



## Relationship between Dose and Duration of Administration of Potassium Bromate on Selected Electrolytes and Hepatorenal Parameters in Male Albino Wistar Rats

Samuel Y. Gazuwa<sup>1\*</sup>, Jonathan D. Dabak<sup>1</sup>, Kiri H. Jaryum<sup>1</sup> and Ige Oluwa<sup>1</sup>

<sup>1</sup>Department of Biochemistry, University of Jos, P.M.B 2084, Jos, Nigeria.

### *Authors' contributions*

*This work was carried out in collaboration among all authors. Author SYG conceptualised and designed the work. Authors JDD and KHJ managed literature searches. Authors SYG and IO wrote the protocol and managed the analyses of the study. Author IO wrote the first draft of the manuscript. Statistical analysis was performed by author SYG. All authors read and approved the final manuscript.*

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### **ABSTRACT**

**Aim:** To monitor the effects of dosage and duration of administering  $KBrO_3$  on some electrolytes and hepatorenal parameters in male albino Wistar rats.

**Study Design:** 24 rats, mean weight of 181.3 g were grouped into 4 with 6 rats of each. Experiment spanned over 12 days. In the control group, animals were fed standard diet. Animals in the test groups were fed diet containing 67, 100 and 167 mg/kg dose of  $KBrO_3$  according to body weight. 2 rats from each group were sacrificed on the 4<sup>th</sup>, 8<sup>th</sup> and 12<sup>th</sup> days.

**Place and Duration of Study:** University of Jos; 1 month including writing the report.

**Methods:** Spectrophotometric and titrimetric techniques were applied. InStat3 statistical software was used to analyse the data obtained.  $P \leq 0.05$  was considered significant.

**Results:** on the 4<sup>th</sup> day at 67mg/kg dose, showed raised serum activities (IU) of ALT,  $41.0 \pm 9.6$ ,

\*Corresponding author: Email: [gazuwas@unijos.edu.ng](mailto:gazuwas@unijos.edu.ng), [sygazuwa@gmail.com](mailto:sygazuwa@gmail.com);

and AST,  $130.2 \pm 31.53$ , ( $P=.05$ ). At 100 mg/kg dose, serum activities of ALT,  $52.12 \pm 1.12$ , AST,  $180.0 \pm 0.41$ , and level (g/L) of Total Proteins, TP,  $67.77 \pm 0.35$ , were elevated ( $P=.05$ ). On the 8<sup>th</sup> day at 67 mg/kg dose, there were no significant increases ( $P>.05$ ). At 100 mg/kg dose, only AST activity,  $98.0 \pm 43.86$ , increased ( $P=.05$ ). Levels of urea (UR) and creatinine (CR) were lower than the control at both 60 and 100 mg/kg dose. At 167 mg/kg dose, level of TP and activities of ALT, and AST increased ( $P=.05$ ) relative control. On the 12<sup>th</sup> day, treatments at 67 mg/kg dose raised the activities of ALT and AST ( $P=.05$ ). At 100 mg/kg dose, level of creatinine,  $106 \pm 19.2$   $\mu\text{mol/L}$ , was significantly ( $P=.05$ ) elevated. For urea, mmol/L, test groups results ( $4.26 \pm 1.39$ ;  $6.70 \pm 2.01$ ;  $21.07 \pm 2.21$ ) were higher ( $P=.05$ ) relative control group. Activities of AST and ALP were raised ( $P=.05$ ). On the 12<sup>th</sup> day at 167 mg/kg dose, TP, ALT, AST and ALP significantly ( $P=.05$ ) elevated implying toxicity of  $\text{KBrO}_3$  is both dose and duration of exposure-dependent. On 4<sup>th</sup> and 8<sup>th</sup> day of treatment, mean level of  $\text{Cl}^-$  was significantly ( $P=.05$ ) raised whereas  $\text{HCO}_3^-$  was not significantly ( $P>.05$ ) increased. 12<sup>th</sup> day of experimentation resulted in dose, and duration of exposure dependent increase concentration of  $\text{Cl}^-$  ( $P=.05$ ).

**Conclusion:** This compound could potentially cause injury to, especially hepatocytes and nephrons. It can also perturb the redox status of the cell with its attendant metabolic consequences; hence, moderate use is imperative.

**Keywords:** Potassium; bromate; renal; hepatocytes; nephrons; liver; kidney.

## 1. INTRODUCTION

Bromate is a chemical compound that contains bromine anion (Bromine–base oxonion) and it includes sodium bromate. It is produced by the introduction of bromine into a solution of sodium carbonate; potassium bromate is a flour enhancer that acts as a maturing agent [1]. It has been in used as a food additive for years and acts principally in the late dough stage giving strength to the dough during the late proofing and early baking [1]. Being a strong oxidant, bromate is highly reactive and if use is not regulated, could spoil the bread (generation of reactive oxygen species) making the bread harmful. Bromate is a carcinogen and toxic in human and experimental animals [2].

It has been reported to be nephrotoxic in both man and experimental animals [3]; also, it induces renal cell tumors, mesotheliomas of the peritoneum, and follicular cell tumors of the thyroid [4]. Lethal oral doses of bromate in humans have been estimated to be between 154 and 385 mg/kg body weight while serious poisoning result at doses of 46-92 mg/kg weight [5]. Oral doses of 185-385 mg/kg body weight results in irreversible toxic effects such as renal failure and deafness in humans while lower doses are associated with vomiting, diarrhoea, nausea and abdominal pain [5,6].

## 2. MATERIALS AND METHODS

### 2.1 Chemicals/Reagents

- i. Determination of total protein: This was achieved using reaction kit containing

- appropriate and assorted reagents and chemicals.
- ii. Reagents for serum Albumin determination: Succinate buffer, Bromocresol green, Preservative for BCG, albumin Tris buffer albumin standard.
- iii. Reagents for serum Aminotransferase (AST and ALT) assay: Phosphate buffer, L–Aspartate,  $\alpha$ –Oxoglutarate 2,4–dinitrophenylhydrazine, L–Alanine and  $\alpha$ –Oxoglutarate.
- iv. Reagents for Alkaline phosphatase (ALP) assay: phosphate substrate, sodium thymolphthalein
- v. monophosphate buffer, magnesium chloride, ALP colour developer, sodium hydroxide, sodium carbonate, ALP standard and thymolphthalein.
- vi. Reagents for Urea determination: ethylene diamine tetra acetate (EDTA), sodium nitroprusside, urease, diluted phenol sodium hypochlorite and sodium hydroxide and standard for calibration.
- vii. Reagents for Creatinine (CR) determination: standard for calibration, Picric, NaOH and Trichloroacetic acid (TCA)

### 2.2 Methods Applied

#### 2.2.1 Experimental rats and treatments

Twenty (24) male albino Wistar rats (*Rattus norvegicus*) with average weight of 181.30 g were obtained from the Animal Housing Unit of the Department of Pharmacology, University of Jos, Nigeria. They were housed in metabolic

cage for 5 days to acclimatise and had free access to water and standard feed diet. Thereafter, they were grouped into Four (4) of six (6) rats each as follows:

- Group 1: Rats fed normal diet
- Group 2: Rats fed normal diet+  $\text{KBrO}_3$  at 67 mg/kg
- Group 3: Rats fed diet +  $\text{KBrO}_3$  at 100 mg/kg
- Group 4: Rats fed diet +  $\text{KBrO}_3$  at 167 mg/kg

The rats were orally administered diet mixed with appropriate concentration  $\text{KBrO}_3$  once per 24 hours. 2 rats from each group were sacrificed on the 4<sup>th</sup>, 8<sup>th</sup> and 12<sup>th</sup> day of experimentation. In the course of the work, we had a challenge which resulted in losing our sample (167 mg/kg).

### 2.2.2 Collection of blood samples

Prior to sacrifice, animals were anaesthetised using chloroform. Using sterile blade, the animal was dissected longitudinally thereby opening up the internal component of the rat. Blood samples were collected by direct cardiac puncture using sterile needle and syringe. They were then spun in a refrigerated centrifuge machine at 4000 rpm for 35 min; the sera were collected using a sterile plastic dropper and Pasteur pipette for enzyme assay.

Estimation of serum total protein according to Biuret [7]; serum albumin was determined applying Bromo Cresol Green [8]. Activities of the Aminotransferases were assayed by Reitman and Frankel [9].

The activity of alkaline phosphatase was assayed using the King and King [10]. The concentration of urea was determined using Berthelot [11]; creatinine level was determined by Jaffe's [12]. Concentrations of serum bicarbonate and chloride ions were determined by titrimetric [13].

### 2.3 Statistical Analysis

InStat3 statistical software was used to analyse data obtained. One Way ANOVA was chosen to analyse the data.

$P \leq .05$  was considered significant.  $P < .05$ ) this was considered significant.

## 3. RESULTS AND DISCUSSION

This work sought to evaluate the effects of potassium bromate on some electrolytes and hepatorenal parameters in male albino Wistar rats. Potassium bromate is chemical compound having molar mass of 167 g/mol. It is an oxidising

agent used in baking to strengthen dough and enhance elasticity of bread. Typically, 15-30 parts per million (ppm) of potassium bromate is a flour enhancer added to dough as a maturing agent [14]. Normally, baking changes its chemical composition and renders it harmless, leaving no trace in the finished product. However, if too much of the additive is used, or the bread is not baked long enough or at a high enough temperature, then a residual amount will remain, and it poses danger since it is a genotoxic carcinogen [15].

Considering results in this Table 1, (4<sup>th</sup> day of experimentation at 67 mg/kg dose), there was significant increase ( $P = .05$ ) in the activity of the AST, ALT, ALP, and the concentration of UR all test groups with the magnitude being dose-dependent whereas all doses of  $\text{KBrO}_3$  for creatinine were lower than the control group. However, treatment did not increase the concentration of TP, ALB and CR. Also, the activities of serum ALT, AST, ALP and concentration of TP and ALB starting from day 4 to 12 of different concentrations of treatment with potassium bromate ( $\text{KBrO}_3$  mg/kg) body weight, were significantly ( $P = .05$ ) higher compared to the control group values.

Results (8<sup>th</sup> day of treatment) at 67 and 100 mg/kg doses, both urea and creatinine concentrations were lower than control groups values. But, concentration of ALB, and activities of AST, ALP, ALT were raised higher ( $P < .05$ ) relative control group values. Elevation was duration of treatment dependent. Level of TP was lower than control group values.

Here, (on 12<sup>th</sup> day of experimentation), levels of urea and creatinine were significantly higher at all the doses relative control ( $P = .05$ ). It could be speculated generally that, from 0 – 8 days, there was relatively no disruption of kidney cell membrane but as the treatment progressed at different concentrations, there appeared to be disruption of nephritic membranes leading to increase in creatinine and urea concentration in circulation.

Enzymes are used as biomarkers of organs to monitor possible toxicity/injury. Rahman et al. [16] have reported use of enzymes to monitor effects of potassium bromate on the liver. Increase in the activities of ALT, AST and to some extent ALP is associated with injury to, especially the hepatocytes albeit not absolutely due to isomerism. There are several isoforms of the transaminases in different organs in the

**Table 1. Mean activity (IU) of some enzymes and levels of hepatorenal parameters in experimental animals sacrificed on fourth (4<sup>th</sup>) day of administration of the sample**

Samples	UR (mmol/L)	CR ( $\mu$ mol/L)	TP ( $\mu$ mol/L)	ALB (g/L)	ALT (IU)	AST (IU)	ALP (IU)
Control	3.50 $\pm$ 1.01	73.55 $\pm$ 1.86	79.66 $\pm$ 2.63	32.93 $\pm$ 1.82	14.00 $\pm$ 1.09	18.00 $\pm$ 1.05	37.43 $\pm$ 0.98
67mg/kg	4.26 $\pm$ 1.39	70.74 $\pm$ 3.53	69.63 $\pm$ 6.57	31.72 $\pm$ 2.97	41.00 $\pm$ 9.61 <sup>*d</sup>	130.11 $\pm$ 3.53 <sup>*d</sup>	37.97 $\pm$ 7.162
100mg/kg	5.50 $\pm$ 2.01	72.88 $\pm$ 19.21	67.77 $\pm$ 6.04 <sup>*d</sup>	27.41 $\pm$ 4.35	52.00 $\pm$ 13.32 <sup>*d</sup>	180.21 $\pm$ 43.86 <sup>*d</sup>	42.84 $\pm$ 11.14

Values are means of triplicate determinations ( $\pm$ SD).  
<sup>\*d</sup> values differ from the control significantly ( $P \leq 0.05$ )

**Table 2. Mean activity values (IU) of some enzymes and levels of some hepatorenal parameters in experimental animals sacrificed on 8th (eight) day of administration of the sample**

Samples	UR (mmol/L)	CR ( $\mu$ mol/L)	TP ( $\mu$ mol/L)	ALB (g/L)	ALT (IU)	AST (IU)	ALP (IU)
Control	3.50 $\pm$ 1.01	73.55 $\pm$ 1.86	79.66 $\pm$ 2.63	32.93 $\pm$ 1.82	14.00 $\pm$ 1.09	18.00 $\pm$ 1.05	37.43 $\pm$ 0.98
67mg/kg	2.38 $\pm$ 1.39	69.21 $\pm$ 3.53	79.10 $\pm$ 6.57	36.03 $\pm$ 2.97	22.00 $\pm$ 9.61	67.02 $\pm$ 31.53	46.76 $\pm$ 7.16
100mg/kg	2.77 $\pm$ 2.01	72.58 $\pm$ 19.21	74.08 $\pm$ 6.04	33.88 $\pm$ 4.35	26.11 $\pm$ 13.32	98.01 $\pm$ 13.86 <sup>*d</sup>	53.92 $\pm$ 11.14
167mg/kg	3.80 $\pm$ 12.21	76.25 $\pm$ 14.78	71.49 $\pm$ 1.58	33.28 $\pm$ 1.10	31.00 $\pm$ 8.49 <sup>*d</sup>	103.21 $\pm$ 23.34 <sup>*d</sup>	57.57 $\pm$ 28.67

Values are means of triplicate determinations ( $\pm$ SD).  
<sup>\*d</sup> values differ from the control significantly ( $P = .05$ )

**Table 3. Mean activity values (IU) of some enzymes and levels of some hepatorenal parameters in experimental animals sacrificed on twelfth (12<sup>th</sup>) day of administration of the sample**

Samples	UR (mmol/L)	CR ( $\mu$ mol/L)	TP ( $\mu$ mol/L)	ALB (g/L)	ALT (IU)	AST (IU)	ALP (IU)
Control	3.50 $\pm$ 1.01	73.55 $\pm$ 1.86	79.66 $\pm$ 2.63	32.93 $\pm$ 1.82	14.00 $\pm$ 1.09	18.00 $\pm$ 1.05	37.43 $\pm$ 0.98
67mg/kg	5.10 $\pm$ 1.39	75.94 $\pm$ 3.53	82.25 $\pm$ 6.57	37.41 $\pm$ 2.97	29.02 $\pm$ 9.61 <sup>*d</sup>	9631.53 <sup>*d</sup>	52.16 $\pm$ 7.16
100mg/kg	6.70 $\pm$ 2.01	106.0 $\pm$ 19.2 <sup>*d</sup>	79.84 $\pm$ 6.04	35.69 $\pm$ 4.35	34.03 $\pm$ 13.32 <sup>*d</sup>	112.0 $\pm$ 43.86 <sup>*d</sup>	65.11 $\pm$ 11.14 <sup>*d</sup>
167mg/kg	21.07 $\pm$ 2.21	309.29 $\pm$ 1.7 <sup>*d</sup>	69.26 $\pm$ 1.58 <sup>*d</sup>	31.72 $\pm$ 1.10	43.02 $\pm$ 8.49 <sup>*d</sup>	136.0 $\pm$ 23.34 <sup>*d</sup>	98.61 $\pm$ 28.67 <sup>*d</sup>

Values are means of triplicate determinations ( $\pm$ SD).  
<sup>\*d</sup> values differ from the control significantly ( $P = .05$ )

body. Therefore, increase in activity amino transferases alone may not absolutely be the hepatic form Per et al. [17] of the enzyme; other biomarkers of the liver have to be analysed before conclusions are drawn. Generally, damage to liver cells may result in elevation of the activities of transaminases in the serum and decrease in the organs [18]. From this work, increases in serum activities of these enzymes relative control suggest the likelihood of damage to hepatocytes or the plasma membrane causing leakage of these enzymes from the organ into circulation owing to compromised integrity of organ due to the presence of potassium bromate (KBrO<sub>3</sub>). This compound was independently reported to be toxic and necrotic to hepatocytes [19,20,21].

However, increase in the activities of AST and ALT in the serum might be due to interference with protein metabolism in the cell or inhibition of the enzymes which agrees with the findings of [22]. Also the concentration of total proteins and albumin in the sera decreased. This could be due to chronic liver disease or inhibition of activities of enzymes of protein metabolism. The measurement of the activities of "marker" enzymes in tissues and sera can be used in assessing the degree of assault and the toxicity of chemical compound on organ/tissues [23,24]. Measuring the level of TP and ALB in sera can also be used to monitor tissues/organ damages caused by these chemical compounds [25]. Furthermore, assaying for AST, ALT and ALP are of clinical and toxicological importance as changes in their activities are indicative of hepatocytes damage by toxicants or in disease conditions [26].

ALP, a marker enzyme of the plasma membrane and endoplasmic reticulum [27], is frequently used to assess the integrity of the plasma membrane [28]. Any alteration in the activity of this enzyme in the tissue/organ indicates likely damage to the external boundary of plasma membrane [29]. From our results, there is increased activity of serum ALP in the rats administered different doses of KBrO<sub>3</sub> mg/kg body weight compared to the control value. This could cause decrease in ALP activity in the organ because, ALP will leak into the blood circulation. The reduction in ALP activity following the administration of different concentrations of KBrO<sub>3</sub> might be adduced to either loss of membrane components (including ALP) into the circulation, inactivation of the enzyme molecule or inhibition of the enzyme activity at the

molecular level. Also, there was decrease in total protein and albumin serum concentration as the serum ALP increased. These may be due to inhibition of protein metabolism enzymes. It may also be due to reduction in concentration or total absence of specific phospholipids required by this membrane bound – enzyme to express its full activity. Enzyme from diseased or damaged tissues may become recognisable in the serum presumably by leakage through altered cell membrane [30]. The corresponding increase in serum ALP activity of the treatment compared to control indicated damage may have been inflicted on the plasma membrane of the liver, which might have resulted in the compromised integrity of the cell membrane. Such leakage of ALP from the tissues could be attributable to disruption of the ordered lipid bilayer by the presence of reactive oxygen species generated by the KBrO<sub>3</sub> leading to escape of detectable quantity of ALP out of the cell into the blood circulation. The presence of oxygen in the KBrO<sub>3</sub> might have caused the oxidation of the polyunsaturated fatty acids which makes up the lipid bilayer and hence its disruption. Such increase in the serum activity of ALP and decrease/reduction in the tissues ALP or organ would have hindered adequate transportation of required ions or molecules across their cell membranes which could lead to their deficiency in the cells. The increases in serum creatinine and urea levels are indication of renal toxicity due to pathological changes [31]. Serum creatinine and urea are a source of more sensitive markers in renal failure which is one among the slowly progressive diseases of kidney function characterized generally by low glomerular filtration, GRF, [31]. Therefore, adverse effects of KBrO<sub>3</sub> on renal parameters are dose dependent. Activities of all enzymes were significantly (P=.05) raised relative control groups values.

From Table 4, treatment on 4<sup>th</sup> of day of experimentation resulted in mixed outcomes of the electrolytes analysed. Electrolytes are required for survival of species of animals. Their perturbation results in serious conditions and death. Treatment did not affect the concentration of bicarbonate ions but chloride was significantly elevated (P=.05) relative control group values. Elevation appeared to be directly proportional to dose and duration of exposure. Low levels of the bicarbonate ions results in metabolic acidosis, a condition characterised by low pH which might have a negative impact on progression of kidney dysfunction [32,33].

**Table 4. Mean levels of chloride and bicarbonate following 4, 8 and 12 days of experimentation**

	4 <sup>th</sup> day		8 <sup>th</sup> day		12 <sup>th</sup> day	
	Cl <sup>-</sup>	HCO <sub>3</sub> <sup>-</sup>	Cl <sup>-</sup>	HCO <sub>3</sub> <sup>-</sup>	Cl <sup>-</sup>	HCO <sub>3</sub> <sup>-</sup>
Control	110± 2.66	25± 1.05	110± 2.66	25±1.05	110±2.66	25±1.05
67mg/kg	111± 3.46	24± 1.15	105± 3.46	26±1.15	111±3.46	24±1.15
100mg/kg	113± 2.89	25± 2.89	108± 2.89	25±2.89	113±2.89	20±2.89
167 mg/kg			110.3.12	24±5.66	116±4.24	16±5.66

Values are means of triplicate determinations (±SD)

<sup>d</sup> values differ from the control significantly (P=.05)

On 8<sup>th</sup> day, chloride was raised significantly (P=.05), bicarbonate was not significantly (P>.05). Chloride is the major anion in serum. Extracellular chloride concentration is influenced by concentration of extracellular sodium and bicarbonate. On 12<sup>th</sup> day of exposure, concentration of chloride ion increased with dose and exposure period significantly (P=.05) whereas bicarbonate concentration was not (P>.05).

#### 4. CONCLUSION

The results of this study indicate that administration of potassium bromate at 67 mg/kg, 100 mg/kg, and 167 mg/kg body weight to rats increased the levels of some hepatorenal parameters, and chloride after a period of, particularly twelve days of exposure which probably resulted in leakage of the enzymes into circulation. Hence, it is concluded that potassium bromate adversely affects hepatic, renal parameters and chloride ion level leading, as a consequence, to necrosis of cells of such organs as corroborated by the results obtained.

#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

#### REFERENCES

- Vadlamani KR, Seib PA. Effect of zinc and aluminium ions in bread making. *Cereal Chem.*1999;76(3):355–360.
- International Agency for research on Cancer (IARC). Potassium bromate. In: IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans Lyon, France: World Health Organisation, International Agency for Research on Cancer. 1986;207–220.
- Kurokawa Y, Maekawa A, Takashi M, Hayashi Y. Toxicity and carcinogenicity of potassium bromate – A new renal carcinogen. *Environ Health Perspectives.*1990;87:309–335.
- Uchida HA, Sugiyama H, Kanehisa S, Harada K, Fujiwara K, Ono T. An elderly patient with severe acute renal failure due to sodium bromate intoxication. *Intern Med.* 2006;45:151-154.
- Mark RB. Round up the usual suspects. Potassium bromate poisoning. *N Carolina Med J.* 1993;49:243–245.
- Magomya AM, Yebpella GG, Udiba UU Amos HS, Latayo MS. Potassium Bromate and Heavy Metal Content of Selected Bread Samples Produced in Zaria, Nigeria. *International Journal of Science and Technology.* 2013;2:(2).
- Gornail AG, Bardawill CJ, David MM. Determination of serum Proteins by the Biuret reaction. *Journal of Biological Chemistry.* 1949;177:751-751.
- Dumas BT, Watson W, Biggs HG. Albumin Standards & the measurement of serum albumin with Bromocresol green. *Clinical Chemistry Acta.* 1971;31:87-96.
- Reitman S, Frankel S. A colorimetric method for the determination of serum glutamic oxaloacetate transaminase and serum Glutamic pyruvic transaminase. *American Journal of Clinical Pathology.* 1957;28:56-63.
- Kind PRM, King EJ. Estimation of serum alkaline phosphatase activity by colorimetric methods. *Journal of Clinical Pathology.*1954;7:322-324.
- Berthelot MPE. *Report Chim. Appl.* 1859; 384.
- Bonses RW, Tausskay HH. The colorimetric determination of Creatinine by the Jaffe reaction. *Journal of Biological Chemistry.* 1945;158:581-591.
- Maas AHJ. A titrimetric method for the determination of actual bicarbonate in cerebrospinal fluid and plasma or serum. *Clinica Chimica Acta.* 1970;29(3):567-574.
- Chipman JK, Davies JK, Parson JL, Nair J, O'Neill G, Fawell JK. DNA oxidation by

- potassium bromate; A direct mechanism or linked to lipid peroxidation. *Toxicol.* 1998; 126:93-102.
15. Fatma FK, Mehmet T. Genotoxic effects of potassium bromate on human peripheral lymphocytes *in vitro*. *Mutation Research/ Genetic Toxicology and Environmental Mutagenesis.* 2007;626(12): 48-52.
  16. Rahman MF, Siddiqui MK, Jamil K. Effects of vepacide (*Azadirachtaindica*) on aspartate and alanine aminotransferase profiles in sub-chronic study with rats. *J. Hum. Exp. Toxicol.* 2001;20:243–249.
  17. Per L, Ingalill R, Clive C, Ulf A, Jesper J, Hedberg A, Anders S, Heike H, Ian C, Björn G. *Archives of Biochemistry and Biophysics.* 2007;466(1):66-77.
  18. Mousa MA, Khattab YA. The counteracting effect of vitamin C (L-ascorbic acid) on the physiological perturbations induced by ochratoxin intoxication in African Catfish (*Clariagariepinus*). *J. Egypt Acad. Environ. Dev.* 2003;4:177–128.
  19. Hanley KS, Schmidt E, Schmidt FM. *Enzymes in serum, their volumes in diagnosis*, Charles Thomas Springfield, Illinois. 1986;79–81.
  20. Abdel-Taiwab M, Shalaby AME, Ahmed MH. Effect of supplement dietary L-ascorbic acid (vitamin C) on mercury intoxication and growth performance of Nile tilapia (*Oreochromis niloticus* L). *Ann. Agric. Sci.* 2001;39(2):961–973.
  21. Karmen A, Wroblewski F, La D. Transaminase activity in human blood. *J. Clin. Invest.* 2005;34:126 –130.
  22. Malomo SO. Toxicological implication of ceftriaxone administration in rats. *Nig. J. Biochem. Mol. Biol.* 2000;15(1):33–38.
  23. Yakubu MT, Bilbis LS, Lawal M. Effect of repeated administration of sildenafil citrate on selected enzyme activities of liver and kidney of male albino rats. *Nig J Pure & Appl Sci.* 2003;18:1395– 4000.
  24. Akanji MA, Ngaha EO. Effects of repeated administration of berenil on urinary excretion with corresponding tissue on pattern in rats. *Pharmacol.Toxicol.* 1989; 81:173–179.
  25. Singh NS, Vats P, Suri S. Effect of an antidiabetic extract of *Catharanthus roseus* on enzymic activities in streptozotocin induced diabetic rats. *J. Ethnopharmacol.* 2001;76:269–277.
  26. Shahjahan M, Sabitha KE, Mallika J. Effect of *Solanum trilobatum* against carbon tetrachloride induced hepatic damage in albino rats. *Indian J. Med. Res.* 2004;120: 194–198.
  27. Akanji MA, Olagoke OA, Oleyede OB. Effect of chronic consumption of metabisulphite on the integrity of rat cellular system. *Toxicol.* 1993;81:173–79.
  28. Yakubu MT. Aphrodisiac potentials and toxicological evaluation of aqueous extract of *Fadogiaagrestis* (Schweinf. Ex Heim) stem in male albino rats. *Asian Journal Androl.* 2005;7(4):399-404.
  29. Yakubu MT, Olatunji IK, Akanji MA. Comparative effects of administration of halofantrine hydrochloride and dihydroartemisinin on some enzymes of selected rat tissues. *NISEB J.* 2002;2(3): 175–180.
  30. Watanabe S, Tajima Y, Yamaguchi T, Fukui T. Potassium bromate induced hyper-uricemia stimulates acute kidney damage and oxidative stress. *J. Health Sci.* 2004;50:647-653.
  31. Nisha R, Srinivasa KSR, Thanga MK, Jagatha P. Biochemical evaluation of creatinine and urea in patients with renal failure undergoing hemodialysis. *J Clin Path Lab Med.* 2017;1(2):1-5.
  32. Gilda D, Bharat B, Sindhagatta V. Fluid and sodium imbalance: Clinical implications. Hindawi books. Open access peer reviewed chapter; 2018. DOI: 10.5772/intechopen.79121
  33. El-Solh AA, Abou PJ, Porhomayon, J. Bicarbonate therapy in the treatment of septic shock: A secondlook. *Internal Emergency Medicine.* 2010;5(4):341-347.

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