

Review Article

Disruptive consequences of monosodium glutamate on male reproductive function: A review

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ABSTRACT

Monosodium glutamate (MSG) is one of the most extensively used flavour enhancers worldwide. Although it is widely regarded as a safe food additive with no recommended daily dosage, its over-consumption has been associated with notably pathophysiological events in various tissues and organs of the body. Previous studies have reported of the neuro- cardio- and hepato- toxic effects of its excessive exposure. Moreover, the food additive instigates metabolic dysfunction. It has been established that MSG damages male reproductive accessory organs like prostate glands and epididymis. In addition, it impairs serum enzymatic activities and serum levels of testosterone, gonadotropin-releasing hormone, luteinizing hormone and cholesterol. Reduced sperm count, sperm motility, sperm morphology, and sperm viability, imbalances in male reproductive hormones, alongside alteration in the histoarchitecture of the testes and other male reproductive tissues have also been connected with excessive exposure to MSG. Literature reports affirm the link between the over-consumption of MSG and reproductive organ weight and male sexual behaviour. This review article addresses the multi-systemic effects of exposure to MSG and the possible mechanism of action of the compound with a focus on the negative implications of the food additive on male reproductive functions and the possible role of natural antioxidants in male reproductive functions. Carefully selected keywords were used during the literature search to gather credible and up-to-date information about the subject matter.

1. Introduction

Lifestyle changes, work pressure and socialization have increased the accessibility of processed food to the society and as a result, promote exposure to flavour enhancers, which enhances the palatability of processed food. One major additive that is commonly employed in the world is Monosodium glutamate (MSG). It is found not only in processed foods, but also in many spiced food products, disguised behind ingredient labels and listed under different names (Erb and Erb, 2003;

Appaiah, 2010).

Monosodium glutamate is widely regarded as food additive that is safe for human consumption with no recommended daily dosage (Samuels, 1999). It is being abused in food due to its palatability characteristics and wide availability (Egbuonu et al., 2009). This flavour enhancer contains the sodium salt of L-glutamic acid (Hamza and Al-Harbi, 2014).

According to reports, the acceptable daily intake (ADI) for MSG set by the Joint FAO/WHO Expert Committee on Food Additives is 0.6 g per

Abbreviations: MSG, monosodium glutamate; GnRH, Gonadotropin-releasing hormone; LH, Luteinizing hormone; INS, International numbering system; ADI, average daily intake; LDL, low density lipoprotein; POMC, pro-opiomelanocortin; VIP, vasoactive-intestinal polypeptide; AgRP, agouti related protein.

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kilogram of body weight. This translates to 40 mg of MSG per kilogram of body weight per day (Roberts *et al.*, 2018). MSG is added to various stock cubes in Africa, specifically Nigeria, to enhance the overall flavor and boost the impact, consistency, and complexity of the final preparation of such cubes (Kadir *et al.*, 2011).

There are reports on the harmful effects of MSG on various biological functions (Farombi and Onyema, 2006; Husarova and Ostatnikova, 2013; Shimada *et al.*, 2013), and more specifically on male reproductive system (Igwebuike *et al.*, 2011; Rahimi Anbarkeh *et al.*, 2019). Studies have shown that MSG damages male reproductive accessory organs like prostate glands and epididymis (Hanipah *et al.*, 2018), decrease testosterone and epididymal sperm concentration in rats (Iamsaard *et al.*, 2014), lower serum gonadotropin-releasing hormone (GnRH), luteinizing hormone (LH), testosterone and cholesterol concentrations (Ochiogu *et al.*, 2015) and impairs serum ALT activities. Moreover, the compound causes testicular haemorrhage and apoptotic changes (Oforofuo *et al.*, 1997). Exposure to MSG has also been associated with the etiology of an ovulatory sterility in females (Eweka and Om'iniabohs, 2011).

Several theories have been proposed on how the taste enhancer interferes with male reproductive function. Taste receptors are also expressed in tissues other than the tongue, including the digestive tract, liver, respiratory tract, ovaries, and testes (Damak *et al.*, 2003; Li *et al.*, 2005; Yang *et al.*, 2021). Also, taste signaling factors including the taste receptor families 1, 2 and their downstream molecules, G α and PLC β 2 are reportedly distributed in the testes and epididymis tissues and their functions evidently linked to spermatogenesis, sperm maturation, and fertilization, which are potential targets for regulating male reproduction (Mosinger *et al.*, 2013; Luddi *et al.*, 2019; Jiang *et al.*, 2021; Liu *et al.*, 2022). MSG-induced renal, hepatic, and testicular toxicity has been linked to increased oxidative stress (Hamza and Al-Harbi, 2014; Oforofuo *et al.*, 1997), as the over-production of reactive oxygen molecules and hydrogen peroxide, which causes damage of the DNA and peroxidation of cell membranes, resulting in cell death (Rahimi Anbarkeh *et al.*, 2019).

In this review, the authors address the multi-systemic effects and mechanism of action of MSG, focusing on the male reproductive system.

2.1. Physico-chemical properties of MSG

2.1.1. Chemistry of MSG

Monosodium glutamate (MSG) is the sodium salt of L-glutamic acid, with the IUPAC designation - sodium 2-aminopentanedioate, in which one sodium atom substitutes hydrogen atom in the carboxyl group (Stanska and Krzeski, 2016) (Fig. 1). The compound has a code number of 621 in both the International Numbering System (INS) and the European System for food additives (Mortensen *et al.*, 2017). Monosodium glutamate is a colourless and odourless, crystalline substance that exists as a monohydrate. It has high water solubility (740 g/L); however, it is insoluble in organic solvents.

The food additive, MSG, has a high melting point of 232 °C, so it may be stored at room temperature for a long time without losing quality. The compound decomposes at a temperature above 350 °C, therefore, it maintains its stability during routine food processing (Mortensen *et al.*, 2017).

Monosodium glutamate has a molar mass of 169.111 g/mol and a chemical formula of C₅H₈NO₄Na and IUPAC name as sodium; 4-amino-

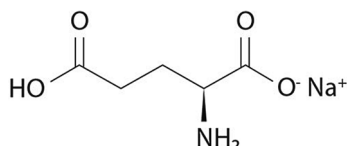


Fig. 1. Chemical Structure of Monosodium glutamate.

5-hydroxy-5-oxopentanoate. Monosodium glutamate appears as white or off-white crystalline powder with a slight peptone-like odor with pH of 7.0. It is freely soluble in water and practically insoluble in ethanol or ether (Zanfirescu *et al.*, 2019).

2.1.2. Monosodium glutamate in foods

The average dietary intake of MSG is about 0.3–1.0 g in European developing countries (Eweka, 2007). However, Asians consume 10 to 20 times the amount of MSG consumed by Europeans and Americans daily, which ranges from 1200 to 3000 mg (Brosnan *et al.*, 2014). In Nigeria, there tends to be an excessive intake of MSG. This is because high MSG content in processed foods is sold without being labeled, therefore, and the compound is frequently advertised and regarded as a safe food additive that requires no specified daily intake limit. Major sources of MSG Fast food includes chips and snack foods; seasoning blends, frozen meals, and soups.

2.1.3. Pharmacology of monosodium glutamate: metabolism and pharmacokinetics

After consumption, MSG is absorbed from the gastrointestinal tract by an active transport system that is particular for amino acids. Under the action of several enzymes, the compound is taken by the cells and catabolized in the cytosol and mitochondria. Several metabolic end-products of MSG like lactate, glutathione, glutamine, alanine, and other amino acids (Burrin and Stoll, 2009) can be found in the stomach, intestines, and colon (Maluly *et al.*, 2017). Besides catabolism, MSG produces alpha ketoglutarate, which enters the tricarboxylic acid cycle and releases energy (ATP) and carbon dioxide. The hepatic portal takes over Ingested glutamate that is not metabolized in the gastrointestinal tract is processed in the liver. The Krebs's cycle converts the metabolites of the compound into energy or excretory products like urea for removal via urine (Burrin and Stoll, 2009). In the central nervous system, MSG activates glutamate receptors, causing the release of neurotransmitters that are important in both physiological and pathological processes (Chakraborty, 2018). It should be noted that there are no guidelines stating the upper limit of MSG in natural food in the literature.

2.2. Multi-systemic effects of MSG

Because of its popularity and effectiveness in boosting food palatability, the projected average daily intake (ADI) of MSG has been on the increase over the years (Sand, 2005). The associated side effects of the over-consumption of the food additive on various systems in a biological organism is widely reported in literature.

The consumption of MSG has been linked to changes in the morphology of heart tissue and cardiac rhythm (Insawang *et al.*, 2012; Liu *et al.*, 2013). MSG supplementation enhances oxidative stress in cardiac tissue, resulting in biochemical changes indicated by raising activities of lactate dehydrogenase, aspartate transaminase, and alanine transaminase (Kumar and Bhandari, 2013).

There are reports on the hepatotoxic effects of over-consumption of MSG, Eweka *et al.* (Eweka *et al.*, 2011) reported on dilated central hepatic veins with lysed erythrocytes and deformed hepatic cells as a result of decreased liver cell membrane permeability following MSG administration in rats. Furthermore, metabolic abnormalities such as obesity, increased adiposity, hyperinsulinemia, elevated triglycerides, and LDL-cholesterol have been associated with exposure to MSG (Granholm *et al.*, 2008) Supplementation with MSG resulted in an increase in oxidative stress markers in the hepatic tissue, which was linked to hepatic lipid peroxidation, reduced glutathione level, catalase and superoxide dismutase activities (Eweka and Om'iniabohs, 2011; Onyema *et al.*, 2006; Nakanishi *et al.*, 2008; Paul *et al.*, 2012; El-Meghawry El-Kenawy *et al.*, 2013).

Monosodium glutamate (MSG) administration has been linked to neurotoxicity and behavioural changes, such as increased aggression, decreased locomotor activity, and muscle weakness (Izumi *et al.*, 2009;

Campos-Sepúlveda *et al.*, 2009; Rivera-Cervantes *et al.*, 2015; Swamy *et al.*, 2014). The aforementioned symptoms are associated with significant alterations in neuronal redox status and higher levels of oxidized lipid, concentration of nitrite, and lower concentration of antioxidants in the brain tissue (Rivera-Cervantes *et al.*, 2015).

Elevated levels of acetylcholinesterase in the brain and serum have been reported post-administration of MSG (Onaolapo *et al.*, 2016; Sadek *et al.*, 2016). Moreover, the compound has been shown to precipitate a reduction in AMP-activated protein kinase activity and elevations in the levels of the apoptosis mediator - Fas ligand in the hippocampus and in the pro-apoptotic Bax protein (Sadek *et al.*, 2016; Dief *et al.*, 2014).

MSG administration in female Wistar rats was reported to cause alteration in the serum progesterone and estrogen level although no significant changes in the uterine morphology (Abdulghani *et al.*, 2022). MSG also causes decreases in the ovarian weight, and some changes in the histology of ovaries such as the congestion of blood vessels of the medulla, and increased atretic follicles were reported (Mondal *et al.*, 2018; Agbadua *et al.*, 2020). Mondal *et al.* (Mondal *et al.*, 2017) reported that MSG suppresses the female reproductive function by impairing the functions of ovary and uterus. Also, MSG during pregnancy adversely influences fetal growth and skeletal development causing several biochemical and histological changes to the maternal and fetal liver and kidney tissues (Shosha *et al.*, 2023).

3. Monosodium glutamate and the male reproductive system

Literature reports affirm the association between exposure to MSG and reproductive organ weight, reproductive hormones, sexual behaviour, sperm indices and reproductive capacity (Kayode *et al.*, 2020; Haddad *et al.*, 2021).

Scientific studies showed that the body weight of rats treated with MSG was significantly increased (Haddad *et al.*, 2021; Abd El-Aziz *et al.*, 2014) with mainly histological alterations including the lumina of the seminiferous tubules and interstitial tissues with exfoliation of spermatocytes and spermatids observed in rats (Nakanishi *et al.*, 2008). The same study reported that many cells of the different types of spermatogenesis appeared necrotic with pyknotic nuclei with dilated congested blood vessels and vacuolar degeneration, thus establishing the deleterious effects of MSG on the testes (Bailey *et al.*, 2004). These are further emphasized below.

3.1. Effect of monosodium glutamate on reproductive organ weight

Organ weight analysis is an important marker of detrimental effects of chemicals in toxicological investigations (Zenick *et al.*, 1994). Studies have shown that changes in the weight of reproductive organs is a significant criterion for detecting changes in the levels of reproductive hormone (Iamsaard *et al.*, 2014).

Significant decreases were detected in the weight of the epididymis, testosterone levels, and sperm concentration (Iamsaard *et al.*, 2014). A decrease in testicular weight of Wistar rats has been reported following exposure to 4 mg/kg body weight of MSG administered intraperitoneally for 15 days (Iamsaard *et al.*, 2014; Nayanatara *et al.*, 2008) and subcutaneously for 75 days (Nosseir *et al.*, 2012). Moreover, intraperitoneal administration of MSG at 2 mg/kg and 4 mg/kg for 65 days reduce testicular and epididymal weights (Fernandes *et al.*, 2012). The weight loss in the reproductive organ weight was evident in the seminal vesicle in MSG-administered rats and rats treated with MSG exhibited partial testicular damage, characterized by sloughing of spermatogenic cells into the seminiferous tubular lumen, and their plasma testosterone levels. This is followed by decreased sperm concentration (Iamsaard *et al.*, 2014).

In addition, the subcutaneous administration of MSG at 2 mg/kg during the perinatal stage (second to the tenth day of life) in male Swiss albino mice increases the quantity of the pachytene phase of primary spermatocyte at day 75, relative to controls. In a similar study,

administration of MSG (4 mg/g) at similar periods to newborn rats led to reduced pituitary glands and testes weights (Iamsaard *et al.*, 2014).

Moreover, twelve weeks of oral exposure to MSG at 8 mg/kg decreased testicular weight of rats (Hamza and Al-Harbi, 2014). Reports also showed that the administration of MSG in Wistar rats at 3 mg/kg and 6 mg/kg for 30 days decreased the size and weight of the epididymis and seminal vesicle (Iamsaard *et al.*, 2014).

Egbuonu *et al.* (Al-Husseini *et al.*, 2022) reported that the ingestion of MSG might adversely alter the functional capacity of the prostate. Another recent study reported the toxic effect of MSG as it caused an elevation in the levels of NFκB in serum, testicular, and epididymis tissue fluid (Al-Husseini *et al.*, 2022). Histological alternation in the reproductive organs was also reported to represent detachment and vacuolation of the seminal epithelium, degeneration of spermatogenesis edema in a lumen in testicular tissues (Al-Husseini *et al.*, 2022). The study by Wang *et al.* (Wang *et al.*, 2021) documented that MSG can cause reproductive toxicity to male mice by damaging GnRH neurons thus the hallmark of male reproductive toxicity. Meanwhile Rahimi *et al.* (Rahimi Anbarkeh *et al.*, 2019) had reported that MSG-ingestion can lead to increase apoptotic changes in the germinal epithelial of the testicle.

3.2. Effect of monosodium glutamate on reproductive hormones

The hypothalamus is the principal higher coordinating centre for reproductive activities. It secretes GnRH, which stimulates the outflow of anterior pituitary hormones, viz; luteinizing and follicle-stimulating hormones, which controls testicular functions by acting on the Leydig's and Sertoli's cells respectively (Ekaluo *et al.*, 2013; Liu and Veldhuis, 2014).

The administration of MSG at 4 mg/kg for 120 days in Wistar rats has been documented to reduce serum concentration of GnRH (Ochiogu *et al.*, 2015), LH (Ochiogu *et al.*, 2015; Nayanatara *et al.*, 2008), FSH and testosterone (Nayanatara *et al.*, 2008). Reports also showed that exposure of Sprague Dawley rats to orally administered MSG at 3 mg/kg, 4 mg/kg and 6 mg/kg for 30 and 48 days respectively, resulted in reduced serum testosterone levels (Iamsaard *et al.*, 2014; Igwebuikwe *et al.*, 2011).

Research affirms that GnRH is under the tight regulation of several neuropeptides (Skorupskaite *et al.*, 2014) e.g. kisspeptin (Uenoyama *et al.*, 2015), neurokinin-B (Krajewski *et al.*, 2010), neuropeptide-Y (Tirassa *et al.*, 1995), pro-opiomelanocortin (POMC), galanin (Gabriel *et al.*, 1988), vasoactive-intestinal ploypeptide (VIP) (Rojas-Castañeda *et al.*, 2016; Yamakawa *et al.*, 2019) and Agouti related protein (AgRP), which are negatively affected by MSG exposure.

The decreased secretion of GnRH following MSG exposure in rats has also been established to be associated with increased generation of reactive oxygen species in multiple organs and tissues including the testes (Hanipah *et al.*, 2018). Impaired secretion of reproductive hormones at the hypothalamus and pituitary levels following MSG administration would compromise testosterone secretion and consequently negatively impact the process of spermatogenesis (Hamza and Al-Harbi, 2014; Pakarainen *et al.*, 2005). It should however be noted that there are limited studies on the effects of MSG exposure on serum level of testosterone.

3.3. Effect of monosodium glutamate on sexual behaviour

MSG has neurotoxic effects and promotes a variety of neuro-behavioral alterations, including anxiety and sadness (Narayanan *et al.*, 2010). The compound is thought to affect the physiology of arousal, sensitization, and libido activities by causing neuroendocrine harm (Nemeroff *et al.*, 1981).

3.4. Effect of monosodium glutamate on sperm indices

Fertility in men is evaluated solely on the quality of sperm produced from the testis. The World Health Organization has set standards for

quality of semen that is necessary for reproduction. In both neonatal and adult animal studies, MSG has been shown to cause oligozoospermia (Lamperti and Blaha, 1976; França *et al.*, 2006; Vinodini *et al.*, 2010) and increase abnormality in sperm morphology (Onakewhor *et al.*, 1998). Onakewhor *et al.* (Onakewhor *et al.*, 1998) also submitted that MSG instigates substantial oligozoospermia and promotes aberrant sperm morphology in male Wistar rats in a dose-dependent manner. This is not surprising as glutamate receptors and transport proteins are widely released in the testicular tissue and sperm cells of mice, rats, and humans (Storto *et al.*, 2001; Hu *et al.*, 2004; Takarada, 2004).

França *et al.* (França *et al.*, 2006) reported histological changes in the testes, as well as a decrease in spermatogenic cells in adult rats exposed to MSG. The presence of unsaturated fatty acids in the plasma membrane layer of the sperm cells and their low concentration of cytoplasmic antioxidants made spermatozoa susceptible to oxidative damage (Jones, 1979). This could be implicated in the documented increase in the death of sperm cells following MSG administration. Increased lipid peroxidation causes oxidative damage to sperm DNA, which affects membrane functions. This resulted in impaired sperm motility and in the growth of spermatozoa (Hamza and Al-Harbi, 2014; Aitken *et al.*, 1989).

The susceptibility of hypothalamus to damages due to exposure to MSG is an indicator to the fact that it may impair the neural activation of the expression of reproductive hormones via the hypothalamic–pituitary–gonadal regulatory axis (Alalwani, 2014). Such impairment may consequently affect the reproductive ability of the affected animals. Administration of MSG to the animal models cause a reduction in the concentration of ascorbic acid in the testicular tissue and this could lead to oxidative damage in rat testes (Vinodini *et al.*, 2010), and in different organs as reported by Moreno *et al.* (Moreno *et al.*, 2005). An earlier study by Giovambattista *et al.* (Igwebuike *et al.*, 2011) showed a significant decrease in the caudal epididymal sperm reserves of the rats that received MSG in comparison to the control rats. Fig. 2 shows the mechanism of MSG induced impairment of male reproductive functions.

4. The protective role of natural antioxidants in MSG induced testicular toxicity

Antioxidants are substances whose presence in relatively low concentrations significantly inhibits oxidation. Owing to the continuous generation of partially reduced forms of oxygen by constitutive metabolic pathways of MSG in the reproductive tissue (Hamza and Al-Harbi, 2014), a number of protective antioxidant enzymes, such as superoxide

dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GSH), glutathione-S-transferase (GST), and other non-enzymatic antioxidants, have been documented to deal with the toxic species (Jubaidi *et al.*, 2019; Kayode *et al.*, 2020). Since oxidation reactions produces free radicals, which start chain reactions that eventually damage the cells, antioxidants acts to terminate these chain reactions by simply removing the free radical intermediates and inhibit other oxidation reactions by being oxidized themselves (Rasheed *et al.*, 2019).

Meanwhile, Antioxidants are abundant in fruits and vegetables, they are as well presents in other foods such as nuts, grains, and some meats, poultry, sweet potatoes, carrots, pumpkin, fish and mangoes (Xianquan *et al.*, 2005). Antioxidants are majorly of two group viz: the primary or natural antioxidants and the secondary or synthetic antioxidants. The natural antioxidants are the chain breaking antioxidants which react with lipid radicals to convert them into more stable products. They are mainly phenolic in structures and include the antioxidant minerals such as selenium, copper and iron; antioxidant vitamins such as vitamin C, vitamin E, and vitamin B; then the phytochemicals such as the flavonoids. However, laboratory studies had significantly demonstrated the role of natural antioxidants of various classes in the prevention and management of MSG induced male reproductive toxicity (Kayode *et al.*, 2020; Rani and Savalagimath, 2017; Hamza and Diab, 2020; Hajjhasani *et al.*, 2020).

4.1. Antioxidant minerals and vitamins effects on MSG-induced reproductive toxicity

Antioxidant minerals are the cofactor of antioxidants enzymes which their absence will definitely affect metabolism of many macromolecules such as carbohydrates. A prominent member in the category of antioxidant mineral is selenium. Selenium has a protective antioxidant effect on several tissues and laboratory studies had demonstrated that the administration of selenium diminished the effect of MSG which induced decrease in testosterone hormone levels and elevated oxidative stress markers. Selenium had a potent antioxidant effect and it is suggested to elevate the antioxidant enzymes significantly, thus decreasing the lipid peroxidation markers as often reported in MSG. Hence, selenium inhibit testicular injury by improving the testicular antioxidant (Hamza and Al-Harbi, 2014; Hamza and Diab, 2020).

Antioxidant vitamins are needed for most body metabolic functions. They include vitamin C, vitamin E, and vitamin B. Since MSG induces

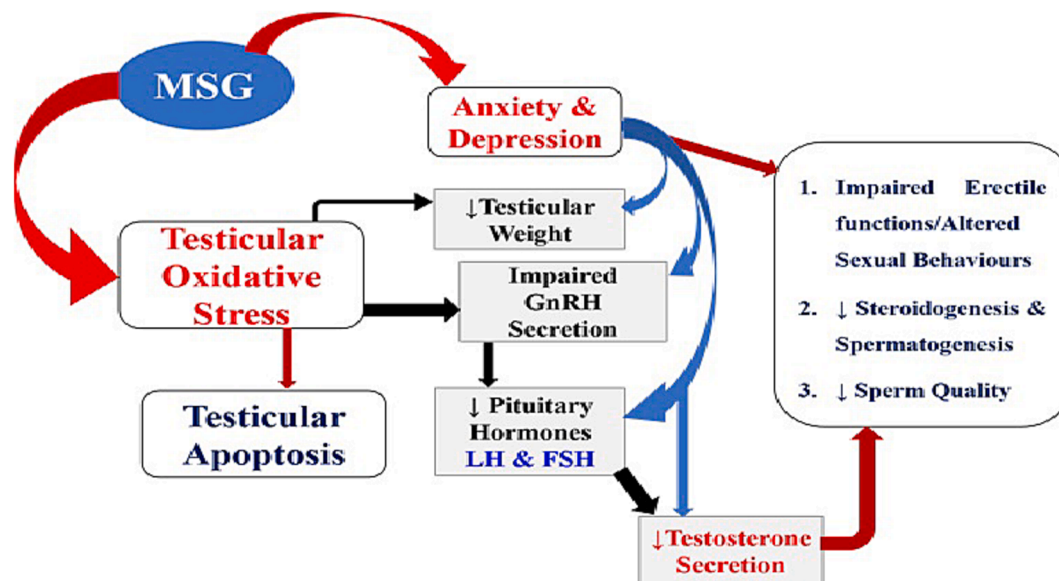


Fig. 2. Mechanism of MSG induced impairment of male reproductive functions.

oxidative stress which leads to generation of free radicals, activation of proteases, phospholipases and endonucleases, transcriptional activation of apoptotic programs and genotoxicity (Kayode *et al.*, 2020; Vinodini *et al.*, 2010). Vitamin C also known as ascorbic acid had been extensively documented for its antioxidant protective role, and is considered the front line of defense against free radicals through its ROS scavenging, reduction of peroxides and repair of peroxidized biological membranes alongside its sequestration of iron. Ascorbic acid contributes to the redox mechanism also by salvaging the other antioxidants vitamin such as vitamin-E, urate, and β -carotene from their oxidized form while also quenching the free radicals present in the lipid membranes thus preventing the lipid peroxidation (El Kotb *et al.*, 2020; van der Loo *et al.*, 2003). Vitamin E as an antioxidant exhibit its protective action against lipid peroxidation by either reducing or preventing oxidative damage and by scavenging lipid peroxyl radicals (Zhang *et al.*, 2015) Antioxidant vitamins are majorly prophylactic agent against MSG-induced reproductive toxicity (El Kotb *et al.*, 2020).

4.2. Phytochemical antioxidant effect on MSG-induced reproductive toxicity

Antioxidant phytochemicals are found in many foods and medicinal plants, playing an important role in the prevention and treatment of chronic diseases that resulted from oxidative stress. They possess strong antioxidant and free radical scavenging abilities, as well as anti-inflammatory action, which are also the basis of other bioactivities and health benefits (Zhang *et al.*, 2015). Examples of antioxidant phytochemicals includes tannins, flavones, triterpenoids, steroids, saponins, and alkaloids (Zhang *et al.*, 2015). Polyphenols and carotenoids are the two main kinds of antioxidant phytochemicals and they include quercetin and flavonoids. Meanwhile, natural polyphenols are the most abundant antioxidants in human diets, their radical scavenging activities are related to substitution of hydroxyl groups in the aromatic rings of phenolics (Rokayya *et al.*, 2014).

Several laboratory studies had reported that plants suggested to have high flavonoids and with high antioxidant properties decreases the reactive oxygen species reportedly generated from the consumption of MSG. A study had recently reported that the high antioxidant level and the active compound contained in some plants can improve the negative effect of MSG in male reproductive functions (Rahayu *et al.*, 2021).

Khaled *et al.* (Khaled *et al.*, 2016) examine the protective effect of propolis on MSG-induced reproductive toxicity and suggested that propolis can be effective in the protection of MSG-induced reproductive toxicity. Mulyani (Mulyani, S., 2016) also in their study examined the effect of mung bean sprouts extract to the morphology and motility spermatozoa in mice exposed MSG reported that increase the percentage of morphology and motility of spermatozoa and attributed the fact that Mung bean sprouts are natural antioxidants as it reported to contains vitamins E and C and zinc (Mulyani, 2016). In another laboratory study quince leaf extract possess a protective effects being a natural antioxidant on the reproductive dysfunction induced by monosodium glutamate in rats (Kianifard *et al.*, 2015), meanwhile, it has been demonstrated that flavonoid compounds from quince have strong antioxidant and immune-regulatory effects (Panche *et al.*, 2016).

El sawy *et al.* (El-sawy *et al.*, 2018) reported that the usage of camel milk as a therapy against MSG used in food industry is very indicative and protective more importantly improve the testicular dysfunctions attributed to MSG-toxicity (El-sawy *et al.*, 2018). Ginger is a medicinal plant, medically used for its antioxidant protection activity and it has a beneficial effect on male reproductive functions had been documented to has protective effects against MSG on the rat testicular tissue (114). Fig. 3 represents the schematics of natural antioxidants in MSG induced reproductive dysfunctions.

5. Conclusion

Monosodium glutamate negatively affects several indices of male reproductive functions by causing: oxidative damage to the reproductive organs, histomorphological alterations to testicular tissues, hormonal dysfunction, and ultimately reduced sperm quality. The safety guidelines on the tolerable limits of MSG in a biological system should be revisited and there should be adequate sensitization of the global populace on its potential toxic effects.

CRedit authorship contribution statement

David Tolulope OLUWOLE: Writing – review & editing. Oladipupo Samuel EBIWONJUMI: Writing – review & editing. Lydia Oluwatoyin AJAYI: Writing – review & editing. Olubunmi Dupe ALABI: Writing – review & editing. Victor AMOS: Writing – review & editing.

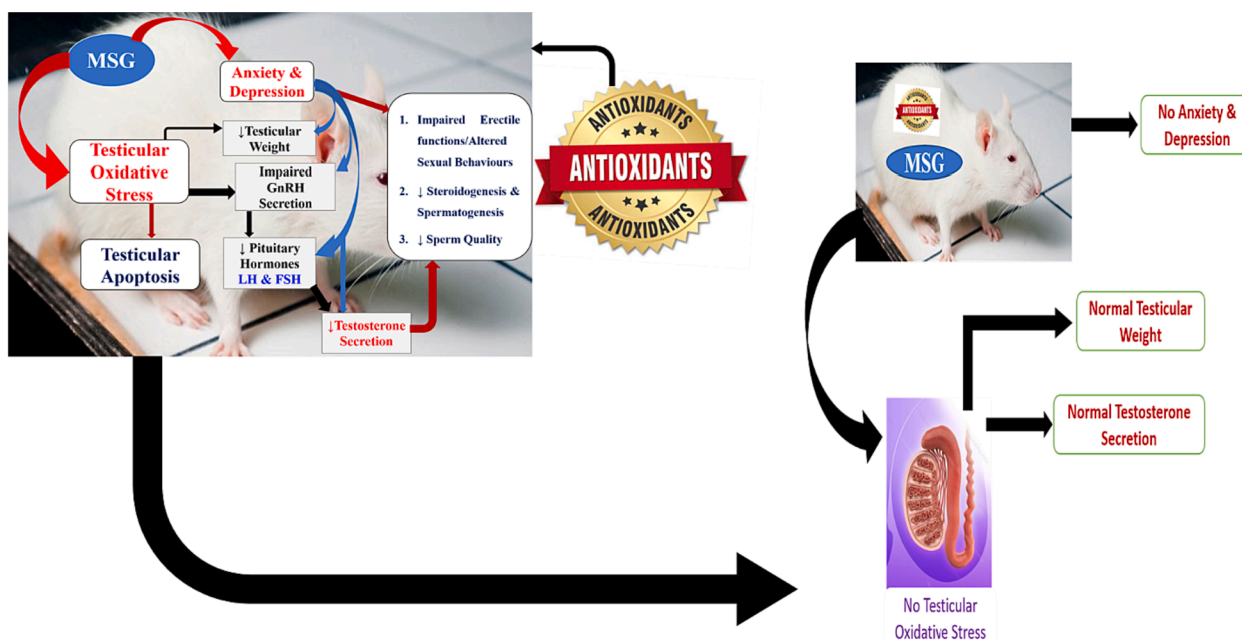


Fig. 3. Natural Antioxidants in MSG induced reproductive dysfunctions.

Grace AKANBI: Writing – review & editing. **Wale Johnson ADEYEMI:** Writing – review & editing. **Ayodeji Folorunsho AJAYI:** Writing – review & editing.

Declaration of competing interest

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Data availability

Data will be made available on request.

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