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An Overview on World's Most Widely Used Food Additive Monosodium Glutamate (MSG) and its Impact on Human Health

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ABSTRACT

Monosodium glutamate (MSG) is an excellent flavour enhancer used to increase the palatability of food items all over the world. MSG blended food stuff creates 'Umami' taste and this unique taste loves everyone. MSG becomes an essential ingredient for all types of processed foods. The interest of using MSG has been growing rapidly with respect to food processing industry since last 30 years. Many researchers have identified MSG as the most controversial food ingredients for its negative impact towards the human health but this fact is not confirmed completely. Excess consumption of MSG contains food items may cause 'neurotoxicity' and different types of disorder. The present review is mainly focused on commercial importance of MSG and its direct and indirect impacts on health. This specific study has pointed out how obesity and other lifestyle related diseases like, diabetes and cardiovascular disease are increasing rapidly day by day in the Indian continental area, may be linked with excess intake of processed food among the people last 40 years in that region. Thus, MSG intake also creates several lifestyle related disorder indirectly. The aim of this review is to aware people about the role of MSG as a food additive and its negative role on health concern.

KEYWORDS: monosodium glutamate; flavour enhancer; excitotoxin; obesity and diabetes

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1. INTRODUCTION

In the 20th Century, rapid development in the science and technology radically changed all the sectors including food processing and food related industry. Industrialization, urbanisation and digitisation changed our socio-economic status as well as our lifestyle. Modern fast lifestyle enforces us to change our food habits. It also radically affects our food taste. Young generation are now habituated intake more and more processed or packed food i.e. 'ready-to-eat' food not only for 'yummy' taste, also it helps them to maintain their fast lifestyle. To increase the taste, keep freshness or to avoid spoilage of food items by microorganisms, 'food additive' and 'food preservative' are almost essential ingredients of the various processed and packaged food stuff.¹ Food additives are chemical substances which are added in the food items in a definite amount mainly to increase or preserve colour, texture and flavour. Some of them also added as an antimicrobial and antioxidant substance.² Thus in the form of different artificial food additive and food preservative, we also consume chemical substances. Various types of food additive in the different trade name are available in the market and extensively mixed in the food items all over the world. But most of the people especially children are still unaware about the impact of additive to the health concern.^{3,4} Among the various food additive monosodium salt of glutamic acid (MSG) is worldwide famous for its flavour enhancing property. MSG is used extensively in the industrial food processing unit and it is also popular for homemade recipes due to its palatability. MSG is one of the cheapest, common food additives which are available in the market and is used widely in crackers, instant nodules, fries items, soups, sauce, processed meats and salad dressings etc. To flourish the food processing industry in India⁵ and also other parts of the world food additive substances are play an important role.

Glutamic acid is a 'non-essential' amino acid which can be synthesized naturally in our body. Some particular glutamate receptors are identified on the taste buds and also in the stomach.^{6,7} Besides our body, it is also available in tomatoes, broccoli, mushrooms, cheeses, seaweed, nuts, legumes, meats, most dairy products and protein bound foods.^{8,9} Only the free form of glutamate can enhance the flavor of foods which is found naturally in very fractional ratio. Due to the existence of free glutamate ions, soy sauce, soy bean paste and so many other fermented or hydrolyzed protein products becomes so tasty. On the other hand, glutamate is the building blocks of protein and glutamic acid plays crucial role, not only in our metabolism system but also act as neurotransmitters¹⁰ to boost our learning and remembering capability.¹¹

Worldwide MSG is very popular because it can introduced 'Umami' flavour in the food items. This salt is mingled into our daily life food chart either as a hidden ingredient labels or listed under other trade names. However, the intake of glutamate salt in excess amount, especially in the

form of artificial food additive like MSG, may causes neurotoxicity and creates numerous side effects.^{12,13,14} It has been well establish by several scientific analysis and survey that excess consumption of glutamate ion for a ‘MSG sensitive persons’ may be dangerous.¹⁵ Flushing, headache, chest pain, numbness, burning, sweating in or around the mouth are the common symptoms observed due to the regular consumption of MSG.

After the 19th century, multinational ‘food brand’ entered into the Indian market as a part of the globalisation. Fast food and processed food industry becomes one of the fastest growing industry in India. Now, urban Indians are very familiar with western food culture and include them as a part of our daily diet. A huge numbers of peoples, especially ‘young generations’ finish either their breakfast or lunch or dinner with this high calorie ‘Fat food’; such as pizza, pasta, burger, fried chicken, instant noodles, chips, canned food and other processed foods. As a result, significant amount of MSG is entered in our body everyday via these types of food items. A joint report was published by the government of Australia and New Zeeland in 2003 indicated that all types of Chinese based meal contain excess amount of MSG (10 to 1500 mg/100 gm).¹⁶ Due to this reason Chinese soups and noodles are so delicious. That means, MSG like food additive indirectly prompt us to eat this ‘junk food’ regularly, perhaps each and every day. However, excess intake of this fast food without regular workout converted us into obese. The rate of obesity has increased almost double among the Indian population compared to past decade. On the other hand, obesity may be increases the chance of various diseases. Recent survey indicates that India will be the biggest ‘hub’ of the Diabetes Mellitus (type –II) in the Asia within 2020.¹⁷ So, in this situation it becomes the biggest challenge for India, to fight against the obesity as well as several lifestyles related diseases, especially for diabetes. So MSG has some indirect effect to generate obesity and obesity related diseases.

Thus, it is the high time to restrict the use of MSG in the food items. Though, the adverse effect of MSG related research has been carried out since long time but significant evidences in this aspect not yet established completely. This review delineates the details of MSG with respect to food and health. This overview does not mean to be exhaustive but rather aims to present a snapshot of the area in as brief a manner as possible. We hope that the discussions will be helpful to unfold the hidden story of MSG both for the new comers who are new to this field as well as for those who already well-versed in the topics under consideration.

2. CHEMICAL IDENTITY

MSG is a white crystallized, odourless sodium salt of glutamic acid (molecular formula: $C_5H_8NNaO_4$, molecular mass 169, density of $1.538g/cm^3$ & melting point $225^\circ C$).¹⁸ It can exist as

glutamate are produced annually and its global market value increases sharply with a projected annual growth rate of 4 per cent.

Brazil is the world's top producing country of sugar cane which is the main raw material of MSG. Thus, several MSG production company was build up in that region. Japan based company 'Ajinomoto' claims that they have almost 30 per cent share of the market; whereas the China-based Fufeng Group is the largest producer of MSG whereas 'Meihua' is the second largest producer. 'Jiali International Corporation' and 'Shanghai Tuo Dong International Trading Co. Ltd' have also a significant share in the MSG market. Thus still MSG market was dominated by 'Asia Pacific' company.²⁹

4. PROCESS OF PRODUCTION

The manufacturing method of glutamate has been shifted from the extraction method to the fermentation method in the 1960s. '*Corynebacterium glutamicum*', is used as a microorganism in the fermentation process.³⁰ The extracted sugar, after adding fermented microorganism and processed, glutamate is accumulated, concentrated and then crystallised via generic bioprocess flow. The most relevant factors influencing L-glutamate formation are the ammonium ion concentration, i.e. control of pH and oxygen concentration of the medium. Therefore, ammonium salt is added in a low concentration at the starting of this fermentation process and is then monitoring continuously throughout the course of the fermentation. In this process proper oxygen concentration are very much essential, because if the oxygen concentration is very low, production of L-glutamate falls sharply and lactic acid, succinic acid accumulates as by-products. On the other hand with an excess oxygen supply, α -ketoglutarate is obtained as a by-product. The fermentation process has the advantage of making mass production at low cost, which was the great impetus for expanding the amino acid market.

5. MSG AND UMAMI TASTE

Professor Ikeda scientifically revealed that glutamate provides the savoury taste to the seaweed soup and termed it 'Umami', which means 'tasty' in Japan.³¹ Commercially it is available in the name of 'Ajinomoto' which means 'essence of taste'.³² However, after 1985 the scientific community included Umami as 'fifth basic taste'. Umami is the feeling that we experience when receptors were subsequently found glutamate rich food in the sensory cells in taste buds on the surface of the tongue.²⁵ Just as sweet is perceived as the 'taste of carbohydrates', Umami is perceived as the 'taste of proteins'.³²

6. MSG AND GLUTAMATE IN FOOD

MSG is chemically indistinguishable from the glutamate that is available in food proteins. Only fractions of the glutamate in foods remain as "free" form, and out of the two isomers, only the L-variety has exclusive flavour-enhancing properties.³³ Commercially available MSG contains over 99.6% L-isomer, which is a higher proportion of L-glutamate that found in the free glutamate ions obtained from fermented naturally-occurring foods. Our bodies metabolize both sources of glutamate in the same way. Glutamate occupies a central position in human metabolism.³⁴ The concentration of glutamate in breast milk is only modestly influenced by the ingestion of MSG because glutamate is virtually impermeable through placenta. On an average, an adult can consumes approximately 13g of glutamate from the protein-rich food in his daily diet, while intake of added MSG is estimates at around 0.55 grams per day.

7. GLUTAMATE-PROTEIN BUILDING BLOCK AND EXCITATORY NEUROTRANSMITTER

Glutamate is the most predominant excitatory neurotransmitter in the body,³⁵ being present in over most of the nervous tissue.³⁶ Glutamate is also used by the brain to synthesize GABA (γ -Aminobutyric acid), the main inhibitory neurotransmitter of the mammalian central nervous system.^{37,38}

By overstimulation of glutamate receptors causes neurodegeneration and neuronal damage which is known as excitotoxicity.^{39,40} Excessive glutamate as excitotoxin performing on the same glutamate receptors, over stimulates glutamate receptors (specifically NMDARs). Due to glutamate excitotoxicity, high levels of calcium ions (Ca^{2+}) influx into the postsynaptic cell.⁴¹ High concentrations of Ca^{2+} trigger a cascade of cell degradation processes involving proteases, lipases, nitric oxide synthase, and a number of enzymes which damage cell structures often to the point of cell death.^{42,43}

Glutamate excitotoxicity triggered by overstimulation of glutamate receptors also contributes to intracellular oxidative stress.^{44,45} When the glutamate concentration around the synaptic cleft cannot be decreased or reaches higher levels, the neuron kills itself by a process called 'apoptosis'. Excessive extracellular glutamate concentrations reverse glutamate antiporter, so glial cells no longer have enough cystine to synthesize glutathione (GSH), an antioxidant.⁴⁶ Deficiency of GSH creates more reactive oxygen species (ROSs) which damage and kill the glial cell. As a result concentration of extracellular glutamate become ceased,⁴⁷ this is another positive feedback in glutamate excitotoxicity. In addition, increased intracellular Ca^{2+} concentrations activate nitric oxide

synthesis (NOS) and the over-synthesis of nitric oxide (NO). As NO is a ROS⁴⁸ excess NO concentration damages mitochondria, adds oxidative stress to the neuron. Excitotoxicity due to excessive glutamate release and impaired uptake occurs as part of the ischemic cascade and is linked with stroke⁴⁸, autism⁴⁹ (some forms of disability) and diseases such as amyotrophic lateral sclerosis and Alzheimer's disease.⁵⁰ On the contrary, decreased glutamate release is observed under conditions of classical phenylketonuria⁵¹ leading to developmental distraction of glutamate receptor.⁵²

8. GLOBAL FOOD PROCESSED MARKET AND MSG

In 2015, Zion Research analysis has published a report to forecasting the global MSG market. According to the report, the global MSG market was valued at USD 4,500.0 million in 2014, and is expected to generate revenue of USD 5,850.0 million by end of 2020, rising at a CAGR of 4.5% between 2015 and 2020.⁵³ The global market analysis reflects that China and Japan is a major consumer of the MSG. Huge demand of MSG in Indian subcontinent and South East Asia indicates rapid growth of food manufacturing sector in that region. North America followed by Europe is also good consumer of MSG due to increasing demand for Asian food. Throughout the world, growth rate of MSG market increases and expected this trend will continue in future.

Food processing industry, restaurants and institutional food service are some of the main application markets for MSG. Chinese food products and fast food items are very much popular among the young generation all over the world. Vastly change in lifestyle, and food habit is primarily responsible for the growth of MSG market in this region. Thus, increasing MSG market in the Asian country also reflected the changing the food habit and lifestyle in that region. Thus, it is clear that MSG market is highly increasing due to increasing demand for flavouring agents. The demands for MSG escalating with increasing growth rate of food processing company. However, rising health issues with the consumption of MSG and various regulatory policies regarding use of MSG in food products is expected to limit the growth of this market.

9. Why MSG is a 'Silent Killer'?

Glutamic acid is one of the essential neurotransmitter of brain and nervous system. Specific glutamates responsive tissues are observe in nerve cell, brain and other parts of body as well. However abnormal function of glutamate receptors⁵⁴ may causes certain neurological diseases such as Alzheimer's disease⁵⁵ and Huntington's chorea.^{56,57,58,59} In 1957, Japanese scientist T. Hayashi was first noted that excess glutamate is harmful and may arrest normal activity of the central nervous system (CNS). In 1957, D. R. Lucas and J. P. Newhouse, noted that single doses of 20-30 gm of sodium glutamate in human life does not affect any permanent illness, but it destroyed the neurons

in the inner layers of the retina of newborn mice.⁶⁰ In April 1968, Robert Ho Man Kwok, a Chinese-American Doctor was claimed that he was faced some strange syndrome i.e. numbness at the back of the neck and general weakness and palpitation after eaten out the Chinese food within 20-30 mins.⁶¹ He was pointed out that it may happen due to presence of excess of MSG in the food and all this fact wrote in the form of letter to the 'New England Journal of Medicine' and also named this fact as "Chinese restaurant syndrome"(CRS).^{62,63,64} This syndrome is also called as 'Chinese food syndrome' or 'monosodium glutamate symptom' complex.⁶⁵

In 1969, Professor John Olney was published his remarkable scientific work in 'Science' and established that the 'negative effect' of MSG was not restricted to the mice retina only, but occurred throughout the brain, and coined the term 'excitotoxicity'.⁶⁶ According to his research, MSG can also overexcite the cells, causing brain damage and other disabilities.⁶⁷ The theory of Olney experiment says, 'newborn mice subcutaneous injections of monosodium glutamate tempted acute neuronal necrosis in several regions of embryonic brain including the hypothalamus'.⁶⁸ As adults, treated animals demonstrated stunted skeletal development, marked obesity, and female sterility. Pathological changes were also noticed in several organs associated with endocrine function'.⁶⁶ Recently scientific study also established that MSG exposures to the young rat develop 'anxiogenic' and depressive like behaviours.⁶⁹ Thus harmful effects of MSG are quite clear, It's ingesting can cause diabetes, adrenal gland malfunction, seizures, high blood pressure, excessive weight gain, stroke and other health problems. It has been reported that MSG is 'neurotoxin' resulting in brain cell damage, retinal degeneration, endocrine disorder and some pathological conditions such as addiction, stroke, epilepsy, brain trauma, neuropathic pain, schizophrenia, anxiety, depression and several neurological diseases.^{70,71} Thus, excess absorption of glutamate in the form of MSG containing food may cause serious damage our nerve and brain cells, which in turns causes several diseases.

10. ADVERSE EFFECT OF MSG

Most food additives act either as preservatives or as enhancer of palatability. The effect of monosodium glutamate was studied extensively and the model study shows its harmful effects. It can initiate severe headache, burning sensation, increase the rate of obesity, increases the asthma and affects the male fertility. It also affects the Kidneys of adult Wistar rat and investigation suggested that the functions of the kidney could have been adversely affected due to the distortion of the cyto-architecture of the renal cortical structures and cellular necrosis associated with the kidney.⁷² Although there is no such strong evidence that MSG is sole responsible element for the different diseases but it can trigger various syndromes as discussed shortly in below.

10.1 HEADACHES

The FIRST adverse report on MSG was from those who believed that eating 'Chinese food' flavored lavishly with MSG was possibly triggering headaches within an hour of consumption. This was called the 'Chinese restaurant syndrome'.⁶¹ It could include other distressing symptoms such as light-headedness, constriction in the chest, stomach pain, and a burning sensation.^{73\}

10.2 INCREASING RATE OF OBESITY, DIABETICS IN INDIA & MSG

Obesity and Diabetes is one of the fast gaining diseases in India, with more than 62 million people becomes currently diabetic.^{74,75,76,77,78,79,80} It will creates negative impact in the socio-economic backbone of the country. Worldwide rate of obesity becomes doubled than the last decades according to the survey WHO (World Health Organisation). People having Body Mass Index (BMI) more than 25 kilogram per metre square have been considered as obese.⁷⁴ Obesity is one of the major risk factor for cardiovascular disease as well as increases the rate of diabetes mellitus.⁸¹ Obesity increases the possibility of obstructive sleep apnoea, certain types of cancer, osteoarthritis and depression.^{82,83} Several researchers have highlighted that obesity responsible for 80-85 per cent of the risk of developing type-2 diabetes. According to Wild et al. the number of diabetic patients are predicted to be almost doubled globally from 171 million (2000) to 366 million within 2030, with a maximum increasing in India.^{74,84} It is predicted that by 2030, in India, 79.4 million people become diabetic, while China (42.3 million) and the United States (30.3 million) will also show significant increases the number of diabetic patient. The situation is quit alarming. Encounter the obesity and diabetes will be one of the biggest challenges for India.

Processed and instant food has become much more accessible in India's food markets. The changing life style enforces us to consume more caloric rich food, resulting increases obesity. 'Fast-food restaurants' and multinational food giants have opened their outlets almost every corner of the Indian street. Now, Indians especially young generation becomes more habituated with the pizza, pasta, burger, sandwich, Chinese, different processed food and soft drinks. All this 'Junk food' contains food additive in the significant amount. The magnificent 'taste' of this 'fat food' creates some sort of addiction.⁸⁵ Several scientific studies indicate that MSG is a risk factor for epidemic obesity as data obtained from both animal models^{86,87,88} and human studies.^{65,89}

In the urban areas most of the school children love to take instant noodles in their breakfast. In June 6, 2015 – The Central Government of India banned nationwide sales of the famous 'banded noodles' for an indefinite period due the presence of excess amount of lead and MSG.⁹⁰ In India, Kerala govt. proposed budgets in 2016 that 14.5 per cent 'fat tax' on burgers, pizzas and other junk food served in branded restaurants.⁹¹ Here we try to relate that, MSG is indirectly link to obesity and obesity in- turns linked to various lifestyle diseases.

Research on mice and monkey provided interesting information that there is a connection between MSG consumption and obesity.^{66,92} This was true for both genders, but especially left great evidence in male mice. There is a tendency to overeat when MSG is added, and it could be due to the effect of MSG on the hormone leptin, which is involved with fat release and satiation and hunger signals.

10.3 ASTHMA ATTACKS

MSG is intricate as a trigger in those prone to asthma attacks. The attack may not happen immediately after consumption and may take up to six hours or more, which could explain why many people don't make the connection between the food and the attack. However According to Allen et.al MSG sensitive persons could be faced severe asthma after taking typical meals contains 5 to 10 gm of free glutamate. They conducted oral monosodium glutamate (MSG) challenges with 32 asthmatic volunteers and reported that 14 reacted to MSG.⁹³ Then several studies reported MSG-induced asthma attacks in asthmatic patients.^{94,95,96,97,98} In 2000, Stevenson claimed that in the previous experiment none of these patients experienced asthmatic reactions after ingesting MSG (one-sided confidence interval of 0–0.066). In conclusion, the link between MSG-and asthma has not been established conclusively.⁹⁹

10.4 EFFECT ON FERTILITY

MSG affected reproductive function of both female and male mice. On administration of MSG females had fewer pregnancies and smaller litters, while males showed reduced fertility. The MSG-treated mice showed increased body weight and decreased pituitary, thyroid, ovary, or testis weights.¹⁰⁰ In female rats also it seemed to interfere with ova and follicle releases, and fertility was disrupted. Even as early as the 1970s, research indicated MSG was involved in pregnancy failures and it will affect the excretion endocrine glands.¹⁰¹ Studies over female albino rats indicates that MSG can destruct the basement membrane, tissue degeneration and atrophy at higher concentration of 0.08mg/kg.¹⁰² MSG has also been shown to promote male sterility in rats.⁷²

11. SIDE EFFECTS & SAFETY STEPS

In 1959, the U.S. Food and Drug Administration (FDA) labelled MSG as "Generally Recognized as Safe" (GRAS), and it has remained that way ever since. However, almost after 10 years later it started showing numerous side effects. From numbness to heart palpitations were experienced by the people after eating MSG and called it "Chinese Restaurant Syndrome" or more appropriately called "MSG Symptom Complex". (FDA) identifies it as "short-term reactions" to

MSG. According to FDA 'MSG Symptom Complex' may appear to those people who have taken "large doses" of MSG or those who are sensitive to asthma.⁹ 'MSG symptom complex' may be appeared within one hour, after eating 3 grams of MSG or more than it on an empty stomach or without other food. This reaction becomes more serious when the MSG is eaten in a large quantity or in a liquid form, such as clear soup. Due to the consistent research on the excitotoxic effects of MSG on the brains of young animals in the 1960s, researchers testified before the U.S. Congress about the danger of using MSG in baby food. As a result, MSG was voluntarily removed from baby foods in 1969. However, under current regulations of FDA (2002), when MSG is added to a food, it must be identified as 'monosodium glutamate' in the label's ingredient list.

12. KEEPING MSG OUT OF THE DIET

The best way of avoiding MSG toxin is to avoid processed food as much as possible and take more and more fresh foods. On the other side, such as is in restaurants, we should order MSG-free menu items, or request them to serve MSG free meal. We should also know what ingredients to be added or watch out for on packaged foods and lookout for many hidden names of MSG. At last, it is very important to become self-conscious and to distribute the proper knowledge of health consciousness to the people, who are really unknown to this fact.

13. CONCLUSION

Monosodium glutamate (MSG) is 'most controversial' flavour enhancer, which can be found in most of the processed food items. MSG is an excitotoxin, causing brain damage, and as well as 'neurotoxin'. The result of rapidly growing food processed industry in India with the help of MSG, will converted India into the biggest hub of diabetes mellitus (type -II) within the year of 2050. Federation of American Societies for Experimental Biology (FASEB) examine the safety of MSG in the 1990s. The FASEB report suggested symptoms such as headache, flushing, numbness, palpitations, tingling, and drowsiness that may occur in some sensitive individuals who consumes greater than the permissible limits of MSG without food. MSG can excite brain cells to death, creates brain lesions, causes leptin insensitivity, contributes to obesity, linked to sudden cardiac death, implicated in strokes, promotes cancer cells growth. Thus, to keep us healthy we have to avoid MSG contain food items from our daily routine. This is only possible if food manufactures can specify the complete list of constituent's and strictly follow the guideline as provided by FASSI (Food safety and standard authority of India). Awareness campaign of 'not to use MSG contain food items' among the consumers have to be increased so that they can actually realise the 'toxic effect' of artificial food additive used in packed food. Moreover, regular random sampling should be continued by the authorised government organisation throughout the year to check out the quality of the food.

If any kind of contamination, malpractices noticed at any stage of manufacturing, packing or as well as during the supply of commercially available food materials, must be taken action in 'strong hand'. Now this is the time to scrutinise the role of MSG as food enhancer in large scale and further research in that field should be encouraged more and more.

14. DECLARATION

Monosodium glutamate is a food additive used in worldwide. Though it has lot of negative effects but up to now MSG is considered a safe food additive by all the governmental agencies. We are just showing various positive and negative effect of MSG from various earlier studies. Though, we have no any competing interests on it.

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