International Journal of Research and Reports in Hematology

2(2): 115-121, 2019; Article no.IJR2H.51578

Hyperglycemic and Hypocholesterolemic Effect of Monosodium Glutamate in Wistar Rats

Emmanuel O. Ogbuagu[1*], Augustine I. Airaodion[2], Victor N. Okoroukwu[3] and Uloaku Ogbuagu[2]

[1]Department of Pharmacology and Therapeutics, Abia State University, Uturu, Nigeria.
[2]Department of Biochemistry, Federal University of Technology, Owerri, Imo State, Nigeria.
[3]Department of Pharmacology and Therapeutics, Gregory University Uturu, Abia State, Nigeria.

Authors' Contributions

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

Article Information

Editor(s):
(1) Dr. Dharmesh Chandra Sharma, ABTO (Associate Blood Transfusion Officer), Incharge Blood Bank, Component and Aphaeresis Uni, G. R. Medical College and J. A. Hospital, Gwalior, India.
Reviewers:
(1) Rupali Sengupta, SNDT, India.
(2) Ioana Stanciu, University of Bucharest, Romania.
(3) Jihan Seid Hussein, National Research Centre, Egypt.
Complete Peer review History: https://sdiarticle4.com/review-history/51578

Original Research Article

Received 03 July 2019
Accepted 15 September 2019
Published 26 September 2019

ABSTRACT

Background: The use of seasonings to enhance the flavor of food has been on the increase in recent times. Different types of seasonings are produced daily and the constituents of these flavor-enhancers are unknown to ignorant consumers. They only want to eat food with good taste without consideration of the effect of these 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 blood sugar and cholesterol.
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, Nigeria in 2011.
Methods: 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

**Corresponding author: E-mail: augustineairaodion@yahoo.com;*

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 into plain test tubes and allowed to clot. The clotted blood was centrifuged at 4000 rpm for 10 minutes in a centrifuge. Serum was collected and analyzed immediately (for glucose) and the remaining refrigerated for further analysis (cholesterol) using standard methods.

Results: 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 blood glucose but decreased cholesterol when compared with control animals.

Conclusion: The elevation of blood sugar by MSG is an indication that it can induce diabetes.

Keywords: Monosodium glutamate; hyperglycemia; hypocholesterolemia; lethal dose.

1. INTRODUCTION

Monosodium glutamate (MSG) is a sodium salt of glutamic acid. 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. It has a carboxylic (-COOH) Fig. 1 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. The difference is that one hydrogen atom at the carboxylic chain has been replaced with a sodium atom, hence, the name monosodium glutamate [1].

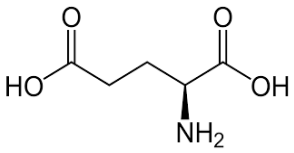

Fig. 1. Structure of glutamate [2]

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. 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].

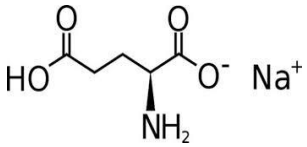

Fig. 2. Structure of Monosodium glutamate [2]

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].

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.

2. MATERIALS AND METHODS

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 (25ºC $\pm$ 2ºC) 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 [14] which involves the use of minimal number of experimental animals. This method of acute toxicity determination makes the following assumptions.

1. Substances more toxic than 1mg/kg body weight are so highly toxic that it is unnecessary to calculate the LD_{50}.
2. LD_{50} values greater than 5000 mg/kg are of no practical interest.
3. 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 into plain test tubes and allowed to clot. The clotted blood was centrifuged at 4000 rpm for 10 minutes in a centrifuge. Serum was collected and analyzed immediately (for glucose) and the remaining refrigerated for further analysis (cholesterol).

2.5 Determination of Blood Glucose and Cholesterol

Blood glucose was determined using previously described method by Airaodion et al. [15,16], while cholesterol was determined by the method described in Owoade et al. [17,18]

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 Fasting Blood Glucose and Serum Cholesterol

The effect of MSG on fasting blood glucose and serum cholesterol is presented in Figs. 3 and 4 respectively.

4. DISCUSSION

Noxious substances abound in the environment. We come in contact with them every day, either directly or indirectly. In either way, they have effect on our health. Some examples of these substances are carbon monoxide (CO), alcohol, tobacco, and additives such as Aspartame, Sulfites, Nitrates/nitrites, and Monosodium Glutamate (MSG). Consumption of monosodium glutamate worldwide with its attendant toxic effect still remains a concern to medical and food scientists. This study sought to evaluate the effect of monosodium glutamate in blood sugar and cholesterol of adult Wistar rats.

In this study, a significant increase was observed in the mean fasting blood glucose of the experimental animals when compared with the control group. This result is similar with the findings of Nagata et al. [19] where MSG was used to induce obesity in type 2 (non-insulin dependent) diabetes mellitus in mice. The elevation in the fasting blood glucose observed in this study might be an indication that MSG could induce diabetes. One main cause of diabetes is an increase in post-prandial hyperglycemia. This

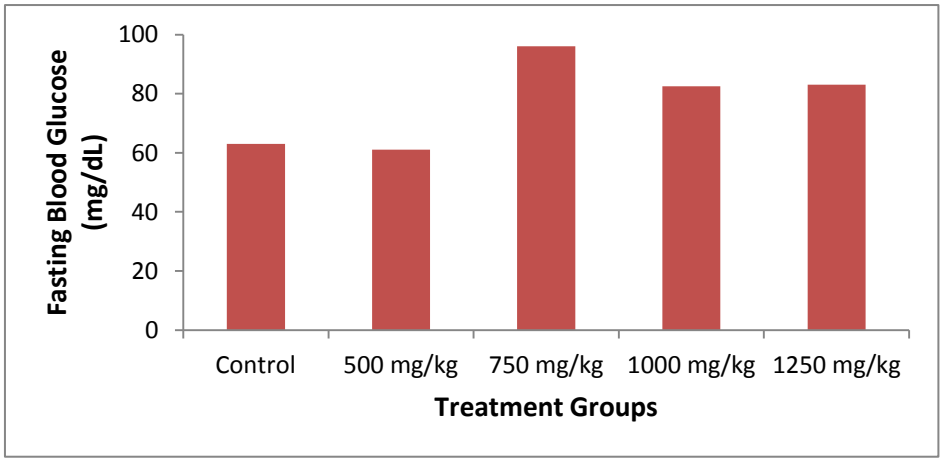

Fig. 3. Effect of MSG on fasting blood glucose levels after 8 weeks treatment

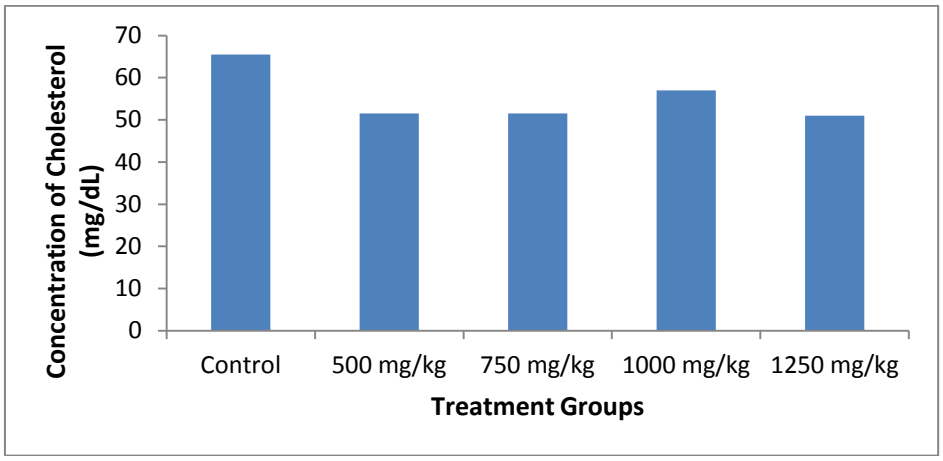

Fig. 4. Effect of MSG on serum cholesterol levels after 8 weeks treatment

is done by increasing the absorption of glucose through the stimulation of the carbohydrate-hydrolyzing enzymes, α-amylase and α-glucosidase, in the digestive tract. Consequently, activators of these enzymes determine an elevation in the rate of glucose absorption and consequently increasing the post-prandial plasma glucose rise [20]. Based on these findings, it could be suggested that MSG may activate platelet aggregation and reduce vasodilatation, exerting compromised role in the prevention of the development and progression of vascular complications caused by the hyperglycemic state [21,22].

Apart from the regulation of carbohydrate metabolism, insulin plays an important role in lipid metabolism. Insulin insufficiency, as in diabetes mellitus, is associated with hypercholesterolemia and hypertriglyceridemia, which have been reported to occur in experimental diabetic rats [23,24,25]. Hypercholesterolemia could result in a relative molecular ordering of the residual phospholipids, resulting in a decrease in membrane fluidity [26]. Accumulation of cholesterol is one of the leading risk factors in coronary heart disease (CHD). Lipid and lipoprotein abnormalities have been shown to play a major role in the pathogenesis and progression of several disease conditions [27]. Surprisingly in this study, a significant reduction was observed in the serum cholesterol level of the experimental animals when compared with the control group. This is in contrast with the study of Savastonon et al. [28] where cholesterol levels of experimental animals were reported to be higher than the control animals. The mechanism for the cholesterol lowering effect of MSG in this study is unclear but it might be due to the inhibition of hepatic cholesterol and possibly triglyceride as well as fatty acid synthesis [29,30].

5. CONCLUSION

The result of this study is an indication that monosodium glutamate has the ability of inducing hyperglycemia and subsequently diabetes, as well as inducing hypocholesterolemia.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Guyton A, Hall J. Textbook of medical physiology, W.B. Saunders Co., Philadelphia; 1996.
2. Airaodion AI, Ogbuagu EO, Osemwowa EU, Ogbuagu U, Esonu CE, Agunbiade AP, Okereke D, Oloruntoba AP. Toxicological effect of monosodium glutamate in seasonings on human health. Global Journal of Nutrition & Food Science. 2019;1(5):1-9.
3. David TW. MSG – Flavor enhancer or Deadly Killer. AU J.T. 2008;12(1):43-49.

4. Chaudhari N, Landin AM, Roper SA. Metabotropic glutamate receptor variant functions as a taste receptor. Nature neuroscience. 2000;3(2):113-119.
5. Kurihara K. Umami the fifth basic taste: History of studies on receptor mechanisms and role as a food flavor. BioMed Research International. 2015;189(402):1-10.
6. Meraiyebu A, Akintayo CO, Uzoechi AC, Okere S. The effects of orally administered Monosodium Glutamate (MSG) on blood thrombocyte, blood coagulation and bleeding in Rats. IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS). 2012;4(1):04-08.
7. Obochi GO, Malu SP, Obi-Abang M, Alozie Y, Iyam MA. Effect of Garlic Extracts on Monosodium Glutamate (MSG). Induced Fibroid in Wistar Rats. Pakistan Journal of Nutrition. 2009;8(7):970-976.
8. Egbuonu ACC, Obidoa O, Ezeokonkwo CA, Ezeanyika LUS, Ejikeme PM. Hepatotoxic effects of low dose oral administration of monosodium glutamate in male albino rats. African Journal of Biotechnology. 2009;8(13):3031-3035.
9. Onyema OO, Farombi EO, Emerole GO, Ukoha AI Onyeze GO. Effect of vitamin E on monosodium glutamate induced hepatotoxicity and oxidative stress in rats. Indian Journal of Biochemistry & Biophysics. 2005;43:20-24.
10. Meraiyebu A, Akintayo CO, Uzoechi AC, Okere S. The effects of orally administered Monosodium Glutamate (MSG) on blood thrombocyte, blood coagulation and bleeding in rats. IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS). 2012;4(1):04-08.
11. Onyema OO, Alisi CS, Ihetuge AP. Monosodium glutamate induces oxidative. Stress and affects glucose metabolism in the kidney of rats. International Journal of Biochemistry Research & Review. 2012; 2(1):1-11.
12. Nwajei JC, Onuoha SC, Essien EB. Effects of oral administration of selected food seasonings consumed in Nigeria on some sex hormones of Wistar Albino Rats. IOSR Journal of Biotechnology and Biochemistry (IOSR-JBB). 2015;1(5):15-21.
13. Kolawole OT. Assessment of the effects of monosodium glutamate on some biochemical and hematological parameters in adult Wistar Rats. American Journal of BioScience. 2013;1(1):11-15.
14. Lorke D. A new approach to practical acute toxicity testing. Arch. Toxicol. 1983;53:275-289.
15. Airaodion AI, Ogbuagu EO, Airaodion EO, Ekenjoku JA, Ogbuagu U. Pharmaco therapeutic effect of methanolic extract of *Telfairia occidentalis* leaves on glycemic and lipidemic indexes of alloxan-induced diabetic rats. International Journal of Bio-Science and Bio-Technology. 2019;11(8): 1-17.
16. Airaodion AI, Ogbuagu EO, Airaodion EO, Ogbuagu U, Ekenjoku JA. Antidiabetic effect of ethanolic extract of *Carica papaya* leaves in alloxan-induced diabetic rats. International Journal of Bio-Science and Bio-Technology. 2019;11(8):93-109.
17. Owoade AO, Adetutu A, Airaodion AI, Ogundipe OO. Toxicological assessment of the methanolic leaf extract of *Bridelia Ferruginea*. The Journal of Phyto pharmacology. 2018;7(5):419-424.
18. Owoade AO, Airaodion AI, Adetutu A, Akinyomi OD. Levofloxacin-induced dyslipidemia in male albino rats. Asian Journal of Pharmacy and Pharmacology. 2018;4(5):620-629.
19. Nagata M, Suzuki W, Izuka S, Tabuchi M, Marayame H, Takeda S. Type 2 diabetes mellitus in obese mouse model induced by monosodium glutamate. Exp. Anim. 2006; 55(2);109-115.
20. Chen X, Zheng Y, Shen Y, Voglibose BAO. One of the most important α- glucosidase inhibitors. Current. Medical. Chemistry. 2006;13:109-116.
21. Airaodion AI, Airaodion EO, Ogbuagu EO, Ogbuagu U, Osemwowa EU. Effect of oral intake of African locust bean on fasting blood sugar and lipid profile of Albino Rats. Asian Journal of Research in Biochemistry. 2019;4(4):1-9.
22. Airaodion AI, Adeniji AR, Ogbuagu EO, Ogbuagu U, Agunbiade AP. Hypoglycemic and hypolipidaemic activities of methanolic extract of *Talinum triangulare* leaves in Wistar rats. International Journal of Bio-Science and Bio-Technology. 2019;11(5): 1-13.
23. Loci AS, Shaabha M, Khazraji AL, Husain A, Twaija A. Hypoglycemic effect of a valuable extract on some blood parameters in diabetic animals. J. Ethnopharmacol. 1994;43:167–171.
24. Ahardh CD, Bjorgell P, Nilson EP. The effect of tolbutamide in lipoproteins and lipoprotein lipase and hormone sensitive

lipase. Diabetes Res. Clin. Pract. 1999;46: 99–108.
25. Frayn KN. Insulin resistance and lipid metabolism. Curr. Opin. Lipidol.1993;4: 197–204.
26. Bopanna KN, Kannan J, Suchma G, Balaraman R, Ranthod SP. Anti diabetic and anti hyperlipidemic effect of neem seed, kernel powder on alloxan diabetic rabbits. Ind. J. Pharmacol. 1997;29:162–167.
27. Rotimi OS, David AO, Olusola AT, Regina NU, Elizabeth AB, Oladipo A. Amoxillin and pefloxacin-induced cholesterol genesis and phospholipidosis in rat tissues. Lipids in Health and Disease. 2015;14:13-30.
28. Savastano S, Disomma C, Belfiore A, Guida B, Orio F, Rota F. Growth hormone status in morbidly obese subjects and correlation with body composition. J. Endocrinal Invest. 2006;29(6):536-543.
29. Airaodion AI, Akinmolayan JD, Ogbuagu EO, Airaodion EO, Ogbuagu U, Awosanya OO. Effect of methanolic extract of *Corchorus olitorius* Leaves on hypoglycemic and hypolipidaemic activities in albino rats. Asian Plant Research Journal. 2019;2(7):1-13.
30. Ogbuagu EO, Airaodion AI, Ogbuagu U, Airaodion EO. Effect of methanolic extract of *Vernonia amygdalina* leaves on glycemic and lipidaemic indexes of Wistar Rats. Asian Journal of Research in Medical and Pharmaceutical Sciences. 2019;7(3): 1-14.

Peer-review history:
The peer review history for this paper can be accessed here:
https://sdiarticle4.com/review-history/51578