INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

Suspected Health Hazards of Monosodium Glutamate -Review

Bhagwat A*., Pardeshi S., Gawali D., Ugale P.G., Gayatri shinde

Smt. shree narmadaben popatlal thakkar institute of pharmacy.

ARTICLE INFO

Published: 17 Dec. 2024
Keywords:
Suspected Health Hazards, Monosodium Glutamate.
DOI:
10.5281/zenodo.14504826

ABSTRACT

Monosodium glutamate (MSG) is a flavour enhancer commonly used in many food products, particularly in Asian cuisine. While generally recognized as safe by regulatory agencies, some research has suggested potential health hazards associated with MSG consumption. Here's a summary of the alleged health hazards: Headaches and Migraines: Some individuals report experiencing headaches, migraines, or other adverse reactions after consuming MSG-containing foods. Neurological Effects: Animal studies have suggested potential neurotoxic effects, including damage to nerve cells and disruption of neurotransmitter function. Obesity and Metabolic Disorders: Research has linked high MSG intake to an increased risk of obesity, insulin resistance, and metabolic syndrome. Allergic Reactions: Some individuals may be allergic to MSG, experiencing symptoms like hives, itching, and difficulty breathing. Asthma and Respiratory Issues: MSG consumption has been linked to asthma exacerbation and other respiratory problems in sensitive individuals. Gastrointestinal Symptoms: Some people report experiencing nausea, vomiting, diarrhoea, or stomach discomfort after consuming MSG-containing foods. Cancer Concerns: Early studies suggested a potential link between MSG and cancer, but more recent research has found no conclusive evidence. It's essential to note that many of these alleged health hazards are based on animal studies, case reports, or small-scale human trials. The scientific consensus is that MSG is generally safe when consumed in moderate amounts. Regulatory agencies like the FDA, WHO, and European Food Safety Authority have established acceptable daily intake levels.

INTRODUCTION

One of the most widely used food additives in the world, monosodium glutamate (MSG) is frequently consumed with commercially processed meals. It can be explained as a glutamic acid salt with sodium. Widely employed as a flavour enhancer, monosodium glutamate (MSG) is made from L-glutamic acid, an amino acid found naturally in a range of dietary products.

***Corresponding Author:** Bhagwat A
Address: *Smt. shree narmadaben popatlal thakkar institute of pharmacy.*
Email : abhibhagwat4507@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Umami, a taste that is unique to MSG, was once thought to be predominant in Asian civilizations before spreading to Western ones much later. Along with sweet, sour, salty, and bitter, Kikunae Ikeda recognized this molecule almost a century ago as the fifth basic taste. MSG can be found in foods strong in protein, like meat or fish, as well as in some vegetables and cheeses, like Roquefort and Parmesan. Apart from its fundamental uniqueness, the umami flavour can intensify flavours overall and make food more palatable. Numerous elements influence this response, but the concentration of the umami molecule and the food matrix are the most crucial ones. **[1]** Over the past 30 years, the use of MSG has grown dramatically; today, the world's demand for it is over three million metric tons, valued at over $4.5 billion. Over two-thirds of the world's MSG consumption was found in Asia, with China leading the way in both manufacturing and exports to other nations. The demand for MSG rose by over 4% year worldwide before to 2020, with China, Thailand, Indonesia, Vietnam, and Brazil expected to have the biggest increases in demand, followed by Nigeria and Brazil. Nonetheless, MSG consumption has been linked in a number of studies included in this review to the onset and advancement of certain metabolic disorders, including obesity, which is a risk factor for other metabolic syndromes like cancer, diabetes mellitus, hypertension, and the male reproductive system, as well as the immune system, kidney, and pregnancy The formation of a hypothalamic lesion, hyperlipidaemia, oxidative stress, leptin resistance, and increased expression of peroxisome proliferator-activated receptors (PPARs) Gamma and Alpha are the mechanisms by which MSG induces obesity. Similar effects of MSG consumption on the induction of diabetes mellitus included decreased mass of pancreatic beta cells, elevated levels of oxidative stress and metabolic rates, decreased transport of glucose and insulin to skeletal muscles and adipose tissue, insulin insensitivity, decreased insulin receptors, and severe hyperinsulinemia. One of the main risk factors for high blood pressure, which can result in hypertension, is dietary salt, an active ingredient in MSG. MSG is added to tobacco to improve its flavor, which leads to smokers consuming more of the product and raising their chance of developing cancer. MSG has both advantages and disadvantages, depending on how much is consumed. The world still consumes a lot of MSG, even in light of the debate about its safety and potential link to the onset and advancement of metabolic diseases. Thus, in addition to helping regulatory bodies further evaluate the daily MSG consumption limit based on metabolic toxicities identified at the various dosages presented in this analysis, this paper will raise public awareness of the need for cautious usage of MSG in foods.[2,3,4]

History

German chemist Karl Heinrich Ritthausen first isolated and identified glutamic acid in 1866 by treating wheat gluten with sulfuric acid . In 1908, Kikunae Ikeda of Tokyo Imperial University used aqueous extraction and crystallization to separate glutamic acid as a taste component from the seaweed Laminaria japonica (Kombu), which he named umami. Not sweet, salty, sour, or bitter, Ikeda observed that dashi, the Japanese soup made with katsuobushi and kombu, had a distinct flavor that had not yet been identified by science . He investigated the flavor characteristics of the glutamate salts magnesium, calcium, potassium, and ammonium glutamate in order to confirm that ionized glutamate was the source of umami. Because of the other minerals, all of these salts tasted metallic and umami. Sodium glutamate was the most readily soluble, flavorful, and crystallizable of them all. Ikeda patented his creation as "monosodium glutamate," and the Suzuki brothers started manufacturing MSG commercially in 1909 under the name Aji-no-moto (essence of taste) . Certain meals that have been seasoned or allowed to ripen have a significant rise in the levels of glutamates and free amino acids. Particularly some cheeses because of their flavor and texture because of their extended ripening process, which increases the amount of amino acids in them. Meat recipes benefit greatly from the addition of these components to their flavor. [5]

Table 1: Natural glutamate content of fresh food -the values is expressed in mg/100g food [6].

Types of Foods	Bound Glutamate	Free Glutamate
Vegetables		
Peas	5.583	200
Corn	1.765	130
Beets	256	30
Carrots	218	33
Tomatoes	238	140
Meat		
Beef	2.846	33
Pork	2.325	23
Fish		
Cod	2.101	9
Mackerel	2.382	36
Salmon	2.216	20
Poultry Products		
Eggs	1.583	23
Chiken	3.309	44
Duck	3.636	69
Milk Product		
Cow	819	2
Human	229	22
Parmesan cheese	9.847	1200

Properties of MSG

Physical properties of MSG are mentioned below:

1) It is a solid, white-coloured compound.

2) MSG is extremely soluble in water but not soluble in organic solvents.

3) The solubility level of monosodium glutamate in water corresponds to 740 grams/L.

4) MSG has no odour or smell.

5) Its melting point is 232 º C.

Chemical properties of MSG

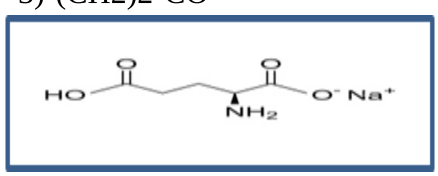
1) The IUPAC name for monosodium glutamate is sodium 2-aminopentanedioate.

2) The chemical formula is C5H8NO4Na.

3) The molecular mass of monosodium glutamate is 169.11 grams per mole.

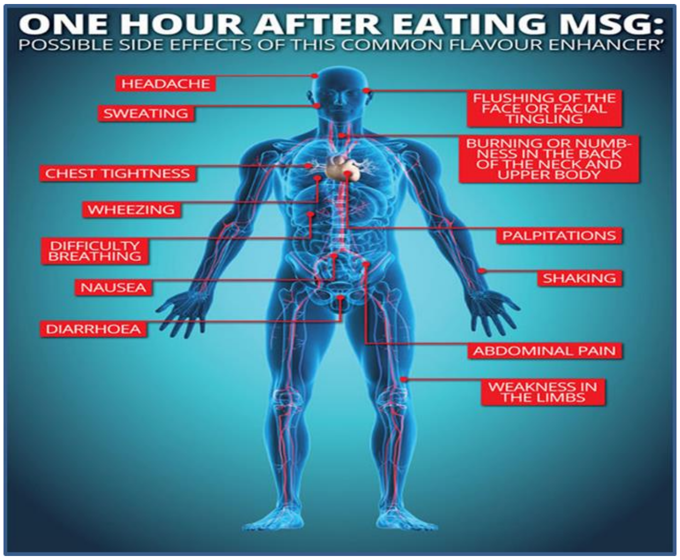
4) The hydrogen ion concentration level (pH) of monosodium glutamate ranges from 6.7 to 7.2.

5) MSG can exist in zwitter ionic form, −OOC-CH(NH+3)-(CH2)2-CO



Chemical Structure Of (MSG)**[7]**

Effect of Monosodium Glutamate (MSG)



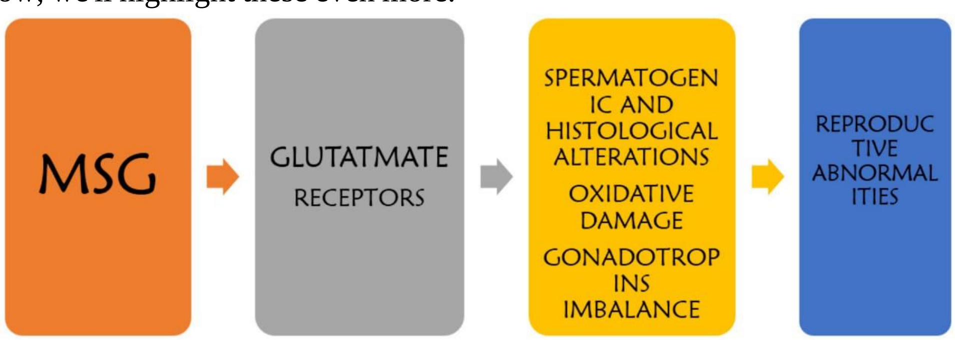
Common side effects of MSG**[8]**

1.Monosodium glutamate and the male reproductive system

The weight of reproductive organs, reproductive hormones, sexual behavior, sperm indices, and reproductive ability are all positively correlated with MSG exposure, according to published data.Studies on rats treated with MSG revealed that their body weight grew dramatically, primarily due to histological changes in the interstitial tissues and lumina of the seminiferous tubules, as well as spermatocyte and spermatid exfoliation in the rats. According to the same study, several of the various spermatogenesis cell types had necrotic appearances, pyknotic nuclei, dilated, congested blood arteries, and vacuolar organelles.Below, we'll highlight these even more. destruction, proving that MSG has a negative impact on the testes.**[9]**

Mechanism of MSG-Induced Testicular Alteration.

MSG may have an impact on male reproductive morphology and function due to its wide range of cellular effects. These effects can include oxidative damage, gonadotropin imbalance, histological changes, and spermatogenic alterations. Ultimately, these effects can lead to male reproductive abnormalities. The evaluation of MSG intake on male reproductive functions in humans appears to be lacking in empirical evidence; the majority of research that are accessible using animal models are extrapolated to human populations.**[10]**



1.1 Oxidative Stress

The presence of adipose tissue in the reproductive system's organs makes them targets for reactive oxygen species (ROS).Following the administration of MSG, studies have shown a discernible increase in testicular oxidative stress and a corresponding decrease in antioxidant/antioxidant enzyme activities, as well as an increase in lipid peroxidation (malondialdehyde, MDA) and decreased antioxidant activity (reduced glutathione, GSH). Sperm DNA damage, lipid peroxidation, sperm membrane malfunction, and reduced sperm motility could result from MSG's increased production of free radicals. Oxidative stress can affect testes and sperm cells because of the high concentration of unsaturated fat (plasma membrane) and insufficient quantities of antioxidants (cytoplasm). It was discovered that sperm membrane damage caused by MSG and elevated ROS production in seminal plasma were present in patients with asthenozoospermia. Sperm motility and viability are directly impacted by this ROS-induced degradation to membrane integrity. Consequently, MSG-induced reproductive damage may be reversed by therapeutic drugs such antioxidants.**[11,12,13,14]**

1.2. Neurotoxicity

The hypothalamic-pituitary-axis pathway (HPA) is disrupted by the neurotoxic impact of MSG, which results in excitotoxicity. An excitatory neurotransmitter like glutamate can generate a significant intracellular calcium influx in neurons, which can ultimately result in the death of a neuron. Progesterone, follicle-stimulating hormone, and luteinizing hormone levels are among the sex hormones whose levels may be lowered by HPA disruption. Sperm quality eventually changes as a result of this. Sex hormones and androgen-dependent reproductive organs, such as the prostate gland, epididymis, and seminal vesicles, are absolutely necessary for spermatogenesis to occur. This means that any disease involving the androgen hormones—testosterone, luteinizing hormone, and follicle-stimulating hormone—will have a detrimental effect on the reproductive tissues. **[11,12]**

1.3 Histomorphological Alterations

There have been earlier reports of modifications to the testicular histology, including edema, poor sperm production, and spermatogenic stoppage. In the meantime, the mice treated with MSG did not exhibit any obvious histological abnormalities, according to another study. In animals exposed to MSG, low levels of spermatogonia have been associated with maturation arrest; this is correlated with low testosterone levels, which impede spermatogenesis. However, testicular histopathology was found to improve in other investigations following the administration of curcumin, vitamin E, and selenium, respectively. Certain treatments, including curcumin, propolis, camel milk, vitamin C, vitamin E, and graviola extract, have been shown to have protective benefits against the histomorphological testicular toxicities caused by MSG. **[15,16]**

1.4 Glutamate Receptor Dysfunction

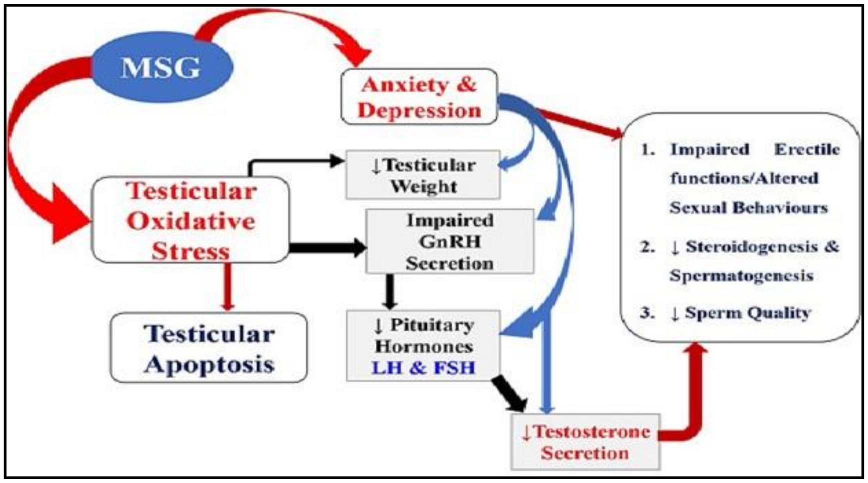
Since MSG directly affects the glutamate transporter on the seminiferous tubule epithelium, glutamate receptors may also play a role in the toxicity of MSG to male reproduction. The endocrine glands, the hypothalamus, the thymus, the ovaries, the liver, the kidney, and the testis are among the organs and tissues that have glutamate receptors. It has been discovered that the testis's morphological changes after MSG treatment are caused by the testis's aberrant expression of the glutamate receptor.**[11]**

Effect of monosodium glutamate on sperm indices

The quality of sperm generated from the testis is the only factor used to assess a man's fertility. Reproductive success depends on semen of a quality specified by the World Health Organization. Studies on adult and newborn animals have demonstrated that MSG increases abnormalities in sperm morphology and causes oligozoospermia.

Spermatozoa were vulnerable to oxidative damage because of the unsaturated fatty acids in their plasma membrane layer and the low levels of cytoplasmic antioxidants in these cells. A sign that

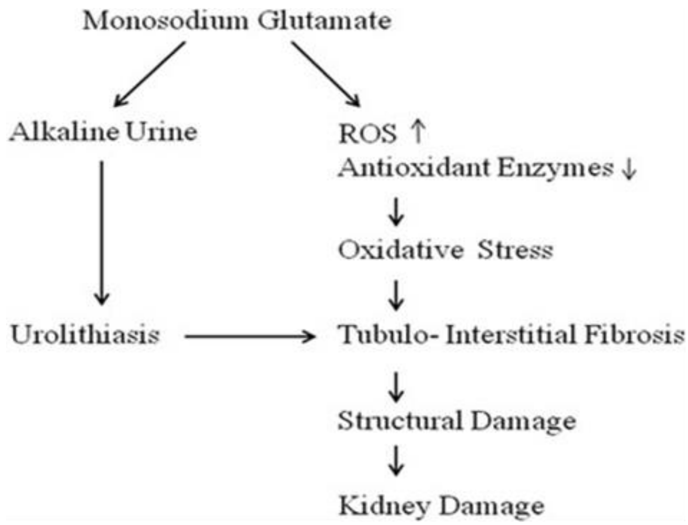
MSG exposure may affect the neuronal stimulation of the expression of reproductive hormones through the hypothalamic-pituitary-gonadal regulatory axis is the hypothalamus's vulnerability to injury.The impacted animals' capacity for reproduction may be impacted as a result of this impairment. According to Moreno et al., giving MSG to the animal models lowers the ascorbic acid content in the testicular tissue, which may result in oxidative damage to the rat testes and other organs. Rats treated with MSG had significantly lower caudal epididymal sperm stores than control rats, according to a previous study by Giovambattista et al. demonstrates the process via which MSG impairs male reproduction. **[17]**



MSG- induced kidney damage

Numerous studies have conjectured that dietary variables, such as MSG, may increase the risk of renal disease. The kidneys are extremely vulnerable to toxins, ischemia, and toxic assaults. Thus, mechanisms resulting in direct or indirect disruptions of the energy metabolism of renal cells will cause damage to the cells and acute renal insufficiency.

An overview of the long-term renal changes brought on by MSG is shown.MSG can cause modifications to the renal cytoarchitecture, a rise in glomerular hypercellularity, the infiltration of inflammatory cells into the renal cortex, tubular cell edema, and ultimately the degeneration of the renal tubules. The precise pathophysiology of infiltration of inflammatory cells is unknown, despite the fact that it indicates a pathology. Regardless of the toxic principle affecting the kidney, cellular dysfunction is thought to be a significant contributing factor in the development of most morphological alterations that follow. Thus, studying the kidney's ultrastructure in experimental mice receiving long-term MSG treatment may help us comprehend the process underlying the abnormalities that occur during renal damage.**[18]** Food additive monosodium glutamate (MSG) is regarded as a water and environmental contaminant that has an impact on living things' tissues. The purpose of this study was to determine how long-term MSG supplementation affected the kidneys' mesangial cell mass. Four groups of ten mature male rats each were created from the forty. For thirty and sixty days, respectively, distilled water was given orally to control groups 1 and 2. Oral administration of 15 mg/kg Bwt of MSG was given to treatment groups 1 and 2 for 30 and 60 days, respectively. The kidney specimens were taken, fixed with 10% neutral buffered formalin, processed using routine histological procedures, stained with Hematoxylin and Eosin and PAS (Periodic Acid-Schiff) stains, and then analyzed under the microscope. The control and treatment groups were sacrificed. The finding indicated that mesangial proliferative glomerulonephritis was caused by an enlargement of a mesangial mass, which was shown by hypertrophy and hyperplasia of mesangial cells. As a result, the investigation revealed elevated creatinine levels, which point to a disruption in renal function. Bowman's space will relatively enlarge and the glomeruli of renal corpuscles will shrink as a result. Renal filtration abnormalities will emerge from the closure of basement membrane gates and glomerular capillaries during the experiment. It was determined that consuming MSG over an extended period of time causes the glomerular capillary lumen to indirectly narrow, which **results** in kidney failure.**[19]**



An overview of the long-term kidney changes caused by MSG. Renal injury from chronic MSG use and alkaline urine may occur through unidentified pathways. ROS and inflammatory cytokines produced by urolithiasis can also exacerbate interstitial fibrosis. **[19]**

3.Cancer

The occurrence of tumours is the result of a comprehensive influence of multiple factors, not only the impact of the internal factors of the organism, but also the result of external environmental factors such as dietary factors. In a study of colorectal cancer (CRC), researchers found that the viability of cancer cells increased after 24 h of incubation with different concentrations of MSG, as well as an increase in the expression levels of adenomatous polyposis coli (APC) and beclin 1, which are involved in the development and progression of CRC. Therefore, it can be inferred that MSG may exert a promoting effect on the proliferation of CRC cells. Tumours are the consequence of a complex interplay between internal and external environmental elements, including nutrition, in addition to the organism's internal components. Researchers observed an increase in the expression levels of adenomatous polyposis coli (APC) and beclin 1, two factors involved in the initiation and progression of colorectal cancer (CRC), as well as an increase in the viability of cancer cells following a 24-hour incubation period with varying concentrations of MSG. Consequently, it follows that MSG might have a stimulating effect on the growth of colorectal cancer cells.**[20]**

3.1 Colorectal cancer

Globally, colorectal cancer (CRC) is the second most common cause of cancer-related fatalities. Studies conducted in several parts of Saudi Arabia indicate that the younger generation is becoming more susceptible to colorectal cancer. A malignant tumour composed of colon and/or rectum epithelial cells is known as a colorectal cancer (CRC). Numerous variables, both hereditary and environmental, may contribute to it. It has been discovered that 35 percent of CRC causes are either entirely or partially hereditary.

Environmental factors that have been linked to an increased risk of cancer include food intake, smoking, obesity, sedentary lifestyles, and exposure to pesticides and changes in the environment. It has also been suggested that these factors, along with lifestyle choices, may trigger genetic changes that can result in cancer. Genetic anomalies have been linked to the development of colorectal cancer in both familial and sporadic cases. Tumour Protein p53 (TP53), Beclin1 (BECN1), and Adenomatous Polyposis Coli (APC) are a few of the genes implicated in the onset and course of colorectal cancer (CRC).As the most frequently altered gene in all tumours, TP53 is a focus of cancer research. There is mounting proof that a person's food and lifestyle have an impact on their chance of colorectal cancer. Food has direct touch with the colonic epithelium, which allows it to directly alter colon health. Due to potential harmful effects, monosodium glutamate (MSG), a major food flavour enhancer used worldwide, has been the subject of extended research. There is evidence, according to some academics, that eating MSG puts people at risk, particularly young ones. Monosodium glutamate has been shown to have a notable neurotoxic effect on rats' short-term spatial memory through oxidative stress-induced brain tissue apoptosis and degenerative alterations, along with continuous systolic hypotension. Because of its distinct umami flavour, MSG is frequently added to meals as a flavour enhancer. The stomach, small intestine, and colon are among the gastrointestinal tract tissues where it has been discovered that the umami taste receptors T1R1 and T1R3 are expressed. The administration of subcutaneous MSG to mice resulted in hyperinsulinemia, diabetes, hypertriglyceridemia, obesity, hyperlipidaemia, and insulin resistance, according to a study by Hata and colleagues. These abnormalities increased the mice's susceptibility to colon cancer caused by azoxymethane. Furthermore, Shoji et al. used quantitative reverse transcription PCR (qRT-PCR) to measure changes in T1R1 and T1R3 gene expression following MSG stimulation of the tongue. **[21,22,23,24]**

3.2 Lung cancer

In a lung cancer investigation, tissue samples from individuals with non-small cell lung cancer showed a considerable up-regulation of the glutamate receptor SLC1A1. In order to enhance the uptake of cystine by XC- and hence improve the formation of reduced glutathione (GSH) and mitigate the oxidative stress produced during cancer cell proliferation, cancer cells actively ingest glutamate through SLC1A1. Walker-256 cells were subcutaneously implanted after newborn Wistar rats received a 400 mg/kg MSG injection. The findings demonstrated that the tumour volume in the MSG group was greater than that of the control group. Additionally, when MSG (2 mg/kg) and azoxymethane (AOM) were administered to newborn mice, the MSG-AOM group's mRNA expression of the insulin-like growth factor-1 (IGF-1) receptor was higher than that of animals that received AOM alone. These findings suggested that mice treated with MSG are more vulnerable to AOM-induced colon cancer. Gln's conversion to glutamate by glutaminase and subsequent conversion to α-ketoglutarate via the tricarboxylic acid cycle may be linked to this cancer-promoting process. This reprogramming mechanism is essential for ATP generation, preserving redox equilibrium, and controlling cancer cells' energy use.**[20]**

4.Effects of MSG on the immune system

Through research with cell cultures, the impact of MSG on the immune system was evaluated directly. The frequency of sister-chromatid exchanges and chromosomal abnormalities in human cells were considerably and dose-dependently elevated by MSG (250–8000 µg/ml). Nevertheless, there was no change in the indices of nuclear division and replication. Based on these findings, MSG may be able to damage human peripheral blood cells genetically.

B cell viability responded dose-dependently to exposure to escalating MSG doses (1–100 mM). Glutamate increased apoptosis in both naive and memory B cell groups; metabotropic glutamate receptor (mGluR) 7 receptors are most likely the mechanism mediating this action. Similarly, glutamate receptors expressed by naive and memory cells differ. Induction of oxidative stress and death in immune cells is facilitated by differential expression patterns of glutamate receptors.[18]

5.MSG on pregnant and lactating women

Pregnant women usually eat a varied, well-balanced diet, making sure to ingest enough calories to support a healthy pregnancy. The majority of amino acids actively cross the placenta to support fetal growth and development. According to research, the fetus has higher amounts of amino acids than the mother does, irrespective of what she eats. The metabolism and transport of amino acids—particularly glutamate—are critical for fetal development, and these functions are shared by the placenta and fetal liver. Researchers examined the effects of MSG consumption on reproduction and birth in rodent trials. The experiment examined three generations of mice given up to 7.2 g/kg of MSG every day.

No negative impact was noted in any generation, and there was no proof that any newborns had ever experienced brain damage. Researchers have looked into the effects of MSG consumption on breastfeeding and breastfed newborns in addition to studies on the pregnancy. Researchers examined nursing mothers who took 100 mg/kg of body weight of MSG and found no increase in the amount of glutamate in human milk or impact on the infant's glutamate consumption. Baker et al. claim that a newborn baby consumes more free glutamate per kilogram of body weight when nursing than at any other time in its life. The American Academy of Pediatrics Committee declared that MSG does not affect lactating or endanger the consuming child.**[25]**

Throughout their 23-day breastfeeding period, sows receiving experimental diets from day 112 of pregnancy forward. 48 hours following farrowing, litters were standardized. Using the Howema computerized feeding system, sows were fed intermediate diets made by combining high and low diets. The feed was then weighed for each sow and given to each feeding hopper individually, allowing the system to track the daily feed consumption of the sows during lactation. Using the PROC MIXED technique of SAS, data were analysed in a randomized complete block design, with parity serving as the random effect and treatment serving as a fixed effect. The sow served as the experimental unit.

The findings were regarded as trending at $P > 0.05$ and $P \leq 0.10$ and as significant at $P \leq 0.05$. The sows' ADFI values (5.2, 5.2, 5.2, 5.0, and 5.4 ± 0.15 kg/d, respectively) did not differ substantially. Sows drank approximately 45 g of SID Lys day on average. The sows that were weaned to estrus at 5.2, 4.7, 5.3, 5.5, and 4.5 ± 0.32 days, respectively, did not exhibit any variation in the Val:Lys ratio. There were no variations in the average daily litter growth (2.66, 2.64, 2.76, 2.61, and 2.62 ± 0.08 kg; $P > 0.10$) when the Val:Lys ratio was increased. Across the dietary treatments, there were no variations in the weight loss of the sows or the number of babies born. SID Val:Lys levels did not, in general, affect sow reproductive efficiency or piglet growth rate.**[26]**

Important issue related to MSG is exposure during pregnancy.

adverse health effects on kids following MSG supplementation during pregnancy, including reduced serum levels of insulin growth factor and growth hormone, increased body weight, weakened convulsion threshold, and poor Y-maze discriminating learning. The progeny exposed to

MSG in utero displayed altered cerebral morphology and function, as well as elevated expression of genes linked to apoptosis and genetic damage.**[27]**

Natural Product as Safeguards Against Monosodium Glutamate Induced Toxicity .

Vitamins

Vitamin E

One of the most significant antioxidants found in a regular diet is vitamin E, which offers protection against a number of diseases that affect humans (. Rats were given 0.6 mg/g bw of MSG, which caused oxidative stress and hepatotoxicity by inducing LPO, lowering GSH levels, and increasing the activities of GST, SOD, and catalase in the liver. When Vitamin E (0.2 mg/g bw) and MSG (0.6 mg/g bw) were given together, the LPO improved, the GSH level rose, the hepatic SOD activities of GST and catalase were decreased, and the serum activities of ALT, AST, and GGT were decreased . A considerable reduction in MDA levels and the number of atresia follicles, as well as an increase in FSH levels and the number of primary follicles, indicate that the administration of combination vitamin C and E protected MSG-induced ovarian damage (. The significant concentrations of vitamin E, polyunsaturated fatty acids, and lignans found in herbal oils, including sesame oil, account for their potent antioxidant properties . Rats that received sesame oil orally saw a reduction in MSG-induced liver damage, as seen by a drop in AST and ALT as well as oxidative stress markers, and an improvement in lipid profile. Moreover, α-tocopherol, the primary component of vitamin E, protected against MSG-induced nephrotoxicity for 180 days at a dose of 200 mg/kg. This was demonstrated by a marked decrease in oxidative stress and lipid peroxidation (reduced MDA and conjugated dienes), an improvement in renal function (reduced urea, uric acid, and creatinine), and an increase in antioxidant defense systems (SOD, CAT, GPx, GST, and GSH) Stated differently, α-tocopherol administered at a dose of 200 mg/kg for 180 days considerably decreased the oxidative stress and cardiac toxicities caused by MSG. As a strong free radical scavenger, α-tocopherol may inhibit the onset of oxidative stress-related illnesses by boosting reduced glutathione levels and lowering lipid peroxidation in the body. Thus, foods containing MSG may benefit from the presence of vitamins, particularly C, D, and E, as protection against MSG-induced toxicity. **[28]**

Vitamins C

Due to the possibility of both vitamins and MSG in the human diet, it is important to assess how they interact to determine whether vitamins will worsen or lessen the negative effects of MSG. Given in conjunction with MSG for 45 days, vitamin C (500 mg/kg) demonstrated a hepatoprotective effect on the liver's parenchymal architecture in rats by lowering cellular proliferation, as demonstrated by a decrease in ki-67 expression and a mutation in a tumour suppressor gene . Based primarily on its extracellular action, induction of apoptosis, induction of cell cycle arrest, and suppression of the expression of genes involved in protein synthesis, vitamin C has anti-proliferative properties. The injection of MSG at a level of 6 mg/g bw for 10 days caused hepatotoxicity and oxidative. When vitamin C (500 mg/kg) and MSG were taken together, there was a substantial reduction in oxidative stress, hepatic toxicity, liver weight, LPO, ALT, and AST activity, as well as decreased hepatic catalase activity. Another study found that giving rats 100 mg/kg of vitamin C orally reduced the toxicity of 2 and 4 mg/kg of MSG on testicular and epididymal weight, sperm motility, sperm count, and abnormalities of the sperm head. Additionally, vitamin C reduced the cytotoxicity that MSG caused in rat thymocytes by upregulating the expression of the Bcl-2 protein.

These findings support the conclusion that MSG has a cytotoxic effect on the germ cells in adult rats' testicular tissue. However, vitamin C, at a dosage of 150 mg/kg, has an advantageous effect on reducing the cytotoxicity caused by the administration of MSG because of its antioxidant properties. A number of other MSG-induced toxicities, such as histological alterations in the rat oviduct, hepatotoxicity, sperm toxicity, obesity, and neurobehavioral alterations in adolescent rats, have been shown to be protected against by vitamin C.**[29]**

Vitamin D

It was discovered that vitamin D protects against obese rats produced by MSG. MSG-administered rats displayed increased body weight and water and food intake. On the other hand, taking MSG and vitamin D together dramatically reduces the rate of weight growth (176). Elbassuoni et al. reported similar outcomes, stating that vitamin D and L-arginine prevent oxidative stress, reduce food consumption, and lower body weight to prevent liver and kidney damage caused by MSG. Renal function indicators, urea, and creatinine levels in rats increased, indicating both kidney injury and the MSG-induced oxidative liver, which was demonstrated by an increase in renal MDA and a decrease in liver TAC.

The liver and kidney were protected against hepatic and renal impairment caused by MSG by concurrently administering vitamin D or L-arginine. This was demonstrated by a decrease in blood ALT and AST levels as well as a decrease in serum urea and creatinine, which are markers of renal injury. Furthermore, vitamin D may be useful in preventing MSG-induced steatohepatitis in nascent and adult animals. Additionally, it has been proposed that a diet high in vitamin D may help minimize liver damage in expectant mothers who eat MSG-containing foods.**[30]**

Solanum Lycopersicon (Tomato)

Reproductive toxicity and infertility are among the issues raised by MSG use in the food business, as was previously highlighted. When mice were given tomatoes, their spermatozoa's motility and morphology improved after being exposed to MSG. The primary mechanism was previously proposed to be the antioxidant properties of tomato content, specifically lycopene . Of all the carotenoids, lycopene—a naturally occurring bioactive component found in tomatoes—is the most effective at scavenging free radicals .

It was demonstrated that lycopene had exceptional neuroprotective properties against Bcl-2/Bax imbalance, neurotoxicity, and cholinergic dysfunction brought on by MSG . Badawi has recently investigated lycopene's ability to shield against MSG-induced nephrotoxicity in vivo. Adult male albino rats were given an oral dose of 4 mg/kg/day of lycopene for 14 days. This demonstrated that lycopene had protective effects against MSG-induced nephrotoxicity by lowering blood urea nitrogen and serum creatinine levels, inhibiting apoptosis (by increasing Bcl2 and decreasing Bax), and preventing kidney damage **.[31]**

Green tea

It is well established that obesity poses a significant risk for developing chronic illnesses, including metabolic, lung, and colon/breast malignancies , as well as cardiovascular complications. It has been shown that green tea has anti-obesity properties in both experimental and clinical investigations . In order to study obesity and its implications, MSG-induced obesity is an often utilized experimental model. MSG-induced obesity has been linked primarily to its toxic effects on neurons in the hypothalamus's sections that regulate body mass and energy metabolism . Furthermore, a different study has also suggested that GTE may lessen insulin and leptin concentrations and ameliorate obesity generated by MSG . MSG may harm female rats' ovaries, leading to sterility, according to a number of research.Because of its strong antioxidant properties, GTE can shield the ovary from harm caused by MSG. with a different trial, taking MSG orally for 60 days resulted with higher levels of plasma total cholesterol, LDL cholesterol, and triglycerides. On the other hand, after 60 days of treatment with 1.5 ml/rat/day of GTE, there was less rise in body weight in those groups . By improving the liver enzyme activity (significantly reduced activities of LDH, ALT, AST, ALP, and γ-GT in the serum) and the lipid profile (significantly decreased activities of LDH, ALT, AST, TC, γ-GT, TG, LDL-C, and VLDL-C), GTE conjugated with zinc oxide nanoparticles (ZnO/NPs) significantly recovers the hepatotoxicity developed by MSG.**[32,33]**

Zingiber officinale (Ginger)

Since 2000 years ago, ginger has been used as a spice. Furthermore, it has a well-known anti-emetic effect because of its anti-5HT3 receptor action; this effect is mostly utilized during pregnancy . Ginger was shown to have protective properties against MSG-induced neurotoxicity in a study by Hussein et al. By raising the activity of antioxidant enzymes and lowering MDA, a measure of lipid peroxidation, ginger was able to minimize oxidative stress. Additionally, ginga (500 mg/kg oral) treated rats reduced MSG-induced higher levels of Na^+ and Ca^{+2} in the brain while increasing K^+ concentration .

When MSG causes neurotoxicity in male albino rats, has investigated the neuroprotective properties of ginger aqueous extract. Significant increases in the levels of dopamine, serotonin (5-HT), adrenaline, and norepinephrine were observed following a prolonged treatment of 100 mg/kg of ginger extract, according to his observations. The antioxidant and neuroprotective properties of ginger have been verified in a prior study . Because ginger contains zingerone, which has strong anti-inflammatory and antioxidant properties, as well as 6-gingerol and its derivatives, such as 6-shogaol and 6-paradol, it may have these positive effects. **[34]**

Curcuma longa

Numerous health benefits of C. longa, particularly its bioactive component curcumin, have been well-documented. These effects include neuroprotective and anticancer qualities . Curcumin has been demonstrated by Khalil and Khedr to provide protection against MSG-induced neurotoxicity in rats. In rats given MSG, therapy with curcumin significantly reduced TNFα and AChE activity. They proposed that the neuroprotective effect of curcumin could be explained by its anti-inflammatory properties. Another study by Vucic and colleagues found that curcumin therapy of rat thymocytes reduced ROS generation and MSG-induced apoptosis, restored MMP, and increased the Bcl-2/Bax protein ratio . It was also suggested that curcumin's primary method of anti-apoptotic actions was the suppression of the PI3K/Akt signaling pathway in MSG-induced apoptosis. In conclusion, curcumin demonstrated its protective properties against MSG-induced reproductive damage by reducing the frequency of aberrant sperm in male rats and restoring testis weight and sperm count. **[35]**.

REFERENCES

1. Zanfirescu A, Ungurianu A, Tsatsakis AM, Nițulescu GM, Kouretas D, Veskoukis A, Tsoukalas D, Engin AB, Aschner M, Margină D. A review of the alleged health hazards of monosodium glutamate. Comprehensive reviews in food science and food safety. 2019 Jul;18(4):1111-34.
2. Kayode OT, Bello JA, Oguntola JA, Kayode AA, Olukoya DK. The interplay between monosodium glutamate (MSG) consumption and metabolic disorders. Heliyon. 2023 Sep 9.
3. A.I.AiraodionE.O.OgbuaguE.U.Osemwowa U.Ogbuagu.E.EsonuA.P.Agunbiade.P.Oloru ntoba Toxicological effect of monosodium

glutamate in seasonings on human healthGlobal Journal of Nutrition & Food Science201919
4. Henry-Unaeze HN. Update on food safety of monosodium l-glutamate (MSG). Pathophysiology. 2017 Dec 1;24(4):243-9.
5. Bera TK, Kar SK, Yadav PK, Mukherjee P, Yadav S, Joshi B. Effects of monosodium glutamate on human health: A systematic review. World journal of pharmaceutical sciences. 2017 Apr 26:139-44.
6. Institute of Food Technologists. Expert panel on food safety and nutrition. Monosodium Glutamate. Food Technol 1987; 41: 143-5.
7. Tolulope OD, Ebiwonjumi O, Oluwatoyin AL, Dupe AO, Victor AM, Grace A, Johnson AW, Folorunsho AA. Disruptive consequences of monosodium glutamate on male reproductive function: A Review. Current Research in Toxicology. 2024 Jan 9:100148.
8. Kayode OT, Rotimi DE, Kayode AA, Olaolu TD, Adeyemi OS. Monosodium glutamate (MSG)-induced male reproductive dysfunction: a mini review. Toxics. 2020 Jan 22;8(1):7.
9. Hamza, R.Z.; AL-Harbi, M.S. Monosodium glutamate induced testicular toxicity and the possible ameliorative role of vitamin E or selenium in male rats. Toxicol. Report 2014, 1, 1037–1045. [Google Scholar] [CrossRef] [Green Version]
10. Hanipah, E.N.A.; Yahya, N.J.; Ajik, E.M.; Yusoff, N.A.; Taib, I.S. Monosodium Glutamate Induced Oxidative Stress in Accessory Reproductive Organs of Male Sprague-Dawley Rats. J. Sains Kesihat. Malays. 2018, 16, 67–73. [Google Scholar] [CrossRef] [Green Version]
11. El-Sawy, H.B.I.; Soliman, M.M.; El-Shazly, S.A.; Ali, H.A. Protective effects of camel milk and vitamin E against monosodium glutamate induced biochemical and testicular dysfunctions. Prog. Nutr. 2018, 20, 76–85. [Google Scholar]
12. Khaled, F.A.; Yousef, M.I.; Kamel, K.I. The protective role of propolis against the reproductive toxicity of mono-sodium glutamine in male rabbits. Int. J. Chem. Stud. 2016, 4, 4–9. [Google Scholar]
13. Sakr, S.A.; Bada, G.M. Protective Effect of Curcumin on Monosodium Glutamate-Induced Reproductive Toxicity in Male Albino Rats. Glob. J. Pharmacol. 2013, 7, 416–422. [Google Scholar]
14. Das, R.S.; Ghosh, S.K. Long term effects of monosodium glutamate on spermatogenesis following neonatal exposure in albino mice—A histological study. Nepal Med. Coll. J. 2010, 12, 149–153. [Google Scholar]
15. Tolulope OD, Ebiwonjumi O, Oluwatoyin AL, Dupe AO, Victor AM, Grace A, Johnson AW, Folorunsho AA. Disruptive consequences of monosodium glutamate on male reproductive function: A Review. Current Research in Toxicology. 2024 Jan 9:100148.
16. Sharma A. Monosodium glutamate-induced oxidative kidney damage and possible mechanisms: a mini-review. Journal of biomedical science. 2015 Dec;22:1-6.
17. Hussin AM, Tala'a AA, Fadhil SA, Salman HA. The adverse effect of long term intake of Monosodium Glutamate on kidney performance. InIOP Conference Series: Earth and Environmental Science 2021 Oct 1 (Vol. 880, No. 1, p. 012056). IOP Publishing
18. Yang L, Gao Y, Gong J, Peng L, El-Seedi HR, Farag MA, Zhao Y, Xiao J. A multifaceted review of monosodium glutamate effects on human health and its natural remedies. Food Materials Research. 2023;3(1).
19. Al Hargan A, Daghestani MH, Harrath AH. Alterations in APC, BECN1, and TP53 gene

expression levels in colon cancer cells caused by monosodium glutamate. Brazilian Journal of Biology. 2021 Dec 13;83:e246970.

20. BURN, J., MATHERS, J. and BISHOP, D.T., 2013. Genetics, inheritance and strategies for prevention in populations at high risk of colorectal cancer (CRC). Recent Results Cancer Res vol. 191, pp. 157-183. http://dx.doi.org/10.1007/978-3-642-30331-9_9 PMid:22893205.
21. BISHEHSARI, F., MAHDAVINIA, M., VACCA, M., MALEKZADEH, R. and MARIANI-COSTANTINI, R., 2014. Epidemiological transition of colorectal cancer in developing countries: environmental factors, molecular pathways, and opportunities for prevention. World Journal of Gastroenterology, vol. 20, no. 20, pp. 6055-6072
22. BRAY, F., FERLAY, J., SOERJOMATARAM, I., SIEGEL, R.L., TORRE, L.A. and JEMAL, A., 2018. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: A Cancer Journal for Clinicians, vol. 68, no. 6,
23. Bera TK, Kar SK, Yadav PK, Mukherjee P, Yadav S, Joshi B. Effects of monosodium glutamate on human health: A systematic review. World journal of pharmaceutical sciences. 2017 Apr 26:139-44.
24. Greiner L, Graham A, Goncalves M, Orlando U, Touchette KJ. Evaluation of the optimal standardized ileal digestible valine:lysine ratio in lactating sow diets1. J Anim Sci. 2019 Jul 2
25. Zanfirescu A, Ungurianu A, Tsatsakis AM, Nițulescu GM, Kouretas D, Veskoukis A, Tsoukalas D, Engin AB, Aschner M, Margină D. A review of the alleged health hazards of monosodium glutamate. Comprehensive reviews in food science and food safety. 2019 Jul;18(4):1111-34.
26. Hajihasani MM, Soheili V, Zirak MR, Sahebkar A, Shakeri A. Natural products as safeguards against monosodium glutamate-induced toxicity. Iranian Journal of Basic Medical Sciences. 2020 Apr;23(4):416.
27. Ekaluo U, Ikpeme E, Ibiang Y, Amaechina O. Attenuating role of vitamin C on sperm toxicity Induced by monosodium glutamate in albino rats. J Biol Sci. 2013;13:298–301. [Google Scholar]
28. Nandan P, Nayanatara AK, Poojary R, Bhagyalakshmi K, Nirupama M, Kini RD. Protective role of co-administration of vitamin D in monosodium glutamate induced obesity in female rats. J Natl Med Assoc. 2018;110:98–102. [PubMed] [Google Scholar]
29. Sayed Badawi M. Assessment of the possible protective effect of lycopene on monosodium glutamate-induced nephrotoxicity in adult male albino rat. Eur J Anat. 2019;23:215–221. [Google Scholar]
30. Ahmed M. Effect of some food additives consumption on the body weight and toxicity and the possible ameliorative role of green tea extract. Sciences. 2016;6:716–730. [Google Scholar]
31. Huang J, Wang Y, Xie Z, Zhou Y, Zhang Y, Wan X. The anti-obesity effects of green tea in human intervention and basic molecular studies. Eur J Clin Nutr. 2014;68:1075–1087. [PubMed] [Google Scholar]
32. Stoilova I, Krastanov A, Stoyanova A, Denev P, Gargova S. Antioxidant activity of a ginger extract (Zingiber officinale) Food Chem. 2007;102:764–770. [Google Scholar]
33. Vucic M, Cojbasic I, Vucic J, Pavlovic V. The effect of curcumin and PI3K/Akt inhibitor on monosodium glutamate-induced rat thymocytes toxicity. Gen Physiol Biophys.

2018;37:329–336. [PubMed] [Google Scholar].

HOW TO CITE: Bhagwat A*., Pardeshi S., Gawali D., Ugale P.G., Suspected Health Hazards of Monosodium Glutamate -Review, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 12, 2341-2355. https://doi.org/10.5281/zenodo.14504826