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Research Article

Effects of Psychoactive Substances on Some Biochemical Parameters and Histopathology of Kidney in Male Albino Rats

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Abstract

Background and Objective: Psychoactive substances are chemical substances that change brain function and result in alterations in perception, mood, consciousness, cognition or behaviour when taken. This study evaluated the effects of psychoactive substances in the white tips of lizard dung, Indian hemp, *Datura metel* seed and blue dye on some biochemical parameters and histology of male albino rats. **Materials and Methods:** Twenty-five male albino rats weighing 91 ± 9.4 g were used for the study and allotted into five groups with group 1 as control which received potable water, while groups 2-5 received potable water, a mixture of lizard dung with other substances. The substances were administered to the experimental animals for 14 days, at the end of which they were sacrificed, serum samples were collected for biochemical analysis, while the kidney was collected for histological study. **Results:** There were no significant differences in serum electrolyte levels of calcium, sodium, potassium and chloride for control when compared with other experimental groups. The results of the malondialdehyde showed that there was a significant difference ($p < 0.05$) between the control and groups 3 and group 4 and no significant difference ($p > 0.05$) between the control and groups 2 and 5. **Conclusion:** The study revealed that varying types of psychoactive substances elicited varying concentrations of malondialdehyde which reflected the levels of peroxidation. However, this variation among treatments was not significantly different ($p > 0.05$). The study further revealed no aberration in the histology of the kidney suggesting that psychoactive substances have no negative impact in albino rats fed for 14 days.

Key words: Blue dye, *Datura metel* seed, lizard dung, peroxidation, potable water, histology, psychoactive

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Psychoactive substances or psychoactive drugs are chemical substances that change brain function and result in alterations in perception, mood, consciousness, cognition or behaviour when taken¹. The knowledge of using natural products to cure both human and animal diseases has been transmitted from one generation to another which was perfected with experience and gained wide acceptance in recent times². These substances affect or alter to a substantial extent: Consciousness, the ability to think, critical judgment, motivation, psychomotor coordination or sensory perception and have a potential for abuse when used without medical supervision. The use of psychoactive substances is one of the main contributors to the occurrence of road traffic accidents³, associated with a significant public health burden⁴.

Psychoactive substances can be grouped into cannabimimetic, synthetic cathinones and novel stimulants⁵. Caffeine and related stimulants are psychoactive substances widely used in the form of coffee, tea and many soft drinks, nicotine, is currently most often used by smoking tobacco, cigarettes and consumption of alcoholic beverages, which come in many forms, including beer, wine and distilled spirit⁶. Although alcohol, tobacco, marijuana and other psychoactive substances are associated with a spectrum of potential harms to individuals and societies, not all psychoactive substances used are harmful⁷. There is growing evidence that specific interventions can reduce the potential harms associated with the continued use of psychoactive substances⁸.

Psychoactive substances are used as medications in relieving pain, promoting either sleep or wakefulness and relieving mood disorders by western and other systems of medicine⁹. Psychoactive substances used illicitly are widespread in many societies, particularly among young adults, the main reason is to enjoy or benefit from the psychoactive properties of the substances like opiates, cannabis, hallucinogens, cocaine and many other stimulants, as well as hypnotics and sedatives^{10,11}. The illegal use has varying reasons or purposes, the consumption of these substances, for the source of nutrition, of heating or cooling the body, or thirst-quenching, or it may serve a symbolic purpose in a round of toasting or as a sacrament. However, despite the purpose of use, the psychoactive properties of the substance inevitably accompany its use¹². this poses a challenge for psychiatry¹³. Psychoactive substances are associated with the imbalance of a range of neurotransmitter pathways and receptors and consequently with the risk of psychopathological disturbances¹⁴. Psychoactive substances act in the brain on mechanisms that exist normally to regulate functions of mood,

thoughts and motivations⁷ as a result of increased dopamine, cannabinoid (CBI) receptor activation, 5-hydroxytryptamine receptor(5-HT_{2A}) activation, antagonist activity at N-methyl-D-aspartate receptors, K-opioid receptor activation¹⁴. Psychoactive substances all have elicited psychomotor excitation, euphoria, feeling of increased empathy, increased interpersonal openness and self-assurance and increased libido. Overdose can result in numerous adverse effects such as panic and aggression, memory disturbances, hallucinations, memory loss, depression and suicidal thoughts¹⁵.

In recent times, the use of numerous psychoactive substances for therapeutic benefits has prompted the study into these psychoactive agents, white tips of lizard dung, a seed of *Datura metel* and blue dye, as very little research, has been done to understand the effects of the psychoactive substances on some biochemical parameters and histopathology of kidney in male albino rats.

MATERIALS AND METHODS

Study area: The study was carried out at Federal University Wukari, Taraba State for five months between January and May, 2019.

Experimental animals: Twenty-five male albino rats seven weeks old weighing between 91 ± 9.4 g were used for the study. They were procured from Benue State. The animals were randomly assigned into five groups, consisting of five animals per group and were acclimatized for 14 days.

Psychoactive substances: The white tip of lizard dung was sourced from the fence of a house, seeds of *Datura metel* were gotten from a neighbourhood in Wukari and the blue dye was gotten from the Biochemistry Department Laboratory of Federal University Wukari.

Experimental design:

Groups	Treatments received (daily)
Group 1	Potable water (control group)
Group 2	Lizard dung+potable water
Group 3	Lizard dung+HEMP+potable water
Group 4	Lizard dung+HEMP+ <i>Datura metel</i> +potable water
Group 5	Lizard dung+HEMP+ <i>Datura metel</i> +DYE+potable water

The mixture of psychoactive substances was administered orally to the animals for 14 days.

Blood and organs collection: A blood sample was collected by cardiac puncture after 14 days into sterile tubes containing no anticoagulant and their kidneys were collected into a small McCartney plastic bottle under formalin. The blood samples were allowed to clot and serum was obtained by centrifuging at 3000 rpm for 5 min. The supernatant (serum) was collected by simple aspiration using a Pasteur pipette and dispensed into clean tubes for biochemical analysis. The tissue was prepared according to the conventional method described¹⁵.

Biochemical analysis: Biochemical analysis such as the estimation of catalase activity was determined by the method¹⁶. Superoxide dismutase (SOD) estimation as described by Peskin and Winterbourn¹⁷. The estimation of GSH by the procedure of Ro and Rosenzweig¹⁸. The malondialdehyde (MDA) was determined spectrophotometrically according to the method described¹⁹. Serum electrolytes were estimated using a flame photometer manufactured by JENWAY, Models PFP7 and PFP7/Cole-Parmer Ltd., Beacon Road Stone, Staffordshire ST15 the OSA, United Kingdom.

Statistical analysis: All the grouped data (results) were statistically evaluated with Statistical Package for Social Science (SPSS) version 25. Hypothesis testing methods included One-way Analysis of Variance (ANOVA) followed by Duncan's Multiple Range Test. The $p < 0.05$ were considered to be statistically significant. All the results were expressed as Mean $\pm$ SEM.

RESULTS

Homogenate parameters were measured as $\mu\text{mole L}^{-1}$:

Figure 1 shows the homogenate parameters determined for five treated groups as shown in the histogram above. There was no definite pattern in the levels of malondialdehyde. The highest level was observed in group 3 animals while the lowest concentration was recorded for group 3. Significant differences ($p < 0.05$) were observed in the levels of glutathione between the control and the treatments. Superoxide dismutase had its range between 21.10 and 39.25 $\mu\text{mole L}^{-1}$, there were significant differences ($p < 0.05$) in the levels of the control and treatments, with the control having the highest level of 3.19.

Table 1 shows the varying levels of electrolytes concentrations elicited by the treatments, with high levels recorded for sodium while low values were recorded for calcium and potassium. The range for serum chloride

concentration was found to be between 47.47 ± 1.06 and 65.43 ± 2.22 mEq L^{-1} .

Figure 2(a-e) represents the histological observation of different components of psychoactive substances and the control group in albino rats. Mild inflammation shows in group 2 while in other group the condition of the kidney tissues is relatively normal and intact.

DISCUSSION

Psychoactive substances affect mainly the central nervous system and brain function causing changes in behaviour. Many psychoactive substances have the therapeutic function of analgesics or anaesthetics and high addiction potential. Clinical observations demonstrated that adverse effects of psychoactive substances were associated with the addiction period and route of administration^{20,21}.

The range observed for glutathione concentration in this study was between 2.50 and 7.75 $\mu\text{m L}^{-1}$. It was found that glutathione concentration in the kidney of albino rats administered with lizard dung and Indian hemp was significantly increased when compared with other groups and the control. This could be due to the high levels of toxins caused by the administration of these psychoactive substances which elicited a corresponding increase in the synthesis of glutathione in the kidney of experimental animals. Similar results were obtained when comparing the results of this study with that of the study on the importance of glutathione synthesis in human disease²². Lipid peroxidation activity increased significantly in the kidney homogenate of rats, this is due to the toxic effects of oxygen free radicals in the body. This translated to increased levels of malondialdehyde (MDA) as reflected in a significant increase in group 3 (Fig. 1) in response to lipid peroxidation and oxidative stress in the cells. The increase in lipid peroxidation was found to be dependent on double bond concentration. The presence of high serum MDA levels supports the hypothesis that increased oxidative stress, particularly lipid peroxidation contributes to sepsis pathophysiology²³. Oxidative stress occurs when free radical production exceeds the antioxidant capacity of endogenous molecules such as glutathione, superoxide dismutase, thioredoxin and vitamin E²⁴. The results of this study showed that the rats had varying levels of MDA with the lowest value reported for group 4. Although several explanations could account for the unreliability of serum MDA levels in sepsis, lipid peroxidation is not specific to sepsis and may be affected by comorbid conditions, diet and lifestyle behaviours. Increased blood MDA occurs in smokers²⁵ and patients with diabetes mellitus hypertriglyceridemia^{25,26}.

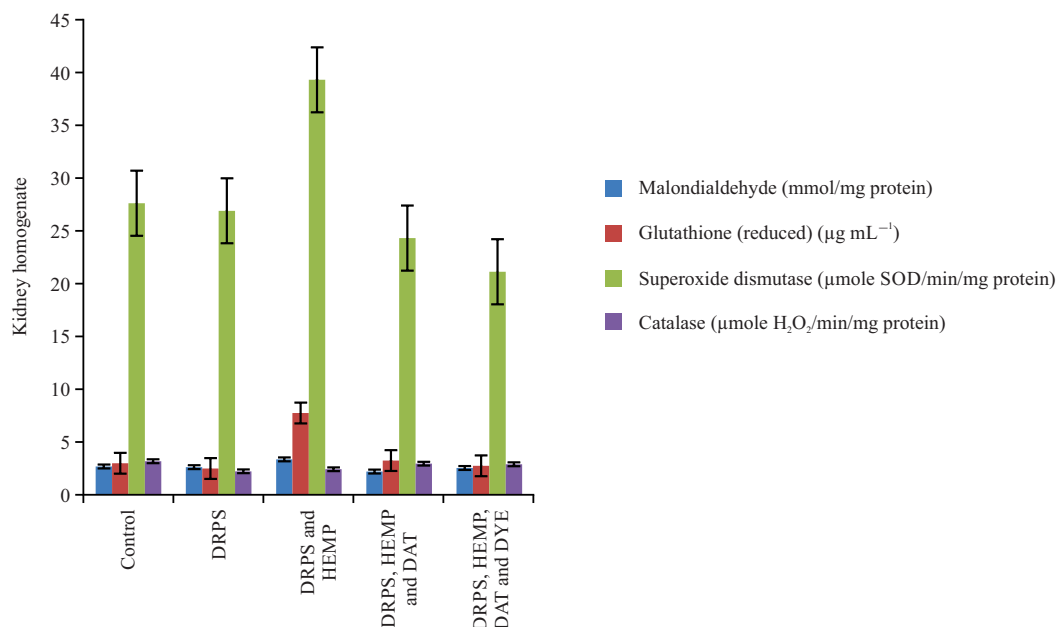


Fig. 1: Showing some serum biochemical parameters

Table 1: Serum electrolytes of experimental rats

Parameters	Calcium (mg dL ⁻¹)	Sodium (mEq L ⁻¹)	Potassium (mEq L ⁻¹)	Chloride (mEq L ⁻¹)
Group 1 (control)	8.31±0.59	101.71±2.53	3.59±0.65	50.57±1.49
Group 2 (DRPS only)	8.35±2.48	87.42±2.96	3.85±0.99	62.24±6.89
Group 3 (DRPS+HEMP)	10.14±1.39	87.55±10.69	2.54±0.64	47.47±1.06
Group 4 (DRPS+HEMP+ <i>Datura metel</i>)	7.85±0.97	97.58±11.06	3.69±0.19	65.43±2.22
Group 5 (DRPS+HEMP+DAT+DYE)	7.88±3.20	90.37±0.91	3.18±0.32	65.33±1.12

It has been found that glutathione participated in many cellular reactions of free radicals and other reactive oxygen species which showed that it effectively scavenges free radicals and other reactive oxygen species such as hydroxyl radical, lipid peroxyl radical, peroxynitrite and hydrogen peroxide directly and indirectly through enzymatic reactions²⁷. The findings in this study showed that group 3 had the highest level of glutathione while the lowest was recorded for group 4. This could be due to the various effects of psychoactive substances in triggering glutathione synthesis. Glutathione (GSH) displays remarkable metabolic and regulatory versatility GSH/GSSG is one of the most important redox couples and played crucial roles in antioxidant defence, nutrient metabolism and the regulation of pathways essential for the whole body homeostasis²⁷.

The range observed for superoxide dismutase varied between 21.10 and 39.25 µmole L⁻¹. Here also, group 3 was noted with the highest level in the kidney homogenate. The levels of catalase activity were significantly different ($p < 0.05$) in the treatments (group 2-5) when compared with the

control. The lower values recorded for treated groups could be a result of inhibition of catalase enzymes by psychoactive substances.

A histological study revealed that kidney slices for group 1, 3, 4 and 5 were normal while group 2 had a mild inflammation, which could be due to the effects of lizard dung on kidney tissue. This could also be because lizard dung could cause inflammation of the kidney possibly as an immune response reaction as elicited in group 2 rats. However, the histology of the kidney of group 3, 4 and 5, were normal.

There were no significant differences in the electrolyte parameters analysed in this study. This could be an indication that the psychoactive substances did not affect the buffering capacity within the blood. This could also be since psychoactive substances affect mainly the central nervous system and brain function causing changes in behaviour²⁸.

The implication of this study is to reveal the effects of psychoactive substances on some biochemical parameters and histology of kidneys in male albino rats. The findings in this study can be applied and translated to what could happen

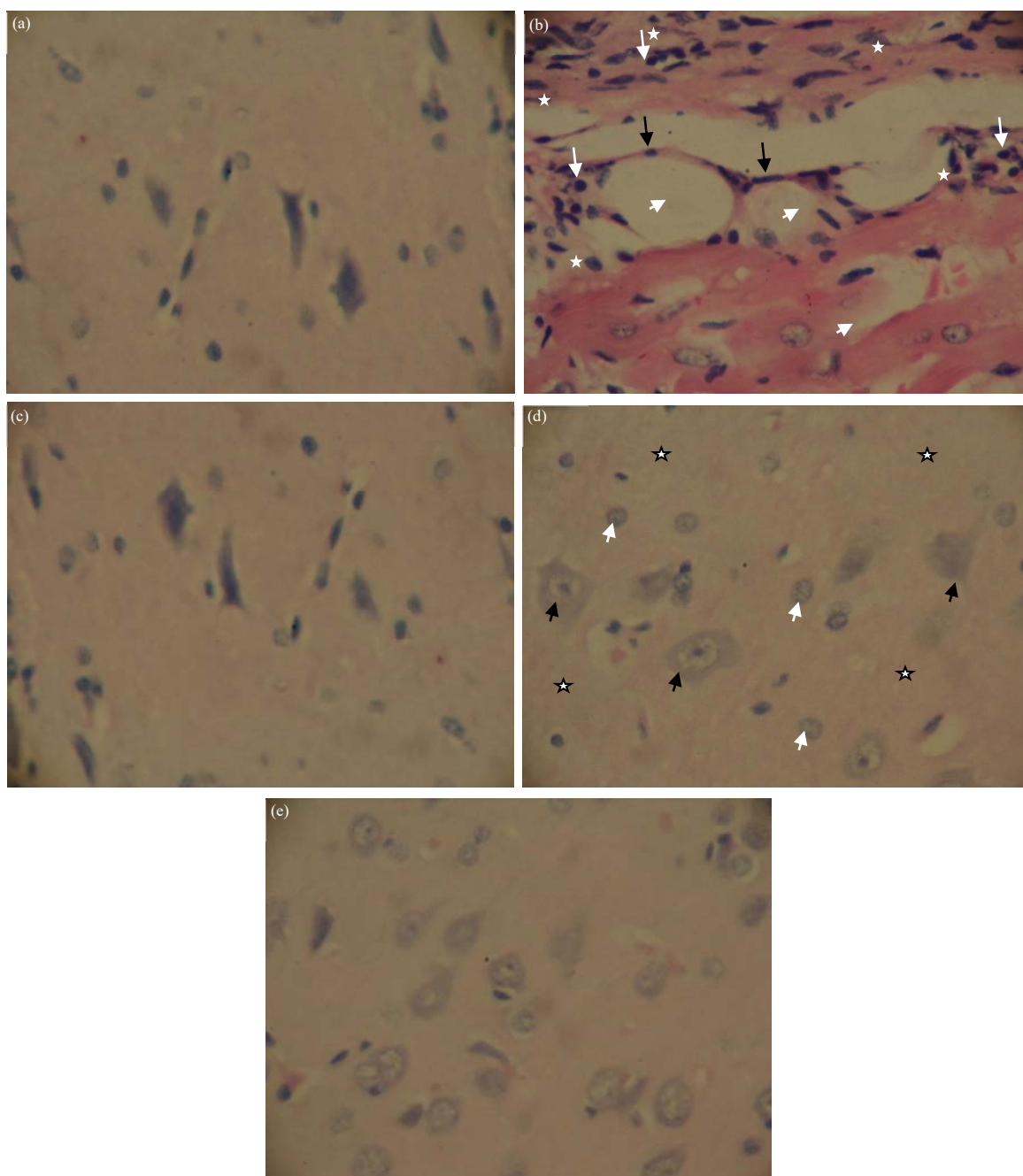


Fig. 2(a-e): Kidney histology of albino rats administered different components of psychoactive substances and the control, (a) Control group 1 kidney of the albino rat fed and received potable water for 14 days, histologically, the kidney tissue is normal, (b) Group 2, kidney of albino rat administered lizard dung and potable water for 14 days, there is mild inflammation as shown by the presence of inflammatory cells (white arrows), fatty degeneration is evident by the replacement of tissue with fat cells (black arrows), (c) Group 3 Kidney of an albino rat administered lizard dung, HEMP and potable water for 14 days, histologically, the kidney tissue is normal, (d) Group 4 kidney of albino rats administered lizard dung, HEMP, *Datura metel* and potable water for 14 days showing normal histology of the kidney tissue, Black arrows: Neurons, White stars: Neutrophil, White arrows: Neuroglia cells and (e) Group 5 kidney tissue of albino rats administered lizard dung, HEMP, *Datura metel*, DYE and potable water for 14 days, showing intact kidney tissue H&E×400

in humans who indulge in the consumption of these psychoactive substances. Hence the findings can be recommended to students and addicts of psychoactive substances so that they can desist from the acts of consumption of conventional and non-conventional psychoactive substances. However, this type of study has its limitations in the area of procurement of some non-conventional psychoactive substances, especially lizard dung, which in this study elicited mild inflammation of kidney histology as shown in group 2.

CONCLUSION

The result of this study showed that the psychoactive substances used had no negative effects and/or structural aberration on the kidney of all the experimental groups when administered for 14 days. Electrolytes (calcium, sodium, potassium, chloride) treatments were not significantly different from control. Hence, it has no effects on the homeostatic system in the experimental animals.

SIGNIFICANCE STATEMENT

This study discovers the effects of psychoactive substances on some serum antioxidant enzymes, electrolytes and histopathology of the kidney in male albino rats. These parameters are good markers for the health of animals. This information could be translated to human parameters and also be beneficial to researchers who will do similar studies in the future.

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