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Preliminary Investigation of the Renal Toxicity of Monosodium Glutamate in Rats Determined by Some Serum Biochemical Markers

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Authors' contributions

This work was carried out in collaboration between all authors. Author HOA designed the study, wrote the protocol and supervised the work. Author AVO carried out all laboratories assays and performed the statistical analysis. Author IFO wrote the first draft of the manuscript. Authors HOA and FSA edited the manuscript. Author IFO worked on the literature review and references in the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

The potential renal toxicity of monosodium glutamate (MSG) following dietary administration for four weeks in Albino rats was preliminary investigated by the measurement of serum electrolytes, urea and creatinine levels. 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

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lowest concentration (4.68±0.16 Mmol/L). There was a significant ($p < 0.05$) 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±0.48mmol/L to 1.4±0.11 Mmol/L. The urea concentration of rats in the experimental groups were significantly ($p < 0.05$) lower than the control group. The creatinine concentration of rats in the experimental groups were not significantly different ($p > 0.05$) from those in the control group. This work has shown that high supplementation of diet with MSG could induce hyperkalemia and hypouremia in rats.

Keywords: Monosodium Glutamate (MSG); electrolytes; urea; creatinine; supplemented diet.

1. 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].

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

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

The kidney major physiological functions include the removal of toxic metabolites and waste products from the blood and the regulation of fluid and electrolytes balance in the body. The kidney function tests include; urinalysis, measurement of serum urea, creatinine, sodium, potassium and serum bicarbonate levels [9,10]. Although some reports are available on the adverse effects of direct administration of MSG in kidney function, there have been a dearth of information of the effect of diet supplemented with MSG on kidney functions in rats. This preliminary study was therefore aimed at investigating the renal toxicity of MSG supplemented in rat feed.

2. MATERIALS AND METHODS

2.1 Reagents

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

2.2 Monosodium Glutamate

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

2.3 Experimental Animals

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

2.4 Experimental Diets

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

2.5 Experimental Design

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

Group A: The rats were fed normal commercial feed pellet and served as the control group
Group B: Rats were fed 0.5% MSG supplemented diets.
Group C: Rats were fed with 1% MSG supplemented diets
Group D: Rats were fed with 5% MSG supplemented diets

2.6 Blood and Serum collection

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

2.7 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].

2.8 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.

2.9 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 ± Standard Error of Mean. Means with difference were separated using the Duncan Multiple Range Test and results were considered significant at $p < 0.05$.

3. RESULTS

Fig. 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 ($p > 0.05$) 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±9.14 Mmol/L) while the group placed on 0.5% MSG supplemented diet had the lowest sodium concentration (140.75±5.77 Mmol/L).

Fig. 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 ($p < 0.05$) 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 ($p > 0.05$) in the chloride ion concentration between the control and experimental groups (Fig. 3).

The effects of monosodium glutamate on serum urea and creatinine levels are as shown in Figs. 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 ($p < 0.05$) 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 concentration of rats in the experimental groups were not significantly different ($p > 0.05$) from those in the control group.

4. DISCUSSION

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

The present preliminary study showed that high intake of dietary MSG in rats altered some physiological biomarkers of kidney physiology. The levels of sodium and chloride were not significantly affected in this study. Inuwa et al. [1] who evaluated the nephrotoxic and hepatoxic effects of monosodium glutamate (MSG) consumption found a similar increasing trend except with chloride ion (Fig. 2). The non-significant ($p > 0.05$) change in the concentration of sodium and chlorine ions in the experimental groups agrees with their findings.

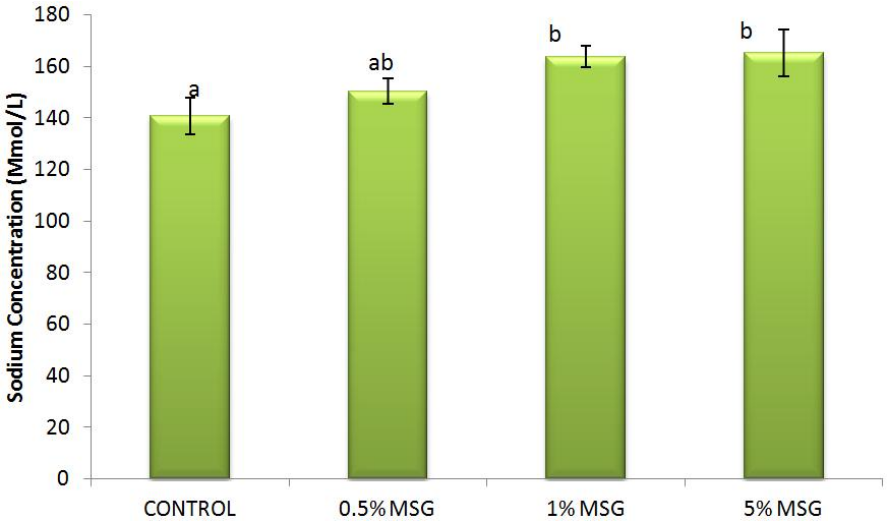

Fig. 1. Serum sodium concentration (Mmol/L) in rats fed MSG supplemented diets
Values are Mean ± SEM (n=5). Bars with different alphabet are significantly (p<0.05) different from control group

The significant ($p < 0.05$) increase in potassium level of the experimental groups (Fig. 3) is consistent with findings of Ilegbedion et al. [4] who evaluated the effect of MSG on electrolyte balance and histology of gastroesophageal mucosa. The potassium ion concentration observed in experimental groups placed on 1% and 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 hyperkerlamia 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 (Fig. 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.

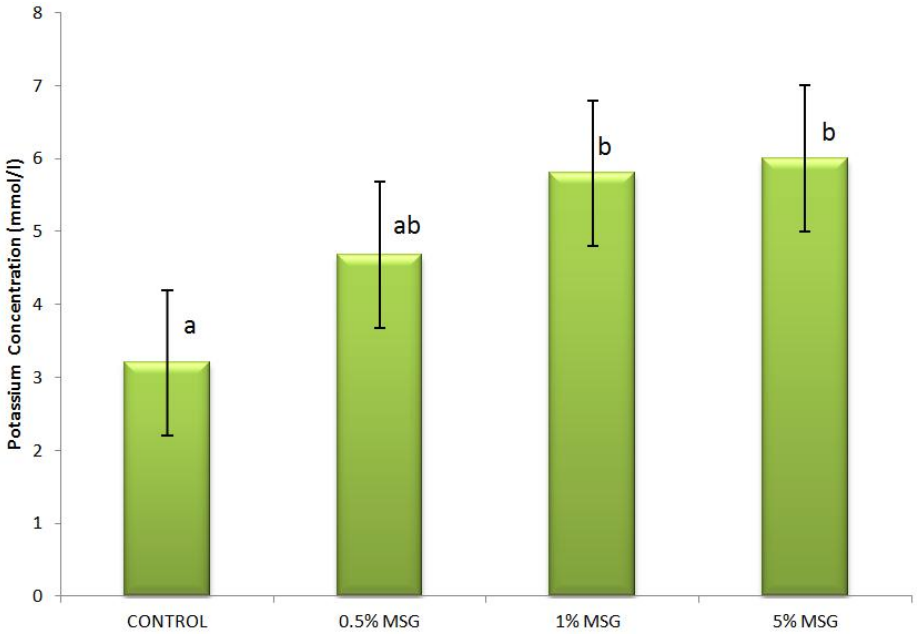

Fig. 2. Serum potassium concentration (Mmol/L) in rats fed MSG supplemented diet
Values are Mean±SEM (n=5). Bars with different alphabet are significantly (p<0.05) different from control group

Serum urea level significantly decreased in the experimental groups (Fig. 4) and this agrees with the result obtained in the study of Manal and Nawal, [5]. It also agrees with the study of Egbuonu 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.

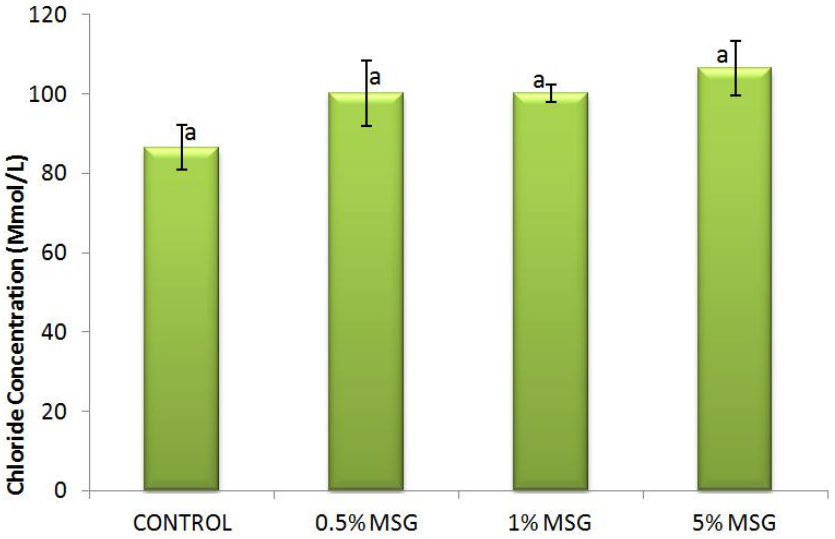

Fig. 3. Serum chloride ion concentration (Mmol/L) in rats fed MSG supplemented diets
Values are Mean±SEM (n=5). Bars with different alphabet are significantly (p<0.05) different from control group

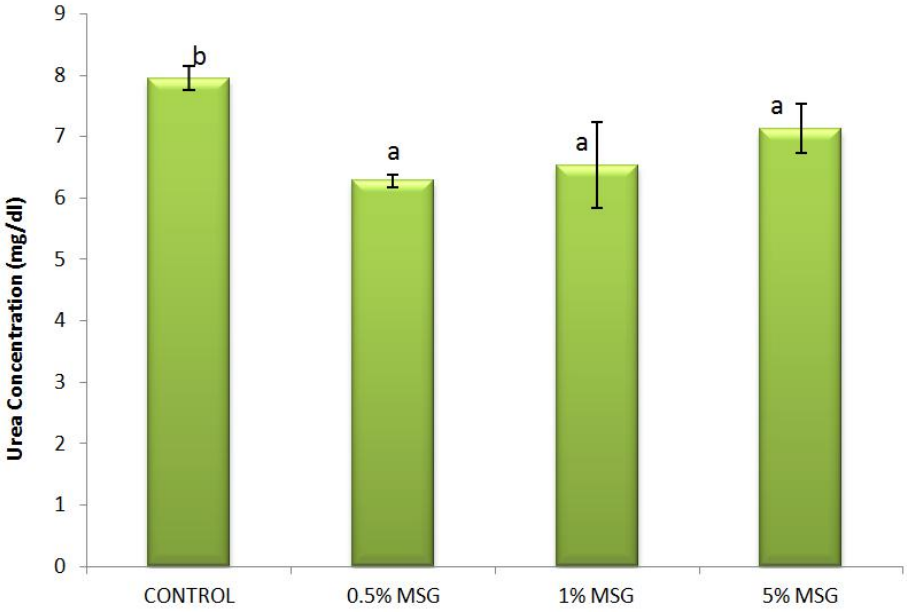

Fig. 4. Serum urea concentration (mg/dl) in rats fed MSG supplemented diets
Values are Mean±SEM (n=5). Bars with different alphabet are significantly (p<0.05) different from control group.

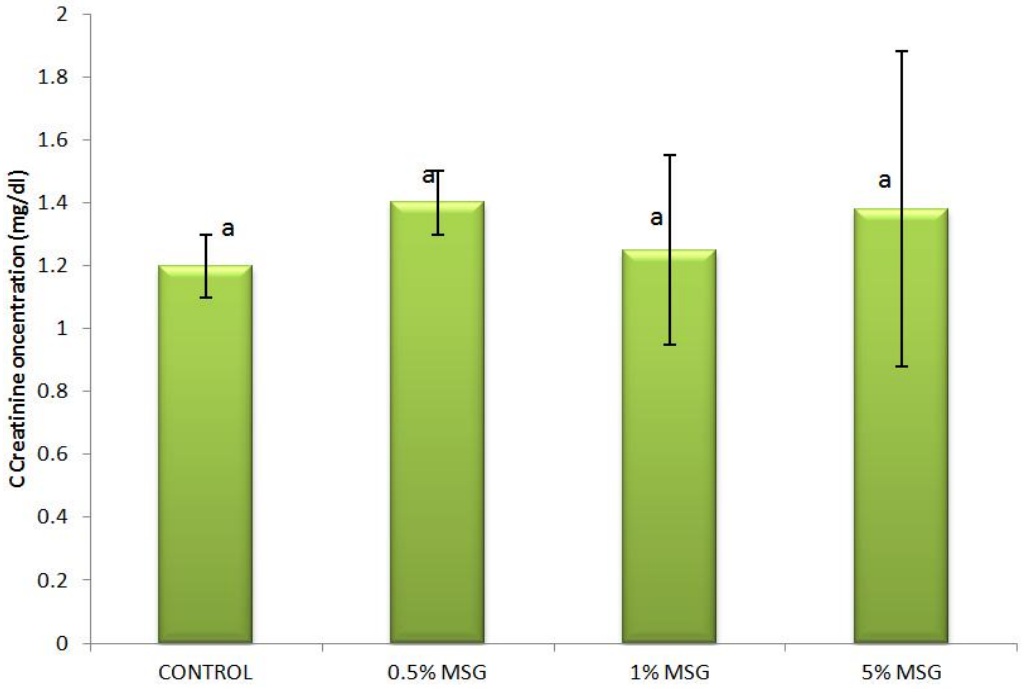

Fig. 5. Serum creatinine concentration (mgl/dl) in rats fed MSG supplemented diet
Values are Mean±SEM (n=5). Bars with different alphabet are significantly (p<0.05) different from control group

5. CONCLUSION

This preliminary study indicated that high dietary intake of MSG given to rats for four weeks in their diet elevated the serum concentration of potassium ion but decreased that of urea, suggesting hyperkalemia and hypouremia in the exposed rats. Further investigation is warranted to determine the specific mechanism(s) of the renal toxicity induced by MSG.

CONSENT

It is not applicable.

ETHICAL APPROVAL

All authors hereby declare that "Principles of laboratory animal care" (NIH publication No. 85-23, revised 1985) were followed, as well as specific national laws where applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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