |
| Grp 2 | 199.76 ± 10.42 $^{b}$ | 107.16 ± 4.76 $^{abc}$ | 45.58 ± 6.48 $^{cd}$ | 21.63 ± 4.33 $^{abc}$ |
| Grp 3 | 181.26 ± 21.04 | 110.23 ± 6.56 $^{abc}$ | 39 ± 1.54 $^{abc}$ | 34.97 ± 3.11 $^{bcd}$ |
| Grp 4 | 163.7 ± 2.57 $^{a}$ | 114.52 ± 2.32 $^{bc}$ | 43.99 ± 1.09 $^{bcd}$ | 37.79 ± 1.27 $^{cd}$ |
| Grp 5 | 162.52 ± 4.74 $^{a}$ | 107.97 ± 4.03 $^{abc}$ | 38.09 ± 1.49 $^{abc}$ | 37.38 ± 6.28 $^{bcd}$ |
| Grp 6 | 175.09 ± 11.18 $^{ab}$ | 117.99 ± 3.03 $^{c}$ | 48.3 ± 3.12 $^{d}$ | 34.68 ± 0.39 $^{bcd}$ |
| Grp 7 | 162.28 ± 12.51 $^{a}$ | 101.84 ± 2.68 $^{abc}$ | 37.64 ± 1.38 $^{ab}$ | 31.74 ± 0.77 $^{abcd}$ |
| Grp 8 | 169.87 ± 4.17 $^{a}$ | 94.48 ± 3.24 $^{a}$ | 39 ± 2.05 $^{abc}$ | 21.5 ± 3.34 $^{abc}$ |
| Grp 9 | 171.3 ± 2.17 $^{a}$ | 94.48 ± 1.84 $^{a}$ | 40.03 ± 2.08 $^{abc}$ | 20.2 ± 0.49 $^{ab}$ |
| Grp 10 | 181.49 ± 3.77 $^{ab}$ | 94.48 ± 5.63 $^{a}$ | 41.16 ± 3.28 $^{abcd}$ | 17.02 ± 7.65 $^{a}$ |
| Grp 11 | 165.6 ± 5.44 $^{a}$ | 93.66 ± 2.9 $^{a}$ | 36.16 ± 1.04 $^{a}$ | 24.37 ± 1.61 $^{abcd}$ |
| Grp 12 | 177.94 ± 6.52 $^{ab}$ | 97.55 ± 7.08 $^{ab}$ | 34.8 ± 1.42 $^{a}$ | 27.15 ± 8.94 $^{abcd}$ |
| Grp 13 | 174.62 ± 5.00 $^{ab}$ | 106.75 ± 1.23 | 35.37 ± 2.13 $^{a}$ | 36.45 ± 3.16 $^{bcd}$ |

Values are expressed as mean ± SD. (n= 4 rats). Means in same column with the same superscript Alphabets are not significantly different at $p<0.05$, while means in same column with different superscript alphabets are significantly different at $p<0.05$

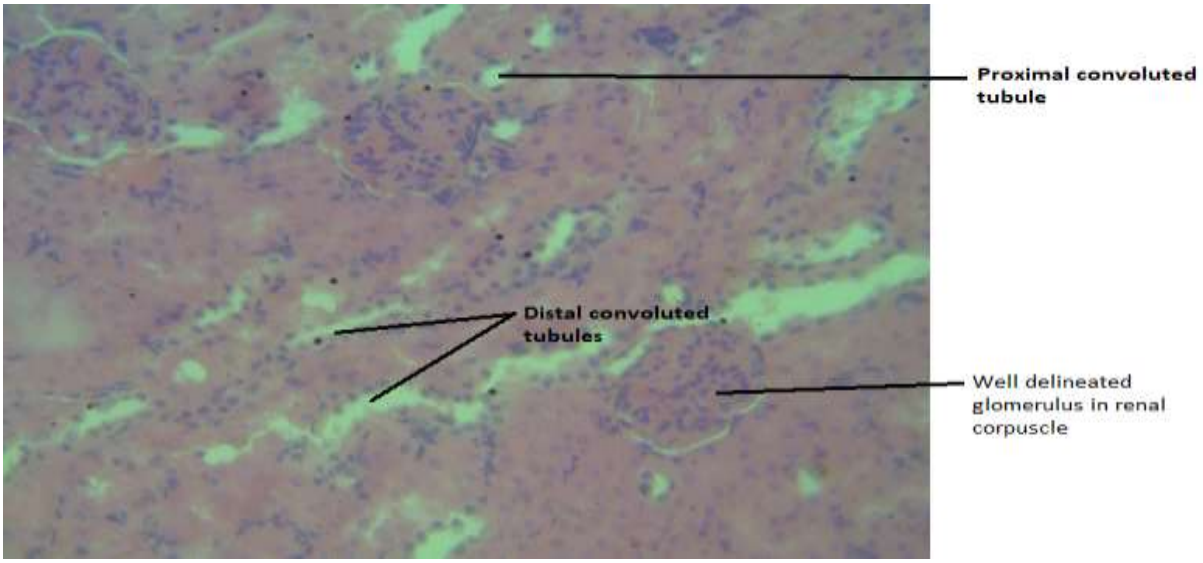


Plate 1: Photomicrograph of the kidney tissue of rats in group 1 (fed with 100g standard rat chow for 30 days), showing the normal features, no abnormalities were seen, using H & E, X40.

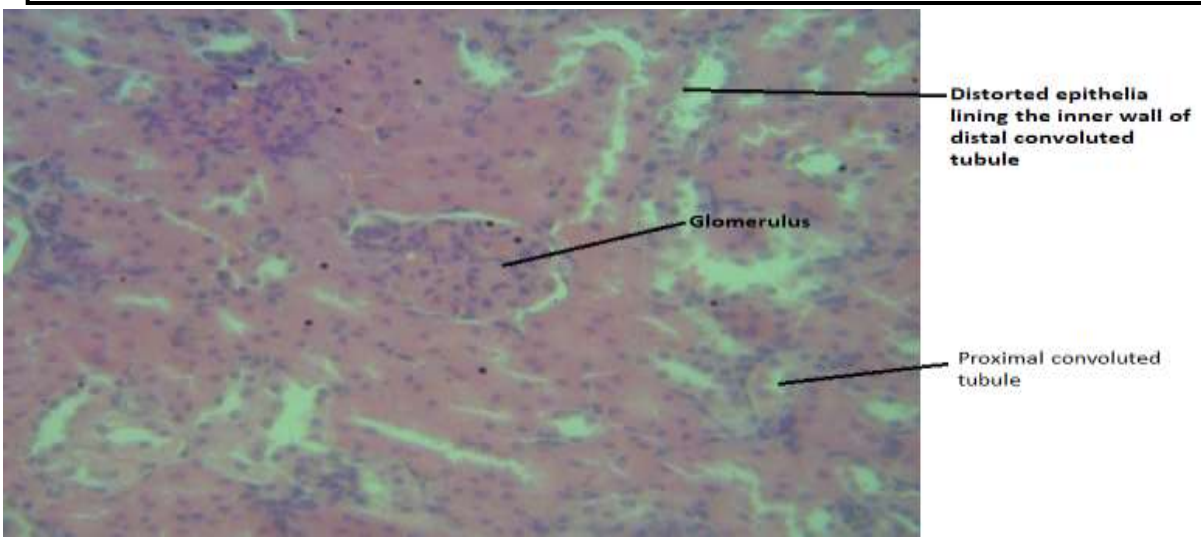


Plate 2: Photomicrograph of the kidney tissue of rats in group 2 (fed with 90g SRC and 10g marijuana diet for 30 days), showing distortion in the distal convoluted tubule, using H & E, X40.

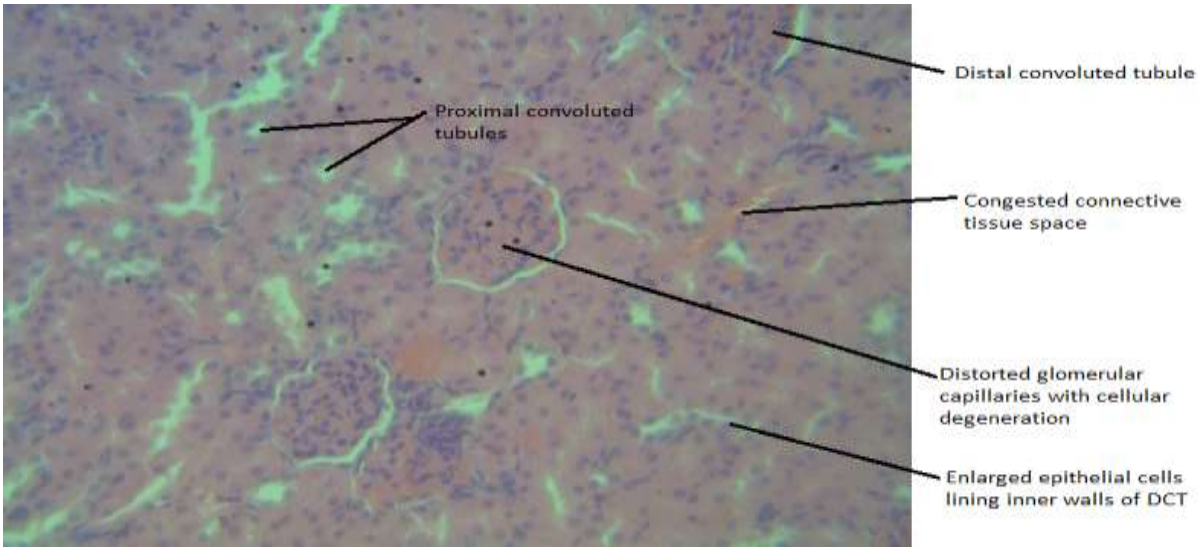


Plate 3: Photomicrograph of the kidney tissue of rats in group 3 (fed with 80g SRC and 20g marijuana diet for 30 days), showing distortion in the connective tissue space, glomelular capillaries and the inner walls of the DCT, using H & E, X40.

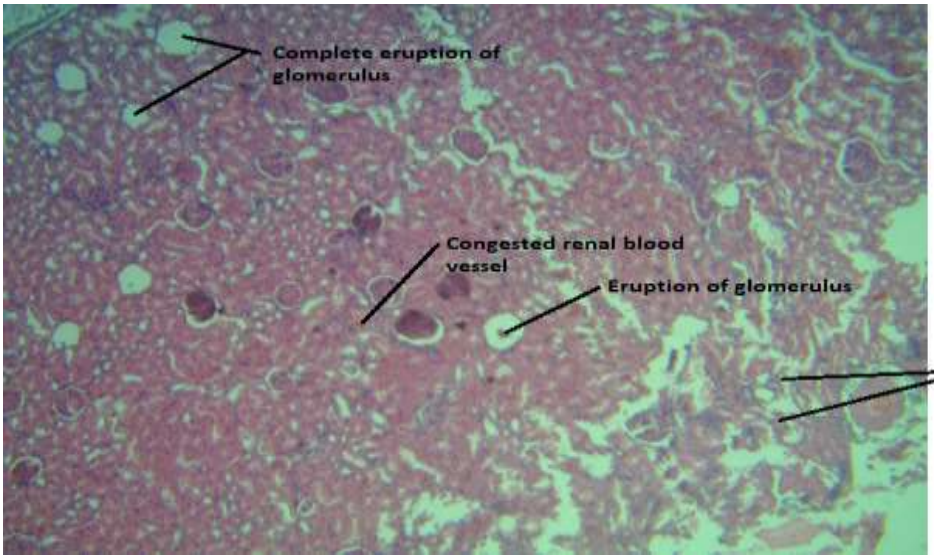


Plate 4: Photomicrograph of the kidney tissue of rats in group 4 (fed with 70g SRC and 30g marijuana diet for 30 days), showing complete eruption of the glomerulus and distortion in the renal blood vessel and connective tissue, using H & E, X40.

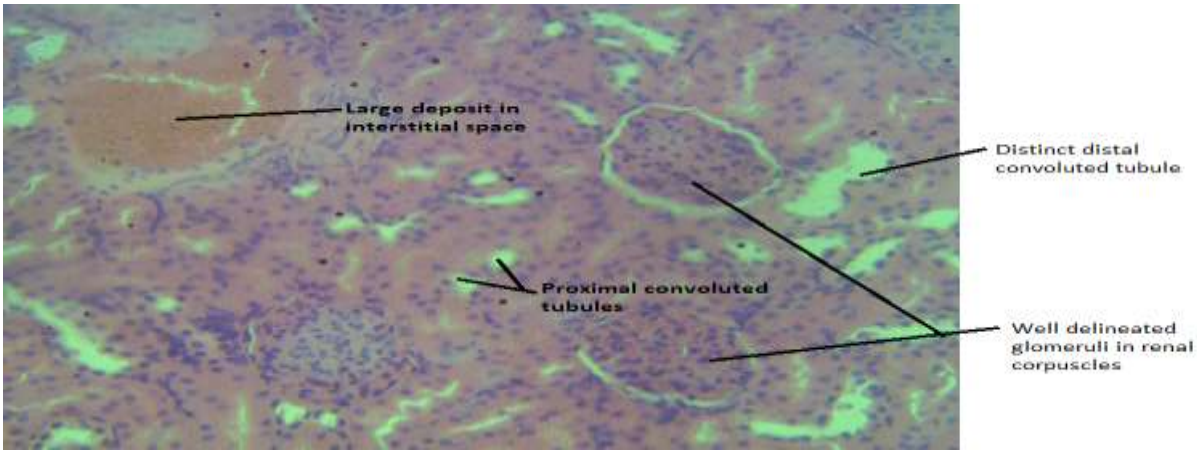


Plate 5: Photomicrograph of the kidney tissue of rats in group 5 (fed with 85g SRC,10g marijuana and 5g ginger diet for 30 days), showing mild distortion in the interstitial space, using H & E, X40.

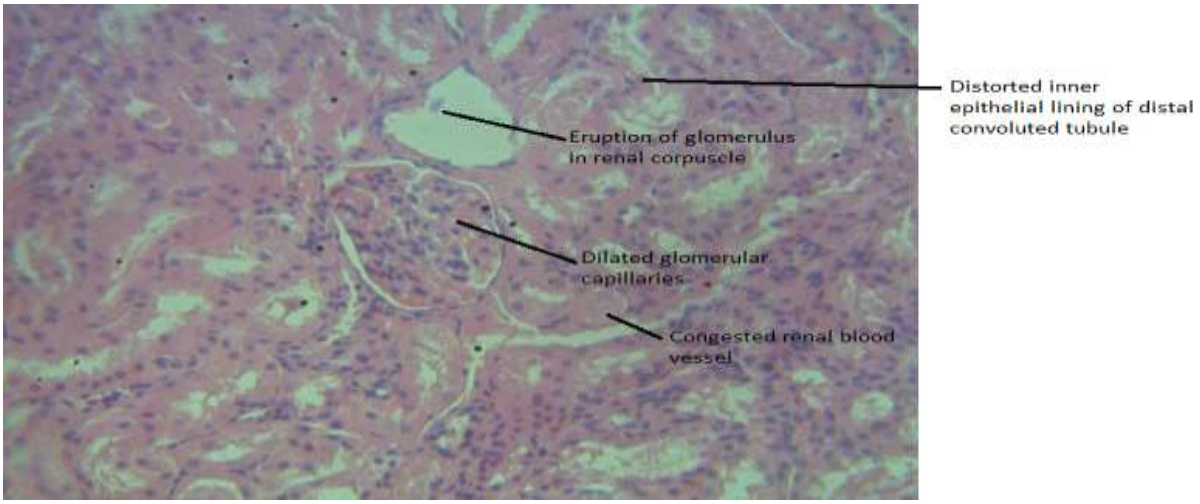


Plate 6: Photomicrograph of the kidney tissue of rats in group 6 (fed with 80g SRC, 10g marijuana and 10g ginger diet for 30 days), showing distortion in the distal convoluted tubule, eruption in the glomerulus, dilated glomerular capillaries and congested renal blood vessel, using H & E, X40.

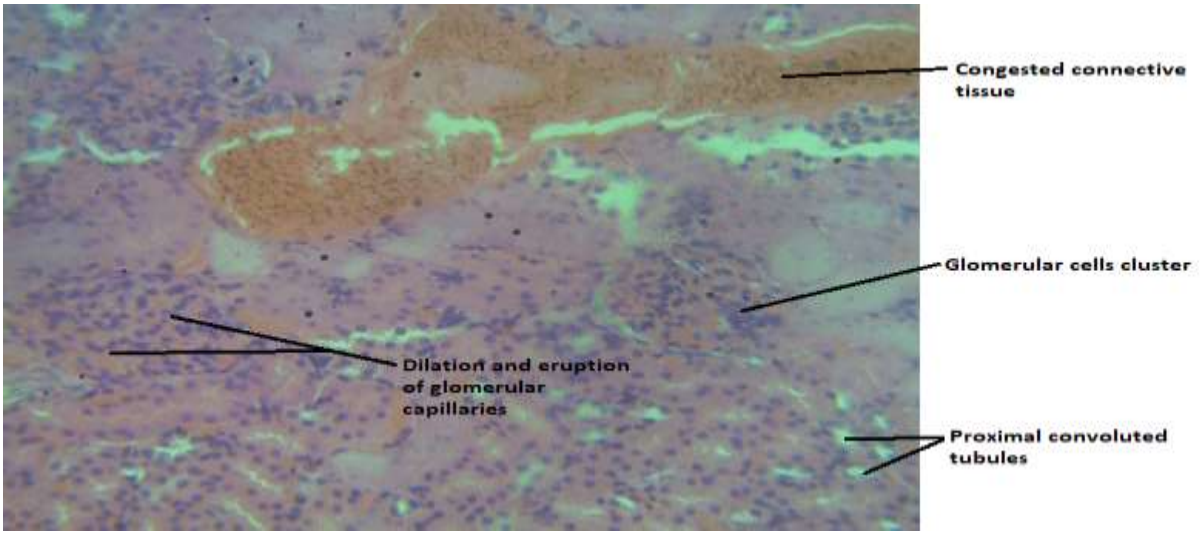


Plate 7: Photomicrograph of the kidney tissue of rats in group 7 (fed with 75g SRC, 10g marijuana and 15g ginger diet for 30 days), showing abnormal features of the glomerular capillaries, congestion in the connective tissue and clustering of the glomerular cells, using H & E, X40.

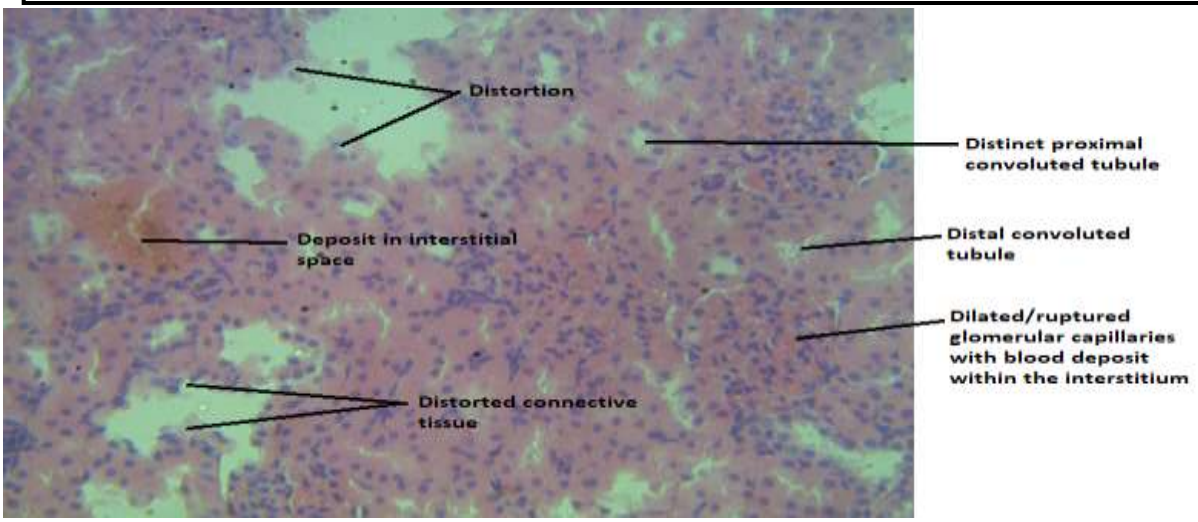


Plate 8: Photomicrograph of the kidney tissue of rats in group 8 (fed with 85g SRC,10g marijuana and 5g turmeric diet for 30 days), showing distortion in the connective tissue, glomerular capillaries and deposit in the interstitial space, using H & E, X40.

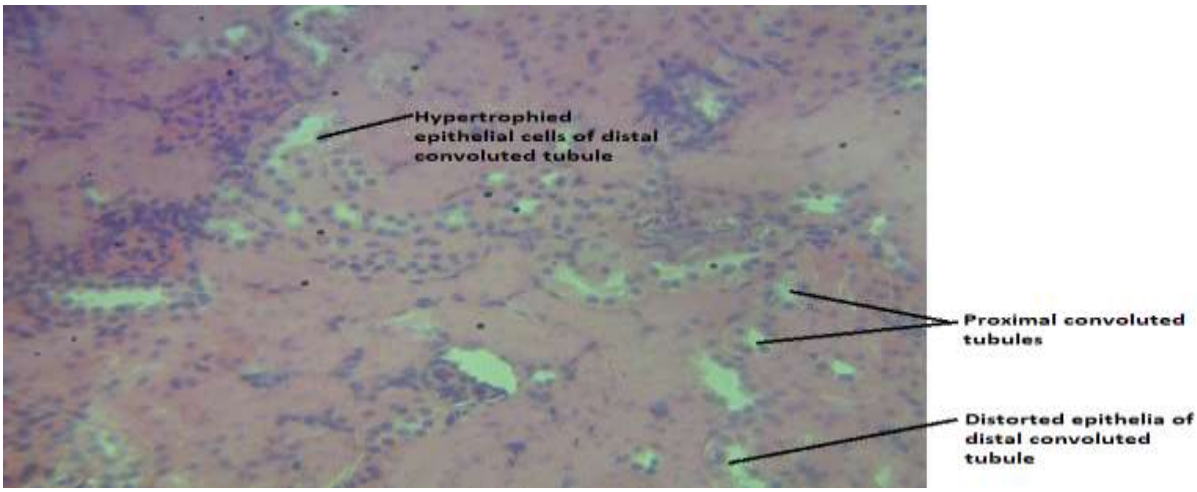


Plate 9: Photomicrograph of the kidney tissue of rats in group 9 (fed with 80g SRC, 10g marijuana and 10g turmeric diet for 30 days), showing hypertrophied convoluted tubule and distortion in the distal convoluted tubule, using H & E, X40.

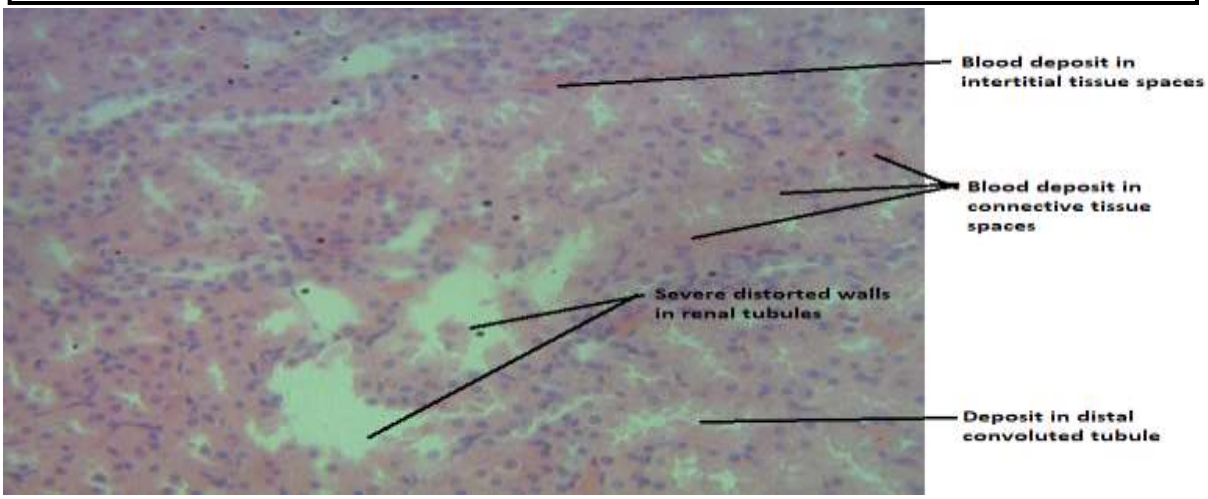


Plate 10: Photomicrograph of the kidney tissue of rats in group 10 (fed with 75g SRC, 10g marijuana and 15g turmeric diet for 30 days), showing blood deposit in the interstitial tissue and connective tissue spaces, distortion in the renal tubules and distal convoluted tubule, using H & E, X40.

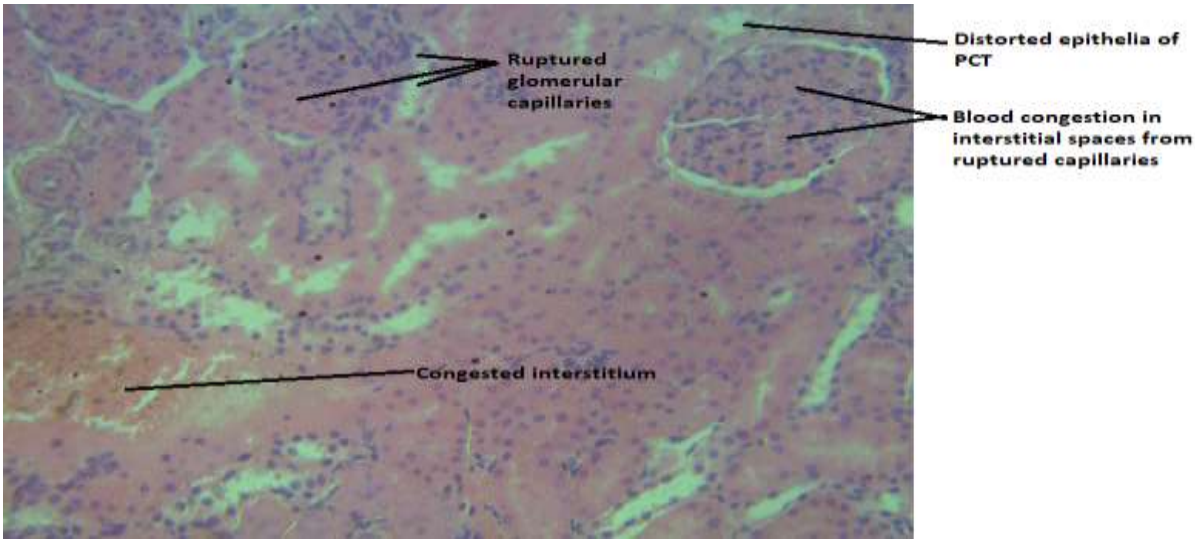


Plate 11: Photomicrograph of the kidney tissue of rats in group 11 (fed with 80g SRC, 10g marijuana and 5g turmeric diet 5g ginger diet for 30 days), showing ruptured glomerular capillaries, distorted distal convoluted tubule, blood congestion in the interstitial space and congested interstitium, using H & E, X40.

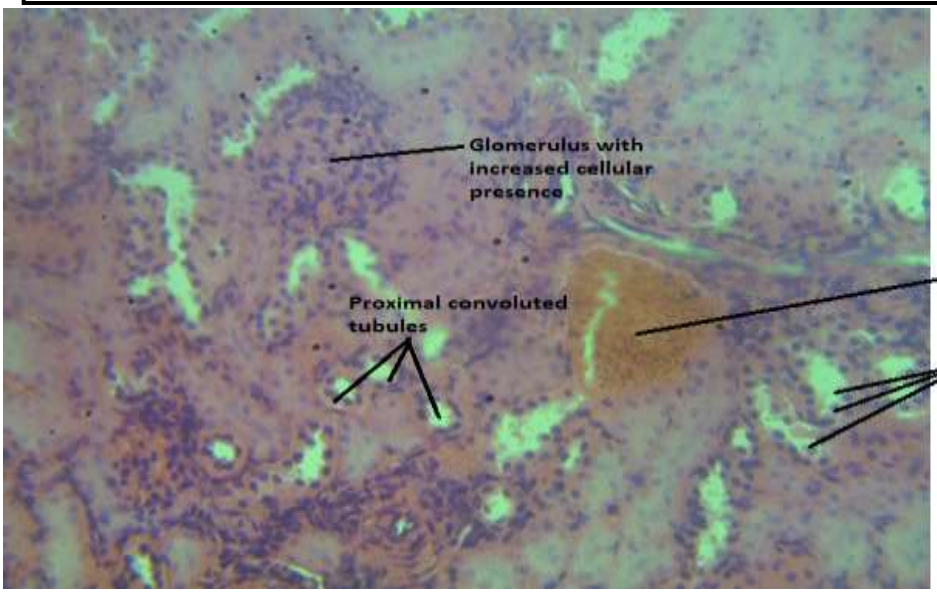


Plate 12: Photomicrograph of the kidney tissue of rats in group 12 (fed with85g SRC,10g marijuana and 2.5g turmeric diet 2.5g ginger diet for 30 days), showing congestion in the blood vessel, hypertrophied lining of the distal convoluted tubule

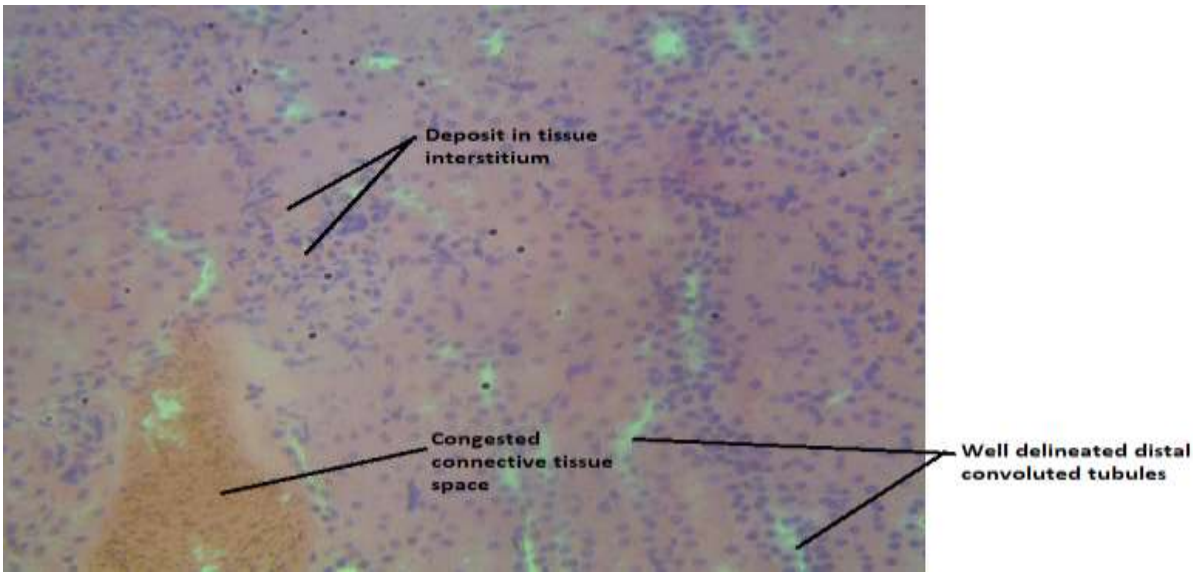


Plate 13: Photomicrograph of the kidney tissue of rats in group 13 (fed with 75g SRC, 10g marijuana and 7.5g turmeric diet 7.5g ginger diet for 30 days), showing mild distortion in the connective tissue space and the tissue interstitium, using H & E, X40.

**DISCUSSION**

Table 2 shows the Ameliorative potential of selected spices on plasma kidney biomarkers on marijuana-induced kidney toxicity in rats. The use of spices not only enhances the flavor of foods but also provides various health benefits due to their bioactive compounds. Selected spices exhibit significant potential in ameliorating plasma kidney biomarkers, thus offering therapeutic avenues for renal protection. The bioactive compounds in these spices contribute to their antioxidative and anti-inflammatory properties,

which can help mitigate kidney damage and improve overall renal function (Khan *et al.,* 2014; Ali *et al.,* 2016; Ghasemzadeh *et al.,* 2017).

Curcumin, the active compound in turmeric (*Curcuma longa*), has been extensively studied for its nephroprotective effects. A study by Singh *et al.* (2015) demonstrated that curcumin effectively reduced renal oxidative stress and inflammation in an animal model of drug-induced kidney damage. The authors noted a significant decrease in plasma levels of creatinine and blood urea nitrogen (BUN), indicating improved renal function. Ginger (*Zingiber officinale*) has also shown promise in improving kidney health. A study conducted by Ghasemzadeh *et al.* (2017) found that ginger extract significantly reduced serum creatinine and BUN levels in diabetic rats, suggesting its protective effect against diabetes-induced nephropathy. The antioxidative properties of ginger are believed to play a key role in mitigating oxidative stress in the kidneys.

The mean plasma chloride, creatinine, and urea levels of the negative control rats (group 3) were significantly lower than those of the normal control (group 1 rats). The mean plasma $K^+$ and $Na^+$ levels of the negative control (group 3) were significantly decreased when compared to the normal control (group 2). The significant increases observed on the mean plasma $Cl^-$ , creatinine, and urea levels as well as the significant decreases noticed on the mean plasma $K^+$ and $Na^+$ levels when compared to the normal control is suggestive to kidney toxicity facilitated by exposure to high dose of marijuana diet which in line with report of Volkow et al. (2014) who in their study, highlighted that THC can induce oxidative stress and inflammation, which may compromise renal cells and lead to an increase in plasma creatinine levels. The mean plasma $Cl^-$, creatinine, and urea levels of marijuana-induced kidney toxicity fed with 10g ginger diet (group 6) for 30 days were significantly decreased in comparison to the negative control values (group 3) while the mean plasma $K^+$ and $Na^+$ of group 6 were significantly increased in comparison to the negative control (group 3) and similar trends occurred in group 7 rats (Table 2). Also, mean plasma $Cl^-$ , creatinine, and urea levels of marijuana-induced kidney toxicity fed with 10g turmeric diet (group 9) for 30 days were significantly decreased in comparison to the negative control (group 3) while the mean plasma $K^+$ and $Na^+$ levels fed with 10g turmeric diet (group 9) for 30 days were significantly increased in comparison to the negative control (group 3) and pattern and changes were perceived in group 12 and 13 fed with 5g turmeric diet 5g ginger and 7.5g turmeric diet7.5g ginger diets (Table 2). The significant decreases observed on the mean plasma $Cl^-$ , creatinine, and urea levels as well as the significant increases perceived on the mean plasma $K^+$ and $Na^+$ levels fed with 10g turmeric diet (group 9) for 30 days in comparison to the negative control, were reflective of the ameliorative potential of singly and combined tumeric and ginger diets. The significant improved observed after feeding with single and combined tumeric and ginger diets for 30 days may be attributed to the antioxidant and anti-inflammatory properties of turmeric and ginger, which could enhance renal health and mitigate damage. The significant increase in plasma potassium and sodium levels suggests a beneficial modulation of electrolyte balance, which is crucial for maintaining cellular function and overall homeostasis. Turmeric and ginger may facilitate better absorption or retention of these essential ions, contributing to improved physiological responses.

Table 3 shows the ameliorative potential of turmeric and ginger diets on oxidative stress kidney biomarkers on marijuana-induced kidney toxicity in rats. The mean plasma nitric oxide level of the rats in group 3 (negative control) were significantly decreased in comparison to group 1 rats (normal control). The mean plasma nitric oxide level of rats in group 6 (80g SRC, 10g marijuana and 10g ginger diet), 7 (75g SRC, 10g marijuana and 15g ginger diet), 8 (85g SRC,10g marijuana and 5g turmeric diet), and 9 (80g SRC, 10g marijuana and 10g turmeric diet) were significantly lower than the negative control (group 3 fed with (80g SRC and 20g marijuana diet) and the normal control (group 1). Also, the mean plasma nitric oxide of rats in group 10 (fed with 75g SRC, 10g marijuana and 15g turmeric diet), group 11 (fed with 85g SRC,10g marijuana and 2.5g turmeric diet 2.5g ginger diet), 12 (fed with 80g SRC, 10g marijuana and 5g turmeric diet 5g ginger diet), and 13 (feed with 75g SRC, 10g marijuana and 7.5g turmeric diet7.5g ginger diet) were significantly increased when compared to those of group 1, 2, and 3 (normal and negative control respectively) (Table 3**).** The significant increase in NO production after feeding with tumeric and ginger diets for 30 days could be indicative that the diets enhanced endothelial

function (which helps in vasodilation and improved blood flow) and reflective of the body's response to combat oxidative stress.

The mean plasma MDA level of rats in group 3 was significantly increased when compared to the group 1 rats. The mean plasma MDA level of rats in group in group 6-12 were significantly decreased after feeding with 80g SRC, 10g marijuana and 10g ginger diet, 75g SRC, 10g marijuana and 15g ginger diet, 85g SRC,10g marijuana and 5g turmeric diet, 80g SRC, 10g marijuana and 10g turmeric diet, 75g SRC, 10g marijuana and 15g turmeric diet, 85g SRC,10g marijuana and 2.5g turmeric diet 2.5g ginger diet, and 80g SRC, 10g marijuana and 5g turmeric diet 5g ginger diet respectively for 30 days in comparison to those of group 2 and 3 (negative control fed with 90g SRC and 10g marijuana diet and 80g SRC and 20g marijuana diet) respectively (Table 3**).** A significant rise in MDA levels could suggest that that marijuana caused an imbalance, leading to oxidative stress. However, the significant reduction in MDA after feeding with diets highlights the potent antioxidant effects of both turmeric and ginger. This results is also suggestive that both turmeric and ginger possess strong anti-inflammatory properties, and the reduction in MDA levels may also indicate a reduction in chronic inflammation.

Also, the mean CAT and SOD activities of rats in group 3 were significantly reduced in comparison to rats in group 1. The mean plasma CAT and SOD activities of rats in group 9-13 fed with 80g SRC, 10g marijuana and 10g turmeric diet, 75g SRC, 10g marijuana and 15g turmeric diet, 85g SRC,10g marijuana and 2.5g turmeric diet 2.5g ginger diet, 80g SRC, 10g marijuana and 5g turmeric diet 5g ginger diet, and 75g SRC, 10g marijuana and 7.5g turmeric diet7.5g ginger diet respectively for 30 days were observed to be significantly increased when compared to the negative control (group 3) as shown in Table 3. The glutathione level of the negative control was significantly decreased in comparison the negative control. Feeding rats in group 9-13 with 80g SRC, 10g marijuana and 10g turmeric diet, 75g SRC, 10g marijuana and 15g turmeric diet, 85g SRC,10g marijuana and 2.5g turmeric diet 2.5g ginger diet, 80g SRC, 10g marijuana and 5g turmeric diet 5g ginger diet, and 75g SRC, 10g marijuana and 7.5g turmeric diet7.5g ginger diet respectively for 30 days resulted in significantly increased glutathione concentration when compared to group 3 rats (Table 3). The significant increases perceived on the mean plasma glutathione level as well as CAT and SOD activities indicate that turmeric and ginger could be yielded cellular amelioration by reducing the accumulation of ROS and preventing oxidative damage to essential biomolecules facilitated by exposure to high dose of marijuana diet.

Elevated plasma triglyceride levels indicate that marijuana, at high doses, may be disrupting normal lipid metabolism. Triglycerides are a form of fat stored in the body and circulate in the bloodstream. An increase suggests that marijuana could be influencing pathways involved in fat synthesis, storage, or breakdown, potentially causing an imbalance in how the body handles fats (Miller *et al.,* 2022). This could be due to changes in the activity of enzymes like lipoprotein lipase or hormone-sensitive lipase, which regulate fat metabolism (Bäckström *et al.*, 2021). High plasma triglyceride levels are often associated with an increased risk of cardiovascular diseases. In humans, elevated triglycerides are linked to conditions like atherosclerosis, hypertension, and heart disease (Dörnyei *et al.,* 2023).

Table 3 shows the Ameliorative effects of selected spices on the lipid profile of marijuana-induced kidney toxicity in Wistar rats**.** The mean plasma triglyceride (TG) of group 3 rats was significantly increased in comparison to that of group 1 (normal control). The mean plasma TG of rats in group 4-13 fed with 70g SRC and 30g marijuana diet, 85g SRC,10g marijuana and 5g ginger diet, 80g SRC, 10g marijuana and 10g ginger diet, 75g SRC, 10g marijuana and 15g ginger diet, 85g SRC,10g marijuana and 5g turmeric diet, 80g SRC, 10g marijuana and 10g turmeric diet, 75g SRC, 10g marijuana and 15g turmeric diet, 85g SRC,10g marijuana and 2.5g turmeric diet 2.5g ginger diet, 80g SRC, 10g marijuana and 5g turmeric diet 5g ginger diet, and 75g SRC, 10g marijuana and 7.5g turmeric diet7.5g ginger diet for 30 days resulted in significant decreases on the mean plasma TG levels in comparison to those of group 1, 2, and 3 (normal and negative control respectively) (Table 4**).** The significant decreases on the mean plasma TG after feeding with turmeric and ginger diet is reflective that the diet could elicit anti-inflammatory properties

The mean plasma total cholesterol of rats in group 2 and 3 were significantly lower than those of group 1. Also, the mean plasma total cholesterol of rats in group 4-7 fed with 70g SRC and 30g marijuana diet,

85g SRC,10g marijuana and 5g ginger diet, 80g SRC, 10g marijuana and 10g ginger diet, and 75g SRC, 10g marijuana and 15g ginger diet were significantly increased in comparison to the negative controls (group 2 and 3)….State the implication. However, the mean plasma total cholesterol of rats in group 8-13 fed with 85g SRC,10g marijuana and 5g turmeric diet, 80g SRC, 10g marijuana and 10g turmeric diet, 75g SRC, 10g marijuana and 15g turmeric diet, 85g SRC,10g marijuana and 2.5g turmeric diet 2.5g ginger diet80g SRC, 10g marijuana and 5g turmeric diet 5g ginger diet, and 75g SRC, 10g marijuana and 7.5g turmeric diet7.5g ginger diet resulted in significantly decreased mean plasma total cholesterol in comparison to the negative control (group 2 and 3). The significant decreases on observed on the mean plasma total cholesterol after feeding diet formulated from single and combined tumeric and ginger did not cause improvement on the metabolism of total cholesterol.

The mean plasma LDL cholesterol level of rats in group 2 and 3 respectively were significantly lower than those of the normal control. The mean plasma LDL levels of rats in group 8-12 fed with 85g SRC,10g marijuana and 5g turmeric diet, 80g SRC, 10g marijuana and 10g turmeric diet, 75g SRC, 10g marijuana and 15g turmeric diet, 85g SRC,10g marijuana and 2.5g turmeric diet 2.5g ginger diet, and 80g SRC, 10g marijuana and 5g turmeric diet 5g ginger diet resulted in significant decreases on the mean plasma LDL cholesterol in comparison to the negative controls (group 2 and 3). Lowering LDL levels is often associated with a reduced risk of atherosclerosis and other cardiovascular diseases. LDL is often termed "bad cholesterol" because elevated levels can lead to plaque buildup in arteries, increasing the risk of heart attacks and strokes. Studies have shown that compounds in turmeric (like curcumin) and ginger can contribute to lipid-lowering effects, thereby supporting heart health (Sharma *et al.*, 2017; Ali *et al.*, 2018). The decreases on the mean plasma LDL level after feeding with tumeric and ginger diet for 30 days is suggestive that turmeric and ginger possess potent anti-inflammatory properties and could reduce inflammation.

Significant regeneration of damage kidney tissues of rats in group plate 6-13 after feeding with high dose of tumeric and ginger diet for 30 days. The regeneration of damaged kidney tissue indicates that turmeric and ginger might have promoted tissue repair and healing in the kidneys. It also indicates that both turmeric and ginger might have potent anti-inflammatory properties.

## CONCLUSION

This study investigated the mitigating marijuana-induced nephrotoxicity: the role of selected local spice diets in Wistar rats. The significant increase in nitric oxide levels after a high dose of turmeric and ginger diet in rats for 30 days likely indicates a beneficial effect on cardiovascular health, immune function, and inflammation regulation, largely due to the bioactive compounds in these herbs. However, it is important to maintain a balance in NO levels to prevent any potential negative effects, such as oxidative damage or neurotoxicity. Significant increases in plasma CAT and SOD levels after a high dose of turmeric and ginger diet for 30 days indicate that these diets might have enhanced the body's antioxidant defense mechanisms of the fed rats. The regeneration of damaged kidney tissue indicates that turmeric and ginger might have promoted tissue repair and healing in the kidneys. It also indicates that both turmeric and ginger might have potent anti-inflammatory properties. These findings suggest that turmeric and ginger could play crucial role in maintaining cellular health and reduce the risk of oxidative stress-related diseases when taken in appropriate doses.

## REFERENCES

Adeyemi, O. S., Akanji, M. A., & Oguntoye, S. O. (2016). "Toxicological Assessment of Cannabis Sativa on Liver Function in Experimental Animal Models." *Journal of Biomedical Science and Toxicology, 10*(2), 35-42

Ali, B. H., Al Za'abi, M., Blunden, G., & Nemmar, A. (2015). "Experimental Nephrotoxicity Induced by Cisplatin: The Protective Effect of Ginger." *Food and Chemical Toxicology, 78*, 130-135.

Ali, B. H., Al Naqeeb, G. M., & Al Suleimani, Y. (2016). "The protective effect of fenugreek (Trigonella foenum-graecum) on nephrotoxicity induced by cisplatin in rats." *Food & Function*, *7*(9), 3803-3812.

Ali, S., Sulaiman, S. A., Mohd, M. N., & Abdul Rahman, R. (2018). The effect of ginger supplementation on lipid profile: A systematic review. *Journal of Medicinal Food*, *21*(5), 433-445.

Bäckström, S., Vetter, H., Nyberg, M., & Lundqvist, C. (2021). Hypertriglyceridemia and lipid dysregulation after marijuana use in rodent models. *Journal of Lipid Research*, *62*, 100073.

Dörnyei, G., Vass, Z., Juhász, C. B., Nádasy, G. L., Hunyady, L., & Szekeres, M. (2023). Role of the Endocannabinoid System in Metabolic Control Processes and in the Pathogenesis of Metabolic Syndrome: An Update. *Biomedicines*, *11*(2), 306.

Ghasemzadeh, A., Jaafar, H. Z. E., & Rahmat, A. (2017). "Ginger (Zingiber officinale R.) and its bioactive compounds: A review on health benefits." *Journal of Food Science and Technology*, *54*(8), 2206-2218.

Khan, A., Safdar, M., & Ullah, N. (2014). "Cinnamon extract improves glucose and lipids of diabetic rats." *Journal of Diabetes & Metabolic Disorders*, *13*(1), 10

Maccarrone, M., Bab, I., & R. S. A. (2017). "Endocannabinoid system: An overview." *Journal of Physiology and Biochemistry*, *73*(4), 585-590.

Miller, D. K., Kolesnik, T. E., & Lewis, M. M. (2022). Chronic Cannabinoid Exposure Induces Dyslipidemia in Rats. *Frontiers in Physiology*, *13*, 788453.

Pertwee, R. G. (2015). "Endocannabinoids and their receptors: A brief history." *British Journal of Pharmacology*, *172*(2), 327-336.

Prakash, D., Suri, S., Upadhyay, G., & Singh, B. N**.** (2017). "Antioxidant and Anti-inflammatory Properties of Ginger (Zingiber officinale): A Review." *International Journal of Health Sciences*, *10*(3), 120-128.

Renard, J., Rushlow, W. J., & Laviolette, S. R. (2017). "What Can Rats Tell Us about Adolescent

Cannabis Exposure? Insights from Preclinical Research." *Canadian Journal of Psychiatry*, *62*(6), 426-434.

Sharma, A., Goyal, R., & Sharma, L. (2017). "Turmeric and Curcumin: Biological Actions and Medicinal Applications." *Current Pharmaceutical Design*, *23*(7), 2326-2340.

Singh, S., Kumar, A., & Kaur, G. (2015). "Curcumin: A potential therapeutic agent for acute kidney injury." *Journal of Renal Nutrition*, *25*(4), 388-394.

Volkow, N. D., Baler, R. D., Compton, W. M., & Weiss, S. R. B. (2014). "Adverse Health Effects of Marijuana Use." *New England Journal of Medicine*, *370*(23), 2219-2227.