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Monosodium Glutamate, Commercial Production, Positive and Negative Effects on Human Body and Remedies – A Review

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ABSTRACT

Monosodium Glutamate is the salt of Glutamate (a most commonly found amino acid). It is used in meat, poultry, seafood, snacks, soups and stews to enhance the natural flavor which is specifically known as "Umami" taste. It is commercially prepared by different species of Corynebacterium. It was found to be very beneficial in taste improvement, recovering from hypertension and hemoglobin deficiency. However it has been found to have negative effects like toxicity, Chinese Resturant Syndrome and sleep disordered breathings. It also been found through different experiments that its negative effects can be reduced by Quercetin, Diltiazem and Vitamin C.

Keywords : Poultry, Meat, Umami, Hypertension

I. INTRODUCTION

MSG : E Glutamate is an amino acid, found naturally. Many proteins and peptides are formed by the glutamate. So glutamate has formed most of the animal tissues. It is also a part of human metabolism. [1], [2]. Naturally glutamate is found in fish, meat and several vegetables.
Monosodium Glutamate is composed of water, glutamate and sodium. Scientists isolated this ingredient (glutamate) from plants in the early 1900s.It is thought to be essential taste component responsible for enhancing flavor [3].

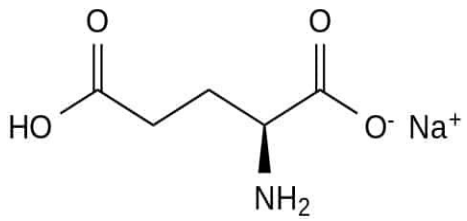


Figure 1

Flavor Enhancement Properties of MSG (Monosodium Glutamate)

In the free state MSG imparts a special flavor to foods. It gives a natural glutamate like flavor [4]. MSG is used in meat and different delicacies to enhance the natural flavors [5], [6].After a scientific research it was found that MSG has a different taste that can not be called sweet, sour, salty or bitter [4], [6].This taste is called "umami". The word umami is derived from Japanese language. It means broth-like or meaty [4], [6].Recently it was found that tongue has a specified receptor for glutamate [7].

II. METHODS AND MATERIAL

Mechanism of Flavor Enhancement

Japan and different countries have been using Monosodium Glutamate (MSG) in many food items. Glutamate was discovered from a seaweed called Kombu in 1908 [8].It is found that free glutamate improves taste and palatability of food. After going to small intestine protein bound glutamate becomes free.

Hence if glutamate is bound with a protein, it can not enhance taste of food. It is suggested that specific receptors are present on tongue and stomach which enhance the taste of food [9], [10].So they play physiologic actions to stimulate gastric vagus nerve [11]. Oriental countries show the higher consumption than that of the western countries. Most commonly it is used in soya sauce [12].

The table 1 is showing the daily consumtion of monosodium glutamate.

Country	Intake of MSG *g/d*
USA	0.55
Netherlands	0.66
Thailand	1.5
Japan	1.42
Indonesia	0.6
Korea	1.57
Malaysia	0.37

Table 2. Occurance of glutamate in some food items. (Institute of food technologists, 1987)

	Bound glutamate(mg /100g)	Free glutamate(mg/100g)
Milk/Milk products		
Cow	819	2
Human	229	22
Parmesan Cheese	9.847	1200
Poultry products		
Eggs	1.583	23
Chicken	3.309	44
Duck	3.636	69
Meat		
Beef	2.846	33
Pork	2.325	23
Fish		
Cod	2.101	9
Mackerel	2.382	36
Salmon	2.216	20
Vegetables		
Peas	5.583	200
Corn	1.765	130
Beets	256	30
Carrots	218	33
Onions	208	18
Spinach	289	39
Tomatoes	238	140
Green Peppers	120	32

1. Production of Monosodium Glutamate

Monosodium glutamate (MSG) is a very good flavor enhancer. In the late 1950s it was first produced by fermentation in Japan. Glutamate can be overproduced by many genera like Micrococcus, *Brevibacterium*, *Corynebacterium* and *Microbacterium*. Reclassified species of *C. glutamicum* are *Brevibacterium lactofermentum* and *Brevibacterium flavum*. These organisms use Embden Meyerhof Parnas glycolytic pathway (EMP), Hexose Monophosphate pathway, Tricarboxylic acid cycle (TCA), and Glyoxylate bypass. For the removal of the intermediates, oxaloacetate is continuously provided. It helps in the synthesis of

biomass and amino acids. In this process production of glutamic acid can be suppressed by the feedback mechanism. During this process repression of PEP carboxylase,citrate synthase and NADP-glutamate dehydrogenase may also occour. NADP-glutamate dehydrogenase enzyme can also be inhibited. It is also found that by regular removal of Glutamate from the system can solve the problem. In this way the l-glutamate titer can increase upto 88g l-1.

Detailed method for the production of Monosodium Glutamate in different steps is given here.

2. Fermentation

Glutamic acid and L-Glutamic acid which is used for the preparation of monosodium glutamate is most commonly prepared by fermentation using bacteria. The most commonly used strains are *Corynebacterium glutamicum* and other bacterium. Other bacterial strains used for the production of L-Glutamic acid are*: C acetoacidophilum, C acetoglutomicum, C alkanolyticum, C callunae, C glutamicum, C lilium, C melassecola, C thermoaminogenes (C efficiens), C herculis, Brevibacterium divaήcatum, B flavum, B immariophilum, B lactofermentum (C glutamicum), B roseum, B sacchorolyticum, B thiogenitalis, B ammoniagenes, B album, B cerinum, Microbacterium ammoniaphilum, B cerinum, M ammoniaphilium*

The most important fermentation ingredients used here are cassava starch, sweet corn, and glucose. In some cases preferably glucose is used for fermentation as it is relatively inexpensive and abundantly available.

Glucose or another suitable fermentation ingredient is added to a fermentation tank 100 containing a fermentation broth which is inoculated with *C glutamicum* or another suitable bacterium. After time of about 48 hours greater than 50% of glucose is converted into to L-glutamic acid. The preferred fermentation tank volume is about 140 cubic meters per kilogram of hydrogen per hour for an output of about 50 grams of L-glutamic acid per liter of fermentation broth for the production of L-Glutamate. After the accomplishment of the fermentation, the L-glutamic acid is extracted from the fermentation broth. The separation from the secondary byproducts is done by conventional separation methods.

3. Preparation of Magnesium Di-glutamate

It is the second step in the Monosodium Glutamate production. Here L-glutamic acid is reacted with magnesium which results in the formation of magnesium di-glutamate and hydrogen gas.

The magnesium is utilized in the form of ^{1}A inch granules, in an exemplary implementation. Utilization of granules helps to increase the surface area of the magnesium so the speed of the reaction is also increased. It is also very helpful in maintaining the safety of the reaction. Other forms of magnesium may also be utilized. For example, magnesium in the form of plates, rods, powder, or alternative sized granules are also found useful. It is also found that utilization of magnesium granules also allows for easier handling of the metal feed. In particular implementations, the magnesium is used in the form of granules that will facilitate easier automatic handling for feed systems and provide the magnesium to the reactor vessel than with larger forms of the magnesium.

Here a first reaction vessel 110 is provided in which magnesium and a L-glutamic acid solution are allowed to react. In the most cases batch reactor is mostly a vessel. It is preferred to use batch reactors in series for the reaction of magnesium metal and L-glutamic acid. The total volume of the batch reactors is typically 3 to 5 cubic meters per kilogram of hydrogen per hour. The reaction between magnesium and L-glutamic acid is slightly exothermic (heat is released in this process). The reaction is relatively slow at NTP (NTP normal temperature and pressure: 20 degrees Celsius and one atmosphere pressure). In another exemplary implementation, five times increase in reaction rate can be done by increasing the reaction temperature to approximately 95°C.

The non-dissolved L-glutamic acid begins to dissolve into the solution after the conversion of L-glutamic acid into magnesium di-glutamate in solution. As the L-glutamic acid is converted into magnesium di-glutamate, it begins to level off at approximately 80% preferably so this step does not exceed 60 minutes.

The chemical reaction for this process is given below.

$$Mg + 2C_5H_9NO_4 \rightarrow Mg(C_5H_8NO_4)_2 + H_2$$

At the end of the reaction enriched solution of magnesium di-glutamate and hydrogen gas is produced. Hydrogen gas and water vapors are expelled out from the reaction mixture in the form of bubbles. The hydrogen gas produced is evacuated from the reactor vessel during the reaction and is bottled separately. In some other cases hydrogen is evacuated, scrubbed, dehydrated and bottled. Then it is either used to provide clean hydrogen gas suitable for use in the food industry or as a fuel.

4. Production of Monosodium Glutamate

In the second and final step magnesium di-glutamate is then reacted with sodium hydroxide, trisodium phosphate, or sodium carbonate. It results in the formation of Monosodium Glutamate. Chemical reactions depicting these processes are given below.

$$Mg(C_5H_8NO_4)2 + 2NaOH \rightarrow 2NaC_5H_8NO_4 + Mg(OH)_2$$

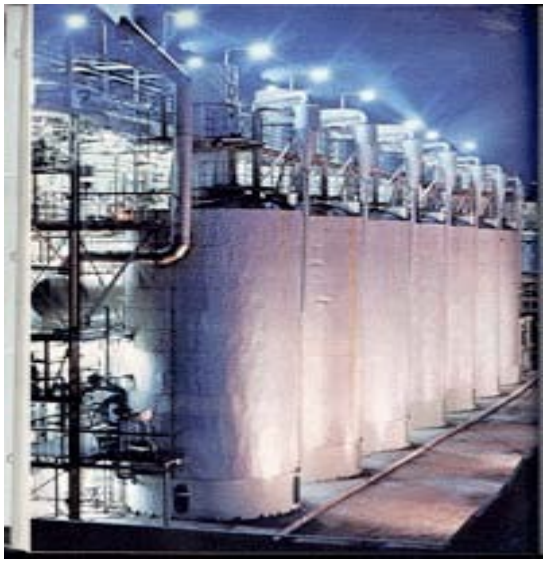
$$3Mg(C_5H_8NO_4)_2 + 2Na_3PO_4 \rightarrow 6NaC_5H_8NO_4 + Mg_3(PO_4)_2$$

$$Mg\ (C_5H_8NO_4)_2 + Na_2CO_3 \rightarrow 2NaC_5H_8NO_4 + MgCO_3$$

A second reaction vessel 120 is used for the reaction of magnesium di-glutamate enriched solution and sodium hydroxide. After that the products are reacted with trisodium phosphate then further this reaction is proceeded with sodium carbonate to form monosodium glutamate in solution. The byproducts are magnesium hydroxide, magnesium phosphate, or magnesium carbonate respectively which are precipitated out. In some cases this step is carried out in a series of batch reactors having a total volume of approximately 3 to 5 cubic meters per kilogram of hydrogen per hour.

Sodium carbonate is the preferred reactant as it is less expensive than sodium hydroxide. Moreover in some implementations, trisodium phosphate is the preferred reactant as its byproduct precipitates more rapidly reducing the processing time.

The solubilities of the secondary byproducts magnesium hydroxide and magnesium carbonate are typically not greater than 0.01% that is ($9.63xlO^{"3}$ g/L), (0.106 g/L), so they are allowing for a preparation of 100 g/L having a maximum monosodium glutamate concentration of 99.9%. Magnesium carbonate can be precipitated most efficiently at high temperatures, in one implementation. Further reduction of precipitation time can be done by agitation for approximately 45-60 minutes. The solubility of the secondary byproduct magnesium phosphate (at most 10 g/L) has a major role in the final step as it allows preparation of 100 g/L having a maximum monosodium glutamate concentration of 90%. After the precipitation of magnesium byproduct into a solid phase, the remaining monosodium glutamate enriched solution can be drained, siphoned off and/or passed through a filter 130. So the precipitates are left behind.



5. Extraction

To extract the monosodium glutamate completely the water should be removed. So, the remaining water is evaporated or removed by utilizing an evaporator 140. Another means to remove water is the use of a dryer to provide dry monosodium glutamate powder. It is done in a series steps to get final concentration.

In one implementation, the extraction is done by decompression method. Partial vaporization of the water present in the monosodium glutamate solution is affected by the decompression. The geometry of the

vessel is made in such a way that it only needs to permit the separation of the vapor phase from the liquid phase.

6. Evaporation

In a particular present disclosure, the reaction product is advantageously heated during decompression. It assists the evaporation of the excess water. The typical setup of decompression stage includes a vacuum condenser which comprises a filter, condenser, vacuum pump and condensate receiving vessel. A Coanda effect pump, steam ejector or any other suitable pump can be used. Other alternative concentrating methods may also be utilized for the extraction. Alternative heating methods include solar and electrical for the extraction. Any other drying method can be used or the combination of different methods can be used.

In the same way a combination of evaporators and dryers may be used to accomplish the process. In order to provide the dry Monosodium Glutamate powder enriched solution may be concentrated using conventional methods prior to using an evaporator or dryer to remove any remaining water. Another way to recover the dry Monosodium Glutamate powder, the monosodium glutamate enriched solution may be concentrated by heating prior to the step of utilizing an evaporator or dryer.

7. Crystallization

A crystallization vessel may be used to crystallize pure monosodium glutamate.

Various changes and modification are to be intended to be encompassed in the annexed claims.

III. RESULTS AND DISCUSSION

Positive Effects of Monosodium Glutamate on Human Body

1. Gustatory Effects

Different scientists have studied that how Monosodium glutamate induces Umami taste. These studies have been extended from receptor level to the cerebral cortex. In 1987 Kurihara explained a mechanism for its perception [13]. He said that Monosodium glutamate produces a chemical stimulus. Taste bud receptors absorb that stimulus and produce certain chemical transmitters. So the sensory nerves are activated by the chemical transmitters. It was also found that this message generated is transmitted to the cortex of the brain. The brain transforms and verifies this message. These findings are related to study on primates. In humans psychological tests were conducted to study the impact of Monosodium glutamate. Same results were found.

Receptor level

Different animals were studied in order to get the idea about the receptors of Monosodium Glutamate. The scientists have found that Carp is having same receptors [14].Moreover Catfish has three different receptor mechanisms for this amino acid [15].According to different studies it was said that taste buds and intrageminal neurons have chemical synapsis in the guinea pig [16]. Moreover taste buds in rats were also studied. Effects of Monosodium glutamate were also studied [17]. It was found that specific receptors were present on their taste buds that help in the production of response and taste perception [18].

Operation

It has many functional effects on body. Urea formation is suggested to be done by the amino acids provided by the glutamate and its metabolites. These are very necessary for liver and intestinal mucosa [19].

Studies done on the brains of rats showed that Monosodium Glutamate promotes neural growth in vitro [20].

Psychological impacts

It is said that it is appetite enhancer in many animals including humans. It has also been proved that its use increases the appetite and energy production in the body [21].

MSG and Hypertension

Form a long time, high blood pressure and health has been studied extensively. World health organization has recommended that, in order to prevent heart disease, per day 5g NaCl should be used. A comparison of MSG and NaCl shows that Monosodium glutamate has less sodium content (12%) as compared to sodium chloride (40%). To investigate the association of MSG with hypertension, only one epidemiological study has been conducted [22]. A new analysis data was provided by Jiangsu nutrition study. It provided the results about different food items which were relished by the Monosodium glutamate. It was suspected that MSG was the major cause of the hypertension. So the effects of the food items seasoned with MSG were studied. In one study they found no relation between MSG and hypertension but the results of another studies contradicted the previous findings. It was very confusing as many Chinese delicacies are using MSG. In the end a strong relationship between MSG consumption and hypertension was found, but these findings do not help to find effect of MSG on blood pressure as they are not relevant to the past inactive drug studies conducted on humans [23], [24], [25].

Reaction to Iron deficiency

Under developed countries have many types of malnutrition problems like iron deficiency. It is estimated that almost 2.5 billion are affected. This deficiency is most common in young children and women. Iron deficiency is determined by the hemoglobin count [26], [27]. It was found that when food of children is enriched with MSG and vitamin A, it can significantly increase the hemoglobin count. Jiangsu Nutrition (JIN) Cohort Study has conducted a research on the relation between MSG and hemoglobin. This study revealed [28] the result which shows that MSG has more positive effect on male as compared to females regarding hemoglobin formation. Their dietary habits and lifestyle was having negligible effects on it. It was suggested to improve their diets in order to improve their hemoglobin level. However it is felt that more research should be carried out before any final conclusion.

2. Contrary Effects of Monosodium Glutamate on Human

Toxicity of Monosodium Glutamate

It is observed that almost every food and cuisine has MSG as an additive. It is used to increase palatability. A recent research has pointed towards its adverse effects on many organs like thymus, kidneys, liver etc [29], [30], [31]. If MSG is used for a very long time, it can cause renal fibrosis [32] and can damage the kidneys by oxidative stress [33]. Oxidative stress is caused by elevation in the quantity of the free radicals. Oxygen radicals and reactive oxygen species are the base for this process [34]. Different factors like cytokines, hormones also contribute to it [35], [36], [37]. A research on rats have shown that MSG can decrease the antioxidant enzymes and can increase lipid per-oxidation. This leads to increase in reactive oxygen species [38], [39]. It was also found that high doses of glutamate increases toxicity in renal culture cells [40]. Reactive oxygen species cause DNA damage, protein modification and other damages that lead to the cell death. So the reactive oxygen species are very harmful for a cell [41], [42], [43]. It has been found that the Reactive oxygen species may alter the glomerular, tubular and interstitial structures of the kidney [44], [45]. Recenty it has been found that it may also damage many tissues like brain or neurons [46], [47], [48]. However the exact mechanism of the damage is still unknown. The only known fact is that it can increase the level of α-ketoglutarate dehydrogenase in the MSG fed rats [33]. So it is concluded that the Oxygen reactive species and α-ketoglutarate dehydrogenase has the more potent effect on the kidneys if MSG is used.

MSG and Chinese restaurant syndrome

"Chinese restaurant syndrome" (CRS) is known since forty years. It is said that its symptoms appear after 20 minutes of having meal. Its symptoms are a sense of paralysis in back of neck that may be felt in arms or

former part of the thorax. The person may have a feeling of instability. Some people may feel vertigo, unconsciousness or a sense of pressure on their face [49]. Many of the researchers were assure that it is caused by MSG but they were not having any experimental evidence to support their opinion. When different experiments were carried out, they found that the amount of MSG used was not enough to bring the symptoms of the Chinese restaurant syndrome [50], [51]. It is said that the symptoms may be due to the high fat and sodium content present in the typical Chinese foods [51].

In 1973 an epidemiological study was carried out to investigate the effect of MSG on the common health in Hawaii. They studied men of age form 45-69 years. They found different symptoms among them like cloudy vision, vertigo or unconsciousness or paralysis of face. These all symptoms are indicate the neurological disorder. It was observed that these symptoms were less observed in the men who do not use MSG in their diet [52].

Reif lehar et al studied the prevalence of the Chinese restaurant syndrome in 1976 [53]. In the survey 1500 people were examined. They observed some common symptoms like headache, vertigo etc.

The same researchers conducted another research on the students and staff of the Harvard University. The survey was conducted in the form of questionnaire and it was having two parts. They wanted to study the unpleasant symptoms in detail [54]. During their survey they did not use the term “Chinese restaurant syndrome”. In the first part of the survey they found that only 6.6% showed the symptoms of Chinese restaurant syndrome. In the second part of the questionnaire they directly asked the subjects that whether they had Chinese restaurant syndrome. They found that 31% respondents thought that they were more prone to that syndrome.

Sleep disordered breathing

It is an ataxia associated with the sleeping. In this disorder a person shows an abnormal respiratory behavior. Abnormal pauses during the sleeping are observed. It is an alarming condition as the person suffering from this disorder may have cardiovascular and pulmonary diseases. It may lead to increase in the morbidity and mortality rate. The person suffering from that disorder sometimes may show another disorder named Obstructive Sleep Apnea. People of different age and body weight may experience it in different ways [55]. Recently Jiangsu nutrition conducted a study. They found that there was a clear relationship between sleep disordered breathing and MSG [28], [56]. Furthermore it was also said that the habit of snoring is also due the usage of MSG.

Adiposis and metabolic perturbation

For this study neonates were administered with the MSG. it was observed that it led to glucose intolerance. Moreover resistance to insulin was also observed. These factors in turn led to obesity [57], [58].

Reproductive Organs

There is a little evidence regarding the effect of MSG on the reproductive system. Experimental work was done only on the animals not humans. Swiss albino mice were used for this purpose. The male mice administered with the MSG at different times during their perinatal period. The doses were injected subcutaneously. Some new born mice were injected double doses. Different results were observed like decreased testosterone level, underweight pituitary gland etc [59].Same experiments were done on the female mice with the same type and method of administration of the doses of MSG. These experiments also created some abnormal conditions in the female mice like elevated number of primary follicles. There was no elevation in the number of the Graffian follicles [60].

These findings are very helpful in studying the effect of MSG but they can be applied on the humans. As experiments are not done on humans and the results may vary.

When same experiments were done on the Wistar rats, many negative effects were observed here too, like the pathological changes in the ovaries. It was also observed that it caused many degenerative effects on th ovaries when high doses were admisnistered [61]. Moreover the lysis of the red blood cells in the stromal cells were also observed [62].

3. How these toxic effects can be avoided?

As soon as the adverse effects of MSG were observed in different animals through experiments it led to another research. The researchers were trying to discover more natural components that could nullify the effects of MSG. Again this was done through more experimental research. So different molecules and antioxidants were studied for their protective effects.

It was found that Vitamin C can be very helpful in this aspect. They administered the MSG with the Vitamin A to some rats. They found that in that case Vitamin A provided protection the intoxication of the nerve cells. When same experiments were done on the male albino rats it was found that Vitamin A provided protection against damage to the cerebral cortex [63].

When the protective effects of Vitamin E were studied it was found to be very protective in the rats. It was said that Vitamin E lowered the lipid peroxidation and also lowered the catalase, superoxide dismutase in the liver. Vitamin E was found to be very effective in increasing the glutathione level [64].
A flavonol named Quercetin is also found to reduce glucose, leptine and creatinine level in the blood. It is also known to elevat the superoxide dismutase and glutathione peroxidase after subcutaneous administration [65].

If rat pups are treated with Dltiazem, it can be protective for it. As it protect the pups from the morphological and functional disorders of the ovaries [66].

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