



# Glutamate and Monosodium Glutamate: Examining the Myths

**B**ecause of the evolving nature of science, researchers rarely, if ever, close the book on studying various foods or food ingredients. Such is the case with monosodium glutamate (MSG). Even though it has been used extensively for nearly a century, it continues to be examined in light of current scientific knowledge and methods of testing. Over the past several years, experts in the fields of pediatrics, allergy, pharmacology, medical psychology, toxicology and food science have reviewed the scientific data on glutamate. This issue of IFIC Review examines the scientific research conducted on glutamate and MSG and summarizes the latest findings.

## *What are Glutamate and MSG?*

Glutamate is one of the most common amino acids found in nature. It is the main component of many proteins and peptides, and is present in most tissues. Glutamate is also produced in the body and plays an essential role in human metabolism.<sup>1,2,3</sup> Virtually every food contains glutamate. It is a major component of most natural protein foods such as meat, fish, milk and some vegetables.

MSG is the sodium salt of glutamate and is simply glutamate, water and sodium. In the early 1900s scientists isolated the ingredient (glutamate) in plants that is the essential taste component responsible for greatly enhancing flavor.<sup>1,2</sup> In the early part of the twentieth century, MSG was

extracted from seaweed and other plant sources. Today, MSG is produced in many countries around the world through a natural fermentation process using molasses from sugar cane or sugar beets, as well as starch and corn sugar.<sup>1,4</sup>

## *Flavor Enhancement Properties*

When present in its “free” form, not “bound” together with other amino acids in protein, glutamate has a flavor-enhancing effect in foods. When MSG is added to foods, it provides a flavoring function similar to naturally occurring free glutamate.<sup>5</sup> MSG is used to enhance the natural flavors of meats, poultry, seafood, snacks, soups and stews.<sup>1,4</sup>

Multidimensional scaling experiments, which are used in sensory research, indicate that MSG falls outside the region occupied by the four classic tastes of sweet, sour, salty and bitter.<sup>4,6</sup> This distinctive taste is known as “umami,” a word coined by the Japanese to describe the taste imparted by glutamate. Westerners often describe this flavor as savory, broth-like or meaty.<sup>4,6</sup> Recently, Dr. Chaudhari and colleagues at the University of Miami School of Medicine identified a specific glutamate taste receptor on the tongue.<sup>7</sup>

Dietary research points to MSG’s potential to enhance food intake in older individuals.<sup>8-11</sup> Over the years, research has shown that losses in taste and smell are major contributors to poor nutritional status among older persons, sometimes even leading to

anorexia. Losses of taste and smell generally occur around 60 years of age and become more commonplace in persons over 70 years of age.<sup>9, 10</sup> Studies find that moderate levels of added MSG in certain foods, such as mushroom soup and mashed potatoes, can increase food intake in an institutionalized older population, thus increasing intake of necessary vitamins, minerals and protein from food.<sup>2, 9, 11</sup>

### ***MSG Consumption and Metabolism***

Current consumption data from the United Kingdom show that per capita consumption of MSG is 4 grams (less than one teaspoon) per week.<sup>12</sup> This is comparable to U.S. estimates of roughly 0.55 grams for the average consumer, spread out through an entire day.<sup>13</sup> In Taiwan, for example, per capita consumption figures are much higher, averaging 3 grams per day.<sup>14</sup>

Still, the human body metabolizes added glutamate in the same manner it metabolizes glutamate found naturally in many foods. Once glutamate is ingested, our bodies make no distinction between the origins of the glutamate.<sup>15, 16</sup> The body does not distinguish between glutamate from foods like tomatoes or MSG added to a tomato sauce.<sup>2, 15, 16</sup> In fact, research now shows that glutamate from food or MSG is important for normal functioning of the digestive tract and digestion.<sup>17</sup>

### ***MSG and Public Health***

In 1958 the U.S. Food and Drug Administration (FDA) designated MSG as a Generally Recognized As Safe (GRAS) ingredient, along with many other common food ingredients such as salt, vinegar and baking powder.<sup>18</sup> There is general consensus in the scientific community, based on numerous biochemical, toxicological and medical studies conducted over four decades, that MSG is safe for the general population, including pregnant and lactating women, and children.<sup>19</sup> In 1995, the safety of MSG for use by the American population was again reinforced in a review by the Federation of American Societies for Experimental Biology (FASEB). The review was conducted by FASEB upon request of the FDA as is periodically done for all GRAS ingredients.<sup>15</sup>

### ***MSG and Food Labeling***

The FDA requires labeling of all ingredients in processed and packaged foods. When MSG is added to a food, it must be included in the ingredient list by its common or usual name, “monosodium gluta-

mate.”<sup>20</sup> When glutamate-containing ingredients are used as a component of a food product, they are required to be listed by their common or usual name (for example, Parmesan cheese, tomatoes, soy sauce, hydrolyzed protein or autolyzed yeast extract).

### ***MSG and Sodium Reduction***

Contrary to popular belief, MSG is not high in sodium. MSG contains only one-third the amount of sodium as table salt, sodium chloride (12 percent versus 39 percent sodium). When small quantities of MSG are used in combination with a reduced amount of table salt during food preparation, the flavor-enhancing properties of MSG allow for far less salt to be used during and after cooking. MSG brings out the best natural flavors in food, working well in reduced-sodium and reduced-fat dishes and can reduce total sodium by 30 to 40 percent without influencing palatability.<sup>21</sup>

### ***Pregnant & Lactating Women***

It is common practice for expectant women to eat a varied and well-balanced diet and consume enough calories to ensure a healthy pregnancy.

To facilitate fetal growth and development, most amino acids are actively transported across the placenta. Research indicates that amino acid concentrations are higher in the fetus, regardless of what the mother consumes.<sup>22</sup> Both the placenta and fetal liver play important roles in amino acid (and specifically glutamate) transport and metabolism important for fetal development.<sup>23</sup>

Because it is difficult to increase blood glutamate to significantly higher levels through dietary intake of MSG, scientists have injected glutamate directly into the bloodstream to observe any effect.

Pitkin and colleagues intravenously administered large amounts of MSG into pregnant monkeys to increase glutamate levels in the mother’s bloodstream. On examination, no increases in the fetal glutamate levels were found with doses up to 220 mg/kg of maternal weight. The authors further concluded that the placenta is virtually impermeable to glutamate, even at high levels.<sup>24</sup> Research suggests there is typically a net loss of glutamate from fetal blood into the placenta.

In rodent studies, researchers investigated effects of dietary intake of MSG on reproduction and

birth. The study looked at three generations of mice that were fed a daily intake of up to 7.2 g/kg of MSG. No adverse effect was observed in each generation, nor was there evidence of any incident of brain lesions in the neonates.<sup>25</sup>

Besides research on the fetus, scientists also investigated the effect of MSG ingestion on lactation and breast-fed infants. Upon examination of lactating women who consumed MSG at 100 mg/kg of body weight, researchers noticed no increase in the level of glutamate in human milk, and no effect on the infant's intake of glutamate.<sup>2</sup>

Likewise, studies show that breastfeeding infants are able to detect and prefer the taste of naturally occurring free glutamate, which is 10 times more plentiful in human breast milk than cow's milk.<sup>26, 27</sup> According to Baker and colleagues, a newborn infant, through breastfeeding, ingests more free glutamate per kilogram of body weight than during any other period of its life.<sup>28</sup>

Additionally, in December 1993 the American Academy of Pediatrics Committee on Drugs reviewed the effects of food and environmental agents on breastfeeding. In the report, the Committee stated that MSG has no effect on lactation and poses no risk to the consuming infant.<sup>29</sup>

## **Children**

It has been speculated that children would metabolize oral MSG more slowly than adults. However, research conducted by Stegink and colleagues at the University of Iowa showed that children as young as one year old metabolize glutamate as effectively as adults.

In the study, infants were fed beef consommé providing MSG at various dosage levels of 0, 25 and 50 mg/kg of body weight. Researchers measured the infant's plasma glutamate levels and, after comparing the children's plasma levels to those of adults, found no higher plasma glutamate values for children.<sup>30</sup> Additionally, scientific evidence has not implicated MSG in attention deficit hyperactivity disorder or other behavioral problems in children.

For the general population, MSG does not pose a health risk. Based on the scientific evidence upholding the safety and efficacy of MSG, the Select Committee on GRAS Substances (SCOGS) concluded in 1980 that there is no evidence that demonstrates reasonable grounds to suspect a hazard to the

public when glutamic acid or its salts are used at current levels and manners now practiced.<sup>31</sup>

## **MSG and Neurological Effects**

In the brain, glutamate serves as a neurotransmitter in addition to its general role in protein and energy metabolism. Neurotransmitters are stored in nerve endings and are used by nerve cells to inhibit or excite other nerve cells or target cells, such as muscle or endocrine cells.

Concerns were raised in the late 1960s by John Olney, M.D., of Washington University, that high doses of MSG may adversely affect brain function. Dr. Olney examined the possibility of MSG-induced brain lesions through injection or force-feeding methods in rodents. In one study, Olney subcutaneously injected neonatal mice, ages 2 to 9 days old, with single dosages of MSG. The amount of MSG injected varied from 0.5 g/kg to even larger dosages of 4 g/kg of the neonate's body weight, inducing brain lesions and a variety of other physiological effects in the rodents.<sup>32</sup>

However, the dosages of MSG used in these studies were extremely high and the methods of injection, as well as force-feeding, do not accurately represent the way humans consume MSG. Interestingly, Olney's results could not be duplicated when large amounts of MSG were added to the diet.

Indeed, studies evaluating the normal dietary ingestion of MSG in food, including amounts exceeding 40 g/kg body weight (5,000 times higher than normal amounts ingested), found no harmful effects on the brain.<sup>1</sup>

Following Olney's observations, early research conducted by Bazzano, D'Elia and Olson compared large amounts of glutamate fed to adult humans and gerbils. The study involved 11 human adult males who consumed diets containing MSG dosages up to 147 g per day for a maximum of 42 days (200 times higher than normal consumption). During that time, researchers did not observe any sign of adverse reactions to the dosage and concluded that very high oral doses of glutamate are well tolerated, with no neurological changes by adult gerbils or humans.<sup>33</sup>

Takasaki and colleagues noted in their findings that when mice were given MSG orally with food, plasma glutamate rose significantly less than after injections of similar doses without food. The researchers observed that pregnant, weaning and

lactating mice fed large amounts of MSG in the diet at up to 14, 42 and 42.8 g/kg body weight respectively, did not develop brain lesions. Furthermore, plasma glutamate levels in mice that were fed large amounts of MSG in the diet were much lower than those required to induce brain damage. Takasaki and colleagues concluded that MSG in the diet does not cause any acute or long-range adverse effect on the brain.<sup>34, 35</sup>

William Pardridge, M.D., further illustrated that dietary glutamate does not enter the brain because the blood-brain barrier maintains a transport system for acidic amino acids, such as glutamate, to effectively exclude circulating glutamate from the brain. Pardridge also showed that the levels of brain glutamate do not rise or fall with changes in plasma glutamate levels.<sup>36</sup>

Substantiating Pardridge's observations, Brian Meldrum, M.D., of the London Institute of Psychiatry in Britain, reported on amino acids' role as dietary excitotoxins that may contribute to neurodegenerative disorders. After reviewing numerous studies of various fields, he concluded that, "the dietary consumption of glutamate has not been shown to cause neuropathology in man."<sup>37</sup>

Meldrum also affirmed that the blood-brain barrier and the very powerful glial and neuronal uptake systems for glutamate help keep the extracellular concentration of glutamate low in the brain.<sup>38</sup>

In 1994, John Fernstrom, Ph.D., professor of psychiatry, pharmacology and behavioral neuroscience at the University of Pittsburgh, reviewed literature examining the influence of food intake and ingestion of acidic amino acids, such as glutamate, on the formation of neurotransmitters and any possible repercussions on brain function.

Fernstrom pointed out that while glutamate is a neurotransmitter, it does not have ready access to the brain from the circulation system or the diet. After reviewing over 20 published studies, Fernstrom stated that the abundance of scientific evidence indicates that dietary glutamate does not present a risk to normal brain function.<sup>39</sup>

Quentin Smith, Ph.D., professor of pharmaceutical sciences at Texas Tech University Health Sciences Center, further illustrated the importance to human health of the blood-brain barrier in maintaining neural glutamate concentration independent of that of the circulatory system.<sup>40</sup> With recent advances in the understanding of barrier amino acid transport systems, future research may yield improved ways to treat human disease.

The weight of scientific evidence has shown that MSG as consumed in food does not impair brain function or pose risk to public health. As further concluded in the World Health Organization's Food Additive Series, scientific examinations have shown a lack of MSG mutagenicity, teratogenicity or carcinogenicity.<sup>26</sup> This lack of evidence was also supported by the 1995 FASEB report.<sup>15</sup> The FASEB review found no evidence linking MSG consumption to any serious long-term neurological problems in the general public, including Huntington's disease, Lou Gehrig's disease (Amyotrophic Lateral Sclerosis) or Alzheimer's disease.

### Natural Glutamate Content of Foods

	Bound Glutamate (mg/100 g)	Free Glutamate
<b>MILK/DAIRY PRODUCTS</b>		
Cow's	819	2
Human	229	22
Parmesan Cheese	9,847	1,200
<b>POULTRY PRODUCTS</b>		
Eggs	1,583	23
Chicken	3,309	44
Duck	3,636	69
<b>MEAT</b>		
Beef	2,846	33
Pork	2,325	23
<b>FISH</b>		
Cod	2,101	9
Mackerel	2,382	36
Salmon	2,216	20
<b>VEGETABLES</b>		
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

Source: Institute of Food Technologists.<sup>1</sup>

## *Hypersensitive Reactions*

Allergic reactions to environmental agents, such as pollen, are typical, whereas the occurrence of an allergic reaction to foods or food ingredients is rare. In fact, recent research has indicated that nearly 30 percent of adults believe they have a food allergy, when in reality less than two percent of the adult population is hypersensitive to foods or food additives.<sup>41</sup>

Physicians have documented many psychological factors that play a role in perception of food allergy or food sensitivity.<sup>42, 43</sup> Likewise, Parker and colleagues reported in 1993 that individuals with unconfirmed reactions to foods were influenced by popular news media.<sup>44</sup> However, many questions still persist about MSG's role in food hypersensitivity.

In 1991, after reviewing the literature on MSG and food allergy and safety, a panel of the American College of Allergy, Asthma and Immunology concluded that MSG is not an allergen and reaffirmed its safety as a food ingredient.<sup>45</sup> More recently, Ronald Simon, M.D., department of allergy and immunology, Scripps Clinic, La Jolla, California, conducted a well-designed, double-blind, placebo-controlled study of 65 subjects with chronic urticaria. None of the subjects exhibited positive reactions to doses of 2.5 g of MSG.<sup>46</sup>

## *MSG and Food Intolerances*

In 1968, Robert Ho Man Kwok, M.D., described a collection of symptoms he allegedly experienced after eating Chinese food. He coined the phrase "Chinese Restaurant Syndrome" (CRS) to describe these symptoms, which included numbness at the back of the neck and a feeling of pressure in the face and upper chest muscles.<sup>47</sup>

As a consequence of Kwok's account, Kerr and colleagues developed a subjective questionnaire to assess the prevalence of CRS in the population. The survey employed listed 18 adverse symptoms related to food, of which three were related to CRS. Of the 3,222 general households that responded to the survey, 43 percent reported food-related adverse reactions, but only 1.8 percent reported possible CRS symptoms.

Adding to this, data from the Centers for Disease Control (now Centers for Disease Control and Prevention) in Atlanta showed that reported reactions to MSG accounted for less than one percent of food related complaints between 1975 and 1987.<sup>49, 50</sup> In 1995, the FASEB report stated its discomfort with

the use of the term CRS because of its pejorative tone and the inherent limitations of the implied circumstances of exposure.<sup>15</sup>

After anecdotal reports of MSG inducing CRS, Morselli and Garattini examined 17 males and seven females, between 18 and 34 years of age in a double-blind crossover challenge.<sup>51</sup> The researchers administered 3 g doses of MSG in 150 ml of beef broth and evaluated the subjects every 20 minutes for a three-hour period. The participants were divided into two groups: one group that received the MSG broth the first day and another group that received the MSG broth on the following day.

Upon examination, no difference in subjective symptoms were observed between the MSG group and the control group. These symptoms included tightness in the chest, flushing and headache. However, no participant in either group experienced the burning sensation that is typical of CRS. There was also no significant difference in the number of times each single symptom occurred or how many participants experienced symptoms. Based on these observations, the researchers concluded that there is no evidence that CRS is associated with the ingestion of MSG.<sup>51</sup>

Richard Kenney, M.D., of George Washington University, tested over 200 individuals from 1972 through 1980.<sup>52, 53</sup> In his studies, Kenney found that sensations reported after MSG administration were seen at high concentrations of MSG and were not reproducible from day to day. He also found no correlation with blood glutamate levels or blood chemistry measurements, and that they were not correlated with any objective measurements.

He further tested 60 subjects with orange juice, spiced tomato juice, black coffee, flavored milk and a two percent MSG solution. Upon examining reactions, Kenney found that six subjects responded to coffee, six to spiced tomato juice and only two to the MSG solution, indicating that MSG was not unique in producing symptoms typical of CRS.<sup>52, 53</sup>

In 1986, Kenney conducted a double-blind placebo-controlled investigation of subjects who believed they adversely reacted to MSG. Subjects were given a soft drink solution for four days, and on two of the days the solution contained 6 g of MSG. Two of the six subjects reacted to both solutions and the other subjects reacted to neither solution. Kenney further noted that while a reaction

## What is a Double-Blind Placebo-Controlled Study?

Considered the “gold standard” for testing potential adverse reactions to a substance, double-blind placebo-controlled studies provide dependable findings that are free of bias introduced by either the patient or the researcher.

In this type of study, neither the subject nor the researcher conducting the study knows whether the test substance or a placebo has been administered. For the results to be valid and to ensure the subject cannot violate the “blindness,” the placebo and the test substance must look, smell and taste similar, if not identical.

The “blindness” of the study is crucial. It eliminates the possibility of a participant’s personal beliefs to undermine the study’s validity, as well as the researcher’s expectations to influence the test results.

and colleagues surmised that the histamine levels in some foods may be the cause for the adverse reactions consumers associate with restaurant meals.<sup>57</sup>

Though numerous studies have evaluated MSG’s possible causative role in food hypersensitivity, a majority of scientific challenges have failed to reproduce the adverse reactions many individuals associate with ingestion of MSG.<sup>58</sup> Studies measuring objective responses such as blood pressure, heart rate, skin temperature and muscle tone have been unable to detect differences between persons fed MSG and placebo.

may occur to an extremely large ingestion of MSG, the reaction is usually transient and benign.<sup>54</sup>

Additionally, Jonathan Wilkin, M.D., of the Medical College of Virginia, studied 24 individuals, 18 of whom described a history of flushing upon ingesting MSG. After failing to provoke flushing when using 3 g or 5 g of MSG, Wilkin determined that MSG-provoked flushing is rare.<sup>55</sup>

In 1993, Tarasoff and Kelly published a study examining the sensory side effects possibly caused by ingesting MSG.<sup>56</sup> Using a randomized double-blind crossover study, seventy-one healthy participants were administered five different treatments, which included two placebos and three different doses of MSG (1.5, 3 and 3.15 g) in a random order. Neither the researchers nor the subjects knew which or how much of the test material was being consumed.

Two hours after ingestion, each subject was interviewed and half reported they experienced more than one symptom regardless of MSG content. While the most common reaction was none at all, the next significant symptom reported was tingling and thirst, which was experienced by the subgroup of strong reactors. Thus, similar to Kenney, Tarasoff and Kelly found that the small number of effects seen were statistically insignificant and that MSG in food had no discernible effect for healthy individuals.<sup>56</sup>

Interestingly, Chin and colleagues explained that histamine toxicity produces symptoms individuals may interpret as being CRS related. Therefore, Chin

For decades, anecdotal reports have suggested that a small percentage of the population may be sensitive to MSG. However, these reactions have been observed to be mild and transitory.<sup>15, 59</sup>

Recently, a rigorous double-blind, crossover placebo-controlled study investigated whether MSG could cause postprandial symptoms after ingestion of Indonesian meals.<sup>60</sup> The researchers found no differences in symptoms after ingestion of MSG or placebo.

In 1998, in the largest study to date, Geha and colleagues reported results from a multicenter study (Harvard University, Boston; Northwestern University, Chicago; and the University of California in Los Angeles) of 130 subjects who believed they were sensitive to MSG.<sup>61</sup> Using double-blind placebo-controlled testing conditions, no adverse reactions could be reproduced with MSG or placebo in the presence of food. Any observed reactions were mild, transient and not life threatening.

### *MSG and Asthma*

Early, poorly controlled studies suggested that MSG might induce, as well as exacerbate, asthma.<sup>62</sup> However, follow-up double-blind challenges have not replicated those results.<sup>63</sup> Researchers at the Harvard Medical School measured the pulmonary reactions of asthmatic participants in a double-blind, randomized crossover study. Participants received either a placebo or MSG in a dose of 25 mg/kg of body weight. After comparing reactions on placebo day and MSG day, as well as those reactions of three

subjects who reported a history of food sensitivity, researchers saw no difference in pulmonary reactions. Thus they concluded that MSG does not induce asthma and it is unnecessary to advise asthmatics to avoid MSG.<sup>64, 65</sup>

In 1991 and 1993, researchers from the National Institutes of Health's Institute of Allergy and Infectious Diseases presented data analyzing the possible association of MSG to asthma.<sup>66, 67</sup> In one study, they challenged 13 non-asthmatics and 30 asthmatics with a total dose of 7.6 g of MSG administered through a single-blind oral challenge. Upon observation, none of the non-asthmatics experienced any change in pulmonary reactions and only one asthmatic participant experienced some discomfort.

However, when the asthmatic patient was challenged through double-blind placebo-controlled effort, no effect was seen. Thus, researchers concluded that "7.6 g of MSG ingested over two hours posed no respiratory hazard to normal subjects and to the asthmatic population in the study."<sup>66</sup>

The FASEB review of MSG—while demonstrating its safety for the general public—suggests potential exacerbation of asthma. The FDA found this linkage to be unsupported by existing data and requested that additional well-controlled clinical studies, if available, be submitted to the agency.<sup>68</sup>

In 1998 and 1999, two well-controlled, blinded food challenge studies addressing the question of MSG-induced asthma were published.<sup>69, 70</sup> In the first study, double-blind placebo-controlled oral challenges using 5 g MSG were administered to 12 subjects with clinically documented asthma, all

of whom believed their asthma was exacerbated by MSG.<sup>69</sup>

In the second study, single-blind placebo-controlled oral challenges using 2.5 g of MSG were administered to 100 mild-to-severe asthmatics, 30 percent of whom believed their asthma was exacerbated by MSG.<sup>70</sup> MSG-induced asthma was not observed among any subjects in either study.<sup>69, 70</sup>

## Summary

It is apparent that there is no shortage of research conducted on this ubiquitous ingredient and its potential health effects.<sup>3</sup> Because MSG is one of the most intensely studied food ingredients in the food supply and has been found safe, the Joint Expert Committee on Food Additives of the United Nations Food and Agriculture Organization and World Health Organization placed it in the safest category for food additives.<sup>26, 71</sup>

Subsequently, in 1991 the European Community's Scientific Committee for Food confirmed the safety of MSG. Based on the extensive scientific data, and in view of large normal dietary intake of glutamates, the committee determined that specification of an Acceptable Daily Intake (ADI) level was unnecessary.<sup>72</sup>

The American Medical Association's Council on Scientific Affairs and the National Academy of Sciences have determined that MSG, at current consumption levels, is safe.<sup>13, 73</sup> Finally, the 1995 FASEB evaluation, sponsored by the FDA, reaffirmed MSG's safety as a food ingredient for the public and noted the lack of scientific information reporting negative effects of MSG on human health in the general population.<sup>15, 74</sup>

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