

Monosodium glutamate and some non-communicable diseases

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ABSTRACT

Monosodium glutamate (MSG), also known as sodium glutamate, is a white odourless crystalline powder that is derived from L-glutamic acid, a naturally occurring amino acid in a variety of food products, especially those rich in protein. Glutamate is a key component in determining the flavour of these foods. MSG adds a special taste to food, due to this special taste; many food producers use it for their products. Currently, people are busy with their technology-based busy work schedules in different sectors and in such a fast-paced life; they have minimal time for meal preparation, which makes most of them depend on “ready-made foods” or “junk foods”. Moreover, even when they prepare their own meals, they still make use of ready-made condiments, spices, and seasonings containing MSG. The majority of such foods have harmful effects on human health. Widely using MSG in ready-made fast food significantly affects the appetite centre, resulting in overweight and different adverse impacts on humans and experimental animals. This paper helps to create global awareness of the harmful impact of MSG on human health and recommends the consumption of natural seasonings and spices as an alternative to MSG.

INTRODUCTION

Monosodium glutamate (MSG), also known as sodium glutamate, is a sodium salt of glutamic acid. It is a white odourless crystalline powder and contains 78% glutamic acid, 21% sodium, 1% contaminant, and water ($C_5H_8NO_4Na$)¹. Water ionizes MSG into free sodium

KEYWORDS

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‘READY TO EAT FOODS’

CONDIMENTS

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um ions and glutamic acid, which is an organic compound consisting of five carbon atoms². MSG is one of the most widely employed food taste enhancers and is added to a variety of products at concentrations ranging from 0.1-0.8% of weight³. MSG is a flavour enhancer derived from L-glutamic acid, a naturally occurring amino acid in a variety of food products⁴. Glutamate is one of the most common amino acids (amino acids are monomers of macromolecules called proteins) found in nature, and virtually every food contains glutamate, especially those rich in protein and foods such as carrot, algae, mushrooms, onion, cabbage, potato, egg yolk, cheese, soy sauce, and shrimp². It is the main component of many proteins and peptides and is present in most tissues. Glutamate is also produced in the body and plays an essential role in human metabolism⁵. It is known as a nonessential amino acid, and it usually exists in two forms: bond and free⁶. Glutamate is a key component in determining the flavour of these foods; however, it only functions as an enhancer when it is

in its “free” form, not when it is bound to other amino acids in proteins⁷. Only a fraction of the glutamate in foods remains in a “free” form. When MSG is added to foods, it provides a flavour similar to that of naturally occurring free glutamate⁸. MSG has a unique flavour and a distinctive taste that falls outside the region of the four classic tastes: sweet, sour, salty, and bitter. This taste is called “Umami” by the Japanese, “Xien Wei” in Chinese, and “savory, broth-like” or “meaty taste” in English². MSG adds a special taste to food due to this special taste; many food producers use it for their products^{9,2}. MSG is also used as a food additive (E621) in the form of hydrolysed protein or as a purified monosodium salt¹⁰. Food additives are substances that are added to food for a specific purpose, and they are either natural or industrial¹¹. Although these substances do not have their own taste or flavour, they can improve or enhance the original taste/flavour of the food to which they are added^{6,12}.

The use of MSG became popular because of the development of the food industry over the past 30 years. It is used as a food additive in frozen entrees, crackers, canned tuna, soups, processed meats, dietary supplements, infant formula, salad dressings, and some types of cheese and vegetables (tomato, mushroom, and broccoli). It is also used to enhance the natural flavour of meat, seafood, poultry, snacks, soups, and stews^{4,10,13}. Of the two isomers of MSG, the l-glutamate and the d-glutamate enantiomers, the L-glutamate enantiomers only exert flavour-enhancing effects. However, various companies have prepared MSG with 99.6% naturally predominant l-glutamate to enhance the flavour of fast food for commercial purposes, which is greater than the percentage of free glutamate ions found in natural foods¹⁴. In addition to increasing taste and palatability, MSG also contributes to the improvement of flavour characteristics such as complexity, mouth-fullness, continuity, and mildness^{15,6}. This savory taste sensation of MSG increases the attraction to a specific type of food or food product. Packaged and processed foods such as frozen foods, potato chips, salty snacks, sauces, sausages, and any other packaged products contain MSG. Because MSG is contained in so many products, it is almost impossible to make a list that encompasses all of them¹⁶⁻¹⁸.

The safety of MSG is approved by official agencies worldwide. The Food and Drug Administration stated that MSG is safe when it is used in limited amounts. MSG intake of 16.0 mg/kg of body weight is generally regarded as safe¹⁹. In 2017, the European Food Safety Authority (EFSA) re-evaluated the safety of glutamate, and an “acceptable daily intake” of 30 mg per kilogram of body weight was established⁴. However, the

safe dose of MSG for long-term daily intake has not yet been specified²⁰. Information regarding the amount of glutamate ingested by humans is scarce in the literature²¹. According to Henry-Unaeze²², the estimated daily MSG exposures in Europe (United Kingdom) and Africa (Nigeria) were 600 and 560-1000 mg/capita/day, respectively. Furthermore, in East and Southeast Asia, MSG exposure was 2-3 times greater than that reported in Europe: 1500-3000 mg/capita/day in Taiwan, 1100-1600 mg/capita/day in Japan, and 1600-2300 mg/capita/day in South Korea²². The daily consumption of MSG at doses of 80, 160, and 320 mg/kg body weight is equivalent to 1.5, 3, and 6 teaspoons of MSG for adults, respectively²⁰. MSG consumption as an additive accounts for approximately 5-10% of the total daily glutamate intake from various dietary sources²³. This does not necessarily exonerate MSG toxicity. For example, the ingestion of free unbound glutamate may lead to transiently high or rapidly changing plasma concentrations, which are not obtained when glutamate is gradually released from dietary protein and other food sources, which makes it harmful²⁴. In addition, MSG causes Chinese restaurant syndrome (CRS) by causing symptoms such as back-neck burn, blistering on the arms or anterior thorax, flushing, dizziness, syncope, and facial pressure, which occur just 20 minutes after consuming a ready-made food rich in MSG²⁵. Some of the reactions associated with MSG are headaches, nausea, flushing, accelerated heartbeat, chest pain, sweating, pressure or numbness in the face, and weakness²⁶. The addition of food additives and MSG to almost all processed foods has increased the consumption of MSG. It is therefore critical to identify potential risks and raise public awareness about MSG consumption^{27-29,13}. Furthermore, it is not easy to conduct an experimental trial to identify the chronic effect of MSG on non-communicable diseases in humans, as there are several complications, ethical implications, and dietary instructions. However, rodent models are very productive for this purpose¹³. Exposure of rats to MSG was found to damage hypothalamic nuclei³⁰, glycosuria³¹, and overactivation of glutamate receptors in the brain.

PRODUCTION OF MONOSODIUM GLUTAMATE (MSG)

MSG was first extracted from seaweed (*Laminaria japonica*) by a Japanese chemist called Kikunae Ikeda in 1908³². The commercial production of MSG began in 1909, when it became a seasoning and was named AJI-NO-MOTO⁶.

Mainland China is largely responsible for the recent increases in global production and consumption of MSG. In 2021, mainland Chinese's production and consumption accounted for the majority of both world production and consumption of MSG³³. Mainland China is also the world's largest exporter of MSG³³. Africa accounted for approximately 4% of the world's MSG consumption in 2021³³. Africa has no MSG producers and relies entirely on imports to satisfy demand. Mainland China has replaced Brazil as the major supplier of MSG to Africa. Nigeria is the largest market for MSG, as it accounts for approximately half of Africa's MSG demand. Africa's consumption of MSG is expected to increase at an average annual rate of 2.8% during the forecast period³³. The reason for the increased MSG consumption in West Africa is its common use in food, such as soup, rice, noodles, and potatoes¹⁰.

THE USE OF MONOSODIUM GLUTAMATE (MSG) IN FOODS

MSG is mostly used in the food processing industry and is used mainly for the processing of convenient, instant and fast foods such as snacks, canned food, and frozen food⁶. The food processing industry is the largest segment of the MSG market. In addition, it is directly sold to consumers, restaurants, and institutional foodservice providers as a condiment and seasoning blend⁶. MSG has been used for more than 100 years to season food²⁶. Food seasoning is a substance that adds flavour to food, for example, bouillon cubes. Seasonings can also be used to replace common salt in a great variety of other industrially prepared food items as well as in the preparation of food in restaurants, and home kitchens¹². The addition of various ingredient mixtures and seasonings to various food items changes the food composition^{34,2}. Reports have indicated that the major active ingredients in flavour enhancers are salt (NaCl) and MSG³⁵. It has been reported that different food industries, cafeteria, and restaurants add a high amount of MSG, and their aim is to enhance the flavour of the fast food formulation^{36,37,12}. Foods containing MSG have a high glycaemic index and high energy density, increasing both the glycaemic index and energy density. This is because of the high amounts of salts in the form of MSG (instead of common salts such as sodium chloride), trans-fatty acids, saturated fatty acids, and hydrogenated fats with low levels of dietary fibre^{36,37,12}. Therefore, a greater intake of food from these sources means a greater intake of MSG.

NON-COMMUNICABLE DISEASES (NCDs)

Non-communicable diseases (NCDs) are chronic diseases resulting from a combination of genetic, physiological, environmental, and behavioural factors³⁸. The four major NCDs include cardiovascular diseases, cancer, diabetes, and chronic respiratory diseases. Non-communicable diseases are an essential global cause of death and are responsible for more than 70% of deaths worldwide³⁹. Non-communicable diseases are silent killers threatening health without causing any symptoms until the problem progresses to an advanced stage⁴⁰. Annually, non-communicable diseases are responsible for 41 million of the 57 million fatalities worldwide, 15 million of which are premature (30-70 years)³⁹. The burden is greatest in low- and middle-income countries, where 78% of global NCDs fatalities and 85% of premature deaths occur⁴¹. The increasing prevalence of non-communicable diseases in low medium-income countries (LMICs) in the sub-Saharan African (SSA) region has reached epidemic levels. An important component implicated in the high morbidity and mortality in this region is the western pattern of life and high urbanization⁴².

Non-communicable diseases have multiple genetic, environmental, and behavioural determinants. However, the epidemiological shift observed in the last few decades is primarily attributable to changes in a few major modifiable risk factors, including dietary factors³³. A lot of evidence confirms that the increase in unhealthy diets is among the major drivers of the global NCD pandemic^{33,43}. In 2017, 11 million adult deaths were attributable to dietary factors³³. Inadequate intake of fruits, vegetables, and dietary fibre and high intake of salt, sugar, alcohol, and fats lead to NCDs^{33,43}. All over the world, unnecessary modification of food habits and delicious foods are directly associated with general health issues of people. Currently, people are busy with their technology-based busy work schedules in different sectors, industries, and companies. In such a fast-paced life, they have minimal time for meal preparation⁴⁴. Moreover, even when they prepare their own meals, they still make use of ready-made condiments and seasonings. For these reasons, most of them are dependent on "ready-made foods" or "junk foods", either from the canteen or nearby cafeterias or street-side local restaurants. These "ready-made foods" or "junk foods" contain MSG, as food producers use it to increase taste and palatability^{45,46,13}. Ready-made foods or junk foods have become increasingly popular among people with the arrival of pizza, hamburgers, fried chicken, chips, hot dogs, Chinese stir-fried noodles, French fries, cheese chili, and some other snacks and

“spicy yummy” food items from either local restaurants or cafeteria^{45,46,13}. Over the past few years, the regular consumption of chemically processed foods with food additives has markedly increased worldwide. This type of food triggers addictiveness towards specific foods containing MSG^{47,48}. Globally, there is a positive link between the consumption of such kinds of food and their impact on human health⁴⁷.

RISK FACTORS OF NON-COMMUNICABLE DISEASES (NCDS)

The risk factors for non-communicable diseases include metabolic-physiological-related conditions like obesity, high blood pressure, high fasting plasma glucose, and high blood cholesterol. Also, behaviour-related activities (including smoking, low physical activity, unhealthy diet consumption, and excessive use of alcohol) are risk factors⁴¹. Dietary risk is defined as eating a diet low in whole grains, nuts, seeds, fruit, vegetables, fibres, legumes, omega-3 fatty acids, polyunsaturated fatty acids, milk, and calcium, as well as a diet high in sodium, trans fats, red or processed meat, and sugar-sweetened beverages (SSB)⁴¹. In our diet, the main source of sodium is salt, but it can also be obtained from sodium glutamate, which is used as a food additive in many processed foods. A greater intake of dietary sodium is associated with increased blood pressure⁴⁹. Excessive salt consumption is linked to adverse health outcomes, such as an increased risk of hypertension (increased blood pressure), which in turn leads to stroke and heart disease⁵⁰.

In 2019, approximately 1.9 million deaths worldwide were attributed to a high-salt diet³³, and the number of deaths increased by 42.8% from 1990 to 2019⁵¹. An estimated 2.5 million deaths could be prevented each year if global salt consumption were reduced to the recommended levels⁵². Salt intake reduction is also known to be one of the most cost-effective or even cost-saving non-communicable disease control measures⁵³. The maximum daily intake of dietary sodium recommended by the WHO is 5 g for adults, but currently, most pop-

ulations consume much more^{54,49}. The importance of sodium reduction as a practical prevention measure for cardiovascular disease is widely known^{55,50}. However, salt intake in almost all countries exceeds the World Health Organization's (WHO's) recommendation^{56,50}. High salt intake was reported as a leading dietary risk factor for more than 3 million deaths and 70 million disability-adjusted life years in 2017^{57,50}. Salt reduction is an urgent issue worldwide⁵⁰. MSG can be used to reduce sodium in foods by replacing sodium with MSG, and it contains approximately 12% sodium, which is two-thirds less than that contained in table salt²¹.

The safety and toxicity of MSG have become controversial in the last few years because of reports of adverse reactions in people who have eaten foods that contain MSG. Many studies have confirmed the adverse reactions of MSG^{58,59,2}. MSG reportedly causes headache, vomiting, diarrhoea, irritable bowel syndrome, asthma attacks in asthmatic patients, and panic attacks². The safe dose of MSG for long-term daily intake has not yet been specified. Widely using MSG as a food additive in ready-made fast food enhances the palatability of the meals but significantly affects the appetite centre, thereby resulting in overweight and different adverse impacts on humans and experimental animals⁶⁰. Researchers have proposed that there is a positive relationship between fast food consumption and obesity¹². Bawaskar et al²⁵ and Banerjee et al¹³ demonstrated that the consumption of fast food rich in MSG causes several symptoms, such as burning sensations in different parts of the body, blistering on the arms, occasionally on the anterior thorax, weakness, fatigue, and palpitations just after 20 minutes of eating a meal. Manufacturers are expected to indicate on the label that a product has MSG, and consumers are expected to read the list of ingredients before buying canned and other processed goods²⁶. Although manufacturers indicate on the label that a product has MSG, the exact amount used is not always specified. Earlier reports^{61,4} suggested that very minimal doses (i.e., 0.6 and 1.6 mg/g body weight for two weeks or 100-500 mg/kg body weight for three weeks) of MSG have harmful effects on humans and experimental animals (Figure 1).

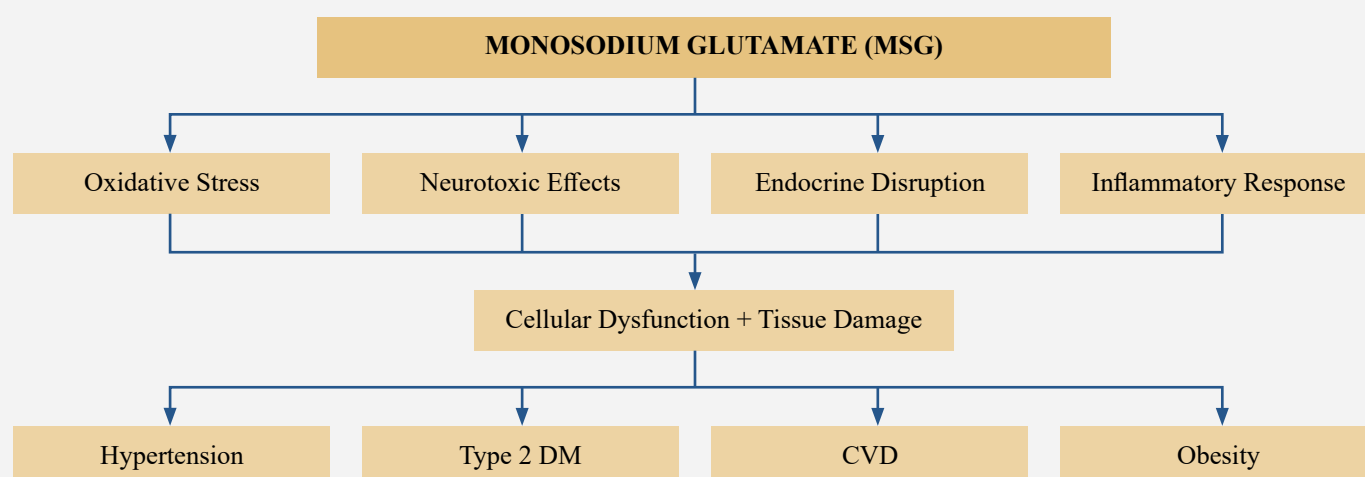


Figure 1. Mechanisms by which MSG may be harmful.

MONOSODIUM GLUTAMATE (MSG) AND SOME NON-COMMUNICABLE DISEASES

Cardiovascular Diseases

Diabetes, smoking, high blood pressure, high BMI, stress, high cholesterol levels, poor nutrition, and insufficient physical exercise are risk factors for the incidence of CVDs⁴¹. Earlier, evidence suggested that the administration of MSG during a certain period leads to oxidative stress (OS) in the heart with elevated levels of cardiac marker enzymes such as lactate dehydrogenase (LDH), aspartate transaminase (AST), and alanine transaminase (ALT)^{62,13}. Cardiovascular diseases are complex, and many metabolic disorders, especially oxidative stress, play a role in their development⁶³. A study by Banerjee et al¹² revealed that an MSG mixed with a high-lipid diet (HLD) provokes severe hepato-cardiac anomalies by altering redox equilibrium, the inflammatory response, and programmed cell death, activating the NF-κB and mitochondrial caspase-mediated pathways.

Arrhythmias

Rhythmias are irregularities in the heartbeat, including when it is too fast or too slow. A resting heart rate that is too fast (above 100 beats per minute in adults) is called tachycardia, and a resting heart rate that is too slow (below 60 beats per minute) is called bradycardia.

Liu et al⁶⁴ administered MSG intravenously (i.v.) to healthy rats at 0.5 g/kg body weight and 1.5 g/kg body weight. In healthy rats, a single dose of 0.5 g/kg body weight intravenous (i.v.) MSG caused a decrease in heart rate, while 1.5 g/kg body weight intravenous MSG caused bradycardia (slow heart rate). In another study, forty male Wistar albino rats were divided into 3

groups. The control group was injected intraperitoneally with physiological saline for 7 days. The second group was injected intraperitoneally with MSG at a dose of 4 mg/g body weight/day for seven consecutive days and then kept without any treatment until the 45th day of the experiment. The third group was injected intraperitoneally with MSG at a dose of 6 mg/g body weight/day for 7 consecutive days and then kept without any treatment until the 45th day of the experiment. MSG significantly elevated heart rate; serum levels of total cholesterol, low-density lipoprotein, and triglycerides; the atherogenic index; troponin T; the activities of serum lactate dehydrogenase and creatine kinase-MB; malondialdehyde concentration; and P53 protein expression in cardiac muscle. In addition, it induced myocardial degeneration, cellular infiltration, collagen deposition in cardiac muscle, and periodic acid-Schiff staining. The study indicated that MSG exerted long-lasting functional and structural alterations in the heart of male albino rats⁶⁵. Konrad et al⁶⁶ proposed that MSG-induced obesity is also associated with hypertension, bradycardia, and vagal-sympathetic effects. Injection of MSG led to bradycardia, enhanced mean blood pressure and reduced heart rate variability. Moreover, MSG-induced obesity is caused by the accumulation of extra fat in adipose tissue due to cholesterol upregulation, which ultimately leads to cardiovascular disorders³⁵. A significant observation reported by Geha et al⁶⁷ was that eating ready-made Chinese foods produced a noticeably rapid heart rate with some other symptoms in humans (e.g., CRS). According to the above reports, MSG-induced cardiac anomalies are caused by alterations in cardiac marker enzymes and dyslipidaemia, disturbances in the balance between free radical and antioxidant levels, OS, necrosis of cardiomyocytes, and cardiac arrhythmia¹³.

Hypertension/high blood pressure

Hypertension or increased blood pressure is defined as a systolic and/or diastolic blood pressure greater than or equal to 140/90 mmHg⁴¹. Several risk factors could be involved in the occurrence of high blood pressure, including high salt intake, being overweight or obese, excessive use of alcohol, low or lack of physical activity, stress, and smoking. Hypertension is an established risk factor for cardiovascular disease (CVD) and contributes to 1 in 7 cardiovascular-related deaths⁶⁸.

Nattaya et al²⁰ investigated the effects of MSG on arterial blood pressure (ABP) and renal excretory function in male Wistar rats. Male Wistar rats were divided into 2 groups ($n = 24$ each), namely, the sham operation (SO) and 2-kidney-1-clip (2K1C) groups, to establish normotensive and hypertensive models, respectively. Four weeks after the operation, each group of rats was further divided into 4 subgroups ($n = 6$ each), and they were orally administered either distilled water or MSG at doses of 80, 160, or 320 mg/kg body weight/day once a day for 8 weeks. All doses of MSG significantly increased the ABP in both the SO and 2K1C groups. Long-term intake of 320 mg/kg BW MSG significantly decreased the renal excretion of salt and water in both the SO and 2K1C groups. The study concluded that MSG consumption contributed to an increase in oxidative stress, which could lead to alterations in cardiovascular and renal function²⁰.

Epidemiological studies have reported the association between dietary MSG consumption and hypertension. The frequent consumption of high-salt food from these sources, i.e., ready-to-eat food, food away from home, home food cooked with bouillon cubes or MSG, was found to be positively associated with hypertension⁶⁹. In addition, an association between ready-to-eat food and hypertension was observed in one study among individuals who regularly purchased ready-to-eat or instant food that contains high amounts of MSG⁷⁰. Another epidemiological study also investigated the association of MSG with hypertension⁷¹. In this study, when blood pressure was evaluated at baseline, there was no association between MSG intake and the incidence of hypertension. However, at follow-up, an association between MSG intake and blood pressure appeared. When the data were adjusted for a number of covariates, it was found that there were significant interactions for MSG intake and blood pressure among participants who took hypertension medication⁷¹.

Diabetes Mellitus

The prevalence of diabetes mellitus has increased over the years. The conservative estimate for the prevalence of diabetes in 2019 was 9.3% (463 million people), which is expected to increase by 2030 to 10.2% (578

million) and by 2045 to 10.9% (700 million)⁴¹. MSG consumption was associated with diabetes⁷².

Chevassus et al⁷³ investigated the effects of monosodium (l)-glutamate on insulin secretion, glucose tolerance, and insulin sensitivity during an oral glucose tolerance test in healthy volunteers. Eighteen healthy volunteers, aged 19-28 years (mean 22 years) and weighing 52-81 kg (mean 68 kg), were included in a randomized double-blind placebo-controlled crossover investigation. The subjects were assigned to receive a single oral 10 g dose of monosodium (l)-glutamate or placebo. They were both packaged in identical capsules to mask the taste of glutamate and maintain the integrity of the blind. The two treatments were separated by a 7-day washout. On the morning of each test day, the subjects were admitted to the Clinical Investigation Centre under fasting conditions for at least 12 hours. Two baseline venous blood samples were taken at 15-minute intervals. Then, the treatment (20 capsules of monosodium (l)-glutamate or 20 capsules of placebo) was administered simultaneously with an oral glucose load (75 g). Blood samples were taken at 15, 30, 45, 60, 75, 90, 105, and 120 minutes after the start of the oral glucose tolerance test (OGTT). The results showed that the 75 min insulin response (area under the curve (AUC) (0, 75 min)) was significantly correlated with the AUC (0, 75 min) of glutamate concentrations ($r = 0.485$, $p = 0.049$), while glucose tolerance was not affected. They concluded that oral glutamate is able to amplify glucose-induced insulin secretion in a concentration-dependent manner in humans at concentrations in the low micromolar range.

An animal study conducted by Nagata et al³¹ demonstrated the effects of MSG on diabetes. MSG injections (2 mg/g body weight) were given to newborn mice. This resulted in the following: elevated fasting blood glucose levels, glycosuria, insulin, triglycerides, and cholesterol levels, and ultimately type 2 diabetes³¹. In another study carried out by Ogbuagu et al⁷⁴, MSG was supplemented at 500, 750, 1000, and 1250 mg/kg body weight/daily for 8 weeks. They found that because of MSG supplementation, fasting blood glucose increased in all MSG groups (except those receiving 500 mg/kg body weight/daily). For this reason, the study showed that the increase in blood glucose by MSG is an indication that it can induce DM⁷⁴. In addition, 4 mg/g body weight parenteral MSG in mice caused insulin resistance⁷⁵. Insulin resistance (IR) and hyperinsulinemia are responsible for the development of obese neonatal rats exposed to MSG. The administration of MSG (4 g/kg bw/daily after birth for 5 days) increased total cholesterol and insulin levels, leading to metabolic syndrome (MetS)-like features in mice⁷⁶.

METABOLIC RISK FACTORS OF NON-COMMUNICABLE DISEASES

Metabolic Syndrome

Metabolic syndrome is a collection of diseases, including obesity, hyperglycaemia, dyslipidaemia, high blood pressure, diabetes, steatosis of the liver, and cardiovascular disorder (CVD)⁷⁷. Metabolic syndrome is also known as insulin resistance syndrome, Reaven syndrome, dysmetabolic syndrome, and syndrome X (SX)⁷⁸. Individuals with metabolic syndrome must have at least hypertension, high levels of triglycerides, decreased levels of 'good cholesterol', and elevated levels of blood sugar¹³. All these factors will additionally alter insulin signalling in the brain and the release of free fatty acids from adipose tissue, which also triggers glucose production in the liver and very-low-density lipoprotein (VLDL), and they simultaneously reduce the level of 'good cholesterol'⁷⁷. Moreover, some factors, including a lack of physical activity, an inflammatory response for a prolonged period, an elevated level of leptin, malfunction of mitochondria, genetic susceptibility, pancreatic dysfunction with the destruction of β -cells and increased levels of free fatty acids, and reduced uptake of glucose in skeletal muscle with increased production in the liver, have been identified. All these factors stimulate the progression of metabolic syndrome via the alteration of insulin signalling⁷⁷.

Epidemiological surveys on humans have also proposed that MSG in the diet promotes metabolic syndrome^{79,13}. A study showed a positive correlation between metabolic disorders and MSG among Thailand's rural people^{79,13}. It has been reported that the consumption of high doses of MSG may cause neurotoxicity, cardiotoxicity, hepatic and renal disorders, and metabolic disorders^{80,4,6,27}. In addition, MSG consumption leads to disruption of energy balance and disturbs the leptin-mediated hypothalamus signalling pathway, leading to obesity^{81,13}.

In animal studies, there are reports on the effects of MSG and metabolic syndrome. Subcutaneous (SC) MSG injections (2 mg/g body weight) given to newborn mice resulted in central obesity⁸². Olguin et al³ carried out preliminary research to evaluate the eventual effects of the oral intake of MSG as a food additive on adult IIMb/Beta obese and diabetic rats by adding 1 g/kg body weight of MSG to commercial feed. Twelve male rats (70 days old) were randomly divided into two groups. The control and MSG treatments (with 1 mg of MSG/g of feed) were used. The rats were housed in individual cages and given food and water for 40 days. An important finding of the study was the significantly greater relative weight of the retroperitoneal

fat pads in the MSG group. This abdominal fat depot is usually considered one of the risk factors for metabolic syndrome and can be considered a negative effect of the addition of MSG. It also induces diet-dependent hepatic steatosis. The important and original contribution of the research lies in the fact that MSG levels are frequently reached in the human diet when it is used as a food additive. In this research, the negative effects of MSG were manifested as larger abdominal fat depots and greater relative liver weight, as well as liver steatosis, and these are two risk factors for metabolic syndrome³.

Obesity

Obesity, defined as a body mass index (BMI) ≥ 30 kg/m², is a metabolic disorder with an increasing worldwide prevalence. Obesity is a chronic, relapsing disease that represents a global public health challenge⁸³. It has long been recognized as an independent risk factor for a variety of chronic diseases, such as type 2 diabetes mellitus (T2DM), dyslipidaemia, hypertension (HT), stroke, and cardiovascular disease (CVD)⁸⁴. Indeed, BMIs above 29 kg/m² were linked to the development of T2D at 10 times greater than normal⁸⁵.

Epidemiological studies have reported the association of dietary MSG consumption with metabolic disorders such as obesity or above average weight^{86,87,50}. A cross-sectional and longitudinal study in healthy Chinese subjects correlated MSG intake with an increased risk of being overweight irrespective of total calorie intake and physical activity⁸⁶. In a study on 32 volunteers, it was shown that there is a link between the addition of MSG as a flavour enhancer to soup and increased food intake and hunger⁸⁸. A study provided MSG to some families for use in meal preparation for 10 days, and MSG consumption was at 4.0 ± 2.2 g/day. MSG intake increased the prevalence of metabolic syndrome (MetS) and BMI in a dose-dependent manner, independent of total energy intake and level of physical activity. Every 1 g increase in MSG intake significantly increased the incidence of MetS by 1.4-fold and overweight by 1.16-fold⁷⁹. Some studies on animal models reported that the addition of MSG was associated with increased energy intake and obesity⁵⁰. MSG supplementation (mixed with diet) at 500, 750, 1000 or 1250 mg/kg bw/daily for 8 weeks was observed to increase body weight gain in Wistar rats (n=40). Bodyweight gain was greater in the group that consumed 750 mg/kg bw/daily than in the other groups⁷⁴. Exposure of rats to MSG at the neonatal stage can severely damage hypothalamic nuclei (the arcuate nucleus and ventromedial nucleus), which results in increased body weight, fat deposition, decreased motor activity, and growth hormone secretion³⁰. The

potential link between MSG and obesity includes the effect of MSG on energy balance by increasing the palatability of food and disrupting the hypothalamic signalling cascade of leptin^{89,2,87}. Leptin is a hormone that signals to the brain that a person has had enough to eat, and it shuts off the appetite and increases caloric intake. Leptin signalling problems, called leptin resistance, are factors in obesity. The MSG stimulation of orosensory

receptors and improvements in the palatability of meals influence weight gain. Monosodium glutamate causes a reduction in the secretion of growth hormones, leading to stunted growth and irreversible obesity and excessive weight, essentially due to the accumulation of excess fats in adipose tissue, which arises from high cholesterol levels and leads to cardiovascular diseases and endocrinological disorders² (Table 1).

Table 1. Reported negative effects of monosodium glutamate (MSG) and their potential link to non-communicable diseases.

Effect	Associated Non-Communicable Disease(s)	Proposed Mechanism	References
Obesity	Obesity, Metabolic Syndrome	Appetite stimulation via hypothalamic damage or leptin resistance	He et al, 2008 ⁸⁶ ; Insawang et al, 2012 ⁷⁹
Insulin Resistance	Type 2 Diabetes Mellitus	Pancreatic β -cell dysfunction and impaired glucose metabolism	Nakanishi et al, 2008 ⁸²
Insulin Resistance	Type 2 Diabetes Mellitus	Pancreatic β -cell dysfunction and impaired glucose metabolism	Nakanishi et al, 2008 ⁸²
Migraine and Headaches	Chronic Neurological Conditions	Vasodilation or reaction to food additives	Geha et al, 2001 ⁶⁷

NATURAL ALTERNATIVES TO MONOSODIUM GLUTAMATE (MSG)

Locust Beans

Locust bean (*Parkia biglobosa*) is used as a seasoning material for cooking in different parts of Nigeria. It is very popular among the people of Nigeria, where it is called (iru) in Yoruba, (ogiri) in Igbo, (dawadawa) in Hausa, and (okpeai) in Igala language. It can be fresh or dry. Locust bean is high in lipids (29%), proteins (35%), and carbohydrates (16%)². The mineral elements present in locust bean are calcium, potassium, magnesium, iron, and phosphorus⁹⁰. The level of crude fibre in locust bean is high, which is considered advantageous since high fibre contents are desirable in meal, as it is known to be most effective in maintaining human health, such as reducing body weight, diabetes, stroke incidence, and heart health. Locust beans have the ability to minimize the effect of MSG on human health. It can be used as an alternative to seasonings containing MSG. Airaodion et al⁹¹ carried out a study to investigate the effect of African locust bean on the fasting blood sugar and lipid profiles of ten adult male albino rats with body weights of 100 and 120 g. The rats were divided randomly into 2 groups of five rats each. Animals in group 1 were administered normal saline solution, while those in group 2 were administered extracts of African locust bean. The animals were exposed to African locust bean and saline solution at a dose of 3 ml per 100 g body weight 12 hours via the oral route of administration for fourteen days. Locust

bean significantly decreased the fasting blood sugar, total cholesterol and triglyceride levels but significantly increased the HDL cholesterol level compared with those in the control group ($p < 0.05$). LDL-C was not significantly different between Locust bean-treated animals and control animals. The study concluded that Locust bean can serve as prophylaxis and remedies for several diseases caused by hyperglycaemia and hyperlipidaemia, such as diabetes and coronary heart disease. This is because increased blood sugar and hyperlipidaemia have been implicated in diabetes, and cholesterologenesis is a major cause of atherosclerosis and subsequent cardiovascular diseases.

In addition, another study was carried out on humans by Ognatan et al⁹² to identify the possible effect of the consumption of fermented African locust bean seeds on the prevention of hypertension. Two populations were identified and compared: one was in a region (Bogou) where the condiment made from African locust bean seeds is highly consumed, and the other was in the region of Goumou Kope where they do not eat it at all. Blood pressure and heart rate were significantly lower in the group of people living in Bogou's region, where African locust bean was consumed, than in the group not consuming Goumou kope ($p < 0.001$). The magnesium level increased significantly in the Bogou group compared to that in the second group ($p < 0.0001$). Lower levels of low-density lipoprotein-cholesterol (91 ± 36 vs. 110 ± 44 mg/dL, $p = 0.01$) and triglycerides (111 ± 6 vs. 129 ± 6 mg/dL, $p = 0.028$) and higher levels of high-density lipoprotein-cholesterol (63 ± 2 vs. 48 ± 3

mg/dL, $p < 0.001$) were detected in subjects who regularly consumed fermented African locust bean seeds. Furthermore, the plasma glucose concentration was significantly lower in the Bogou group than in the Goumou-Kope group (68 ± 16 vs. 76 ± 15 mg/dL, respectively; $p < 0.001$). They concluded that fermented seeds of African locust bean exert an antihypertensive effect.

Garlic

Garlic (*Allium sativum*) is a species of the onion family. The bulb is widely used as a culinary spice and is an antioxidant; thus, it has numerous health benefits. Garlic also contains enzymes, calcium, copper, iron, manganese, phosphorus, potassium, and selenium. The vitamins in garlic include vitamin A, vitamin B1 (thiamine), vitamin B2 (riboflavin), vitamin B6, and vitamin C⁹³. It also contains some bioactive compounds, such as flavanols (e.g., catechin), and flavonols (e.g., kaempferol, myricetin, and quercetin)⁹⁴. Garlic has antioxidant, anti-inflammatory, antiobesity, antidiabetic, anticancer, cardioprotective, immunomodulatory and antibacterial properties⁹⁵. The cardiovascular protective effects of garlic are related to the inhibition of oxidative stress and lipid peroxidation and the control of angiotensin-converting enzymes and nitric oxide (NO) and hydrogen sulfide (H₂S) production. Moreover, garlic powder can reduce blood pressure, cholesterol (total and low-density lipoprotein cholesterol), and platelet aggregation⁹⁵. Fermented garlic reduces obesity by impeding lipogenesis and controlling lipid metabolism⁹⁵. The daily intake of garlic in various forms recommended by the WHO is 2-5 mg of oil, 2-5 g (one to two cloves) of raw garlic/fresh garlic, 0.4-1.2 g of dry powdered garlic, and 0.3-1 g of dry extract⁹⁶. As a dietary supplement, the American Dietetic Association recommends 600-900 mg of garlic per day⁹⁷.

Turmeric

A report by Airaodion et al³⁵ showed that turmeric (*Curcuma longa*) contains flavonoids and other antioxidants. Rhizomes contain vitamin C, minerals (e.g., iron, calcium, and sodium), flavanols (e.g., catechin), and flavonols (e.g., kaempferol and myricetin)⁹⁴. Turmeric also contains curcumin, a biologically active polyphenolic compound. Therefore, turmeric has the propensity to annul the effect of MSG on the body². In addition to potentially direct antioxidant activity, curcumin can induce the expression of phase II antioxidant enzymes, including glutamate-cysteine ligase (GCL), the rate-limiting enzyme glutathione synthesis. Glutathione (GSH) is an important intracellular antioxidant that plays a critical role in cellular adaptation to stress⁹⁸. Preclinical evidence suggests that the antiox-

idant, anti-inflammatory and glucose-lowering activities of curcumin and its analogues may be useful in the prevention and/or treatment of type 2 diabetes⁹⁹. In a nine-month, randomized, double-blind, placebo-controlled study in 237 subjects with impaired glucose tolerance (prediabetes), no progression to overt diabetes was reported with daily ingestion of a mixture of curcuminoids (0.5 g), while 16.4% of placebo-treated participants developed diabetes¹⁰⁰. In addition, curcumin supplementation was shown to reduce insulin resistance and improve measures of pancreatic β -cell function and glucose tolerance. Curry powder contains turmeric along with other spices, but the amount of curcumin in curry powder is variable and often relatively low¹⁰¹. Curcumin extracts are also used as food-colouring agents. Because of its ability to help balance glutamate levels, scientists have suggested the introduction of combinations of curcumin and MSG to the market¹⁰². For nutritional purposes, curcumin is normally applied at a dose of 5-500 mg/kg, depending on the food category¹⁰³. An acceptable daily intake (ADI) of 3 mg/kg b.w./day is recommended for adults and older individuals¹⁰⁴. However, curcumin has been found to be quite safe in animals and humans, even at doses up to 8 g/day¹⁰³.

Ginger

Ginger (*Zingiber officinale*) is used as a spice in food and beverages and in traditional medicine as a carminative and antipyretic agent and in the treatment of pain, rheumatism, and bronchitis¹⁰⁵. Its extracts have been extensively studied for a broad range of biological activities, including antibacterial¹⁰⁶, analgesic and anti-inflammatory, antiangiogenic and antitumour¹⁰⁷ activities. It is also used for the treatment of gastrointestinal disorders, including gastric ulceration¹⁰⁸. It contains minerals (e.g., potassium, copper, magnesium, silicon, manganese), vitamins (e.g., A, E, C, B1, B2, B3, B5, B6, B9, and B12)¹⁰⁹. It also contains flavanols (e.g., catechin), flavonols (e.g., myricetin), curcuminoids (e.g., curcumin), alkaloids, carotenoids, tannins, flavonoids, saponins, cardiolides, and steroids⁹⁴. Garlic is rich in vitamins, and it has been suggested that the toxicity of MSG can be overcome by the use of certain kinds of vitamins, such as vitamin A, C, D, and E¹¹⁰. The antioxidants contained in these vitamins can prevent the action of MSG in the body (MSG causes cellular death through oxidative stress). With the known benefits of vitamin C, it can reduce the adverse effects of MSG. Research has shown that vitamin C is an antioxidant that can eliminate free radicals produced in the body³⁵. Vitamin E exerts protective effects against diseases, which may be attributed to its powerful antioxidant properties. Research has shown that MSG induces ox-

oxidative stress and that vitamin E significantly reduces oxidative stress. As an antioxidant, it protects against the damaging effects of free radicals, which may contribute to the development of diseases⁹³.

Many bioactive compounds in ginger, such as phenolic and terpene compounds, have been identified. The phenolic compounds are mainly gingerols, shogaols, and paradols, which account for the various bioactivities of ginger¹¹¹. Ginger and its bioactive constituents, including gingerenone A, 6-shogaol, and 6-gingerol, have shown anti-obesity effects, and the underlying mechanisms are mainly related to the inhibition of adipogenesis and the enhancement of fatty acid catabolism. Studies have demonstrated that ginger has the potential to prevent and manage several diseases, such as cardiovascular diseases¹¹², obesity¹¹³, and diabetes mellitus¹¹⁴. The major pungent component in ginger is [6]-gingerol. This was administered to mice at 100 mg/kg body weight. It significantly decreased fasting blood glucose; improved glucose tolerance in type 2 diabetic mice; and lowered plasma triglyceride, total cholesterol, free fatty acid, low-density lipoprotein, and plasma insulin levels¹¹⁵.

A study was conducted by Wang et al¹¹⁶ to assess daily ginger consumption and explore its correlation with chronic diseases among adults and to further analyse how different levels of ginger intake affect the incidence of chronic diseases. The study was a large cross-sectional study of 4628 participants (1823 men and 2805 women aged 18 to 77 years). They found that daily ginger consumption was associated with a decreased risk for hypertension (odds ratio [OR], 0.92; 95% confidence interval [CI], 0.86-0.98) and coronary heart disease (CHD) (OR, 0.87; 95% CI, 0.78-0.96) in adults aged ≥ 18 years. Differences were also observed in adults aged ≥ 40 years for hypertension (OR, 0.92; 95% CI, 0.87-0.99) and CHD (OR, 0.87; 95% CI, 0.78-0.97). Again, the probability of illness (hypertension or CHD) decreased when the daily intake of ginger increased. Furthermore, the intake of dried ginger powder could reduce respiratory exchange ratios and promote fat utilization by increasing fat oxidation in humans¹¹⁷. With these biological activities, ginger can minimize the effect of MSG on human health².

Curry (*Murrayakoenigii*)

Curry is a combination of spices (turmeric, cumin, coriander, paprika, cardamom, and other spices) and herbs. It contains fat, protein, minerals (iron, calcium, and sodium), carbohydrates, fibre¹¹⁷, and phytochemicals such as flavanols (e.g., catechin), flavonols (quercetin and kaempferol)⁹⁴. It also contains carbazole (murrayanol, murrayagetin, marmesin-1"-O-rutinoside, mukoe-

nine-A, -B, and -C, murrastifoline-F, bis-2-hydroxy-3-methyl carbazole, bismahanine, biskoquinone-A and bismurrayquinone A, koenoline, mukoline, and mukolidine). Phytochemicals in curry have antioxidant, antidiabetic, cytotoxic, anticancer, immunomodulatory, antiobesity, antihyperlipidemic and hepatoprotective properties¹¹⁸.

CONCLUSIONS

The harmful effects of MSG described in this paper represent a silent threat posed by the consumption of this popular additive and flavour enhancer to society. This study demonstrated that MSG is dangerous to human health. Regular high-dose intake of MSG for a long period can lead to some non-communicable diseases. No food processing company shows the quantity of MSG used as a seasoning substance in their products. Therefore, when consumers use these 'ready-to-eat foods', condiments, and seasonings containing MSG, they are unaware of the quantity of MSG they consume. In addition, restaurants and food service institutions do not specify whether they use it at all, but they do use it. Restaurants use MSG instead of salt to improve the taste of specific foods, and surprisingly, they have proudly declared that they have not used food additives in their restaurant or foods¹⁵.

There is a need for nutritional education on the hazardous effects of MSG to enlighten the public. Regulatory bodies that are responsible for food labelling should ensure proper food labelling, as the amount of MSG added to foods is not specified. In addition, natural herbs and spices should be promoted.

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