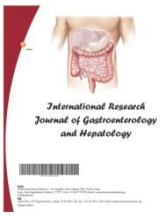

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Effect of Monosodium Glutamate on Body Weight and Alanine Aminotransferase Activity in Wistar Rats

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Authors' contributions

This work was carried out in collaboration with all authors. Author EOO conceptualized designed and also managed the analyses of the study. Author AIA wrote the manuscript. Author VNO and author JAE managed the literature searches. Author UO wrote the protocol and performed the statistical analysis. All authors read and approved the final manuscript.

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ABSTRACT

Background: In recent days, the use of seasonings to enhance the flavor of food has been increased. A variety of seasonings are produced now days and the constituents of these flavor-enhancers are unknown to ignorant consumers. The consumers were preferred to eat food with good taste without consideration the effect of additives on their health. These seasonings contain monosodium glutamate (MSG) which really spiced the food.
Aim: This study sought to investigate the effect of MSG on body weight and alanine aminotransferase activity.

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Place and Duration: This research was carried out at the Department of Pharmacology and Therapeutics, College of Medicine and Health Sciences, Abia State University, Uturu, and the Department of Chemical Pathology, St. Anthony's Hospital Ltd. Aba, both in Abia State, Nigeria in 2011.

Methods: MSG (3g/satchet containing 99% MSG) was obtained from a Grocery Store at New Market, Aba in Abia State, Nigeria. Forty Wistar rats were used for this study. Fifteen of the rats were used for acute toxicity test (LD_{50}) and twenty-five for the experiment. The 25 Wistar rats were divided into five groups of 5 rats each. Animals in groups A, B, C, and D were respectively administered 500 mg/kg, 750 mg/kg, 1000 mg/kg and 1,250 mg/kg of MSG thoroughly mixed with standard feed for eight weeks. Animals in group E received equal amount of feeds without MSG added. This group served as the control group. At the end of 8 weeks, animals were fasted overnight and anaesthetized using diethyl ether. Blood samples were collected by cardiac puncture and ALT activity was determined using standard method.

Result: The LD_{50} was taken to be 500 mg/kg, which is the median of 200 mg/kg which did not kill any of the animals and 800 mg/kg that killed all its animals. MSG was observed to increase weight gain as well as ALT activity when compared with control animals.

Conclusion: The elevation of ALT activity by MSG is an indication that it can induce hepatotoxicity.

Keywords: Monosodium glutamate; body weight; alanine aminotransferase; hepatotoxicity; obesity.

1. INTRODUCTION

Monosodium glutamate (MSG) is a sodium salt of glutamic acid [1]. It is usually a white powder. Water ionizes it into free sodium ions and glutamic acid, which is an organic compound consisting of five carbon atoms [2]. It has a carboxylic (-COOH) group and an amino ($-NH_2$) group attached to an "alpha" carbon atom (a carbon atom joined directly to the – COOH group). It is an alpha amino acid. The molecular formula of MSG is $C_3H_8NNaO_4$ and its molecular mass is 169.11 $gmol^{-1}$. MSG has the same basic structure of amino acids, with an amine group ($-NH_2$) and carboxylate ion instead of the carboxylic group ($-COO^-$). MSG has almost same structure with glutamate [2]. The difference is that one hydrogen atom at the carboxylic chain has been replaced with a sodium atom, hence, the name monosodium glutamate [1].

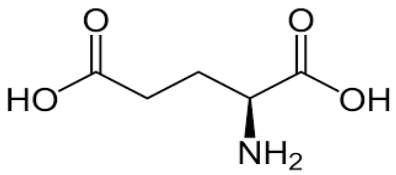

Fig. 1. Structure of glutamate [2]

Monosodium glutamate (Fig 2) has a distinctive taste that falls outside the region of the four classic tastes: sweet, sour, salty, and bitter. This taste is called "Umami," also referred to as "Xien Wei" in Chinese or "savory, "broth-like" or "meaty taste" in English. Due to this special taste, many food producers use MSG to enhance the flavor of their product [3]. Recently, Chaudhari et al. [4] identified a specific glutamate taste receptor on the tongue. Three umami substances (glutamate, 5-inosinate, and 5-guanylate) were found by Japanese scientists, but umami has not been recognized in Europe and America for a long time. In the late 1900s, umami was internationally recognized as the fifth basic taste based on psychophysical, electrophysiological, and biochemical studies [2]. Three umami receptors (T1R1 + T1R3, mGluR4, and mGluR1) were identified. There is a synergism between glutamate and the 5-nucleotides. Among the above receptors, only T1R1 + T1R3 receptor exhibits the synergism [5]. Since glutamate and 5-inosinate are contained in various foods, umami taste is induced by the synergism in daily eating [5].

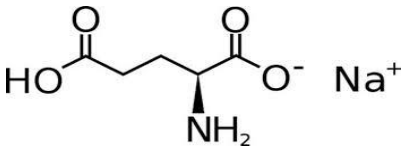

Fig. 2. Structure of monosodium glutamate [2]

The safety and toxicity of MSG had become controversial in the last few years because of reports of adverse reactions in people who have eaten foods that contain MSG. Many studies had confirmed the adverse reactions of MSG [1,6,7].

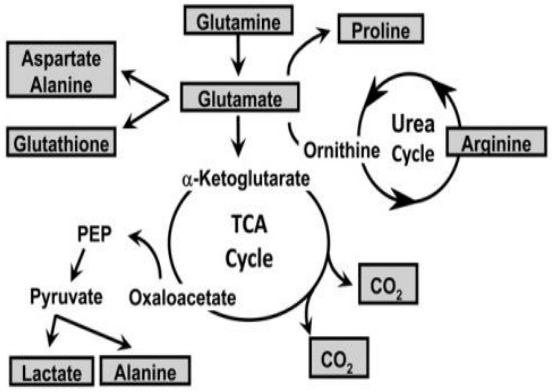

Fig. 3. Metabolic fates of dietary glutamate in the intestine [2]

MSG has been reported to cause headache, vomiting, diarrhea, irritable bowel syndrome, asthma attacks in asthmatic patients and panic attacks [1]. Obuchi et al. [7] studied the effect of garlic extracts on MSG induced fibroid in Wistar rats and reported that MSG alone increased total protein, cholesterol and estradiol (estrogen), which in turn, induced fibroid in the rats. However, treatment with garlic extracts near-completely abrogated/mitigated any effects that have been induced by MSG alone. Egbuonu et al. [8] reported a study aimed at investigating the potentials of low concentration administration of monosodium glutamate in inducing hepatotoxicity in male albino rats. In that study, it was observed that treating rats with monosodium glutamate at a low concentration (5 mg/kg of body weight) could be hepatotoxic without significant cholestasis or pathologies of the bone. Onyema et al. [9] reported that MSG at a dose of 0.6 mg/g body weight induced the oxidative stress and hepatotoxicity in rats and vitamin E ameliorated MSG-induced oxidative stress and hepatotoxicity. Meraiyebu et al. [10] reported that MSG increased the number of platelets, bleeding time and clotting time in MSG-treated rats. Onyema et al. [11] tested the hypothesis that alteration in glucose metabolism following MSG administration might be a contributor to the changes in the markers of oxidative stress observed in the animals. The pattern of induction of oxidative stress and alteration of glucose metabolic enzymes in the animals was an indication that oxidative stress induced by MSG in the renal tissues of rats might be contributed by increased tissue glucose concentration resulting from enhanced renal gluconeogenesis [11]. Nwajei et al. [12] reported that four selected food seasonings (labeled IS, KC, SMC and BS) commonly consumed in Nigeria adversely perturbed some sex hormones: testosterone, Estrogen and progesterone of Wistar albino rats due to the presence of MSG in these seasonings. Kolawole [13] investigated the effect of orally administered MSG on food consumption, body weight and some biochemical and hematological parameters in adult Wistar rats and reported that MSG at the doses or 5 – 15 mg/kg body weight was not hazardous to health. Furthermore, Ogbuagu et al. [14] has previously reported that MSG has hyperglycemic and hypocholesterolemic effect on Wistar rats.

2. MATERIALS AND METHOD

2.1 Collection of Monosodium Glutamate

The Monosodium Glutamate (3 g/satchet containing 99% MSG) was obtained from a Grocery Store at New Market, Aba in Abia State, Nigeria.

2.2 Collection of Animals

Forty (40) adult Wistar rats with body weight between 160 and 200 g were obtained from the animal house of the Department of Pharmacology and Therapeutics, College of Medicine and Health Science, Abia State University, Uturu, Nigeria. They were acclimatized for seven days before the study. All the animals were handled in accordance with the standard guidelines for care and use of laboratory animals. The animals had access to standard animal feed purchased from a local commercial supplier and water *ad libitum* and housed under standard condition of temperature (25°C $\pm$ 2°C) under 12 hours light-darkness cycles. Fifteen (15) of the rats were used for acute toxicity test and twenty-five (25) for the experiment.

2.3 Acute Toxicity Test (LD_{50} Determination)

The acute toxicity test (LD_{50}) was determined using a modified version of the method proposed by Lorke [15] which involves the use of minimal number of experimental animals. This method of acute toxicity determination makes the following assumptions.

I. Substances more toxic than 1 mg/kg body weight are so highly toxic that it is unnecessary to calculate the LD_{50}.
II. LD_{50} values greater than 5000mg/kg are of no practical interest.

III. An approximate figure for the LD_{50} is usually adequate to estimate the risk of acute intoxication.

The LD_{50} is taken as the median concentration that killed 50% of the test animals. The median lethal dose was estimated as the geometric mean of the least dose at which none of the animals died and highest concentration at which all the animals died. The 15 animals used in the determination of LD_{50} were divided into five groups of 3 each. Groups A, B, C and D were administered 100 mg/kg, 200 mg/kg, 400 mg/kg and 800 mg/kg of MSG respectively through the intraperitoneal route of drug administration while group E was similarly treated but with saline solution. This group served as the control group. The animals were constantly observed for 24 hours for signs of toxicity and death.

2.4 Experimental Design

A total of 25 adult Wistar rats were divided into five groups of 5 rats each. Animals in groups A, B, C, and D were respectively administered 500 mg/kg, 750 mg/kg, 1000 mg/kg and 1,250 mg/kg of MSG thoroughly mixed with standard feed for 8 weeks. Animals in group E received equal amount of feeds but without MSG. This group served as the control group. At the end of 8 weeks, animals were fasted overnight and anaesthetized using diethyl ether. Blood samples were collected by cardiac puncture.

2.5 Determination of Alanine Aminotransferase Activity

The activity of alanine aminotransferase was determined by the method of Reitman and Frankel [16].

2.6 Statistical Analysis

Data were subjected to analysis using Microsoft excel 2016.

3. RESULTS

3.1 Acute Toxicity Test

One of the animals in Group D (administered 800 mg/kg body weight) died within the first 30 minutes of administration. After 12 hours of observation another one died in Group D. The remaining one in group D and one in group C died overnight. The LD_{50} was then taken to be 500 mg/kg, which is the median of 200 mg/kg which did not kill any of the animals and 800 mg/kg that killed all its animals.

3.2 Systemic Effect of MSG

Two weeks into the study, most of the animals in the experimental group became hyperactive. Four weeks later, one of the animals in the group fed with 1250 mg/kg of MSG developed bulging of eyeballs (exophthalmus), and had several bouts of seizures before its demise six days later.

3.3 Effect of Monosodium Glutamate on Body Weight and ALT Activity

The effect of MSG on weight gain and alanine aminotransferase activity after 8 weeks of treatment is presented in Figs. 4 and 5 respectively.

4. DISCUSSION

Food seasoning is a substance that adds flavor to food, for example salt, peppers, and other spices. Spices are vegetable substances of indigenous or exotic origin which are aromatic and have hot piquant tastes, used to enhance the flavor of foods or to add to them the stimulant ingredient contained in them [2]. Seasonings can also be used to replace common salt in a great variety of other industrially prepared food items as well as in the preparation of foods both in restaurants, catering, home kitchen etc. Such seasonings are particularly suitable for soups, beefs, and other foods in which salty, and/or spiced seasonings are used. The ingredient mixture and seasonings when added to various food items change the food composition [17]. There are several brands of food seasonings readily available in the open markets, in-street shops and supermarkets. These include: star maggi, knorr, royco, doyin, jumbo (cubes), Onga, Mixpy, Benny, Aluba shrimp seasoning (powdered), A-one, Vedan, Aji-no-moto, Salsa and Tasty (monosodium glutamate). Reports have indicated that the major active ingredients in flavor enhancers are salt (NACL) and monosodium glutamate (MSG). Other ingredients include: Hydrogenated palm oil, Caramel, Colour, Soyabeans, Locust beans, Maltodextrin, Corn starch, Chicken fat, Disodium guanylate, Disodium inosilate, Hydrolyzed plant/Vegetable, protein, tomatoes, natural spices etc. [18]. This study sought to investigate the effect of MSG on body weight and ALT activity.

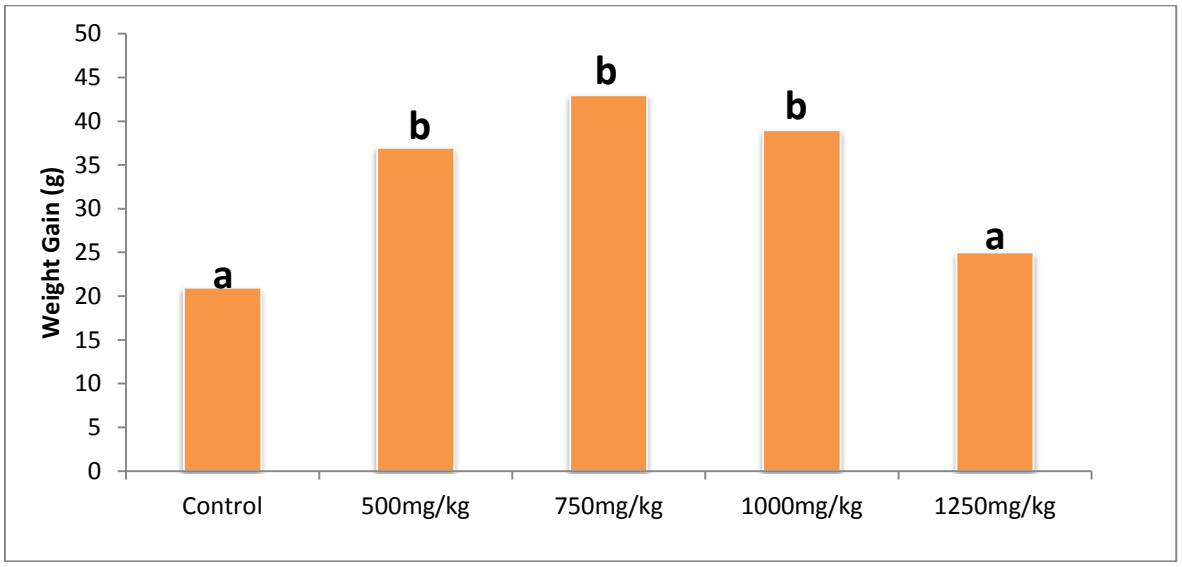

Fig. 4. Effect of monosodium glutamate on weight gain after 8 weeks of treatment
Bars with different letters are significantly different at p<0.05

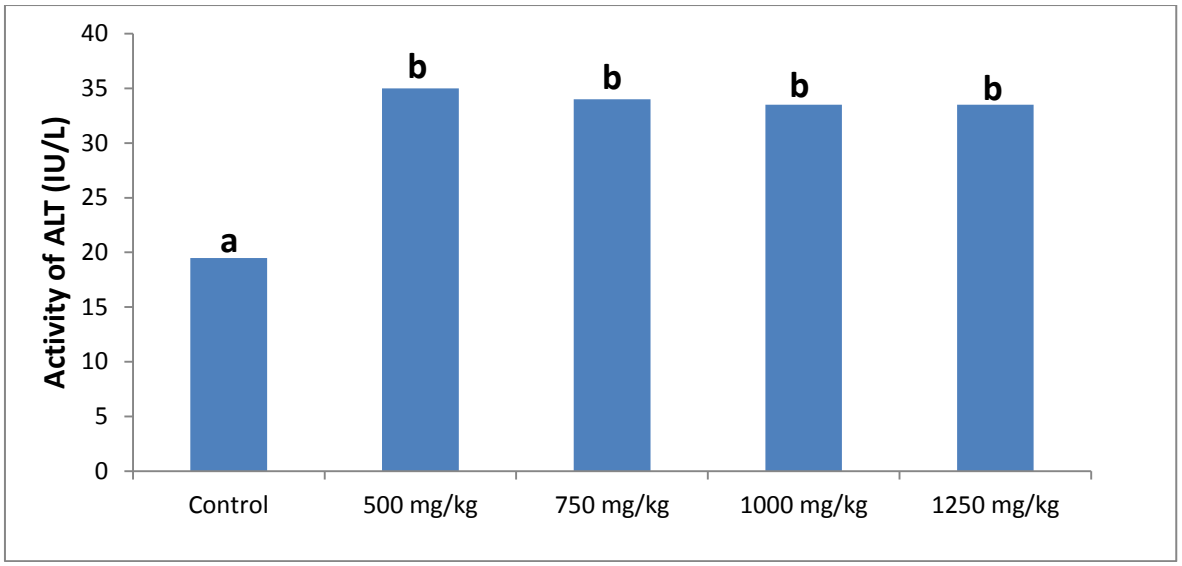

Fig. 5. Effect of monosodium glutamate on alanine aminotransferase activity after 8 weeks of treatment
Bars with different letters are significantly different at p<0.05

In this study, MSG was observed to significantly increase weight gain especially in animals fed with 500, 750 and 1000 mg/kg body weight respectively. This increased weight gain might probably be due to the stimulation of lesion in the arcuate nucleus of the hypothalamus, resulting in increased caloric intake above utilization [19]. Monosodium glutamate has also been reported to increase appetite and improves the palatability of poor quality diet [20]. This increase in body weight following treatment with MSG might also be that MSG stimulates the pancreas, resulting in hyperinsulinaemia. The excess insulin in the blood increases the conversion of glucose to glycogen and its storage in the adipose tissues as fat [21]. Nevertheless, the growth of an organism comprises many factors including physiological, biological and cellular processes [22].

Studies on the tissue enzyme alterations might reflect the metabolic abnormalities and cellular injuries in some organs. The liver has extremely important function in detoxification and excretion

of metabolic wastes and xenobiotics [23,24]. Exposure to toxic chemicals causes alterations in liver enzyme activities [25-27]. Alanine aminotransferase (ALT) is considered most reliable hepatocellular injury because it is solely confined to the liver, unlike AST and ALP which are also abundantly present in other body organs such as the kidneys, brain, and hearts [28,29]. In this study, a significant increase in the activity of ALT was observed in the experimental rats when compared with the control group. ALT is a sensitive marker of liver damage [30,31], therefore the increase in ALT activity by 1%, 10.7% and 28.1% in rats fed with MSG of 750 mg/kg, 1000 mg/kg and 1250 mg/kg respectively, may perhaps be an indication of liver damage. MSG could dissociate easily to release free glutamate. The deamination of glutamate produces ammonium ion (NH_4^+) that could be toxic unless detoxified in the liver via the reactions of the urea cycle. Thus the possible ammonium ion overload that may occur as a result of an increased level of glutamate following MSG intake could damage the liver, as well as induce oxidative stress in the MSG fed rat, consequently releasing the ALT enzyme that may lead to its observed elevation. The result seemingly agrees with the findings of Farombi and Onyema [32] that the activity of ALT increased in male rats that were fed with MSG. Thus, it could be concluded that MSG may be hepatotoxic at 750 $mgkg^{-1}$ and above and should be avoided in patients with hepatic dysfunction. Furthermore, ALT has been reported to be a strong positive indicator of insulin resistance, diabetes mellitus and obesity which are risk factors of coronary heart disease [33-37]. This might be suggestive that MSG has the propensity to induce or increase the risk factors of diabetes mellitus as well as obesity.

5. CONCLUSION

This study revealed that consumption of MSG at 750 mg/kg body weight for about eight weeks has the capacity to increase body weight significantly and thus might induce obesity on the long-run. The significant increase in the activity of ALT due to MSG consumption might also imply that MSG is hepatotoxic therefore; the use of MSG at even low dose should not be encouraged because of the possible adverse implications.

CONSENT

It is not applicable.

ETHICAL DISCLAIMER

Animal ethic Committee approval has been collected and preserved by the author.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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