

Changes in some Electrolytes and Biochemical parameters in Rats fed Monosodium glutamate

ABSTRACT

The effect of monosodium glutamate (MSG) on serum electrolytes, urea and creatinine levels was evaluated in Albino rats. The rats were randomly divided into four (4) groups based on the proportion of MSG supplemented in their diets. Group A was fed with commercial chow (control) while groups B, C and D were placed on 0.5, 1.0 and 5.0% MSG supplemented diets respectively. The serum electrolytes, urea and creatinine were analyzed using TECO Diagnostic kits. The sodium and chloride concentrations in the experimental groups were not significantly ($p > 0.05$) different from the control group. Group fed 5% MSG supplemented diet had the highest potassium concentration (6.00 ± 0.83 Mmol/L) while the group placed on 0.5% MSG supplemented diet had the lowest concentration (4.68 ± 0.16 Mmol/L). There was a significant ($p < 0.05$, $F = 30.21$) difference in the potassium ion concentration between the experimental groups and the control group. The urea concentration ranged from 6.28 ± 0.10 Mmol/L to 7.13 ± 0.36 Mmol/L in the experimental groups whereas the creatinine concentration ranged from 1.38 ± 0.48 mmol/L to 1.4 ± 0.11 Mmol/L. The urea concentration of rats in the experimental groups were significantly ($p < 0.05$, $F = 25.66$) lower than the control group. The creatinine concentration of rats in the experimental groups were not significantly different ($p > 0.05$, $F = 2.88$) from those in the control group. This work has shown that high supplementation of diet with MSG could induce hyperkalemia and hypourcemia in rats.

Key words: *Monosodium Glutamate (MSG), electrolytes, urea, creatinine, supplemented diet*

INTRODUCTION

Monosodium glutamate (MSG) is a chemical food additive used to enhance the flavor of many types of food. It contains about 78% glutamic acid, 22% sodium and water [1]. Glutamate is one of the most common amino acids in nature [2] and is the main component of many proteins and peptides of most tissues (plant and animal). It is a non-essential amino acid as it can be produced in the body independent of its availability in ingested foods [3].

MSG has a trade name; “Ajinomoto” which is marketed by West African Seasoning Company Limited It is commonly referred to as “Vedan” or “White Maggi” and available in markets as well as open stores in Nigeria. Monosodium glutamate when added to food provides a taste referred to as “umami” which differ from the four classic tastes of sweet, sour, salt and bitter. As a food additive, monosodium glutamate is described and listed on food labels as a “Flavouring” or “Hydrolysed vegetable protein”. Through its stimulation of the sensory receptors and improving the palatability of meals, monosodium glutamate influences the appetite positively and induces weight gain [4].

33 Despite its taste stimulation and improved appetite enhancement, reports indicate that monosodium glutamate
34 may be toxic to humans and experimental animals [5]. Several communities in Nigeria often use monosodium
35 glutamate as a bleaching agent for the removal of stains from clothes. There is a growing apprehension that its
36 excellent bleaching properties could be harmful or injurious to the tissues, and organs of the body or worse still
37 inducing terminal diseases in consumers when ingested as a flavour enhancer in food. In the sixties, the
38 symptoms associated with MSG were referred to as “Chinese Restaurant Syndrome” which began 15 to 30
39 minutes after eating in certain Chinese restaurants, and lasted about 2 hours with no lasting effects. These
40 symptoms ranged from burning sensation of different parts of the body, headache or numbness in the face to
41 chest pain, nausea or vomiting, sweating, paresthesias, heart palpitations and tremors [1]. In recent years there
42 have been much concern about possible adverse effect of MSG on human and animals and MSG is believed to
43 cause neurotoxicity, impaired vision and endocrinal disorder in human subjects. It has also been associated with
44 some pathological conditions such as schizophrenia, anxiety, Parkinson’s disease, epilepsy, stroke and
45 Huntington’s disease [6].

46 Despite evidence of negative consumer response to MSG, reputable International organizations and nutritionists
47 have continued to endorse monosodium glutamate and reiterated that monosodium glutamate has no adverse
48 reactions in humans [7]. Recognized International organization such as the Food and Drug Administration
49 (FDA) and also a regulatory food safety body in Nigeria; National Agency for Food and Drug Administration
50 Control (NAFDAC) have reported that MSG be maintained on the “Generally Recognized as Safe” (GRAS) -
51 list of foods [8].

52 The Kidney is a paired organ located in the posterior abdominal wall, whose major functions include the
53 removal of toxic metabolites and waste products from the blood and regulation of the amount of fluid and
54 electrolytes balance in the body. Kidney function tests include; urinalysis, measurement of serum urea,
55 creatinine, sodium, potassium and serum bicarbonate levels [9, 10]. Although some reports are available on the
56 adverse effects of direct administration of MSG in kidney function, there have been a dearth of information of
57 the effect of diet supplemented with MSG on kidney functions in rats. This study therefore aimed at evaluating
58 the changes of some electrolytes, urea and creatinine levels in rats fed MSG supplemented diets.

59 **Materials and method**

60 **Reagents**

61 TECO diagnostics Kits (Anaheim, U.S.A.) were used for the determination of serum electrolytes, urea and
62 creatinine. All the chemicals used were of analytical grade.

63 **Monosodium Glutamate**

64 Ajinomoto a brand of monosodium glutamate manufactured by Ajinomoto Co., Inc. Tokyo, Japan marketed by
65 West African seasoning company limited was purchased from the Ultra-modern market in Minna Niger State,
66 Nigeria. It was stored and protected from direct sunlight.

67 **Experimental Animals**

68 Healthy Wistar albino rats weighing between 120-150g were obtained from animal house centre, college of
69 Health Science, Benue State University Makurdi, Nigeria. They were conveniently housed in the Department of
70 Biochemistry laboratory, Federal University of Technology, Minna, under standard environmental conditions
71 (temperature 27 ± 2 °C, 70% relative humidity and 12hrs day light/night cycle). The rats were allowed free
72 access to commercial growers feed pellets (product of Bendel Feeds and Flour Mills, Ewu, Edo State, Nigeria)
73 and water *ad libitum*. They were then allowed to acclimatize to the laboratory condition for two weeks before
74 the commencement of the experiment. The cages were cleaned regularly throughout the experimental period.
75 Animals were catered for in compliance with internationally accepted principle for humane handling and use of
76 laboratory animal.

77 **Experimental Diets**

78 Three different levels of supplementation with MSG (0.5, 1.0 and 5.0%) diets were prepared by adding 5g, 10g
79 and 50g of MSG to 995g, 990g and 950g of standard feed respectively. The feeds were pelletized according to
80 the method of Larry, [11].

81 **Experimental Design**

82 A total of twenty (20) rats were randomly divided into four groups (A-D) of five (5) rats each and were fed
83 MSG supplemented commercial diets for four weeks.

84 Group A: The rats were fed normal commercial feed pellet and served as the control group

85 Group B: Rats were fed 0.5% MSG supplemented diets.

86 Group C: Rats were fed with 1% MSG supplemented diets

87 Group D: Rats were fed with 5% MSG supplemented diets

88

89 **Blood and Serum collection**

90 After four weeks of feeding the rats with supplemented diets containing different proportion of monosodium
91 glutamate, the rats were anesthetized using cotton wool soaked in chloroform and blood was collected by
92 decapitation into clean lithium heparinized bottles. The blood thus collected was allowed to stand for 10 minutes
93 at ambient temperature to clot. Thereafter, the serum was separated by centrifugation at 1000 rpm for 10
94 minutes.

95 **Determination of Serum Electrolytes**

TECO diagnostic kit was used for the determination of serum sodium ion concentration according to the method of Maruna [12], potassium ion [13] and chloride ion [14].

Determination of Urea and Creatinine Levels in Rats

Urea and creatinine were determined using TECO diagnostic kit according to the methods of Alexander and Griffith, [15] and Wilding and Kennedy, [16] respectively.

Statistical Analysis

Data were subjected to Analysis of Variance (ANOVA) using the statistical package for Social Science (SPSS) 16.0 window versions. Results were presented as Mean $\pm$ Standard Error of Mean. Means with difference were separated using the Duncan Multiple Range Test and results were considered significant at $p < 0.05$.

Results

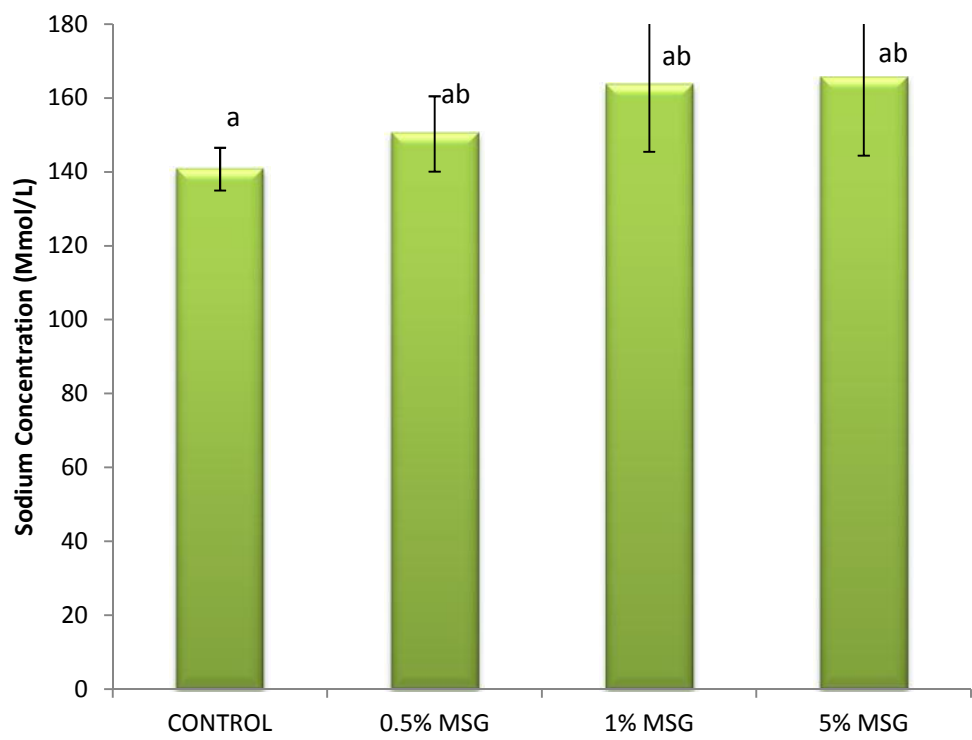
Figure 1 shows the effect of monosodium glutamate on serum sodium concentration of rats fed with diets supplemented with MSG. In the experimental groups, there was a general increase in sodium ion concentration with increased level of supplementation of MSG fed diet. However, there was no significant difference ($p > 0.05$, $F = 3.08$) in the concentration between the experimental groups and the control group. The experimental groups supplemented with 5% MSG had the highest sodium ion concentration (165.25 ± 19.14 Mmol/L) while the group placed on 0.5% MSG supplemented diet had the lowest sodium concentration (140.75 ± 5.77 Mmol/L).

Figure 2 shows the effect of monosodium glutamate on serum potassium concentration of rats fed diet supplemented with MSG. The potassium ion concentration ranged from 4.68 ± 0.16 Mmol/L in the group placed on 1.0% MSG supplemented diet to 6.00 ± 0.83 Mmol/L in the group supplemented with 5% MSG. There was significant ($p < 0.05$, $F = 30.21$) difference in the potassium ion concentration between the control group and the experimental groups.

Rats placed on diet supplemented with 5% MSG, had the highest chloride ion concentration (106.50 ± 6.89 Mmol/L) while the groups placed on 0.5% and 1% MSG supplemented diet had similar concentrations of 100.25 ± 8.23 Mmol/L and 100.25 ± 2.18 Mmol/L respectively. There was no significant difference ($p > 0.05$, $F = 4.35$) in the chloride ion concentration between the control and experimental groups (Figure 3).

The effects of monosodium glutamate on serum urea and creatinine levels are as shown in Figures 4 and 5 respectively. The urea concentration of rats placed on 0.5% MSG supplemented diet was 6.28 ± 0.10 mg/dL while those fed with 1% and 5% supplemented diets were 6.53 ± 0.66 mg/dL and 7.13 ± 0.36 mg/dL respectively. The urea concentration of rats in the experimental groups were significantly ($p < 0.05$, $F = 25.66$) lower than the control group. The creatinine concentration ranged from 1.25 ± 0.33 mg/dL in group fed 1% MSG supplemented diet to 1.88 ± 0.48 mg/dL in rats placed on 5% MSG supplemented diet. The creatinine

128 concentration of rats in the experimental groups were not significantly different ($p > 0.05$, $F = 2.88$) from those
129 in the control group.

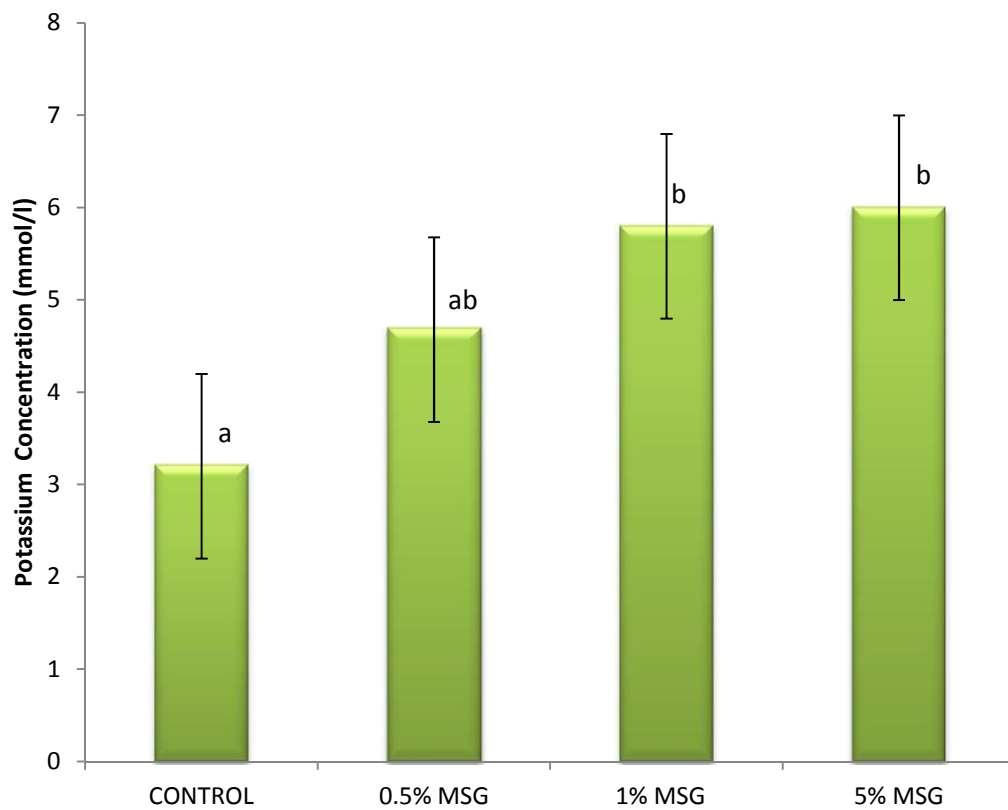


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131 **Figure 1: Serum sodium concentration (Mmol/L) in rats fed MSG supplemented diets** Values
132 are **Mean $\pm$ SEM** (n=5). Bars with different alphabet are significantly ($p < 0.05$) different from Control group.

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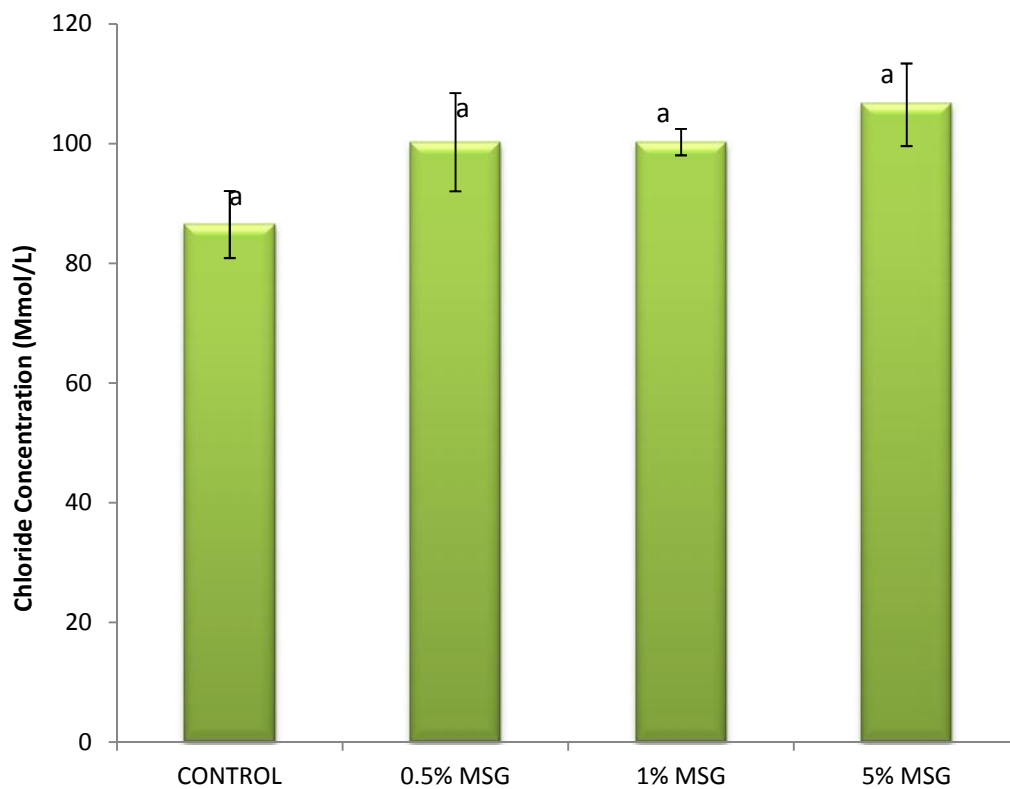
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136 **Figure 2: Serum potassium concentration (Mmol/L) in rats fed MSG supplemented die** Values
 137 are **Mean $\pm$ SEM** (n=5). Bars with different alphabet are significantly (**p < 0.05**) different from Control group.

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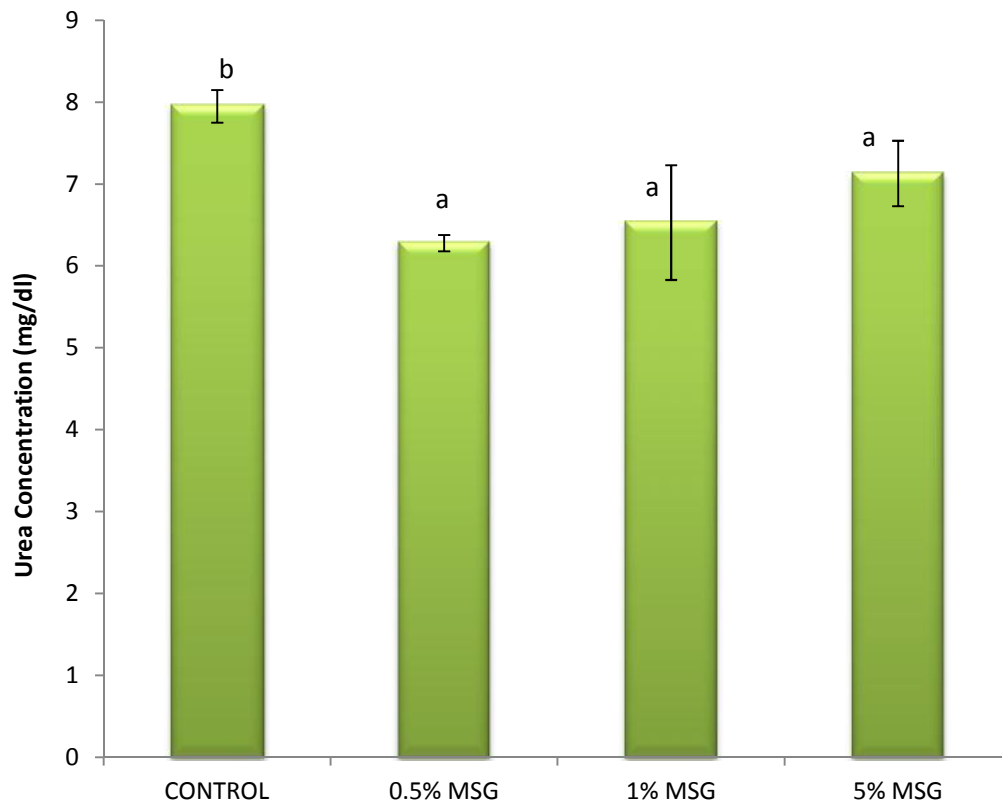
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140 **Figure 3: Serum chloride ion concentration (Mmol/L) in rats fed MSG supplemented diets**

141 Values are **Mean $\pm$ SEM** (n=5). Bars with different alphabet are significantly (**p < 0.05**) different from Control

142 group.

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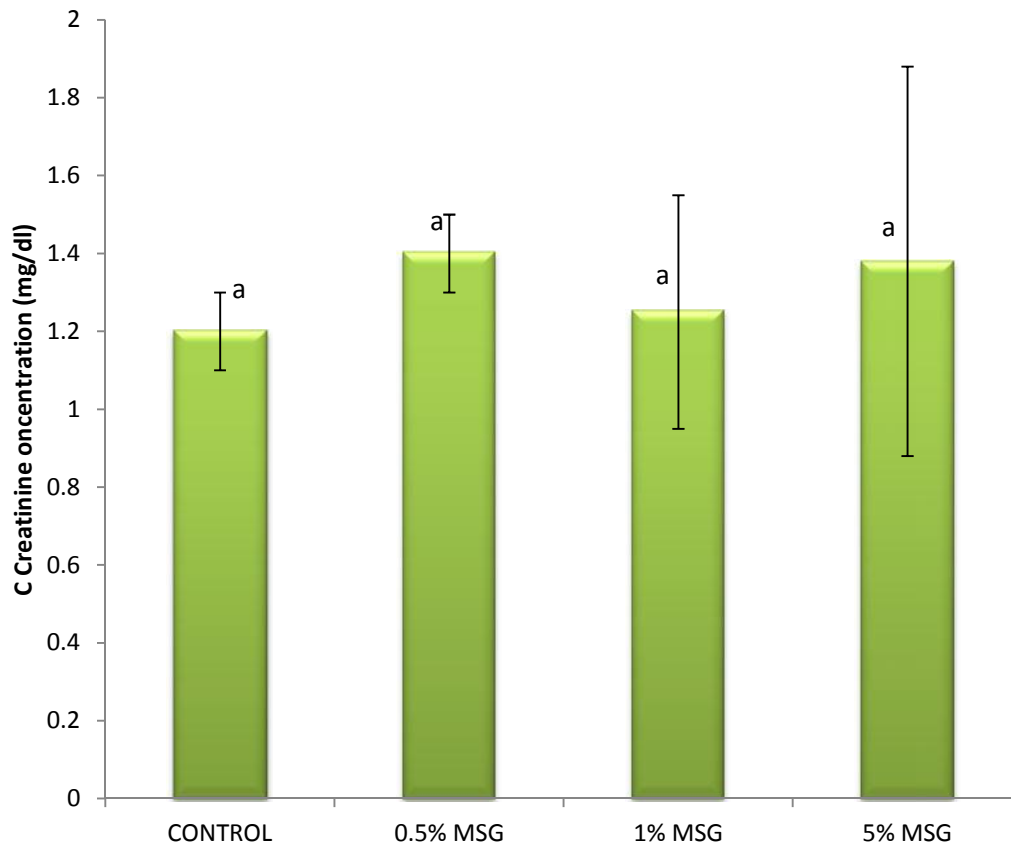
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Figure 4: Serum urea concentration (mg/dl) in rats fed MSG supplemented diets

Values are **Mean $\pm$ SEM** (n=5). Bars with different alphabet are significantly (**$p < 0.05$**) different from Control group.



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149 **Figure 5: Serum creatinine concentration (mg/dl) in rats fed MSG supplemented diet** Values are
 150 **Mean $\pm$ SEM** (n=5). Bars with different alphabet are significantly (**$p < 0.05$**) different from Control group.

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152 DISCUSSION

153 Globally, dietary MSG has been consumed in large amount to induce preferences for foods [17]. Serum
 154 electrolytes are among the most commonly used laboratory tests for the assessment of a patient's diseased state.

155 The present study showed an increasing trend in the concentration of electrolytes with increasing MSG
 156 supplementation. Inuwa et al., [1] who evaluated the nephrotoxic and hepatotoxic effects of monosodium
 157 glutamate (MSG) consumption found similar increasing trend except with chloride ion (Figure 2). The non-
 158 significant (**$p > 0.05$**) change in the concentration of sodium and chlorine ions in the experimental groups also
 159 agrees with their findings.

160 The significant (**$p < 0.05$**) increase in potassium level of the experimental groups (Figure 3) is consistent with
 161 findings of Ilegbedion et al., [4] who evaluated the effect of MSG on electrolyte balance and histology of
 162 gastroesophageal mucosa. The potassium ion concentration observed in experimental groups placed on 1% and
 163 5% MSG supplemented diets was higher than the normal range 3.5 and 5.3 mmol/L [18]. Values higher than this

range may point at a condition referred to as hyperkalemia. Peterson and Levi, [19] reported that renal excretion is the major route of potassium elimination. William, et al., [20] reported that hyperkalemia may ensue when there is renal failure. Serum potassium is generally believed to rise above the normal limit only at the latter stage of chronic kidney disease (CKD) [21]. Eweka, [8] also reported the distortion of the cyto-architecture of the renal cortical structures and cellular necrosis associated with the kidney of rats administered MSG. Therefore, the concentration of potassium ion might have been elevated in the experimental groups possibly as a result of kidney dysfunction which may have resulted in poor excretion. Potassium homeostasis may also be altered by changes in acid-base balance, insulin, aldosterone and gastrointestinal and skin damages [19]. Moreso, according to He et al., [22], there are overwhelming evidences that laboratory animals exposed to MSG suffer neuroendocrine disorders. Ahmed and Wiesberg., [23] and Soliman, [24] had previously reported findings which explained that excess parathyroid hormone (PTH) increases basal levels of cytosolic calcium which affects the permeability of the cellular membrane to potassium thus decreasing extra renal disposal of potassium in chronic kidney disease.

Serum creatinine is a vital indicator of renal function [5, 8]. The concentration of serum creatinine in the experimental groups was not significantly ($p > 0.05$) different from the control (Figure 5). The findings was not in agreement with that reported by Manal and Nawal, [5] who observed a significant rise in creatinine concentration and reported that administration of MSG may be attributed to alteration of the renal functional capacity. Inuwa et al., [1] also reported a significant elevation of creatinine level and suggested that MSG might have either interfered with creatinine metabolism leading to increased synthesis or the tissues might have compromised all or part of its functional capacity of tubular excretion [25]. The contrast observed might have resulted from either the concentration of MSG administered or the route of administration to the experimental animals.

Serum urea level significantly decreased in the experimental groups (Figure 4) and this agrees with the result obtained in the study of Manal and Nawal, [5]. It also agrees with the study of Egbonu et al., [26] who reported a significant ($p < 0.05$) reduction in urea concentration although was not in agreement with the work of Thomas et al., [27] who reported the protective effect of *Piper longum* Linn. on MSG induced oxidative stress in rats. The significant reduction in serum urea concentration throughout the experimental groups might have resulted from impairment of the urea cycle (a down regulation of the urea synthesis) or increased excretion through the urine, probably as a result of MSG-induced toxicity.

Conclusion

This study indicated that administration of MSG supplemented diet elevated the concentration of potassium ion but decreased that of urea, suggesting hyperkalemia and hypourcemia in the exposed rats.

References

- 197 [1] Inuwa, H.M., V.O. Aina, B. Gabi, A.I. ola., and J. Leehman, 2011. Determination of Nephrotoxicity and
198 Hepatoxicity of Monosodium Glutamate (MSG) Consumption. *British J. Pharmacol. Toxicol.*, 2(3): 148-
199 153
- 200 [2] Alao1, O.A. J.O. Ashaolu O.K. Ghazal and V.O. Ukwenya, 2010. Histological and biochemical effects of
201 monosodium glutamate on the frontal lobe of adult Wistar rats. *Int. J. Biomed. Health Sci.*, 6(4), 197-203.
- 202 [3] David, T.W. 2008. MSG–Flavor Enhancer or Deadly Killer. *Assump. Uni. J. Tech.*, 12(1): 43-49.
- 203 [4] Ilegbedion, I.G., F.M. Onyije and K.A. Digba, 2013. Evaluation of MSG on Electrolyte Balance and
204 Histology of Gastroesophageal Mucosa. *Middle-East J. Sci. Res.* 18 (2): 163-167.
- 205 [5] Manal, S.T., and A. Nawal, 2012. Adverse Effects of Monosodium Glutamate on Liver and Kidney
206 Functions in Adult Rats and Potential Protective Effect of Vitamins C and E. *Food Nutri. Sci.*, 3: 651-659.
- 207 [6] Mozes, S., and Z. Sefcikova, 2004. Obesity and changes of Alkaline Phosphatase Activity in the Small
208 Intestine of 40 and 80-day old rats subjected to early postnatal overfeeding of monosodium glutamate.
209 *Physiol. Res.*, 53:177-186.
- 210 [7] Adrienne, S. 1999. The toxicity of MSG, a study in suppression of information. *Account. Res.*, 6(4): 259-
211 310.
- 212 [8] Eweka, A.O. and F.A.E. Om’Iniabo, 2007. Histological studies of the effects of monosodium glutamate
213 on the small intestine of adult Wistar rat. *Electron J Biomed*, 2, 14-18.
- 214 [9] Burtis, C. and E. Ashwood, 1999. “Tietz Textbook of Clinical Chemistry,” W. B. Saunders Company,
215 London.
- 216 [10] Stryer, L. 2006. “Biochemistry,” W.H. Freeman and Company, New York.
- 217 [11] Larry, H.P. 1990. Pelleting’s history and development. *Feed manag.*, 41(10): 51-72.
- 218 [12] Maruna, R. F. L. 1958. Colorimetric Determination of Sodium in human serum and plasma. *Clinica*
219 *Chimica Acta.*, 2: 581.
- 220
- 221 [13] Henry, R.J. 1974. *Clinical Chemistry, principles and Technique* (2nd edn). Harper and Row: New York;
222 525.
- 223 [14] Tietz, N.W. (1995). *Clinical Guide to Laboratory Tests*, 3rd Edition. W. B. Saunders Company.
224 Philadelphia. PA pp. 518-519.
- 225 [15] Alexander, R.H., and J.M. Griffith, 1992. *Clinical/Nutritional Biochemistry. Basic Biochemical Methods*.
226 2nd edn. Wiley-Liss, New York. John Wiley & Sons
- 227 [16] Wilding, P., and J.H. Kennedy, 1977. *Manual of routine methods in clinical chemistry for use intermediate*
228 *laboratories WHO Lab./78.1* p. 25-28.
- 229 [17] Prescott, J. 2004. Effects of added glutamate on liking for novel food flavors. *Appetite*, 42(2): 143-150.
- 230 [18] Dileep, N.L., J.P. Andrew, Lewington and P. Simon, Allison. (2013) *Basic Concepts of Fluid and*
231 *Electrolyte Therapy. Die Deutsche Bibliothek publishe Germany*, pp 23-28.

- 232 [19] Peterson, L.N and M. Levi, 2003. Disorders of potassium metabolism. In: Schrier RW, ed. Renal 2007.
233 Histological Studies of the Effects of and Electrolyte Disorders. 6th ed. Philadelphia, PA: Lippincott
234 Williams & Wilkins, pp 171-215.
- 235 [20] William K.B., K.D. Richard, A.E. Ben, A. Nafiu and F.L. Edwin, 2012. Relationship between parathyroid
236 hormone and electrolytes in chronic kidney disease. J. Med. Res., 1(8): 103-111.
- 237 [21] Korgaonkar, S., A. Tilea, B. W. Gillespie, M. Kiser, G. Eisele, F. Finkelstein,... and R. Saran, 2010. Serum
238 potassium and outcomes in CKD: insights from the RRI-CKD cohort study. Clin. J. Am. Soc. Nephro.,
239 5(5): 762-769.
- 240 [22] He, K., Du, S., Xun, P., Sharma, S., Wang, H., Zhai, F., & Popkin, B. (2011). Consumption of
241 monosodium glutamate in relation to incidence of overweight in Chinese adults: China Health and
242 Nutrition Survey (CHNS). Am. J. clin. Nutr., 93(6): 1328-1336.
- 243 [23] Ahmed, J., & Weisberg, L. S. 2001. Hyperkalemia in dialysis patients. In *Seminars in dialysis* (Vol. 14, No.
244 5, pp. 348-356). Blackwell Science Inc.
- 245 [24] Soliman, A.R, M. Akmal and S.G, 1989. Parathyroid hormone interferes with extrarenal disposition of
246 potassium in chronic renal failure. Nephron, 52: 262-267.
- 247 [25] Vinodini, N. A., A.K. Nayanatara, C. Ramaswamy, V.R. Anu, D.K. Rekha, G.K.M. Damadara, B. Ahamed,
248 and R.B. Shabarinath, 2010. "Study on Evaluation of Monosodium Glutamate Induced Oxidative
249 Damage on Renal Tissue on Adult Wistar Rats," J. Chinese Clin. Med., 5 (3): 144-147.
- 250 [26] Egbuonu, A.C.C., P.M. Ejikeme and L.N. Obasi, 2010. Influence of sub-chronic oral exposure to high
251 monosodium glutamate on some serum markers of the renal functions in male Wistar rats. African J.
252 Biochem Res., 4(9): 225-228.
- 253 [27] Thomas, M., K.S. Sujatha, and S. George, 2009. Protective effect of *Piper longum* Linn. on monosodium
254 glutamate induced oxidative stress in rats. Indian J. Exper. Biol. 47(3): 186-192.
- 255