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MONOSODIUM GLUTAMATE'S (MSG) NEUROTOXIC EFFECTS ON BRAIN HEALTH

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Abstract

Globally, Monosodium glutamate (MSG) is a flavor enhancer that is used all over the world. MSG is an umami-flavored flavor enhancer. Together with salty, sour, bitter, and sweet, umami is the fifth basic taste. MSG is utilized in the food sector as a flavor enhancer with an umami taste that increases the fleshy, savory taste of food, much like glutamate that occurs naturally in foods like stews and meat soups. Many studies have been done on the safety of MSG, which has been used to season food for more than a century. Humans can metabolize relatively large amounts of glutamate under normal circumstances because exopeptidase enzymes naturally produce it in the gut during the hydrolysis of proteins. MSG is still consumed in large quantities even though its safety has been called into question. This paper contributes to our understanding of the molecular pathways, such as the umami taste signaling pathway and different brain glutamate regulation mechanisms, that underlie MSG-induced neurotoxicity. MSG has been connected to obesities, metabolic diseases, Chinese restaurant syndrome, neurotoxic and negative effects on reproductive organs. Studies conducted on both humans and animals have shown that even trace amount of MSG are harmful. The recommended daily intake of MSG is 0.3–1.0 g. This study uses recent and historical data from investigations on humans and animals to review a few common harmful effects of MSG on the body organs. The future application of MSG, as well as actions taken and potential dietary substitutions for MSG to remove its toxicity and related public health concerns, are all covered in this study. The conclusion was that MSG should be avoided in diets as much as possible because it is more harmful than helpful to the general public's health.

Introduction:

With the chemical formula C5H8NO4Na and the IUPAC name sodium 2-aminopentanedioate,The sodium salt of glutamic acid is called monosodium glutamate. Its molar mass is 187.12 grams/mole and its melting point is 232°C. The white, crystalline powder known as monosodium glutamate dissolves easily in water. Additionally, it dissolves in ether, but not in alcohol, acetone, benzene, methanol, or acetic acid. In 2017, Henry-Unaeze. In 1866, German chemist Ritthausen became the first to isolate pure glutamic acid by hydrolyzing gliadin at acidic pH. Gliadin is a major element of wheat. Then, in 1908, when the kelp-like algae (seaweed) was used to make a stew stocks, Japanese chemist Kikunae Ikeda found that the flavor was due to glutamic acid. Under the brand name Ajinomoto the synthesis of monosodium glutamate began for sale in 1909. Following that, MSG was added to food all over the world to improve its flavor. Since 1957, genetically modified bacteria that secrete glutamic acid through their cell walls have been used in

bacterial fermentation to produce monosodium glutamate from sugar corn and beet. Following filtering, concentration, acidification, crystallization, and conversion to its monosodium salt, glutamic acid is next processed (Henry-Unaeze, 2017). The sodium salt of the amino acid glutamic acid is called monosodium glutamate, or MSG. Worldwide, fermentation using Corynebacterium glutamicum or related organisms produces 1.9 million tons of monosodium glutamate annually (Nakamura, 2008). Since these bacteria utilise biotin (Vitamin B7) as a cofactor, they are biotin auxotrophs. When producing MSG, producers prefer to use sugars. The sugar sources used are cassava tubers, sugarcane, and starch hydrolysates derived from corn. Ammonia and ammonium salts are the forms in which nitrogen is introduced. To complete the process, vitamins and other nutrients are added. Glutamate only builds up in the medium when there is a shortage of biotin. Standard raw materials like sugar molasses, which are composed of biotin, could not be used because biotin limits were in place. If oleate or glycerol-auxotrophic bacteria are employed, or if penicillin is added, the bacteria are not limited by biotin and can produce large amounts of glutamate.

2.0 Methods

A systematic review of the literature was carried out using MeSH (Medical Subject Headings) and PUBMED to find all relevant articles. Only English-language articles were accepted for publication, with a focus on the majority of work done between 2008 to 2024. This made up half of the cited material; relevant, earlier research was not missed. The search strategy for preclinical studies contained the following keywords: Umami substance, umami molecule, flavor enhancer, and monosodium glutamate MSG causes toxicity through: oxidative balance, heart toxicity, liver toxicity, obesity, insulin resistance, metabolism, pain, and neurotoxicity. After conducting eligibility analysis and cross-checking, a total of forty papers were chosen in accordance with PRISMA (Transparent reporting of systematic reviews and meta-analyzes) guidelines for systematic reviews (http://www.prisma-statement.org/).

3. Preclinical research evaluating the effects of MSG

3.1. MSG's effects on diabetes and obesity

Obesity has become more widely recognized as a serious global health concern in recent decades due to MSG (Dehghani et al., 2019; Hajian & Heidari, 2019). Among other human diseases, it contributes to the development of dyslipidemia, hypertension, diabetes, cancer, and coronary heart disease (Hajian & Heidari, 2019). Two important factors associated with a lower risk of diabetes are dietary and lifestyle modifications (Dow et al., 2019). The free usage of food additives such as MSG has been connected to obesity (Leshchenko et al., 2012). In animal models, this has also been explained by a number of different mechanisms.

3.2. Evaluation of MSG on Oxidative stress and Hepatotoxicity

Oxidative stress has been linked to the mechanism by which MSG damages the kidney, testicles, liver, and brain, among other organs. (2015) Umukoro et al. Oxidative stress is characterized by an increase in reactive oxygen species (ROS), disturbance of the metabolism of cells and the breakdown of molecules such as proteins, lipids, nucleic acids, and carbohydrates. . According to studies by Dow et al. (2019) and Saeidnia and Abdollahi (2013), oxidative stress is associated with osteoporosis, diabetes, inflammatory bowel disease,

cardiovascular disease, atherosclerosis, and carcinogenesis. Pavlovic et al. claim that MSG decreased Bcl-2 expression, which in turn increased rat thymocyte apoptosis (Pavlovic et al., 2006). Depending on the rats' age, the time of administration, and other factors, MSG caused nociception and oxidative stress in the animals and the sensitivity of specific brain and spinal cord regions (Rosa et al., 2018). Elshafey et al. (2017) discovered that oxidative stress, the cause of the MSG-induced liver damage, was indicated by elevated lipid peroxidation, decreased antioxidant enzymes, and fibrosis.

3.3. Assessment of Neurotoxicity with MSG

Glutamate, the main component of MSG, is the brain's primary excitatory neurotransmitter and when consumed in excess has been related to neurological symptoms. On the other hand, a neurotransmitter taken in excess can become an excitotoxin, a substance that damages cells by causing them to become unduly excited. According to Hajihasani et al. (2020), glutamate can become neurotoxic when its equilibrium is disturbed, which can cause enzymatic cascades that ultimately result in cell death. Furthermore, according to Miranda et al. (2016), MSG has been connected to neuroendocrine disorders like hypophagia, which can lead to obesity, insulin resistance, altered analgesic responses, glucose intolerance, chronic inflammation, and metabolic dysfunction. Hypophagia can also cause anxiogenic and depressive behaviors. Recent research on rats exposed to mild doses of MSG revealed diminished short-term memory and learning capacity in the hippocampus's forebrain. In a different study, rats' memory was impaired due to MSG's inhibition of the hippocampus's Na^+, K^+-ATPase enzyme activity (Ramalho et al., 2018). Impact of Monosodium Glutamate (MSG) on human health are shown in figure 1.

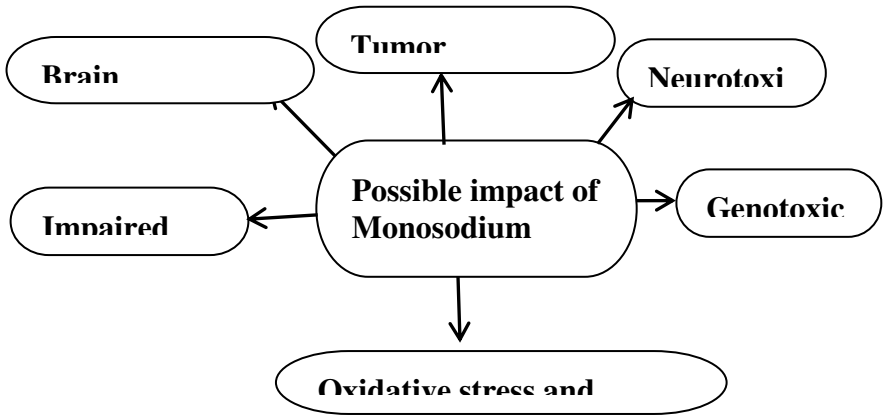

Fig. 1. Impact of Monosodium Glutamate (MSG) on human health

3.4. Analyzing the Genotoxicity of MSG

Numerous studies have shown that several flavor enhancers, such as MSG, are genotoxic (Lestari et al., 2017). Human peripheral blood cells have been shown to be genotoxic to MSG in vitro. (Ataseven et al., 2016). Several other researchers have also shown that MSG has genotoxic effects (Turkoglu, 2015). Some scientists, on the other hand, disagree and maintain that MSG is not carcinogenic (Rogers, 2016).

3.5. Effect of MSG as Poisoning

MSG is known by a number of names, such as MSG syndrome, Chinese restaurant syndrome, hot dog headache, and glutamate-induced asthma. The "Chinese restaurant syndrome" refers to the symptoms that some people experience after eating Chinese food, and it was first discovered in the 1960s. A group of symptoms known as monosodium glutamate poisoning are caused by consuming too much MSG. Among the warning signs and symptoms are headaches, flushing, sweating, palpitations, weakness, chest pain, and nausea (Geha et al., 2000). Other symptoms include tingling, burning, and numbness in the face and neck. MSG also effected the reproductive problems. Furthermore, MSG lowers serum levels of cholesterol, gonadotropin-releasing hormone, luteinizing hormone, and testosterone as well as serum enzymatic activities. Excessive exposure to MSG has also been linked to altered testicular and other male reproductive tissue histoarchitecture, sperm motility, morphology, and viability, as well as imbalances in male reproductive hormones.

3.6. MSG and cancer

Prior research has indicated a potential correlation between MSG consumption and carcinogenesis through the inhalation of tobacco-flavored cigarettes, as illustrated in Figure 2. Steatosis and steatohepatitis, which resembled the preneoplastic lesions frequently seen in non-alcoholic fatty liver disease in humans, were linked to obesity induced by MSG, per one such study. During this study Hargana et al. (2021) showed that the MTT assay, which measures the viability of cancer cells, showed a notable increase in the quantity of live cells following a 24-hour treatment with MSG at different concentrations.

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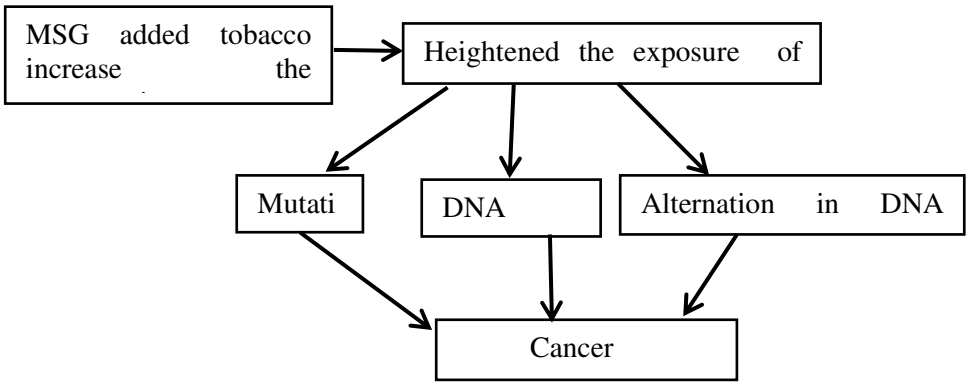

Fig 2. Prediction of MSG added tobacco as cancer induction

4. Mechanisms of Neurotoxicity of MSG:

4.1. Excitotoxicity: The process known as excitotoxicity causes damage or death to neurons when glutamate receptors are activated excessively or for an extended period of time. excessive glutamate receptor activation, which results in the death and damage of neurons. Since glutamate is the brain's main excitatory neurotransmitter and is involved in memory and learning. Damage to neurons, leading to conditions like Alzheimer's, Parkinson's, and Huntington's.

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4.2. By oxidative stress: MSG causes the production of reactive oxygen species (ROS), which have been shown to cause cellular damage through a chain reaction of oxidation and reduction reactions that result in the formation of free radicals.

4.3 By inflammation: Due to presence of MSG pro-inflammatory pathways are activated which contributing to neurodegeneration.

4.4. Disruption of blood-brain barrier: Due to presence of MSG it allowing toxins to enter the brain. Due to entry of toxins it might damage the brain functioning.

4.5. Neurotransmitter imbalance: Several types of meurotransmitters like dopamine, serotonin etc are present in the body. MSG Altering levels of dopamine, serotonin, and other neurotransmitters and causes incorrect signaling.

5. Prevention and Mitigation of the effect due to MSG:

As result of several studies showed that MSG causes various adverse effect on animals model of research. This similar type of effect also causes in human beings. Hence, its prevention and mitigation is very important. By avoid MSG-containing foods; Choose natural, whole foods; Read labels carefully; Cook from scratch and Consider MSG-free alternatives we will overcome on the effect of MSG.

6. Conclusion:

We would like to conclude by saying that while MSG has demonstrated its worth as a flavor enhancer, several studies have raised the possibility of harmful consequences associated with this widely used food additive. These harmful effects include neurological disorders, obesity, abnormalities in the physiology of adipose tissue, liver damage and reproductive problems. It's possible that these risks were previously underappreciated. People continue to use MSG in ever-increasing amounts while remaining ignorant of the potential risks. It is clear from evaluating several earlier studies that there are more risks associated with consuming MSG than advantages. To avoid these risks, it is strongly advised that an alternative to MSG be made available, as it may contribute to the development of numerous other illnesses, such as organ failure, which may ultimately result in death. Further research is necessary to validate the use of MSG as a salt flip still. Furthermore, studies continue to investigate MSG's neurotoxic effects

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