

Research Article



Monosodium Glutamate Induces Physiological Stress by Promoting Oxygen Deficiency, Cell Mediated Immunosuppression and Production of Cardiovascular Risk Metabolites in Rat

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ABSTRACT

The effects of Monosodium glutamate (MSG), a popular food additive, on hematopoietic and cardiovascular risk variables in animal have not been reported till date. We report here the effects of MSG on the said variables in rat model. Adult female rats of Charles foster strain weighing about 100-120 gms were administrated MSG at a dose level of 0.8gm/kg/day, 1.6gm/kg/day, 2.4gm/kg/day, respectively for 30 days. It has been seen that the mean body weight increases significantly in the entire MSG treated groups in a dose dependent manner, and the absolute and relative organ weights of ovary, uterus, heart and liver increases significantly in MSG treated groups of rats in comparison with control rats. We found significant decrease in red blood cell (RBC) and white blood cell (WBC) counts, and hemoglobin concentration in peripheral whole blood in MSG treated groups of rats. Further we found significant increase in the concentration of serum total glucose, protein, cholesterol, triglycerides, very low density lipoprotein (VLDL), glycerol free triglycerides and low density lipoprotein (LDL); and decrease in high density lipoprotein (HDL) in a dose dependent manner in MSG treated rats. From the study we may conclude that MSG suppresses the physiologic functions of the organ systems presumably by reducing the availability of oxygen in tissues through inhibiting the erythropoiesis process for the formation of RBC; by suppressing the cell mediated immunity through reducing the formation of WBC; and by increasing the production of cardiovascular risk metabolites under the influence of hypothalamic pathways emanating from the hunger and satiety nuclei.

Keywords: Cardiovascular risk metabolites, Cell mediated immunity, Erythropoiesis, Monosodium glutamate.

INTRODUCTION

Monosodium glutamate (MSG) is a hydrated sodium salt of naturally occurring L-glutamic acid. It is generally used as a food additive to process fast foods, specially the Chinese dishes to enhance the flavor of the food, so that the appetite and taste stimulation of the humans are enhanced.^{1,2} MSG has a characteristic taste called "Umami", which is considered distinct from the four other basic tastes (sweet, sour, salt, and bitter). The optimum palatability concentration for MSG is between 0.2- 0.8% with the largest palatable dose for human beings is about 60mg/Kg body weight. Human beings are exposed to external monosodium glutamate through MSG added dietary sources. Glutamic acid is one of the essential normally occurring endogenous excitatory neurotransmitter found in nervous system. It facilitates neurotransmission process through neuro- neuronal synapses in some areas of human brain and neuro-somatic synapses in some organ systems of the human body. Overstimulation of the glutamate system by the endogenous glutamate seems to be associated with a number of toxic and diseased states. Glutamate from external sources can have effects also. Absorption of MSG through intestinal barriers into the blood allows the accumulation of MSG in the tissues due to its characteristics pharmacokinetic behaviors. It has been reported that, low levels of MSG produce in some people a group of symptoms often called Chinese restaurant syndrome. These sensitive individuals may react to as little as 1 to 2 gm of MSG with burning or tingling sensations in upper part of the body and occasionally

event chest pain.³⁻⁶ There is a possibility of the severe toxic syndromes as results of the overstimulation of the glutamate system due to overloading of exogenous glutamate in the tissues. The modes and mechanisms of action of MSG in human excitotoxicity have not been reported till to date systematically.

Therefore, the aim of the study was to examine the effects of MSG on some cellular and biochemical variables of the whole blood; and mean body weight and organ weights of some vital organs in female albino rats.

MATERIALS AND METHODS

Reagents and Chemicals

All common chemicals used for the study were of analytical grade. MSG was purchased from Sigma Chemicals Co. (USA).

Animals

Studies were performed on female albino rats of Charles Foster (CF) strain weighing 110-120 gm. The animals were maintained in Environmental Physiology Laboratory in the Department of Physiology, University of Kalyani, following the protocols approved by the Kalyani University Animal Ethics Committee. Animals were kept in equal light-dark cycle (12 h light and 12 h dark) and fed standard laboratory chow and water *ad libitum*.

Animal grouping and treatment schedule

After seven days of acclimatization to the laboratory environment the animals were randomly divided into four



groups each containing 10 animals (n=10). The animal grouping for the chronic study is as follows.

	Animal grouping
Control	Received no test elements
Treated I	Received 0.8gm MSG/kg/Day (5% of LD ₅₀ of MSG) for 30 days
Treated II	Received 1.6gm MSG/kg/Day (10% of LD ₅₀ of MSG) for 30 days
Treated III	Received 2.4gm MSG/kg/Day (15% of LD ₅₀ of MSG) for 30 days

Sample collection and preparation

After the completion of the treatment duration of 30 days, the animals were sacrificed by cervical dislocation on the 24th hour after the application of last dose. Whole blood was collected by cardiac puncture and used for hematological study. For the biochemical study serum was prepared following the centrifugation of whole blood at 4000 rpm for 10 minutes and kept in -20° C.

Body weight and absolute organ weight

The body weight of the rats was measured from the first day of the treatment up to the last day of the treatment period in every ten alternate days. The weight of rats taken on the day of the application of first dose, was considered as the initial body weight, and the body weight taken on the day of sacrifice was considered as the final body weight. Ovary, uterus, heart and liver were dissected out from each group, free from adherent tissue and weighed to get absolute organ weight. The body weight of each rat was assessed using a sensitive balance. The relative organ weight of each animal was then calculated as follows:

$$\text{Relative Organ Weight} = \frac{\text{Absolute Organ Weight (gm)}}{\text{Body Weight of rat on sacrificed day (gm)}} \times 100$$

Hematological evaluation of whole blood

The hematological variables of the whole blood were estimated following the standard laboratory protocol. Red Blood Cells (RBC) and White Blood Cells (WBC) were counted using improved Nuebauer hemocytometer.⁷ Hemoglobin concentration was determined by hemoglobinometer by Sahil's Acid Hematin method.⁷

Biochemical study of serum

Serum protein contents were estimated by the method of Lowery et.al, 1951.⁸ Serum glucose, serum cholesterol and serum triglyceride levels were estimated by using commercial kits (Glucose test kit, Autospan, Mfg.Lic.No.G/924, Ref: Old: B0112, New: 93DP100-74, Cholesterol test kit, Autospan, Mfg.Lic.No.G/221, Ref: Old LG052 New: 71LS200-60, Triglycerides test kit, Autospan, Mfg.Lic.No.G/221, Ref: Old LG061 New: 72LS100-40, respectively), according to the kit instructions.

Statistical analysis

The results were expressed as mean±S.E.M. The significance of the difference between control and treated groups were determined by the Student *t*-test and the results were considered as significant at p≤0.05.

RESULTS

Effect of MSG on the body weight and organ weight of ovary, uterus, heart, and liver

It has been seen that the mean body weight of MSG treated groups of rat's increases significantly in all the treated groups in a dose dependent manner compared to control groups of rats (Table 1). It has also been seen that the absolute and relative organ weights of ovary, uterus, heart and liver increases significantly in MSG treated groups of rats in comparison with control rats (Table 2).

Table 1: Showing the body weight of MSG treated and control rat groups. Values are represented as mean ± SEM (n=10), *p<0.05, **p<0.01 vs. control.

Treatment design	Mean body weight	
	Initial body weight (gm)	Final body weight (gm)
Control	110±2.58	119.2±2.29
Treated I	110±3.65	122±2.44 *
Treated II	110±3.33	123±3.13 *
Treated III	110±4.3	125.8±3.91 **

Effect of MSG on RBC and WBC count; and Hemoglobin concentration of whole blood

We found significant decrease in RBC count in all MSG treated groups of rats in a dose dependent manner compared to control groups; but the white cell counts significantly decreased only in group III treated rats compared to the control group (Table 3). Further, we found significant decrease in hemoglobin concentration of the whole blood in all treated groups of rats in comparison with control group (Table 3).

Effect of MSG on some metabolic biochemical variables in blood

We found significant increase in the concentration of serum total glucose, total protein, total cholesterol, triglycerides, very low density lipoprotein (VLDL), glycerol free triglycerides and low density lipoprotein (LDL); and decrease in high density lipoprotein (HDL) in a dose dependent manner in treated rats compared to control groups of rats (Figure 1).

DISCUSSION

MSG is used as food additive to enhance the appetite and also to stimulate the taste perception to foods of the human beings. In this study the mean body weight and organ weights of some vital organs like uterus, ovary, heart and liver have been studied in MSG treated rats in order to study the effect of MSG on hypothalamic hunger



and satiety centers that control the body weight homeostasis. In our study we found significant increase in mean body weight and organ weights of uterus, ovary, heart, and liver. The results suggest that glutamic system in hypothalamic hunger-satiety centers may shift the balance towards the hunger centers due to the results of

the overstimulation by the exogenous glutamate. Thus, intake of food was increased as a result of the enhancement of appetite to MSG added foods. Overeating, in turn causes the increase in body weight due to increase in bodily tissue mass.

Table 2: Showing the absolute and relative organ weight of MSG treated female rats. Values are represented as mean \pm SEM (n=10), *p<0.05, **p<0.01, ***p<0.001 vs. control.

Groups	Ovary		Uterus		Heart		Liver	
	Absolute weight	Relative weight	Absolute weight	Relative weight	Absolute weight	Relative weight	Absolute weight	Relative weight
Control	0.052 \pm 0.033	0.065 \pm 0.005	0.138 \pm 0.011	0.120 \pm 0.009	0.476 \pm 0.009	0.397 \pm 0.014	3.880 \pm 0.119	3.492 \pm 0.086
Treated I	0.044 \pm 0.004	0.054 \pm 0.003	0.192 \pm 0.02*	0.163 \pm 0.010 **	0.462 \pm 0.048	0.418 \pm 0.006	4.504 \pm 0.133**	4.413 \pm 0.138***
Treated II	0.077 \pm 0.004	0.075 \pm 0.002	0.246 \pm 0.007***	0.197 \pm 0.005***	0.472 \pm 0.010***	0.396 \pm 0.007	4.840 \pm 0.165***	4.143 \pm 0.115***
Treated III	0.076 \pm 0.004	0.084 \pm 0.005*	0.261 \pm 0.008***	0.220 \pm 0.011***	0.485 \pm 0.044**	0.440 \pm 0.010*	4.868 \pm 0.179***	4.264 \pm 0.116***

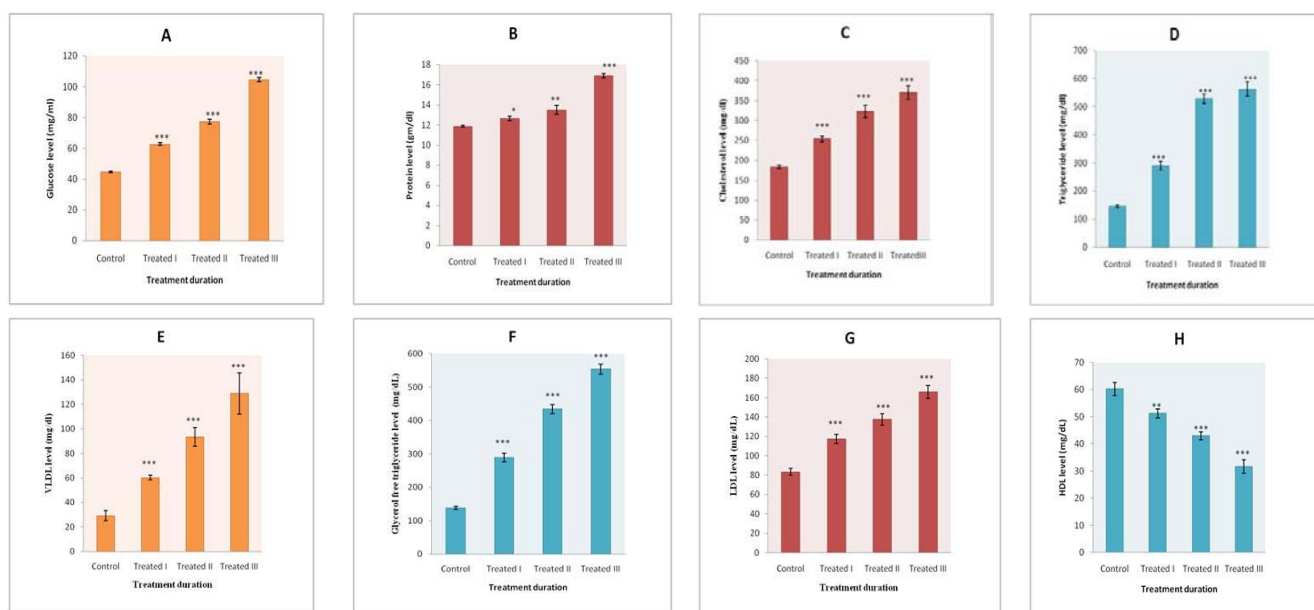


Figure 1: Showing the total serum glucose (A), protein (B), cholesterol (C), triglycerides (D), VLDL (E), glycerol free triglyceride (F), LDL (G) and HDL (H) concentration of MSG treated female rats. Values are represented as mean \pm SEM (n=7), *p<0.05, **p<0.01, ***p<0.001 vs. control.

We found significant decrease in the red blood cell and white blood cell counts and decrease in hemoglobin concentration of the whole blood of the MSG treated groups of rats. The concentration of hemoglobin depends on the RBC counts in whole blood. The hemoglobin concentration decreases with the reduction in RBC count. In our study we observed significant decrease in RBC count and hemoglobin concentration of whole blood of MSG treated rats. These results suggest that decrease in hemoglobin concentration might be due to decrease in the number of RBC count in MSG treated rats. Moreover, the WBC count was found to be decreased in MSG treated rats. From these results we may suggest that MSG

impairs the hematopoietic process in the bone marrow that causes speciation of blood cells, specially the RBC and WBC; and causes the release of blood cell species to the peripheral blood circulation. MSG may suppress the hematopoietic system presumably by exerting cytotoxicity in pluripotent stem cells in bone marrow that undergoes to speciation through mitosis.

In our study we found significant increase in the serum concentration of total glucose, total protein, total cholesterol, triglycerides, LDL-cholesterol, VLDL-cholesterol, and glycerol free triglycerides level, and decrease in HDL-cholesterol in MSG treated rats. Our

result is supported by the report of Egbunu et.al.2010c, who stated that MSG treatment significantly increases the serum cholesterol concentration.^{9,10} Our results suggest that exogenous glutamate affects the metabolic profiles in body presumably by altering glutamate mediated signal transduction mechanism. The cardiovascular risk factors like total cholesterol, LDL- cholesterol and triglycerides have been increased in MSG treated rats. On the other hand the concentration of cardiovascular protective metabolites like HDL-cholesterol is decreased in MSG

treated rats. From the results we may suggest that MSG enhance the cardiovascular risks by increasing the concentration of cardiovascular risks metabolites. In our study we found significant increase in glucose concentration in the MSG treated animals. This might be due to inhibition of the entry of glucose into the cells either by the deficiency of insulin or by insulin insensitivity; or by the increase in glycogenolytic activities in the liver.

Table 3: Showing changes in the RBC count (cu/mm²), WBC count (cu/mm²) and Hemoglobin concentration (gm/dL) of whole blood in MSG treated (treated I, 5% of LD₅₀; treated II, 10% of LD₅₀; treated III, 15% of LD₅₀) and control group of female rats. Values are represented as mean±SEM (n=7), *p<0.05, **p<0.01, ***p<0.001 vs. control.

Hematological variables	Treated groups			
	Control	Treated I	Treated II	Treated III
Red blood cells	9.49±0.078	8.58±0.115***	7.14±0.175***	6.80±0.126***
White blood cells	8.50±0.246	8.73±0.116	8.033±0.195	7.44±0.313*
Hemoglobin conc.	13.14±0.305	12.11±0.317*	11.45±0.289**	10.25±0.173***

CONCLUSION

From the study we may conclude that MSG suppresses the physiologic functions of the organ systems by reducing the availability of oxygen in tissues through the inhibition of the production of red blood cells, the cell mediated immunity by suppressing the production of WBC, and by increasing the cardiovascular stress as a result of the induction of metabolism related to the production of cardiovascular risk metabolites with the active involvement of the hypothalamic hunger-satiety neuronal pathways.

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