REVIEWS

A Mini Review About Monosodium Glutamate

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Abstract

Monosodium glutamate (MSG) is salt of sodium and glutamic acid. It is most commonly known as a flavouring enhancer in food processing, which provides umami taste that intensifies the meaty, savory flavor of food, as naturally occurring glutamate does in foods such as stews and meat soups. The amino acid glutamic acid it is naturally presents in food. Globally, commercial MSG's consumption is increasing, markable high in Asia. Likewise, its production has known improvements regarding both method and technical equipment. Although MSG's safety was evaluated by international organizations (EFSA, FDA) as safe and the limits were set up, there are studies concern about its side effects such as obesity, asthma, migraine headache, etc. The European Union classifies it as a food additive permitted in certain foods and subject to quantitative limits. The increase in commercially MSG use has raised the concern of both scientists and consumers about its safety. Therefore, due to a need of full comprehension about MSG, it is necessary to give more attention in studying it. Advantage in the development of analysis methods and technical equipments should be exploited to obtain higher accuracy result. This review provides a brief and general information about MSG with updates in its research.

Keywords: flavour, food additives, food safety, monosodium glutamate

Introduction

Nowadays, food additives aren't a new term anymore. Every day, a huge amount of food is needed to meet requirement of the world hunger, which is increasing rapidly out of control. Food additives have an important role in handling this challenge. By supporting the production, they help producers to ensure not only quantity but also quality of the products when they come to consumers hands. According to EC 1333/2008 'food additive' shall mean any substance not normally consumed as a food in itself and not normally used as a characteristic ingredient of food, whether or not it has nutritive value, the intentional addition of which to food for a technological purpose in the manufacture, processing, preparation, treatment, packaging, transport or storage of such food results, or may be reasonably expected to result, in it or its by-products becoming directly or indirectly a component of such foods. Their two basic functions are assuring the inocuity of foodstuff and preserving their sensorial qualities. Depending on the function they have in the product, food additives are divided in 27 classes, among these: preservatives, antioxidants, emulsifiers, and so on (Pașca et al., 2018).

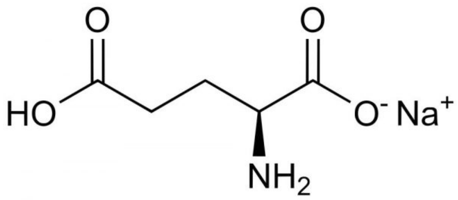

Figure 1. MSG's molecular formula (Uses, effects and properties of monosodium glutamate (MSG) on food & nutrition, n.d.)

Table 1. Free glutamic acid content in foods (Cebi et al., 2018)

Food item	Free glutamic acid (mg/100g)
Cow's milk	2
Human milk	22
Cheddar cheese	182
Chicken	44
Beef	33
Pork	23
Tomato	246
Potato	180

Flavour enhancer is one of food additives groups. Even though, they don't have their own taste or flavour, these substances have the ability to improve or enhance the original taste/flavour of food in which they are added. The best-known representative for this group is glutamic acid and its salts, especially monosodium glutamate. They are now used widely as food additives, but still, there are questions about its safety to human body. This review provides a brief and general information about MSG with updates in its research, without being exhaustive (*Regulation (EC) No 1333/2008 of the European Parliament and ... - EUR-Lex*, n.d.).

Glutamate and monosodium glutamate

Monosodium glutamate (MSG), also known as sodium glutamate is the sodium salt of L-glutamic acid, an amino acid. Its IUPAC's name is sodium 2-aminopentanedioate, with one sodium atom replaces for one hydrogen atom in carboxyl group. Both in the International Numbering System (INS) and the European system for food additives, MSG has a code number 621 (Codex, 1989).

Natural occurrence

In food industry, the term "glutamate" refers to all the forms of glutamic acid and its salts, which is one of the most common amino acids found in nature. It is known as a non-essential amino acid and can be synthesized by cells. It usually exists in two forms: bond and free. Glutamate is found in many foods, especially those rich in protein. In the the structure of proteins and peptides, glutamate is bonded with other amino acids. In bonded form, it is tasteless. Free glutamate, has the "umami" taste, being present in various foods, in different concentration ranges, some of which are naturally rich in glutamate. Umami taste has been widely accepted as the 5th basic form of taste, along with the other 4 basic tastes of sweet, sour, salty and bitter (Zhang et al., 2017). High levels of free glutamate are contained in seaweed, cheese (roquefort and parmesan), fish sauce, tomato, mushrooms, broccoli, potato, etc. (Kochem & Breslin, 2017; Stańska & Krzeski, 2016). Generally, some kinds of protein hydrolysis increase the content of glutamate, such as cured cheese or ham.

History

The name "glutamate" is derived from wheat gluten, when a German chemist Karl Heinrich Ritthausen conducted experiments with this material and sulfuric acid, to first discover and identify L-glutamic acid (the natural form of glutamate) in 1866. Until 1908, the most outstanding property of glutamic acid and its salts were found out by a Japanese scientist Kikunae Ikeda. It started from an observation concerning the dominant taste of dashi, a Japanese soup base. According to Ikeda, the taste of dashi is mild but clearly distinct from the four basic tastes. After a process of isolation from the main ingredient of dashi, seaweed *Laminaria japonica*, he discovered

Table 2. Some physical properties of MSG (PubChem)

Property	Measurement
Molecular weight	169,11 g/mol
Hardness	Hard
Appearance	Solid (Room temperature)
Color	White
Odor	Odorless
Form	Crystalline powder
Melting point	232°C
Solubility in water	~740 g/L (25 °C)

that the substance in charge of that special taste is L-glutamic acid (Lindemann, 2002). Its taste was named umami, a word derived from the Japanese adjective *umami* (delicious). Its salts were also researched and concluded that all of them confer the umami taste. In 1909, monosodium glutamate was commercially produced with the name Ajinomoto, the world's first umami seasoning. Nowadays, the brand has expanded its presence in 35 countries and regions throughout the world, bring this additive to table of every family.

Physical and chemical properties

Monosodium glutamate particularly is an odorless white crystalline solid, being usually available in form of a monohydrate. It has high water solubility (~740 g/L) but it is practically insoluble in organic solvents. This substance isn't hygroscopic or affected by light and it has a high melting point. Therefore, it can maintain its quality for long-term even if it is stored at room temperature. The MSG has high stability to high temperature (it decomposed above 350°C), this property making it be stable during normal food processing. In solution, MSG is an ampholyte, the acting as an acid or as base depending on pH. When glutamate is free from the weak ionic bond between sodium and glutamate, it can participate in a variety of reactions, under specific conditions. For instance, in the presence of reducing sugars and high temperature, the Maillard reaction can occur (Giovanni, 2002).

Food processing applications

In food processing, MSG is used as additive, being a flavour enhancer and providing the umami taste. It is contributing to the improvement of few flavour characteristics such as complexity, mouth-fullness, continuity and mildness. MSG has also the ability to mask or suppress off-flavours, undesirable tastes due to unintentional changes. A lot of food products are processed at high temperatures, which may lead to the decomposition or losses of aroma substances. Moreover, MSG is water-soluble, hence, it can be mixed easily in food, during or after the thermal treatment. Moreover, the processing of foods (e.g. cooking, ripening) has as result an increase in glutamate due to the release of amino acids by the hydrolysis of proteins. On the other hand, by increasing the level of glutamate, the content of added sodium chloride may be lowered. Adding salt to food is a traditional way to enhance the flavour and richness of products. But high salt intake badly effects the health causing cardiovascular system and kidney problems. Due to glutamate, the sodium content of recipes can be lowered by up to 40% but still keep the palatability, which meets the requirement of both producers and consumers (Yamaguchi & Takahashi, 1984). However, adding glutamate doesn't always mean enhancing flavour. The use of an excessive amount of glutamate, much higher than the limit, may have a negative impact on the taste. The recommended amount of added glutamate to enhance the taste of food is at 0.1–0.8% by weight, which is related to the amount of natural free L-glutamate in tomato or parmesan cheese (Beyreuther et al., 2007).

Due to our tongue design, humans can feel tastes while foods are masticated. Surface of tongue contains special tissues called papillae, which act as taste detectors, consisting in dozens of receptors. From these receptors, information is transmitted to the brain, and we perceive the taste of the food. In this case, MSG is a molecular stimulus, which is detected by most of the taste buds on the tongue and on other regions of the mouth. By stimulating glutamate taste receptors on the tongue, MSG enhances the savory taste (known as umami) and causes foods to elicit a "meatier" flavor. Researchers have found that

Table 3. Detection thresholds for five taste substances in water % (wt./v) (Yamaguchi & Takahashi, 1984)

MSG	Sucrose	Sodium Chloride	Tartaric Acid	Quinine Sulfate
0.012	0.086	0.0037	0.00094	0.000029

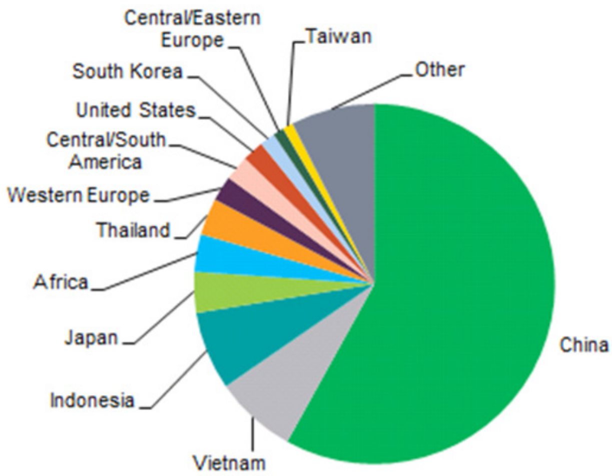

Figure 2. World consumption of MSG in 2018 (IHS Markit)

receptors that are responsible to identify the umami taste as modified forms of mGluR4, mGluR1 and taste receptor type 1 (T1R1 + T1R3) can be found in almost every region of the tongue (Uses, effects and properties of monosodium glutamate (MSG) on food & nutrition, n.d.) (Roper & Chaudhari, 2017). The MSG sensibility also varies widely among individual consumers. However, its presence is generally considered to be easily recognized with small concentration (Yamaguchi & Ninomiya, 2000). According to Table 3, reported detection threshold for MSG is as low as 0.012 g/100 mL, or 6.25 ×10-4 M. The threshold for MSG was found to be lower than the threshold for sucrose, approximately equal to NaCl, and higher than the thresholds for quinine and tartaric acid. The umami taste will have stronger intensity when MSG acts in synergy with disodium guanylate (GMP) or disodium inosinate (IMP). The detection threshold of MSG is therefore markedly lowered (Yamaguchi, 1967).

MSG consumption

Most of MSG is used in food industry and mainly for processing of convenience, instant and fast foods. It is also directly sold to the consumers and institutional foodservice providers as condiments and seasoning blends. In addition, MSG is used in animal feeds in a negligible amount.

MSG production capacity is largely concentrated in Asia, as well as the highest consumption in 2018. In particular, China takes the lead in production and consumption of MSG in the world, followed by few Southeast Asian countries such as Indonesia, Vietnam, and Thailand. This growth can be explained by the improved living standards, dietary culture and patterns, ongoing development of the food processing industry, and the increase of population and urbanization. Key manufacturers in the monosodium glutamate market like Ajinomoto Company, Kyowa Hakko Kogyo Co Ltd, Vedan Vietnam Enterprise Corporation Ltd also have their origin in Asia. The Ajinomoto Company is the world's largest manufacturer of sodium glutamate, with manufacturing sites in Peru, Brazil, Japan, the United States, China, and France among others.

Besides Asian region, other regions accounted for a small share of world MSG consumption. Some developed countries such as Western European countries, United States and Canada, have tendency to care more about health and the preference for clean label foods is expected to reduce the MSG consumption in these regions (Asioli et al., 2017).

Toxicity and safety

MSG has been used for more than 100 years to season food, with a number of studies conducted on its safety (Bera, 2017). Concern about the hazard of MSG for health has been debated all over the world for many decades. The concern started from a syndrome named "Chinese Restaurant Syndrome", which was first described by Kwok in 1968. It includes a group of adverse symptoms that occur in some people after eating food from Chinese restaurants. Their symptoms may include headache, numbness, dizziness, palpitation, chest pain, back pain, etc.(Freeman, 2006; Niaz et al., 2018; Williams & Woessner, 2009). Some suggested that these symptoms may be caused by MSG, which is used generously to a great extent for seasoning in Chinese restaurants. So far, there have been many research studies regarding this issue but no consent has been reached. Further studies are required to evaluate whether or not a causal relationship exists between MSG ingestion and headache (Obayashi & Nagamura, 2016b). Therefore, nowadays, there are two main opinions about MSG: harmful and harmless.

Since 1958, glutamate has been listed as a Generally Recognized as Safe (GRAS) substance by the U.S Food and Drug Administration (FDA). Its safety is proven by numerous biochemical, toxicological and medical studies, hence, nowadays it is used as a food ingredient (USDHHS, 1958). Until 1971, MSG's safety was first officially evaluated by JECFA. At that time, an Acceptable Daily Intake (ADI) of 0–120 mg/kg body weight was set.

The safety of glutamic acid and its salts as flavor enhancers was evaluated by the Joint FAO/WHO Expert Committee on Food Additives in 1971, 1974 and 1987, and it allocated an "acceptable daily intake (ADI) not specified" based on the conclusion that the total intake of glutamate arising from their use at levels necessary to achieve the desired technological effect and from their acceptable background in food do not represent a hazard to health(Obayashi & Nagamura, 2016a). A numerical ADI was considered unnecessary, hence, glutamate group was listed in ''ADI not specified'' group (JECFA, 1988). The Scientific Committee for Food of the Commission of the European Communities (SCF) (1991) conducted a similar safety evaluation reaching the same conclusion, namely that for glutamate an ''ADI not specified'' could be allocated. It is set considerate to very low toxicity and no toxic effects of MSG are seen during animal testing when large amounts are given in the diet. In 2017, the European Food Safety Authority (EFSA) re-evaluated the safety of glutamate and an "acceptable daily intake" of 30mg per kilogram of body weight for MSG and related glutamates was established (EFSA, 2017) (Zanfirescu et al., 2019). This safe level of intake is based on the highest dose at which scientists observed no adverse effects on test animals in the toxicity studies.

On the opposite side, MSG is described as having potential side effects related to few health problems. A study by He et al., 2008 from China concluded that glutamate intake may indirectly increase the risk of overweight in humans. The study of Geha et al., 2000 also tried to find if there is any reaction of body to glutamate. Although there were claims that glutamate might cause headache or other symptoms, they failed in proving that these were reproducible symptoms (Bera, 2017). Besides, MSG was suspected to cause asthma (Woods et al., 1998). This study showed the alarming results with 13 from the total of 32 subjects experiencing a reduction of breathability. However, other studies (Schwartzstein et al., 1987) and (Germano et al., 1991) with similar protocol didn't obtain the same results, proving that there isn't a consistent relationship between glutamate and asthma symptoms. Migraine headache worsening is also one of the effects that MSG is described to trigger. However, this effect isn't supported by any clinical data (S. Jinap & Hajeb, 2010).

Furthermore, the numerous negative effects reported by preclinical studies (oxidative stress, hepatotoxicity, neurotoxicity, cardiac toxicity, impaired fertility, tumor develpoment, pathological fetal development, inflammatory response) (Ataseven et al., 2016; El-Meghawry EL-Kenawy et al., 2013; Eweka et al., 2011; Eweka & Om'iniabohs, 2011; Hernández-Bautista et al., 2014; Khalaf & Arafat, 2015; Kohan et al., 2016; Matousková et al., 2015; Nakadate et al., 2016; Sadek et al., 2016; Swamy et al., 2013) are a matter of debate, as several shortcomings of these studies are apparent, namely: lack of adequate control groups, small sample size, methodological flaws, lack of dosage accuracy, or usage of extremely high doses far exceeding those unattained in normal diets. The use of MSG still remains a subject of controversy (Zanfirescu et al., 2019).

Different reports revealed increased hunger, food intake, and obesity in human subjects. Limited studies have been carried out on humans to check possible hepatotoxic, neurotoxic, and genotoxic effects of monosodium glutamate. The literature showed that increased consumption of MSG may be associated with harmful health effects. So, it is recommended to use common salt instead of it (Kazmi et al., 2017). More studies with robust methodology are required to assess causal links to disease (Chinna & Karupaiah, 2013). In spite of the controversies over safety of MSG, has not yet been generally accepted to be toxic to humans (Rim, 2017).

Although reports informed about adverse effects in some individuals exposed to glutamate, there still hadn't been any officially scientific evidence linking dietary glutamate or other forms of free glutamate to any serious, long-term medical problems (Zanfirescu et al., 2019).

Potential benefits

For all the flak it receives, MSG may have some indirect health benefits. MSG contains 61% less sodium than table salt. One study found that partially swapping table salt for MSG could reduce the sodium content of a soup by 32% without negatively affecting its taste (Selamat Jinap et al., 2016). A review mentions the above study with several others that have also used MSG to preserve taste while reducing sodium in soups, stocks, seasonings, instant noodle products, meats, and snacks like chips and nuts. Taste was best preserved when salt was only *partially* replaced with MSG (Maluly et al., 2017). Also, there are some evidence suggests potential benefits for elderly people with appetite issues (Yamamoto et al., 2009).

Regulations

Those arguments above have raised the awareness of consumers in MSG consumption. As far as consumers are concerned, the EU has limited the content of L-glutamate and salts present in food products, both individually or in combination (LMA ≤ 10g/kg). For salt substitutes, seasoning and condiments, the regulation specifies the use as quantum satis (sufficient to obtain the desired technological effect) (Council of European Union, 2011). In America, monosodium glutamate used as an ingredient in food shall be declared by its common or usual name monosodium glutamate (Code of Federal Regulations- CFR, 2019). Some of the glutamate in foods is in a "free" form; and only this free form of glutamate can enhance the flavor of foods (e.g. tomatoes, certain cheeses, and fermented or hydrolyzed protein products: soy sauce and soy bean paste, hydrolyzed yeast). While FDA requires that these products be listed on the ingredient panel, the agency does not require the label to also specify that they naturally contain MSG (USFDA, 2012).

In contrast, few organizations deal with MSG negatively. GIMDES, the Halal Certifying Body in Turkey, has assumed that MSG is harmful to human health and must not be used in food production. Therefore, this organization refuses to certified any food product that contained MSG. In Pakistan, the government has also banned on all the trading activities of monosodium glutamate salt. These announce to strongly influence the acceptability of products containing added glutamate. Due to the preference of consumers on products which don't contain glutamate, many manufacturers are labeling their products as ''No MSG'', ''No MSG Added'' or ''No Added MSG''. Consequence of such labels is that they generate and reinforce beliefs that glutamate is harmful or an unsafe ingredient (Selamat Jinap et al., 2016). Label information has been shown to create expectations for a food's sensory properties and acceptability, and influence evaluations of the product.

MSG production

MSG commercial production began early in 1909, when it became a seasoning and was named AJI-NO-MOTO, which is now one of the most well-known brands. There are three general methods in glutamate industrial production: extraction, chemical synthesis and fermentation.

Extraction method

Extraction is a classic method, which exploits natural sources to obtain amino acids. It is basically a hydrolysis process of protein with the presence of inorganic acids as the hydrolyzing agent. After hydrolyzing, filtration and crystallization are repeatedly performed to isolate amino acids from protein hydrolysate. This is based on the fact that at different pH, each crystalline form of glutamate has different solubility. For glutamate extraction, wheat gluten is an industrially ideal source due to its high content of L-glutamine. The total glutamate content of protein in wheat gluten is approximately 36% by weight. The process includes 3 main steps: extraction, isolation and purification.

Due to the insolubility in water, gluten is obtained by washing the starch from dough. Then, crude gluten is hydrolyzed by heating with aqueous HCl. A part of amino acids will transform into the hydrochloride form, others will react with carbohydrates resulting a black residue, which needs to be removed. Among the hydrochlorides of amino acids, L-glutamic acid hydrochloride is impressively less soluble in concentrated HCl, make it easier to be separated. Therefore, after filtering, the protein hydrolase is subsequently concentrated under reduced pressure, the addition of concentrated HCl in purpose to lower the pH. Finally, cooling allows the L-glutamic acid hydrochloride salt to crystallize.

In the isolation step, the crystal is separated from the liquid and redissolved in water. By adding alkali hydroxide of sodium or potassium, L-glutamic acid isoelectric point is obtained (approx. 3.2). There are 2 polymorphs in L-glutamic acid crystals: metastable α-form and plate-like β-form. The α-form grows better than the β-form in solution containing other amino acids (Sano, 2009a)a professor at the Tokyo Imperial University, began his research to identify the umami component in kelp. Within a year, he had succeeded in isolating, purifying, and identifying the principal component of umami and quickly obtained a production patent. In 1909 Saburosuke Suzuki, an entrepreneur, and Ikeda began the industrial production of monosodium l-glutamate (MSG. Therefore, at this pH, mainly the crude L-glutamic acid in the α-form will be obtain.

The crude separated L-glutamic acid in the presence of sodium bicarbonate in water becomes monosodium glutamate solution. The solution is simply decolorized by activated carbon and filtering. Monosodium L-glutamate (MSG) is formed after the concentration of the solution is concentrated by heating and cooled down.

The method is easily controlled and requires simple equipment, hence, it is suitable to be apply in handmade or small-scale facilities. Raw materials are cheap and highly adequate for supplying. The dominance of α-form growth when crystalline improves purity because the crystals do not contain other amino acids. Besides wheat starch, another protein source that could be used in MSG production, are de-oiled soybean flake or waste products from beet sugar industry. The method has several disadvantages such as low productivity, environmental and safety problems. Strong acid as HCl will gradually erode equipment, reduce their using duration. In addition, vapors containing hydrogen chloride gas pose some safety issues on workers' health.

Chemical synthesis method

Due to increasing demand for MSG, besides extraction, chemical synthesis, along with fermentation, are other ways to commercially manufacture MSG. There are numerous potential chemical starting materials to synthesize glutamic acid such as acrylonitrile, acrylates, acetoacetic ester, butyrolactone, etc. Among them, acrylonitrile is the most preferred for manufacturing, due to its oxo reaction.

This process is prominent because acrylonitrile is an inexpensive chemical. Other materials such as carbon monoxide, hydrogen cyanide, ammonia, and water are also low-cost. Most other processes involve appreciable molecular weight losses of the reagents used. Another advantage of the process is the possibility of recovery of the needed hydrogen cyanide as a by-product from the propylene-ammonia route to acrylonitrile. Also, it is a continuous operation, with all materials present in a liquid phase that is contained at high temperature under pressure (Sano, 2009b)a professor at the Tokyo Imperial University, began his research to identify the umami component in kelp. Within a year, he had succeeded in isolating, purifying, and identifying the principal component of umami and quickly obtained a production patent. In 1909 Saburosuke Suzuki, an entrepreneur, and Ikeda began the industrial production of monosodium L-glutamate (MSG. This partly ensures the safety for workers when acrylonitrile is known as having acute effects via inhalation exposure. The process has a 66% efficiency. The oxo reaction made the synthesis of β-cyanopropionaldehyde from acrylonitrile possible, which is the key intermediate for the synthesis of glutamic acid. β-Cyanopropionaldehyde is then treated with hydrogen cyanide and ammonia, followed by simple acidic or basic hydrolysis to obtain DL-glutamic acid.

The biggest disadvantage of chemical synthesis is that the product exists as a racemic mixture, including two enantiomeric forms, both D and

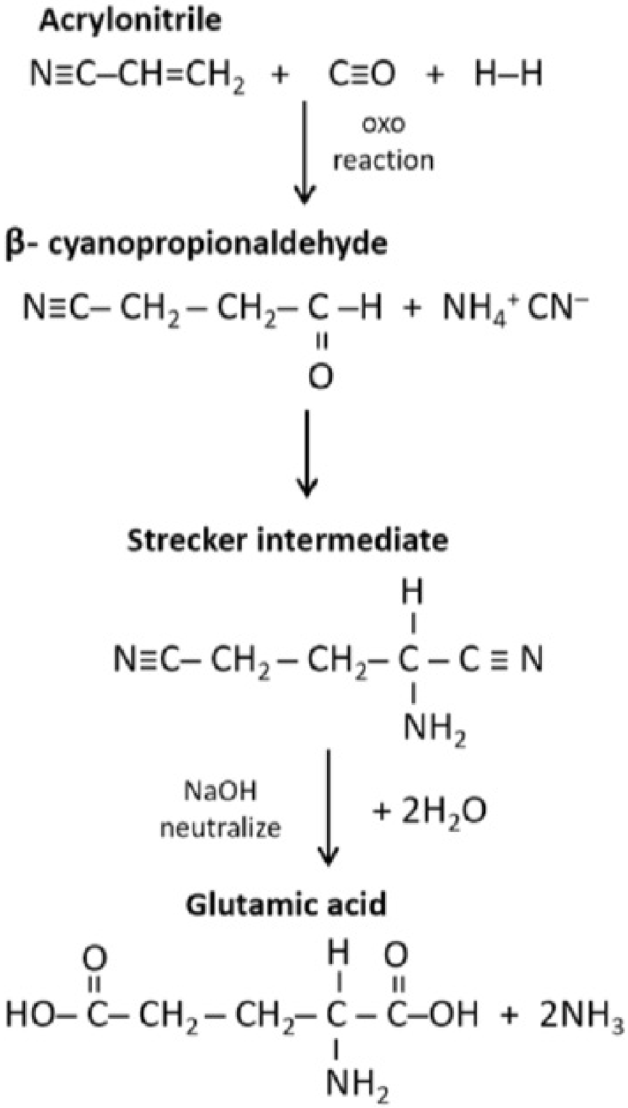

Figure 3. Chemical glutamic acid synthesis process from acrylonitrile (after Ault, 2004)

L isomer. In the case of glutamic acid, L isomer is desired, meanwhile, D isomer is tasteless. Therefore, to obtain the pure final product, L isomer must be isolated from the racemic mixture.

Fermentation method

In early years of MSG's commercial manufacture, extraction and chemical synthesis were mainly used, although, there were limits which concerned low yield, environmental unfriendly process and health concerns. Plus, the increasing demand of consumers, it directed the producers to prefer biosynthesis method, fermentation, which meets most of the requirements. In this method, L-glutamic acid is synthesized in large amount by specific microorganism strains cultures. Since the first industrial fermentation technology for L-glutamate was developed, many bacteria useful in glutamate production have been isolated, including *Corynebacterium glutamicum*, *Brevibacterium lactofermentum*, and *Brevibacterium flavum* (Sano, 2009a)a professor at the Tokyo Imperial University, began his research to identify the umami component in kelp. Within a year, he had succeeded in isolating, purifying, and identifying the principal component of umami and quickly obtained a production patent. In 1909 Saburosuke Suzuki, an entrepreneur, and Ikeda began the industrial production of monosodium l-glutamate (MSG. These bacteria can utilize various types of sugar (e.g. glucose, fructose, sucrose, maltose, ribose, etc.), for cell growth and L-glutamic acid biosynthesis. For industrial production, starch (tapioca, sago, etc.), cane molasses, beet molasses, or sugar is generally employed as the carbon source. A suitable source of nitrogen is essential for L-glutamic acid fermentation. Ammonium salts such as ammonium chloride or ammonium sulfate and urea are assimilable. However, the ammonium ion concentration needs to be controlled as its detriment to both cell growth and product formation. Also, the pH tends to become acidic when ammonium ions are assimilated and L-glutamic acid is excreted. Gaseous ammonia has a great advantage over aqueous bases in maintaining the pH at 7.0–8.0, the optimum for L-glutamic acid accumulation (Shyamkumar et al., 2014)3 and 5% sodium alginate concentrations were used for production and reusability of immobilized cells for 5 more trials. Results: The results revealed that 2% sodium alginate concentration produced the highest yield (13.026±0.247 g/l by C. glutamicum and 16.026±0.475 g/l by mixed immobilized culture. The process includes 3 main steps: fermentation, isolation and purification. Fermentation processes occurs in clean and sterilized tanks, which contain starter culture, nutrient source as glucose and ammonia, growth factors as minerals and vitamins. Variables like pH, temperature, addition of nutrient and dissolved oxygen concentration must be controlled. Since the fermentation is aerobic, oxygen is continuously supplied and each tank has paddles for stirring. After the glutamate accumulation reaches an adequate amount, the tank is centrifuged and filtered to remove microorganism and impurities. The clear liquid is then concentrated under reduced pressure, the pH is adjusted to 3.2, allow the crystallization as described above.

The disadvantage of this method is that it is a batch process, which may lead to big loss if the process is not controlled properly. However, it just produces the desired L isomer of glutamic acid and the yield can reach as great as 60%. The food industry try to avoid this problem by production of fertilizers from MSG production. MSG industry generates organic and nutrients rich waste resources which can act as a substitute fertilizers and manures to reduce the agricultural costs, soil and water pollution (Singh et al., 2011).

Methods of analysis

The analysis of MSG is complex and there are many studies described concerning of that.

Quantitative analysis

As a substance naturally present in food and also allowed to be used in processing, control and management the content of MSG is extremely important because it relates closely to food safety. Numerous methods of quantitation are described in published articles. A few of them are mostly used currently and worth to be mentioned such as spectrometric (ISO 4134, 1999), flow injection analysis (FIA) technique (Oliveira et al., 2001) and electrophoresis (Aung & Pyell, 2016), using a potentiometric method with a modified multiwalled carbon nanotube based molecularly imprinted polymer (Anirudhan & Alexander, 2015), liquid chromatographic techniques, in particular, high-performance liquid chromatography with various types of detection (UV, fluorescence, etc.) (Veni et al., 2010), determination of glutamate in food samples by heterogeneous membrane with chitosan as ionophore (Isa & Ghani, 2009), or using ninhydrin for color development. In some of these methods, the sample needs a pre-treatment by an enzymatic process. Alnokkari et al., 2013 (Alnokkari et al., 2013) have developed a rapid, sensitive and simple chromogenic method was developed for quantitative determination of monosodium glutamate (MSG) in food samples.

For fast and high accurate evaluation, titration is an efficient method for L-glutamate quantitative analysis. While the Association of Official Analytical Chemists (AOAC) recommends potentiometric titration of previously ion-exchanged MSG, JECFA (1987) proposed the titration with perchloric acid.

Qualitative analysis

For qualitative analysis, methods that are able to separate amino acids in food, are used to detect the presence of monosodium L-glutamate. Paper or thin layer chromatography are recommended as suitable options (FAO/WHO, 2006; Veni et al., 2010).

Besides the laboratory methods that require expensive solvents and equipment, there are also methods for quick test. BioAssay Systems QuantiQuik™ have introduced L-Glutamate quick test strips. The principle is based on the oxidation of glutamate which is catalyzed by glutamate dehydrogenase. The reaction using NAD as a cofactor produces NADH and will reduce a chromogenic reagent. It is convenient due to its

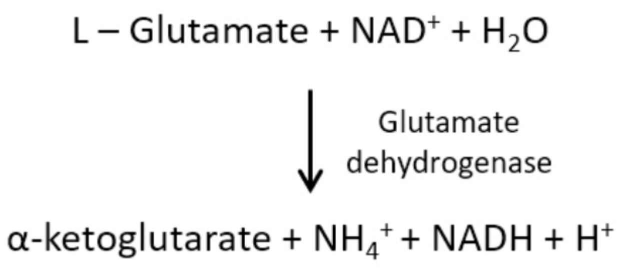

Figure 4. The oxidation of glutamate catalyzed by glutamate dehydrogenase (Veni et al., 2010)

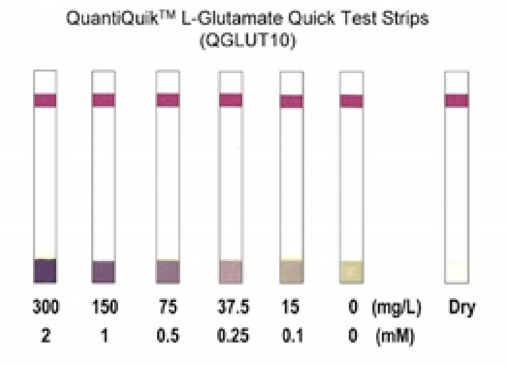

Figure 5. Result reading of L-glutamate quick test strips (BioAssay Systems)

fast, sensitivity and no needed lab equipment, the result can be visual observed. Sample dilution is required and the assay can be performed in under 15 minutes with the use of 20 or 100 µL sample. Wide range of sample can be tested such as instant soup broth, restaurant Pho broth, soy sauce, fish sauce, 2% milk, plasma, serum, and urine.

Conclusions

Monosodium glutamate belongs to "glutamate" group, which is allowed to use as a commercial food additive. It is known as providing umami taste and enhancing food own flavour. Available literature showed that it has a pleasant taste and induced urge to eat more food. The increase in commercially MSG use has raised the concern of both scientists and consumers about its safety. Therefore, due to a need of full comprehension about MSG, it is necessary to give more attention in studying it. More studies are required to assess causal links to disease. Furthermore, intensive research is required to explore MSG related molecular and metabolic mechanisms. Advantage in the development of analysis methods and technical equipments should be exploited to obtain higher accuracy result.

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