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Use of monosodium glutamate in foods: the good, the bad, and the controversial side

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ABSTRACT

Introduction: Monosodium glutamate (MSG) is known as a flavor-enhancing compound and also the fifth basic taste (umami). About the safety of using MSG as a food additive, some studies show indications that there is no threat and others show the opposite. There is no consensus about the advantages and disadvantages of using MSG. **Objective:** To systematically review studies in the international literature on the knowledge of the pros and cons of using glutamate in food. **Methods:** Systematic review of studies published in journals indexed in ScienceDirect and PubMed databases. Articles published until 2020 were included. The aspects involving the advantages and disadvantages were discussed, as well as the health risks related to the MSG intake from diet. **Results:** The revised studies showed that MSG can reduce the amount of sodium in foods without modifying flavor. Although authorities indicate that MSG is safe for human consumption, some studies highlight that health risk is real. The use of MSG is still controversial because there are some misunderstandings in the applied amounts of MSG absorption and metabolism. **Conclusion:** MSG is widely applied in industrial and homemade food. The need for further studies is crucial, and aspects such as metabolism and amounts of MSG effectively consumed must be better evaluated.

Keywords: food additives; health education; taste; flavoring agents; sodium; toxicity.

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INTRODUCTION

Glutamic acid is a very abundant aminoacid found in animal and plant proteins. In its free form, it enhances the original flavor of food and it is commonly used in Asian cuisine. Monosodium glutamate (MSG) is a natural salt of glutamic acid, which acts to promote palatability and is used as a flavor enhancer and also as a food preservative[1-3].

MSG is naturally and abundantly present in several types of food, including meats, seaweed, anchovies, mollusks, tomatoes, cheeses, vegetables, seafood, among others, contributing to the characteristic flavor. It is a non-essential amino acid, being the main excitatory neurotransmitter in the mammalian brain. It is involved in the metabolism, sensory stimulation, and improvement of palate perception[1,4-6].

Nowadays MSG is produced from the fermentation of starch, sugar beet, sugar cane, or molasses, mostly using bacteria of the genus *Corynebacterium*. Formerly it was obtained from algae, but this was a slow and costly process. The production process is similar to other fermentation processes such as the production of yogurt, vinegar, and wine, in which a microorganism is cultivated in culture media containing nutrients that allow, by microbial metabolism, the excretion of a useful metabolite[7-10].

The increased concentration of glutamic acid enhances the umami flavor, demonstrating that the taste is attributed to the glutamic acid ion, being a fundamental component for the perception of this basic taste. There are five basic tastes: sweet, salty, sour, bitter, and umami, which are recognized by specific receptors and transduction pathways. Although umami is the fifth taste, there are some recent developments in molecular biology which have demonstrated that a sixth basic taste, known as kokumi (glutamyl-valyl-glycin) may be included in the future[1,5,11].

Although some studies have shown that MSG is a flavor enhancer and an important factor to increase appetite and to bring some health benefits, other studies suggest the opposite, indicating that MSG consumption is related to the spread of diseases such as idiopathic urticaria, metabolic disorders, neural damages, and neurodegenerative diseases[12-15]. Gagliardi[16] states that excessive stimulation of MSG receptors alters calcium homeostasis and initiates a succession of free radical formation, apoptosis, and mitochondrial dysfunction, resulting in neurotoxicity, neuronal loss, and cell death.

In this way, there is little consensus in understanding the advantages and disadvantages of using MSG[17].

This study aimed to carry out a bibliographic review comparing the advantages and disadvantages of the use of MSG in food products, as well as to evaluate the scientific opinion about the health risks related to its intake from diet.

METHODS

This review was based on the analysis of published studies that addressed the use of MSG in foods, including the benefits of the application and the possible problems of consumption to human health. The articles were consulted in the ScienceDirect database and the PubMed database, using the following keywords: crossing 1 (food, diet, monosodium glutamate, health risk), crossing 2 (food, diet, monosodium glutamate, advantages, disadvantages), and crossing 3 (food, diet, monosodium glutamate, umami, obesity). The inclusion criteria adopted in this systematic review were: a) studies in English; b) between 1950 and 2020; c) published as review articles or research articles.

The results were evaluated to exclude duplicity. After this selection, the studies were carefully read and analyzed. Then, the advantages and disadvantages of the use of MSG in foods were described. Finally, the controversial aspects involving MSG and human health were discussed.

RESULTS

Electronic search in both databases resulted in the identification of more than 200 different studies. Tables 1 and 2 show the results using the different keywords for both databases. It was observed that most studies published on the subject have occurred in the past 20 years, emphasizing the increasing importance of this topic to food consumption and human health. After the inclusion of only research and review articles and the exclusion of studies that were present in more than one situation, due to the different crossings, ~60 studies were considered for this review. Considering these studies, 42% of the articles pointed out positive aspects of MSG, 46% presented negative aspects against MSG and 12% were informative and neutral. Regarding the articles that dealt with clinical trials, 33% were for research with humans, 63% with rats, and 3% with other animals.

Table 1: Crossings performed according to the ScienceDirect database and results obtained.

Keywords	Period	Results	Review articles	Research articles
“food” AND “diet” AND “monosodium glutamate” AND “health risk”	1950-1999	14	2	4
	2000-2020	124	13	21
“food” AND “diet” AND “monosodium glutamate” AND “advantages” AND “disadvantages”	1950-1999	68	5	18
	2000-2020	136	28	14
“food” AND “diet” AND “monosodium glutamate” AND “umami” AND “obesity”	1950-1999	23	0	9
	2000-2020	159	20	41

Table 2: Crossings performed according to the PubMed database and results obtained.

Keywords	Period	Results	Review articles	Research articles
“food” AND “diet” AND “monosodium glutamate” AND “risk”	1950-1999	1	1	0
	2000-2020	16	3	13
“food” AND “diet” AND “monosodium glutamate” AND “advantages” AND “disadvantages”	1950-1999	0	0	0
	2000-2020	0	0	0
“food” AND “diet” AND “umami” AND “obesity”	1950-1999	0	0	0
	2000-2020	21	5	15

DISCUSSION

In response to the objectives of this systematic review, several advantages justify the use of MSG in different food products. However, there are also some health issues related to its consumption that cannot be hidden from anyone.

Advantages of monosodium glutamate: The good side

Palatability improves food selection, ingestion, digestion, and absorption. The five senses are involved with these factors, but umami plays a key role in the taste of food, being transmitted by glutamate and 59 ribonucleotides such as inosinate and guanylate[18]. In addition to the functions in the body, umami can improve the palatability of foods that have low fat and salt content, increasing the intensity of two compounds and prolonging the residual taste, contributing to the selection of foods. It can be used in hospitals as a tool to increase the acceptability of food served, provide beneficial meals, and aid in the evolution of recovery[18,19].

Santos et al.[20] conducted a study with sausages, using 50% and 75% potassium chloride (KCl) to replace sodium chloride (NaCl) and adding monosodium glutamate, taurine, lysine, disodium inosinate, and disodium guanylate to remove sensorial defects caused in taste substitution. The formulation with 50% KCl showed a 44% reduction in sodium and a 127% increase in potassium content. The treatment that used 75% KCl showed a 68% reduction in sodium and an increase in potassium content by more than 200%.

Altug & Demirag[21] researched sensory attributes with 6 trained panelists and acceptability with 93 consumers to check the influence of MSG and its substitutes (yeast extract, mushroom concentrate, tomato concentrate) in chicken soup (0.4% NaCl). There was a significant preference for samples with 0.1% MSG, 0.025% yeast extract, and 0.5% salt compared to the others. The results showed that 43.5% of the judges liked the 30% to 50% sodium reduction and 26.1% preferred sodium reduction lower than 30%, obtaining important reductions in the percentage of sodium without loss in the sensory aspects of food. Yamaguchi & Takahashi[22] studied the sensory characteristics of binary mixtures of MSG (0.7%), NaCl (0.88%), sucrose (0.83%), caffeine (0.06%) and tartaric acid (0.033%). Samples were evaluated by a panel of 20 to 40 men and women, initially in aqueous solution and later at the same concentrations in cooked foods. The experiment confirmed that there was an ideal concentration of MSG that improved palatability. In addition to the studies involving the use of MSG as a sodium reducing agent, MSG participates in several important functions in the human organism, such as urea production, synthesis of other amino acids, platelet coagulation, salivation, appetite, taste, and health in general[23].

Research carried out by Sasano et al.[24] with 102 young and 82 elderly patients with hypogeusia (reduced ability to taste things), lack of appetite, and weight loss used Japanese kombucha (produced by fermenting sugared black or green tea) enriched with MSG (1, 5, 10, 50, 100 e 200 mM). The work evaluated the use of MSG as an alternative way to increase salivary secretion and improve appetite. The results showed that the symptoms were minimized in the majority of patients with hypogeusia due to stimulation of the umami taste[24]. However, the insertion of MSG in excess showed an adverse effect, reducing the palatability, therefore the ingestion of MSG was self-limiting[22].

Recently, the European Food Safety Authority (EFSA) reassessed the use of MSG as a food additive and defined the safe amount in a daily dose of 30 mg/kg body weight. The established amount and safety level were based on the dose with which there were no side effects and toxicity in the animals tested. In the European Union, there is no safe level definition of its consumption, but it is allowed to add glutamate normally up to 10 g/kg of food[25].

In several countries, it is regulated that MSG does not have a maximum limit of 100 g of food. Agencies like the Food and Agriculture Organization for the United Nations (FAO) and the World Health Organization (WHO) also defined glutamate as an additive in the functional class of flavor enhancer[13,26]. The Joint FAO/WHO Expert Committee on Food Additives has assessed the overall safety of MSG, concluding that its consumption presents no risk or danger to health, since its addition is technologically carried out to reach taste parameters and to create the necessary effect on food. For this reason, it was not necessary to specify a parameter for the consumption of monosodium salts[27]. According to Beyreuther et al.[28], the average European glutamate consumption ranges from 5 to 12 g/day, of which 1 g of free MSG, 10 g of protein, and about 0.4 g of added flavor. In Asian countries, the average intake of MSG ranges from 0.3 to 0.5 g/day. A maximum intake of 6000 mg/kg body weight is considered safe. Adults ingest between 10 and 12 g/day of glutamate, regardless of their ethnicity, culinary culture, or food eating habits[29].

In general, MSG has a GRAS (generally recognized as safe) status and an ADI (acceptable daily intake) not specified, meaning that it can be used as a food additive in the necessary amount to achieve the desired technological effect[30].

Disadvantages of monosodium glutamate: The bad side

In 1968 some scientists studied the symptoms of weakness, irregular heartbeat, and numbness in various parts of the body, which were reported after 15 to 20 minutes by people who consumed Chinese food. These symptoms were correlated with the consumption of MSG and generated the first incidences of side effects found after ingestion of MSG, being denominated in Chinese restaurant syndrome (CRS)[31,32].

Another disadvantage of using MSG is linked to the toxicity to the human body. Advances in knowledge about glutamate as a sedimentary substance in the brain show that exogenous glutamate acts on taste receptors, while endogenous glutamate reaches excitatory neurons and triggers the ease of feeding[4]. It is the endogenous excitatory neurotransmitter that is interconnected in memory and also in learning[33].

Some studies have shown negative effects, especially in animals, when MSG was administered, resulting in neurotoxic, genotoxic, and hepatotoxic effects[10]. Onyema et al.[34] observed liver damage in rats treated with MSG (0.6 mg/g body weight) for 10 consecutive days. In the study, an increase in the activity of liver enzymes and lipid peroxidation was also found, inducing oxidative stress and hepatotoxicity in rats, but with the use of vitamin E, these symptoms were reduced. Kayode et al.[35] studied testicular dysfunction in 46 male rats (180±40 g), divided into two groups (control and group with the application of MSG 4 mg/kg for 28 days), concluding that the administration of MSG caused a reduction in testicular glycogen, testicular dysfunction and also changes in the lipid profile. Research has shown that glutamate consumption is linked to the death of neuronal cells, causing an imbalance because it is considered an oxidative stressor and an obstacle in the antioxidant profile[36]. About genotoxicity, tests *in vitro* were carried out to evaluate the possible damage to the genetic material of the cells or to cause severe complications[37]. At seven et al.[38] performed a study using peripheral blood lymphocytes from healthy humans *in vitro*. In this research, the authors evaluated the genotoxic effects of MSG on human lymphocytes. The concentrations of 250, 500, 1000, 2000, 4000, and 8000 μg/mL of MSG were applied to the treated cells for 24 and 48 hours. The results showed a significant increase (regardless of time and dose used) of chromosomal aberrations, sister chromatid exchanges, and micronuclei blocked by cytokinesis when compared to control, showing genotoxic potential *in vitro*[38].

In pregnant rats, single oral doses of 8000 mg/kg administered at the end of pregnancy caused an increase in plasma levels from 100 to 1650 nmol/mL, but no significant increase in plasma levels was observed in fetuses. Infusion of 1 g/h of MSG in pregnant monkeys increased plasma levels 10 to 20 times, but no changes were observed in the fetuses. These reproduction studies used oral administration of MSG indicated that the fetus is not exposed to toxic levels of the maternal diet through transplacental transfer[27].

Another disadvantage commonly associated with the use of MSG is related to the risk of obesity. The MSG used for the induction of weight gain in hospitalized patients showed a positive influence; however, it could also be correlated with obesity in non-hospitalized individuals. MSG applied to obese mice by injection (2 mg/g) once daily for 5 days from the first day of life showed chronic neuroendocrine dysfunction and the animals developed glucose intolerance[39]. Mondal et al.[40] administered daily doses of 0.8, 1.6, and 2.4 g/kg of body weight/day of MSG, for 30 and 40 days by oral tube and found an effect of the consumption of MSG related to the reduction of function of the ovary and uterus, by suppressing reproductive function, increasing serum levels of follicle-stimulating hormone, luteinizing hormone and estradiol, which promote follicular maturation.

A study carried out with 90 pregnant rats weighing between 150±20 g determined the role of MSG in comparison to high-calorie feed. Three groups were studied: the control was carried out with 30 rats fed with food presenting 3.3 kcal/g (23.4% protein, 4.5% fat, and 72.1% carbohydrates), the second group was treated with a diet supplemented with 100 mg/kg of MSG, the third group was fed with a caloric diet presenting 4.47 kcal/g (21% protein, 31% fat, 48% carbohydrates and 50% sucrose). The groups were kept for three months in these controlled conditions, with 4 to 6 animals per cage, kept at a temperature of 25±0.5°C and 12:12 hours in light and dark. The results showed that pregnant rats consuming MSG showed a marked increase in the proportion of body fat and had an impact on the weight of offspring at birth, about the other groups[41].

Dolnikoff et al.[42] observed the relationship between fat content and body weight in 30-day-old rats, injecting 4 g/kg of MSG in the first 10 days of life. Body weight was lower, but the number of lipids in the adipocytes, cell diameter, surface area, and volume were higher in rats that received MSG than in the control group. After subjecting mice to a 6-32-week diet with 0.64 g/kg MSG, there was an increase in serum triglyceride and insulin levels and changes in the liver[43]. The study with rats carried out by Majewski et al.[44] also confirmed the induction of obesity caused by the consumption of MSG, as well as favored a pro-inflammatory environment.

Diniz et al.[45] demonstrated that MSG added to a standard diet via animal feed increased food intake. However, overfeeding also occurred, resulting in negative factors, including induced oxidative stress in the absence of obesity. The study used fiber to prevent changes in glucose, leptin, triacylglycerols, and insulin levels. Anderson et al.[46] investigated, in 28 healthy men, the effects of adding MSG to carrot soup enriched with and without whey protein, on appetite, food intake, and satiety. Five treatments were applied (water as control, carrot soup, carrot soup with 5 g MSG, carrot soup with 36 g protein, and carrot soup with 36 g protein and 5 g MSG). Food intake was not affected in MSG treatments alone and combination with whey protein. However, the addition of MSG decreased the desire to eat and subjective appetite, increased satiety and when the protein was added there was a decrease in blood glucose, an increase in insulin, and also in C-peptide, showing that MSG, in the intestine, can signal protein consumption.

The study by Asero[47] investigated clinical conditions due to the consumption of food additives. A 44-year-old patient with chronic (12 years) urticaria and rhinitis was observed. Initially, 4 weeks were dedicated to a diet without additives, reporting a 60% reduction in urticaria and disappearance of rhinitis in the first 4-5 days. Eight additives and 4 placebos were used to assess symptoms. When MSG was administered at a dose of 100 mg, within 45 minutes severe urticaria appeared, although food additives are rarely the primary cause of chronic urticaria, the additives can aggravate the condition.

Bautista et al.[48] evaluated inflammation markers, biochemical parameters, and glucose homeostasis during the aging process in rats with MSG-induced obesity. MSG (2 mg/kg of body weight dissolved in 0.01 mL/kg of saline solution) was injected subcutaneously into young rats with 2 and 4 days of birth and, later on, days 6, 8, and 10, injections of 4 mg/kg. At four months of age, the rats showed changes in triglycerides and total cholesterol. In addition, the levels of transaminases increased, there was a reduction in adiponectin and levels of glucose tolerance and insulin sensitivity, generating changes in metabolic control and inflammatory increase. However, after 16 months of age, an adaptation was observed in which the changes normalized, weakening the association between obesity and mortality linked to MSG.

The study by Collison et al.[49] evaluated the relationship between a diet with trans fat associated with MSG and the possible effects in rats. Four different treatments were carried out, using feed and drinking water for control, feed and water with 0.64 g/L of MSG, feed with the addition of 8.68% trans fatty acids, feed with the addition of trans fatty acids and 0.64 g/L of MSG in 20 males and 20 females aged 3 to 32 weeks, assessing food intake, body weight, waist circumference, and spatial learning. In addition to generating obesity, abdominal fat, and dyslipidemia, the diet impaired learning and spatial memory, suggesting that these signs were induced when feeding with MSG.

Onaolapo et al.[50] applied doses of MSG of 10, 20, 40, and 80 mg/kg of weight orally to 60 male rats for 28 days. The MSG doses of 40 and 80 mg/kg resulted in neuronal damage to the brain, cerebellum, and hippocampus, increased brain tissue, due to the action of the enzymes superoxide dismutase and catalase, which reduce nitric oxide, in addition to the increase in glutamate and glutamine in plasma, but not in brain tissue.

In general, preclinical studies have associated MSG administration with several health issues such as cardiotoxicity, hepatotoxicity, neurotoxicity, low-grade inflammation, metabolic disarray, premalignant alterations, and behavioral changes[51,52].

The controversial side

Although several studies emphasize the benefits or the health risks potentially related to the consumption of MSG, some studies show controversial information on the subject, highlighting aspects that are not yet clear.

The Joint FAO/WHO Expert Committee on Food Additives reviewed studies using human volunteers and failed to demonstrate that the cause of the symptoms was the ingestion of MSG, and concluded that cross-controlled double-blind trials did not correlate MSG with Chinese restaurant syndrome. However, the Joint did not rule out the hypothesis of intolerance in some individuals[27].

The study by Geha et al.[32], who evaluated the sensitivity of individuals to MSG, with double-blind placebo-controlled and randomized tests, did not obtain reproducible results, because they found only 2 effective responses in 130 participants. Danbolt[33] reported that changes in glutamate transporter activities may have fundamental implications for the functions of the nervous system and peripheral organs. However, the glutamate absorption system was not confirmed as the primary cause of any human disease.

MSG acts by activating the ionotropic and metabotropic glutamate receptors, affecting the nervous system, and the overactivation of the receptors produces excitotoxicity and neuronal death[53]. Swamy et al.[54] induced neurotoxicity by injecting MSG at a concentration of 2 g/kg of body weight intraperitoneally daily for 7 days. After 1 hour, 200 and 400 mg/kg of ethanolic extract from the *Pongamia pinnata* bark were administered orally. There was a significant reduction in lipid peroxidation, increased activity of the enzymes superoxide dismutase, catalase, and glutathione, in addition to altering behavioral and locomotor activity and muscle strength. Neurotoxicity is caused by the excessive accumulation of intracellular calcium along with the increase in sodium level and the reduction of potassium, which triggers many actions in cells, leading to mitochondrial dysfunction and free radical production[13].

Appaiah[55] stated that MSG causes brain damage, impairing cognitive abilities and learning problems, as well as endocrine and emotional complications. However, studies have shown that glutamate enters into the endothelial cells, but the organism does not allow its passage from endothelial cells into the brain[56]. For this reason, studies continue to argue that MSG consumed through food does not present risks and does not generate disease conditions with brain effects or even hormonal imbalances[57].

About genotoxicity, Rogers[58] contradicted the study carried out by Ataseven et al.[38], citing it and explaining that *in vitro* research is not enough for suggesting the symptoms. Reeds et al.[59] also explained that glutamate is compartmentalized and less than 4% of the glutamate consumed is absorbed in the gut passing into the circulation.

Some studies also affirmed that the correlation of the increase of body weight with MSG in rodents using injection was not applicable. The explanation was that almost no percentage of MSG consumed passes from the intestine into the bloodstream, meaning that its normal intake does not access the brain, and consequently its influence on fat metabolism and/or body weight is unlikely. Moreover, injectable studies should not be used with the normal amount of human consumption, since the metabolic pathway of injectable MSG is higher than that normally consumed[57,60].

In 2010 a study conducted in China tracked 1282 people for 5 years, evaluating multiple factors such as lifestyle, energy consumption, age, and sex. The results indicated that there is no association between the ingestion of MSG and a higher prevalence of obesity[61]. Corroborating this study, FAO/WHO considered scientifically that MSG is not considered to be a hazard to human health[13,26].

According to the review article by Zanfirescu et al.[51], further clinical and epidemiological studies are needed, because many of the negative health effects of MSG reported are poorly informed and have flaws in the methodology.

Conclusion

MSG can be used in food as a way to improve palatability and, depending on the results of applications in preparations, it can be used to reduce sodium without changing the sensory quality. However, there is a need for further research in this regard, with the percentage of reduction in each food being evaluated. It is an area in increasing development and the reduction of sodium consumption is linked to disease prevention.

About studies focusing on health safety, although the competent agencies claim that the use of MSG in food is safe, many researchers contradict these results, identifying a series of clearly known problems, involving obesity, heart diseases, and neuropathies, among others. However, the most important limitation observed was related to the application of MSG in animals, because most studies that showed a negative correlation with health were carried out using injectable methods.

The present study observed that more studies (carried out by the scientific community) are needed to evaluate the effects and metabolism of MSG in humans, as well as toxicity and limits of use. These results must be analyzed with caution so that there are no inconsistent results and no real basis for applicability. As long as there is a tiny consensus between scientists and regulatory agencies, the careful consumer should observe the doses of MSG ingested by the sum of the consumed industrialized food products, aiming at a healthy balanced diet.

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