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The toxic effect of Monosodium glutamate as a food additive on some biochemical parameters in male rat

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Abstract

Monosodium glutamate is made up of nutritionally indispensable amino acids and used as a flavor enhancer worldwide. Monosodium glutamate (MSG) is believed to be associated with different health problems. The purpose of this research is to outline the metabolic alterations related to MSG administration in male rats. Rats were orally administrated with MSG at a dosage (15 mg/kg body weight) for three months. We evaluated: body weight, and some biochemical parameters in the blood such as Triacylglycerol, Total cholesterol liver enzymes, kidney function, Thyroid-stimulating hormone (TSH), Iron and hemoglobin (Hb). All data were statistically analyzed. Results: MSG administrated rats showed a highly significant increase in average body weight, Triacylglycerol, Total cholesterol, Liver enzyme, and Kidney function, besidesa significant increase in Iron level with a positive correlation with hemoglobin level, while there is no effect on TSH.

Keywords*: Monosodium glutamate, liver, kidney, TSH, Iron, Hb*

Introduction

The globalization of food systems that yield more processed and inexpensive food, and promote passive overconsumption from energy-dense, Nutrient-poor foods and drinks have been identified as a main driver of the obesity epidemic **(Swinburn *et al.,* 2011)**, with a decrease in physical activity owing to the modernization of lifestyles is also likely involved **(Ng and Popkin, 2012)**.

However, processed food is composed of not only sugar and fat but also a series of other products that are added in order to increase palatability, modify texture, and prolong shelf life. These products are together called food additives. **(Dahiya *et al.,* 2017)**. The use of food additives is one of the most important problems in the health nutrition field **(Helal *et al.,* 2017).**

Food additives are organic elements that are intentionally added to food in small quantities during manufacture or processing to improve the organoleptic quality (color, flavor, appearance, taste, and texture) of the food. One of these food additives is monosodium glutamate (MSG) which widely used as a flavor-enhancingamino acid **(Shi *et al.,* 2014)**.

Monosodium glutamate (MSG), known as AJI-NO-MOTO or white magi, is a salt derivative of the amino acid glutamic acid and is used as a food additive in many commercial food products, e.g. meat, fish, cheese and vegetables **(El-Aziz *et al.,* 2014).** MSG is used to enhance the flavor of many types of food as it stimulates receptors located in the taste buds, providing an expansion of taste (**Sant'Diniz *et al.,* 2005).** MSG is frequently added to processed food, particularly in Asian cuisine, to improve food palatability and acceptance, to increase salivary flow and to reduce oral complaints (**Li *et al.,* 2002).**

Accordingly, the global MSG production and consumption have increased considerably in recent decades **(Shi *et al.,* 2010).** Regarding the association of MSG with increasing risk of

overweight, information obtained from human or experimental studies in animals is controversial and remains to be verified **(Ebert, 2009).** Recent studies on healthy Chinese subjects reported that MSG consumption was positively linked to increased risk of overweight **(He *et al.*, 2011a)**. Additional alarms over MSG have been raised in response to reports of its association with overweight and obesity **(Collison *et al.*, 2010).**

On the contrary, **Shi *et al.* (2010)** reported that MSG intake was not associated with a higher prevalence of obesity or with a clinically significant weight gain in Chinese adults. Data from animal studies suggested a possible link between MSG and obesity, where weight gain was found to be significantly greater in MSG-treated animals, and that this might be independent of an increase in appetite **(Iwase *et al.*, 2000)** or due to an improvement in the palatability of foods by exerting a positive influence on the appetite center **(Hermanussen *et al.*, 2006).**

Other studies demonstrated that MSG did not increase food intake or induce obesity**,** and some even demonstrated that MSG administration to rats was associated with suppression of body weight gain, fat deposition, and plasma leptin levels **(Kondoh and Torii, 2008).**

In another respect, several studies reported damaging effects of MSG; on small doses of 15 and 30 mg/kg for 10, 20, and 30 days; on the gastric mucosa (**Falalieieva *et al.*, 2010)**, ileum), and liver **(Eweka and Om'Iniabohs, 2011)**. These reports indicate that MSG might have some deleterious effects on the gastrointestinal tract, which in turn might be associated with mal-digestion and mal-absorption of ingested foods **(Soliman, 2011).**

The excessive administration of MSG (15 mg/ kg. BW) may lead to liver and kidney damages. It is reported that rats exposed to MSG meet many problems like learning difficulty, gonadal dysfunction, brain damage, obesity, depleted in some of the neurotransmitters like norepinephrine, serotonin, dopamine and their metabolites in the hypothalamus region, and increase in the occurrence of stomach cancer, oxidative stress in the hepatic tissue with degenerative changes in hepatocytes **(Abu-Taweel *et al.*, 2014)**

The purpose of this research is to outline the pathophysiological mechanisms and metabolic alterations related to the dose of (15mg MSG/ kg BW) administration in male rats.

Materials and Methods

Material:

1.1 Animals:

The present research was carried out on a total number of 20 healthy male Spraque Dawley rats, weighing 120-150g were purchased from the lab. Animal House. Faculty of Vet. , Suez Canal University.

They were kept at the Animal House of Veterinary Medicine, Suez Canal University. They were housed in separate metal cages under controlled environmental (20-24^0 C and 55-60% relative humidity) and nutritional conditions. They were maintained on a standard balanced ration for 2 weeks of accommodation, the animals had free access to water and food **(Becker *et al.*, 1996).**

1.2 Bodyweight measurement:

Bodyweight was measured weekly for adjustment dose drugs given according to body weight and taken the average B.W at the end of the study.

1.3 Experimental design:

The present study was carried out on a total number of 20 healthy male Spraque Dawley rats, weighing 120-150g divided into:

A-Control (group A) (n=10): Served as a control group and received a standard balanced diet according to NRC all over the experimental period and were orally administrated with distilled water once daily for 3 months.

B. MSG administrated (group B) (n=10): Received standard balanced diet all over the experimental period and were orally administrated with monosodium glutamate (MSG) at a dose of 15 mg/kg body weight dissolved in 5ml distal water by gastric tube once daily for 3 months **(Egbuonu and Osakwe, 2011).**

The protocol regarding the research was conducted according to the ethical guidelines for

the use of animals in laboratory experiments of the faculty of Vet. Medicine, Suez Canal University, Egypt.

1.4. Sampling:
Blood samples are collected at the end of the third month from all groups after overnight fasting from the medial canthus of the eye using microhematocrit tubes. Blood was divided into 2 tubes; the first tubes (EDTA) as an anticoagulant. This tube was used for the estimation of hemoglobin (Hb).

The second tubeof blood was taken into a clean and dry screw-capped centrifuge tubeand left to clot at room temperature, then centrifuged at 3000 r.p.m for 15 minutes to separate clear serum samples for determination of different biochemical parameters e.g (Triacylglycerol, Total cholesterol, liver enzymes, kidney function test Thyroid-stimulatinghormone and Iron)

2. Methods:
2.1. Determination of Triacylglycerol and Cholesterol:
Determination of Triacylglycerol (TAG)(mg/dl) according to **Siedel *et al.,* (1993)**, and Total Cholesterol (TC))(mg/dl) according to **Allain *et al.,* (1974)** using fully automated auto-analyzer Roche/Hitachi Cobas C311 (Roche Diagnostic, Germany).

2.2. Determination of liver enzymes:
- Determination of Serum alanine aminotransferase (Alanine Aminotransferase (ALT) (U/L), and serum aspartate Aminotransferase (AST) (U/L) activities according to **ECCLS, (1989)** using fully automated auto-analyzer Roche/Hitachi Cobas C311 (Roche Diagnostic, Germany)

2.3. Determination of kidney function:
Determination of serum creatinine (mg/dl) according to **Pardue, (1987)**, and serum urea level (mg/dl) according to **Rock, (1987)** using fully automated auto-analyzer Roche/Hitachi Cobas C311 (Roche Diagnostic, Germany).

2.4. Determination of Serum Thyroid Stimulating Hormone (TSH) (mU/L) according to **Tietz, (2006)** using fully automated auto-analyzer Roche/Hitachi Cobas C311 (Roche Diagnostic, Germany).

2.5. Determination of serum Iron (µg/dL):
Serum Iron level was determined according to **Tietz *et al.,* (1994)** using a fully automated auto-analyzer Roche/Hitachi Cobas C311 (Roche Diagnostic, Germany).

2.6. Determination of Hb (g/dl):
Hemoglobin level was determined by using an automated auto-analyzer (Sysmex 2000).

3. Statistical analysis
The Statistical Package for the Social Sciences (SPSS for Windows, version 20.0; SPSS Inc., Chicago) was used for the statistical analysis. Results were articulated as mean ± SE and all statistical comparisons were made by means of Independent sample T-Test **(IBM Corp, 2011)**.

Results

Table (1). Effect of MSG administration on body weight, Triacylglycerol, Total Cholesteroland liver enzyme at the end of the experiment (after 3months):

Parameters	Control group (group A)	MSG group (group B)
Final average body weight (g)	190.75±6.70	342.00±19.24***
Triacylglycerol (TAG) (mg/dl)	51.00± 4.70	163.00± 15.54***
Total Cholesterol (TC) (mg/dl)	78.25± 2.90	147.50±8.53***
Alanine transaminase (ALT) (U/L)	38.25± 2.21	70.75± 3.70***
Aspartate transaminase(AST) (U/L)	121.00± 8.07	146.00±5.93*

Data are expressed as mean ± SEM. * statistically different from control values p<0.05 ** statistically different from control values p<0.01. *** Statistically different from control values p<0.001

Table (2). Effect of MSG administration on kidney function, TSH, Iron and Hemoglobinat the end of the experiment (after 3months):

Parameters	Control group (group A)	MSG group (group B)
Creatinine (mg/dl)	0.55± 0.06	0.87 ± 0.03**
Urea (mg/dl)	28.00± 2.42	37.00± 0.47*
TSH (mIU /mL)	1.15± 0.10	1.40± 0.09
Iron (µg/dL)	175.00±3.59	272.75±23.5*
Hemoglobin (g/dl)	14.10±0.04	14.30±0.22

Data are expressed as mean ± SEM. * statistically different from control values p<0.05 ** statistically different from control values p<0.01. *** Statistically different from control values p<0.001.

Discussion

Our research illustrates that MSG administrated rats (group B) which received MSG for three months have a highly significant increase in average body weight, triglyceride and total cholesterol (p > 0.001) when compared to Control group (group A) as shown in (Table 1), these results are in agreement with **Collison *et al.* (2010)** who reported that MSG intake may be linked to elevated serum free fatty acids, triglycerides, insulin, and bile synthesis.

Moreover, the potential link between MSG and obesity includes the MSG effect on energy balance by increasing the palatability of food and by disrupting the hypothalamic signaling cascade of leptin action **(He *et al.* 2011)**.

The results of this research showed that MSG administrated rats (group B) have a significant increase in ALT and AST activities when compared to the control group (group A) as shown in (Table 1) and these results are in agreement with **Onyema *et al.*, (2006)** those reported that rats treated with MSG develop symptoms of liver damage.

The results of this study showed that MSG administrated rats (group B1), have a significant increase in creatinine and urea levels (p > 0.05) when compared to Control group as shown in (Table 2), these results in agreement with **Tawfik and Al-Badr, (2012)** who reported that the significant increase in creatinine content of the serum following the administration of MSG may be attributed to the compromise of the renal functional capacity.

Moreover, 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 **(Rao *et al.,* 2015).**

The result of this study showed that MSG administrated rats (group B) have no significant difference in serum TSH levels when compared with the Control group (group A) as shown in (Table 2).

The results of this study showed that MSG obese rats (group B) have significant increase in Iron levels ($p > 0.05$) when compared to control group (group A) as shown in (Table 2), this result nearly similar to those reported by **Bertinato *et al.,* (2013)** MSG administration leads to a significant increase of Fe levels in the spleen, and the administration of MSG increased Fe retention by enhancing Total Iron Binding Capacity (TIBC) in serum.

Also, the results of this study showed that MSG obese rats (group B) have no significant difference in Hb levels when compared with the control group (group A) this result is in agreement with **(Shi, 2012)** who reported that MSG consumption and hemoglobin levels are positively correlated to each other.

Conclusion

The results of the present research have shown that mono-sodium glutamate (MSG) at this dose led to disturbances in metabolism with the increase in more parameters including Triacylglycerol, Total cholesterol, and Iron in serum has been observed, also capable of producing alterations in liver and kidney functions. These alterations appear in the liver and kidney probably because these organs are mainly responsible for detoxification of foreign compounds in the body, but it has not any effect on Thyroid-stimulating hormone, besides it has a positive correlation with hemoglobin. So we recommended avoiding MSG consumption at this dose due to its toxic effects.

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