# Monosodium glutamate – do we have anything to fear?

Zdeňka Panovská, Vojtěch Ilko

Department of Food Analysis and Nutrition
Faculty of Food and Biochemical Technology
University of Chemistry and Technology
Prague, Czech Republic

**Abstract**

Glutamic acid was discovered in 1866 and its taste properties and those of its salts were described in 1907. Its salts soon began to be used as food flavourings as they are characterised by a unique taste different from sweet, salty, sour and bitter. Their flavour has been described by the Japanese word umami which can be translated as a pleasant savoury taste. Discussions about the inclusion of umami among the basic tastes were resolved at the end of the twentieth century when the receptors for its perception were discovered. Salts of glutamic acid are presently among the most widely-used additives, though their effects on human health are the subject of considerable discussion. This paper attempts to summarise the most common concerns and our current knowledge of this substance.

*Additive, glutamic acid, salts of glutamic acid, umami*

## Introduction

The Internet is an information medium that enables the extremely rapid sharing of information. This information is not, however, necessarily based on science, but it spreads extremely quickly so long as it is sufficiently shocking or people find it interesting. One topic that is the subject of much discussion on the Internet is food safety. We all consume food, for which reason information about food is not just of interest to a small section of the population. Articles of the type "The Quiet Killer E621 – Monosodium Glutamate (MSG)" or "The Truth, the Whole Truth and Nothing But the Truth About MSG" (Truthinlabeling 2014) have begun appearing on the Internet in recent years. Monosodium glutamate is, according to these sites, responsible for destroying nerve cells and is a cause of obesity, migraine and damage to the hypothalamus induced by high doses during breastfeeding. It is said to cause autism, attention deficit disorders, hyperactivity and diabetes. It is said to be responsible for Alzheimer's disease, to interfere with the retina and cause glaucoma, and to lead to aggressiveness, stomach ulcers, gastritis and other diseases in man. A brief summary about MSG is given in this article.

### The history of glutamic acid

Asian nations have used extracts of seaweeds such as *Laminaria japonica* and sauces made from fermented fish to improve the flavour of the food dishes they make for centuries, though for a long time it was not known what caused this taste. The word umami was already in use in Japanese during the Edo period to describe a delicious, sharp taste or to mean to enjoy a taste, etc. In 1866, the German scientist Karl Ritthausen was the first to isolate naturally occurring glutamate from acidic wheat hydrolysate in the form of L-glutamic acid. In 1907, Professor Kikunae Ikeda, a Japanese chemist at Tokyo University, isolated glutamate from a broth of dried Kombu seaweed (*Laminaria*) and found that the basic component responsible for improving the taste of certain fermented dishes and the cause of the umami taste, the impression of which is described as meaty, salty-sour, etc., was glutamic acid (Yamaguchi and Ninomiya 2000). In 1908, he had glutamate patented, joined up with Mr Suzuki and obtained a certificate from the Japanese Minister of the

**Address for correspondence:**
Doc. Dr. Ing. Zdeňka Panovská
Department of Food Analysis and Nutrition
Faculty of Food and Biochemical Technology
University of Chemistry and Technology
Technická 3, 166 28, Prague, Czech Republic

Phone: +420 220 443 176
E-mail: zdenka.panovska@vscht.cz
www.maso-international.cz

Interior confirming that AJI-NO-MOTO (the Japanese commercial name for glutamate) was harmless in relation to health and safety. Industrial production of monosodium glutamate for use in the food industry began in 1910. This was the very first industrial use of monosodium glutamate in the world. In 1946, the company was given its present name of Ajinomoto Co., Inc.

In the years 1910 to 1956, the monosodium glutamate production process was slow and costly. It was not until 1956 that Japanese scientists succeeded in producing glutamic acid by means of the fermentation of starches. Pure monosodium glutamate is most commonly produced industrially from the hydrolysate of yeast cultivated on substrates containing starch (primarily potatoes, flour, sugar beet, grain, tapioca starch, molasses, etc.). Additional substances responsible for the umami taste have also been discovered over the course of the years. Dr Kodama, a student of Professor Ikeda, discovered the nucleotide inosine-5′-monophosphate (IMP) in 1913. Guanosine-5′-monophosphate (GMP) and xanthosine-5′-monophosphate (XMP) were discovered in 1960, followed by others. Thirty-one dipeptides and tripeptides that induce the umami taste have been described in the literature, while other compounds have also been described (Van den Oord and Van Wassenaar 1997).

Although the umami taste was the subject of much discussion throughout the whole of the 20th century, the receptors for perceiving the taste of salts of glutamic acid were not discovered until the end of the century. Chaudhari et al. (2000) discovered the taste receptor for L-glutamate, known as taste-mGluR4, which regulates the activity of the receptor cells. Nelson et al. (2002) discovered the T1R1+3 receptor broadly tuned for amino acids which is stimulated by L-amino acids. These discoveries made it possible to include the umami taste among the basic tastes as they meet the conditions on which scientists have agreed, i.e.:

- the existence of specialised receptors and cells (taste receptor cells) capable of changing a chemical signal into an electric signal must be proven,
- different specific sensations must exist for the given stimulus,
- the signal transmitted from the oral cavity to the brain stem must be carried by a special neural pathway.

## The glutamic acid content in the human body

Glutamic acid is an amino acid that is found in both plant and animal proteins. It occurs in all living organisms, generally in bound form as part of proteins. The human body contains 14 – 17% proteins, of which around 1/5 is made up of glutamic acid. An adult person weighing 70 kg has an average of 12 kg of amino acids bound in proteins (of which 2 kg is made up of bound glutamic acid) and around 200 g of proteins in free form (of which 10 g is glutamate). The human body synthesises an average of around 50 g of glutamate daily. Protein in food is broken down (hydrolysed) in the stomach and intestines in the human body by the action of hydrochloric acid and enzymes. In healthy individuals, the body keeps the amount of glutamic acid under control and the excess amounts are not stored in the body. The largest amount of free glutamate is found in the muscles (6 000 mg), the brain (2 250 mg), the liver (670 mg) and the blood plasma (40 mg) (Bellisle 1999). Human saliva also contains a small amount of glutamate (1.5 ppm) (Yamaguchi and Ninomiya 2000).

Glutamic acid and glutamine are not considered essential amino acids as they can be synthesised endogenously in sufficient amounts from other amino acids and precursors. Glutamate is known to be absorbed from the intestine by a transport system specific for amino acids. There are evidently four transport systems for free amino acids. One of these is specific to aspartic acid and glutamic acid and would seem to be slower than the others. During intestinal absorption, a large proportion of glutamic acid is transaminated,

as a result of which the content of alanine in the blood increases. Glutamine and glutathione are other products of metabolism. Ingestion of an extremely large amount of glutamate results in increased hepatic metabolism of glutamate which leads to the release of glucose, lactate, glutamine and other amino acids into the circulation. It must, however, be said that these results come from experiments on animals and that it has been shown that the oral administration of glutamate with food, particularly food rich in saccharides, significantly reduces the maximum concentration in the blood plasma. Experiments have also shown that great differences exist in glutamate levels in the blood if it is consumed with food in contrast to glutamate administered in an aqueous solution (it is not, however, consumed in this form) (Walker and Lupien 2000).

Glutamate is a major excitatory neurotransmitter in the brain. A neurotransmitter is generally a low-molecular chemical that is formed naturally in the nervous system of animals and serves for the transmission of messages. Our knowledge of the synapse has advanced immensely over the last decade, mainly thanks to the use of cellular electrophysiological and molecular biology techniques that enable better study of glutamate receptors and transporters. Although glutamate normally functions as a neurotransmitter, an excess of glutamate can be harmful and may cause cell degeneration. Glutamate may cause neuron death by means of a mechanism known as excitotoxicity – a process involving the death of neuron cells and glial cells due to excessive or long-term activation of excitatory amino acid receptors. Excitotoxicity may, in fact, contribute to a number of neurodegenerative diseases, including ischaemic strokes, Alzheimer's disease, Parkinson's disease and epilepsy. In view of the fact that glutamate may cause neuron degeneration, there are two main approaches to the treatment of neurological diseases. Either an effort is made to prevent neuron degeneration by controlling excitotoxicity, or glutamatergic synaptic transmission and function in surviving neurons is modulated by positive or negative regulation of glutamate receptors (GluRs), i.e. an attempt to prevent neuron degeneration by applying substances reducing the wash-out of glutamate, i.e. by reducing excitotoxicity, or applying drugs increasing glutamatergic neurotransmission (Balazs et al. 2010). Discussion has recently turned to a new treatment for schizophrenia by means of the activation of group II glutamate receptors that act through G-proteins, for which reason they are known as "metabotropic" glutamate receptors (Hons 2006). It is interesting to note that glutamate was used in the 1950s to treat mentally retarded children. No increase in intelligence coefficient was confirmed following its administration, though certain aspects of behaviour did show improvement in more than half of the children studied (Zimmerman and Burgemeister 1959).

In many species of animals, the glutamate levels in the brain are far higher than those in the plasma. The important thing is that L-glutamate has not been proven to cross the blood-brain barrier when there is a larger amount of glutamate in the brain. This is caused by an error in its biosynthesis. Glutamate is biosynthesised in the brain from various precursors, including glucose and glutamine. The excretion of glutamate from the brain is seven times higher than its intake (Bellisle et al. 1999). Many papers have been written on the function of glutamic acid in the brain as this is an extremely important topic. A number of studies have also been performed on livestock animals. The work by the authors who demonstrated the effects of glutamate intake in diets with a threonine deficiency is interesting. The addition of L-glutamic acid showed an effect on threonine and improved the growth of piglets. During the course of serious illness, glutamate is considered a conditionally essential amino acid, particularly in view of the fact that it supports the metabolic needs of the intestinal mucosa when glucose is exhausted or when the intestinal mucosa is damaged during starvation, chemotherapy or radiotherapy.

The study by Rezaei et al. (2013) focused on determination of the safety and effectiveness of food supplementation with monosodium glutamate. Piglets were weaned at 21 days

and fed a diet based on maize flour and soya flour with 0, 0.5, 1, 2 and 4% glutamate. The results showed that dietary supplementation of up to 4% MSG was safe. The first paper suggesting that MSG causes brain damage in the form of degeneration of the retina was published in 1957 (Lucas and Newhouse 1957), though its results were obtained in mice and were not confirmed in man. Heightened interest in glutamate appeared following a paper published in 1968 (Kwok 1968). Symptoms appearing after consumption of large amounts of glutamate in sensitive people, particularly vomiting, water retention in the body, stiff muscles, palpitations and dizziness, were described in the paper. The illness was named Kwok's disease after the author of the paper. As the given symptoms arose mainly following consumption of Chinese food, it has become known in the USA as Chinese restaurant syndrome. This led to increased interest in this issue from scientists, though further studies did not confirm the symptoms, but show rather that symptoms of this kind are seen in sensitive people following consumption of exotic or unfamiliar foods in an unfamiliar environment. A study was performed, for example, in which glutamate was served in capsules, with a placebo also being given, to volunteers who thought they were sensitive to glutamate. The administration of glutamate did not induce undesirable effects in them any more frequently than the placebo. In 1969, Olney (1969) published a report in which monosodium glutamate was allegedly responsible for brain damage, obesity and other disorders. These studies were also performed on (newborn) mice. A direct correlation between the intake of monosodium glutamate in food and adverse reactions has not been confirmed by scientific studies.

## The natural occurrence of glutamate in food

Glutamate is contained naturally in food or is added to food as a flavour enhancer. Man consumes around 10 g of glutamate in bound form and around 1 g in free form in food from natural sources daily. Glutamate occurs in large concentrations (more than 0.1%) in the majority of mushrooms, which gives them their characteristic flavour, and in certain cheeses (Parmesan and Roquefort, in particular) and ripe tomatoes. Large concentrations are found in soya sauce and soup seasonings. Only free glutamate has an influence on taste. The glutamate content in selected foods is given in Table 1 (Bellisle et al. 1999).

## Glutamate as an additive in the legislation

Glutamic acid and its salts (E620 – E625) are among the most widely studied food additives. Food additives are the responsibility of the Joint Food and Agriculture Organisation of the United Nations and the World Health Organisation Expert Committee on Food Additives (JECFA). Evaluation of the safety of monosodium glutamate by the JECFA was performed together with a group of related compounds, i.e. L-glutamic acid and its ammonium, calcium, potassium and sodium salts. These substances were first evaluated at the 14$^{th}$ and the 17$^{th}$ sessions in 1971 and 1974. An extensive study undertaken under the auspices of the World Health Organisation (WHO) and the Food and Agriculture Organisation (FAO 1987) did not, however, confirm any serious effect of glutamate on human health. The finding that a level of 120 mg·kg$^{-1}$ bodyweight (in addition to the natural intake in unmodified foods) is entirely without problem was published (WHO 1988). In view of the absence at that time of data on its intake in infants, and with a view to the finding that neonatal rodents seem to be more sensitive to the neurological effects of high levels of glutamate than adults, it was stated that the ADI does not apply to children less than 12 weeks of age. The Scientific Committee on Food of the European Commission (SCF) re-examined the given data in 1991 and reached conclusions similar to those of the JECFA (Walker and Lupien 2000).

At the present time, glutamate is an approved additive for use in food in the EU in accordance with Regulation (EC) No. 1333/2008. The conditions for its use are laid out

Table 1. Glutamate content in selected foods (Bellisle et al. 1999)

| Food | Bound glutamate [mg·100 g$^{-1}$] | Free glutamate [mg·100 g$^{-1}$] |
|---|---|---|
| | Fish | |
| Cod | 2 101 | 9 |
| Salmon | 2 216 | 36 |
| | Vegetables | |
| Peas | 5 583 | 200 |
| Maize | 1 765 | 150 |
| Spinach | 289 | 39 |
| Beet | 256 | 30 |
| Tomatoes | 238 | 140 |
| Carrot | 218 | 33 |
| Onion | 208 | 18 |
| Pepper | 120 | 32 |
| | Dairy products | |
| Cow's milk | 819 | 2 |
| Breast milk | 229 | 22 |
| Parmesan | 9 487 | 1 200 |
| Camembert | 4 787 | 390 |
| | Eggs / Meat | |
| Eggs | 1 600 | 23 |
| Chicken | 3 309 | 44 |
| Duck | 3 336 | 69 |
| Beef | 2 500 | 33 |
| Pork | 2 325 | 23 |

in the Regulation (EU) No. 1129/2011. According to this regulation, a specific maximum level of 10 g·kg$^{-1}$ individually or in combination, expressed as glutamic acid, is stipulated for E621. It is permitted for use in, for example, the following foods – salt substitutes, flavourings and seasonings (quantum satis = a sufficient quantity). Consumption of glutamate as an additive has risen and amounts to two million tons a year globally (Sano 2009).

There is no particular risk of the given doses of glutamate being exceeded, as the use of high concentrations does not further improve the taste of food. On the contrary, a worsened flavour described as metallic, sickly sweet, bitter, etc. is described, for which reason it is generally added to food at an amount of 0.1 – 0.8% by weight (Chi and Chen 1992).

## Interesting sensory studies in recent years

Umami substances are generally known to be effective flavourings for savoury foods such as meat, fish, seafood, vegetable foods and mixed products made from the given items, though they remain ineffective in sweet and fruit dishes. The relationship between individual taste substances is being subjected to detailed study as they are generally present in foods in large numbers and various concentrations and other factors may also effect the intensification or suppression of subsequent taste.

In the 1960s, Kuninaka (1967) described the taste synergy between glutamate and nucleotides. He demonstrated that mixing glutamate and 5'-ribonucleotides significantly improves the intensity of the taste of the mixture. The detection threshold for MSG is 0.012% by weight and is reduced markedly in the presence of inosine-5'-monophosphate

(IMP). This is caused by the synergetic effect between MSG and IMP. Similar synergetic effects are known to occur in other substances, e.g. sweet substances, though the most pronounced synergetic effects have been found in substances displaying the umami taste. The taste of monosodium glutamate in food is significantly reinforced by the concurrent presence of extremely small quantities of 5'-nucleotides. The proportion of MSG to nucleotides generally falls within a range of 100:1 to 50:1 (Yamaguchi and Ninomiya 1998).

The bitterness of caffeine, for example, is inhibited by the sweetness of saccharose. Interactions of this kind are also being studied in the umami taste, principally its ability to suppress the bitter taste. Suppressing the bitter taste is important because bitterness has a negative hedonistic effect on the acceptance of food (Kim et al. 2015). This has also been confirmed by the work of Santos et al. (2014) who replaced sodium chloride (NaCl) in a product with potassium chloride because sodium chloride is the main source of sodium in the human diet. An increased intake of salt is associated with high blood pressure. In recent years, the WHO and other public health organisations and regulatory agencies have recommended reducing sodium intake. This has also increased demand for meat products with a lower salt content. Research has, however, shown that reducing NaCl may alter the quality of fermented, cooked and dried meat products as sodium chloride ensures microbiological stability, reduces water activity, contributes to the solubility of myofibrillar proteins and develops aroma and structure. For this reason, attention has focused on the effect of the addition of monosodium glutamate and other umami substances on the quality of fermented salamis in which 75% of the NaCl was replaced with KCl and in which it was necessary to mask the bitter taste. The addition of sodium glutamate proved sufficient to eliminate the defect caused by replacing 75% of NaCl with KCl.

The umami taste is also produced by other substances, and attention is being focused on the peptides that may be responsible for the umami taste. The work by the authors who compared the taste of the peptides responsible for the umami taste isolated from two kinds of ham – Jinhua ham (a Chinese ham) and Parma ham (a western ham) – is interesting. The amino-acid sequence of peptides Cys-Cys-Asn-Lys-Ser-Val (CCNKSV) was isolated from Jinhua ham, and Ala-His-Ser-Val-Arg-Phe-Tyr (AHSVRFY) from Parma ham. Peptides isolated from the hams and synthetic peptides were subjected to sensory evaluation. An electronic tongue, which is an instrument that should enhance sensory studies in the future, was used for sensory evaluation (Santos et al. 2014).

Lugaz et al. (2002) described a new specific type of ageusia (inability to detect taste) in man relating to glutamate (MSG). Four tests were used for differentiation by means of comparison with sensitivity to sodium chloride. Only 73% of 109 evaluators showed sensitivity to MSG markedly higher than their sensitivity to NaCl and, therefore, specific sensitivity to L-glutamate. The remaining 27%, who showed no significant difference in sensitivity to solutions of MSG and NaCl, were considered insensitive (hypotasters). The values of sensitivity between insensitive and sensitive were shown to differ by as much as three orders of magnitude.

## Conclusions

Monosodium glutamate is one of the most widely studied food additives, and scientific studies and their evaluation have demonstrated that it allows safe improvement to the taste of foods. According to the American Chemical Society (ACS), monosodium glutamate has been unjustly presented to consumers as unsafe for too long. The American Chemical Society is a not-for-profit organisation established by the American Congress. It has more than 161 000 members and is the largest scientific society providing access to chemical research through its databases, reviewed journals and scientific conferences. In a new video launched in August 2014, the ACS corrects the myths about MSG and explains

the "scientific consensus that this substance enhances taste and is completely safe for the majority of people." A great deal of interesting information can be read on the webpages devoted to glutamate, which are administered by the International Glutamate Information Service (IGIS). The Society for Research on Umami Taste, established in 1982, is also engaged in the research activities.

**References**


Balazs R, Bridges RJ, Cotman CW, Cotman CA 2010: Excitatory amino acid transmission in health and disease. Oxford Scholarship. Available at: http://www.oxfordscholarship.com

Bellisle F 1999: Glutamate and the UMAMI taste: sensory, metabolic, nutritional and behavioral considerations. A review of the literature published in the last 10 years. Neurosci Biobehav R **23(3)**: 423-438

Chaudhari N, Landin AM, Roper SD 2000: A metabotropic glutamate receptor variant functions as a taste receptor. Nat Neurosci **3(2)**: 113-119

Chi SP, Chen TC 1992: Predicting optimum MSG and NaCl concentrations in chicken broth as affected by spice addition. J Food Proc Preserv **16(5)**: 313-326

Commission Regulation (EU) No. 1129/2011 of 11th November 2011 amending Annex II to Regulation (EC) No. 1333/2008 of the European Parliament and of the Council by establishing a Union list of food additives

Regulation (EC) No. 1333/2008 of the European Parliament and of the Council of 16th December 2008 on food additives

Hons J 2000: Nové možnosti farmakologického ovlivnění glutamátergního systému u schizofrenie. Čes a slov Psychiat **2**: 85-90 (In Czech)

Kim MJ, Son HJ, Kin Y, Misaka T, Rhyum R 2015: Umami – bitter interactions: The suppression of bitterness by umami peptides via human bitter taste receptor. Biochem Biophys Res Commun **456(2)**: 586-590

Kuninaka A 1967: A flavor potentiator. Schults HW, Day EA, Libbey LM eds. The chemistry and physiology of flavors. AVI Publ Westport, 517-535

Kwok RHM 1968: Chinese restaurant syndrome". N Eng J Me **18(178)**: 1533-4406

Lucas D R, Newhouse JP1957: The toxic effect of sodium L-glutamate on the inner layers of the retina. AMA Arch Ophthalmol **58(2)**: 193-201

Lugaz O, Pillias AM, Faurion A 2002: A new specific ageusia: some humans cannot taste L-glutamate. Chem Senses **27(2)**: 105-15

Nelson G, Chandrashekar J, Hoon MA, Feng L, Zhao G, Ryba NJP 2002: An amino-acid taste receptor. Nature **416**: 199-202

Olney JW 1969: "Brain lesions, obesity, and other disturbances in mice treated with monosodium glutamate". Sci **164**: 719-721

Rezaei R, Knabe DA, Tekwe CD, Dahanayaka S, Ficken MD, Fielder SE, Eide SJ, Lovering SL, Wu G 2013: Dietary supplementation with monosodium glutamate is safe and improves growth performance in postweaning pigs. Amino Acids **44(3)**: 911-2351

Sano C 2009: History of glutamate production. Am J Clin Nutr **90(3)**: 728S-732S

Santos Dos BA, Campagnol PC, Morgano MA, Pollonio MA 2014: Monosodium glutamate, disodium inosinate, disodium guanylate, lysine and taurine improve the sensory quality of fermented cooked sausages with 50% and 75% replacement of NaCl with KCl. Meat Sci **96(1)**: 509-13

Truthinlabeling "The truth, the whole truth, and nothing but the truth about MSG. Available at: http://www.truthinlabeling.org

Van Den Oorad AHA, Van Wassenaar PD 1997: Umami peptides: assessment of their alleged taste properties. Eur Food Res Technol **205(2)**: 125-130

Walker R, Lupien JR 2000: The safety evaluation of monosodium glutamate. J. Nutr **130(4)**: 1049S-1052S

WHO 1988: Toxicological evaluation of certain food additives. Food Additives Series 22, 31th Meeting of the Joint FAO/WHO Expert / Committee on Food Additives, Cambridge Univ Press, 23-48

Yamaguchi S, Ninomiya K 2000: Umami and food palatability. J Nutr **130(4)**: 921S-926S

Zimmerman FT, Burgemeister B 1959: A controlled experiment of glutamic acid therapy. AMA Arch Neur Psych **81(5)**: 639-648