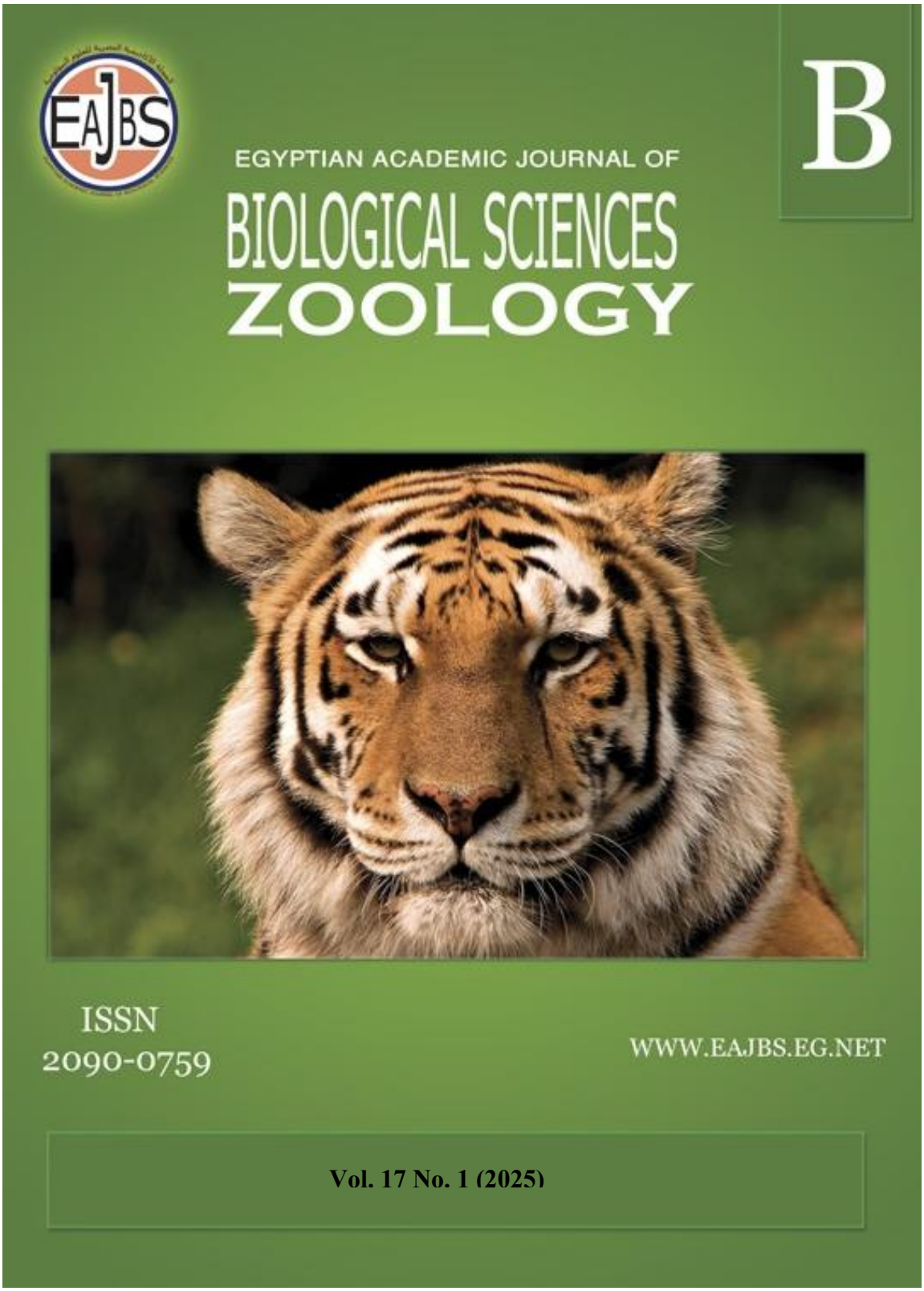

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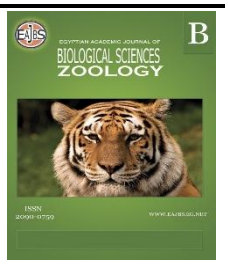

In vivo Appraisal of the Impact of Oral Using of Monosodium Glutamate on Male and Female Rats

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ABSTRACT
One of the many adverse consequences of monosodium glutamate (MSG), a common flavor enhancer, is swelling of the cartilage. Inflammation in articular cartilage was assessed in the current investigation after MSG administration, which may have contributed to the alterations in oxidative stress indicators and articular cartilage histology seen in the animals. In this work, two primary groups of forty-two Swiss albino rats, male and female, were used. The first group's male and female rats were given distilled water orally as their control. The male and female groups of rats in the second group were given oral monosodium glutamate at a high dose of 7g/kg b.wt For a duration of two months. A notable change in histology of chondrocytes in the joints of male and female rats stained using hematoxylin-eosin and Masson trichrome stains. A significant boost in IF-gamma and IL-6 as well as a dramatic reduction in IL-4 levels in treated animals versus control. A slight elevation of sodium level and significant raise of potassium levels in animals groups consumed MSG. Furthermore, a significant rise in ALT, MDA and creatinine levels in the treated animals as well as dramatic reduction in catalase level in the treated animals versus control. The sequence of oxidative stress development and inflammatory cytokine expression in the animals suggests that MSG-induced cellular oxidation stress in the rat cartilage tissues may have led to inflammation and cartilage matrix disintegration.

INTRODUCTION

Monosodium glutamate (MSG) is a flavoring substance that is widely used in food businesses and food outlets. It is available in an extensive range of processed food and is incorporated into food in infinite amounts in eateries, healthcare facilities, and dining areas (Nguyen *et al.,* 2020). The producers of foods do not disclose the quantity of MSG within their package, so it is impossible to estimate how much MSG a normal person uses in a day (Zanfirescu *et al.,* 2019). Naturally shape glutamic acid used in foods is not harmful, but processed artificial glutamic acid is dangerous (Beyreuther *et al.,* 2007). Industrial study indicates that the ideal amount of MSG to add to food is 0.6%. The United States Environmental Protection Agency states that food containing MSG should not be given to infants or children below one-year-old (Chakraborty, 2019; Sedlak *et al.,* 2019).

Numerous researches demonstrated the potentially dangerous impact of MSG on the liver and renal functions, fat cells, hepatic tissue, sexual organs, and the neurological system (Nnadozie *et al.,* 2019; Banerjee *et al.,* 2021). According to these investigations, MSG raises the incidence of several malignancies (Eid *et al.,* 2019), induces cytotoxicity (Pavlovic *et al.,* 2009; Eweka *et al.,* 2011), and promotes oxidative injury to the renal system and other organs (Pavlovic *et al.,* 2007). The immune system and associated organs such as the testes (Abd-Elkareem *et al.,* 2021), ovary (Rohmawati *et al.,* 2014), pancreas (Ajibade *et al.,* 2015),

spleen (Alsalmi *et al.,* 2019), hepatic, and heart tissue may be negatively impacted by MSG (Al-Ghamdi, 2021). There have been reports that eating meals with additional MSG raises the risk of developing various diseases, including overweight (Araujo *et al.,* 2017), insulin resistance, and cognitive impairment (Špolcová *et al.,* 2015).

Bone contains a completely functional glutamate signaling system (Spencer *et al.,* 2007). The role of glutamate signaling in maintaining bone homeostasis is being increasingly understood (Hinoi *et al.,* 2004). Several studies found that glutamate receptors in connective tissues, chondrocytes, osteoclasts, and fibroblasts transporters (Flood *et al.,* 2007). Diseased regions of bone and cartilage in human arthritic tissue and rat antigen-induced arthritis expressed AMPA and the NMDA receptor may be involved in biomechanical responses (Piepoli *et al.,* 2009). In this work the impact of MSG on histology of articular cartilage as well as oxidative markers, elemental levels, inflammatory mediators and other physiological markers in serum samples of male and female rats.

MATERIALS AND METHODS

Chemicals:

Monosodium glutamate (49621) was obtained from Sigma Aldrich.

Animal Model:

Forty-two young male and female albino rats (Age: 12 weeks, 130-140 gm) were split into two groups. The first group: control group contained both male and female animals, orally administrated by 1.0 ml distilled water. The second group, contained animals from both sexes, orally administrated by at a high dose of MSG (7 g/kg b.wt) every day for four months (Thomas *et al.,* 2009). All animal work was done according to ethical guidelines in Zoology Department, Women's College for Arts, Science and Education, Ain Shams University according to ARRIVE guidelines.

Histological Examination:

Rats from both groups were killed by cervical dislocation. Tibiofemoral joint samples were collected, for decalcified by 6% nitric acid for 12 days. Sections of specimens from both groups were processed at 6 µm by a rotary microtome, put on slides, and dyed with (Leica Auto-stained YZ00) with hematoxylin and eosin as mason trichrome to evaluate tissue structure and images will have collected at ×400 (Zeiss microscope., Germany) (Collins *et al,* 2015).

Mediators and Elemental Analysis:

Blood specimens were obtained from the eyes of animals in tubes contained EDTA before killing the rats and rotated at 6000 rpm for 20 minutes at 6°C. The mediators including IF-gamma, IL-4, IL-6 were examined using (Invitrogen kits, USA) by Elisa (Shimadzu, Japan). Sodium and potassium were examined using (diamond kits, UK) using flame photometer (Agilent, USA). All steps were done according to instructions inserted in the protocols inside the kits (Sundaram *et al.,* 2015; Yosri *et al.,* 2022).

Oxidative and Biochemical Markers:

The levels of ALT, creatinine, and catalase, malondialdehyde in serum of the tested groups were examined by the instruction's steps through the used analysis kits (Invitrogen kits, USA) (Garcia-González *et al.,* 2015; Mateen *et al.,* 2016; Conti *et al.,* 2020; Ioannidou *et al.,* 2024).

Statistical Testing:

All outcomes were reported as means ± standard deviation (SD), the statistical variance was calculated using the San Diego, California-based GraphPad Prism 5 software. One way-Anova was employed. Where $P < 0.05$ is considered significant (Eweka *et al.,* 2011; Anbarkeh *et al.,* 2019).

RESULTS

Microscopic Examination:

In this work, the classical shape of chondrocytes could be seen in normal specimens of male and female animals with slight differences upon examination of the samples stained by hematoxylin and eosin stain. The arrangement of chondrocytes could be confirmed by examination of the slices stained by Masson trichrome stain as shown in (Figs. 1 A & B; 2 A

& B). While administration of a high dose of MSG for long time led to enlargement of chondrocytes size with apparent shrinkage of hyaline matrix in rat samples from box sexs upon testing of the specimens stained by H&E as well as Masson trichrome stains as depicted in (Figs. 1 C & D; 2 C & D).

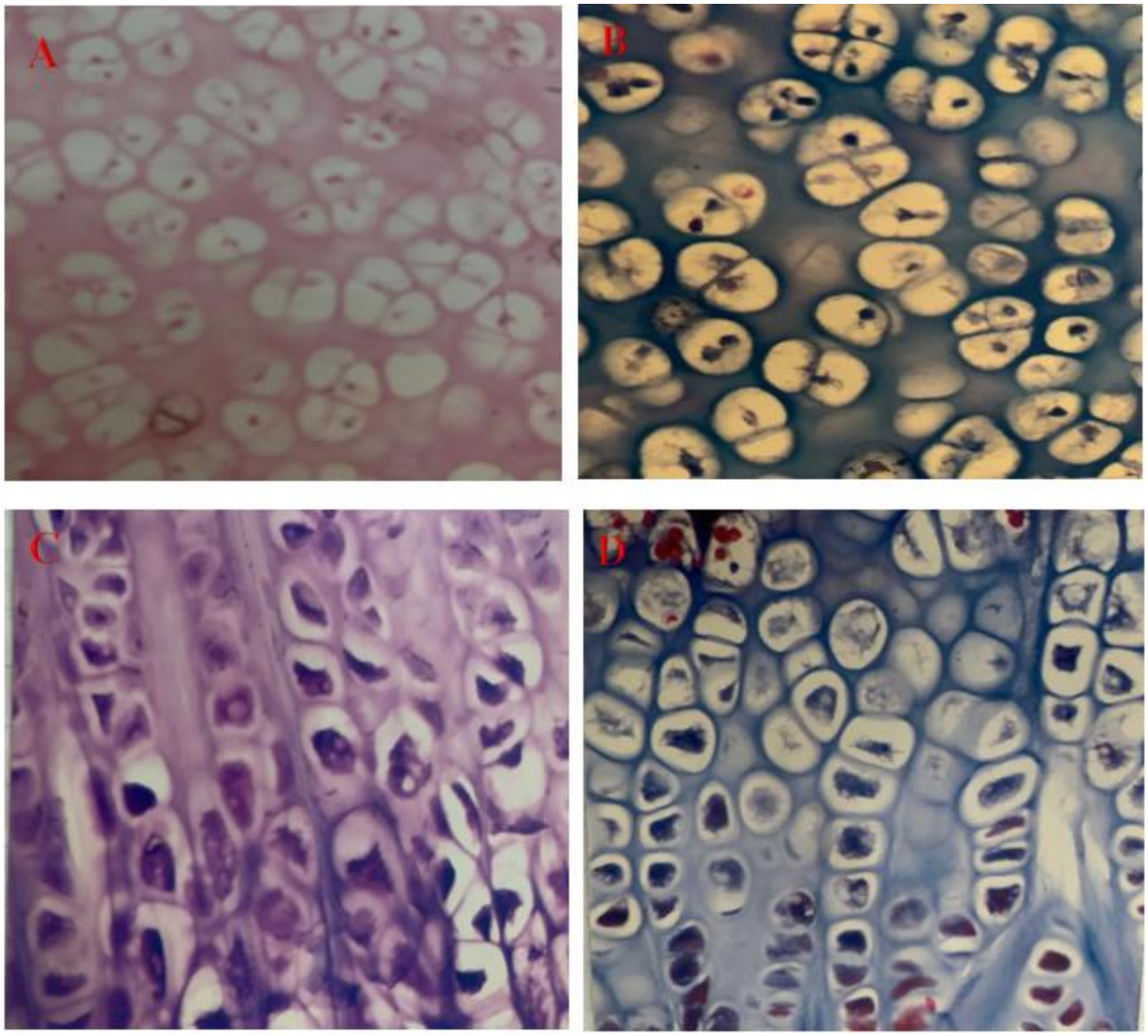

Fig. 1: Photomicrograph of Cartilage showing (A) Normal chonrocytes from normal female rats arranged in Lacunae and seperated by hyaline matrix stained by H&E ; (B) Normal chonrocytes from normal female rats where it took the blue color of Masson trichrome stain ; (C) Inflammed chonrocytes from treated female rats with minimal amonut of hyaline matrix stained by H&E ; (D) Inflammed and irregular chonrocytes arranged in bluish sheets and stained Masson trichrome stain(Magnication X=400).

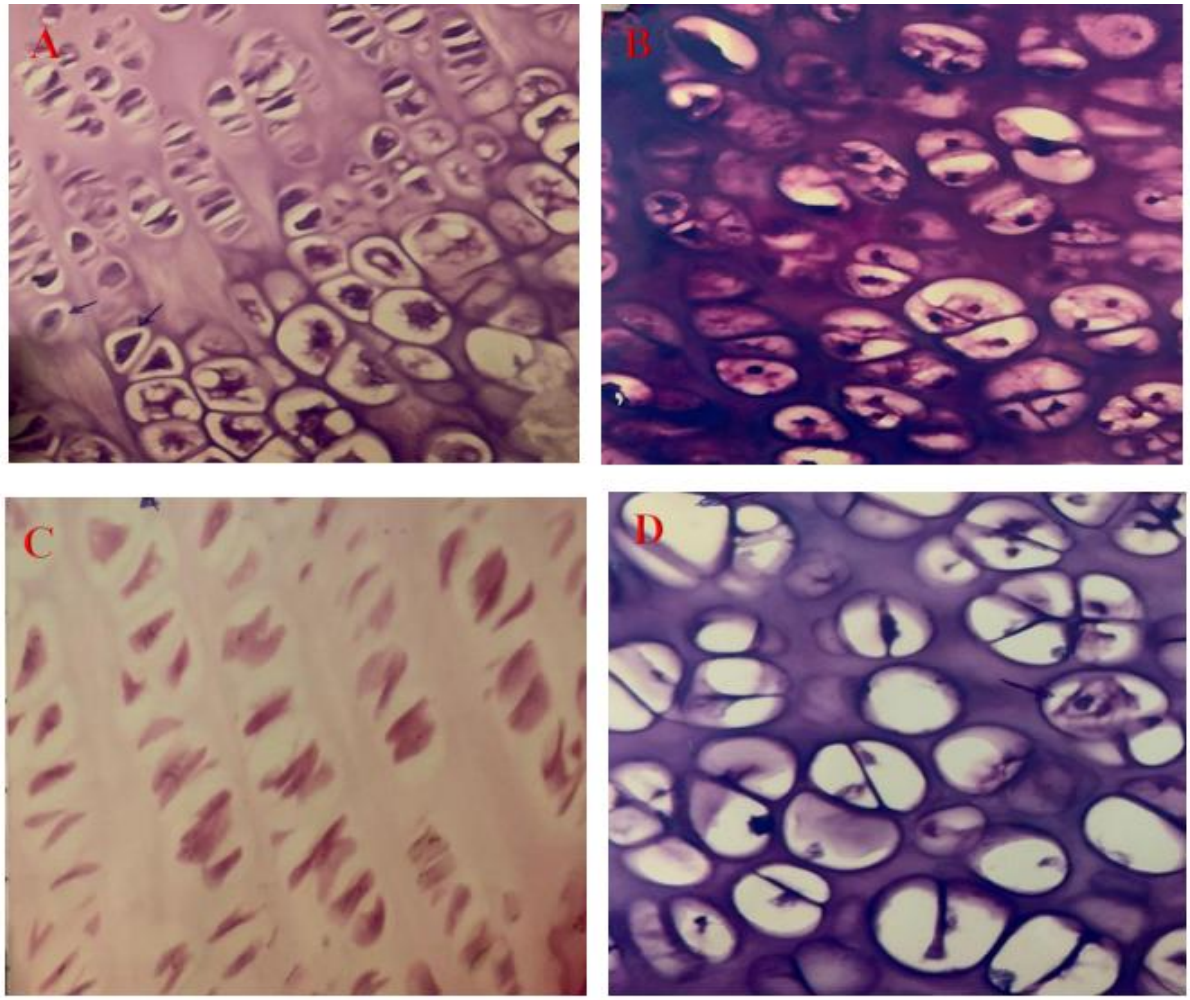

Fig. 2: Photomicrograph of Cartilage showing (A) Normal chonrocytes from normal male rats arranged in Lacunae and seperated by hyaline matrix stained by H&E ; (B) Normal chonrocytes from normal male rats where it obtained the blue color of Masson trichrome stain ; (C) Inflammed chonrocytes from trated female rats with condended chonrocytes with minimal amonut of hyaline matrix stained by H&E ; (D) Inflammed and irregular chonrocytes arranged in bluish sheets and stained Masson trichrome stain(Magnication X=400).

Testing Levels of Cytokines and Elements:

In the current investigation, the assessment of the concentrations of pro-inflammatory cytokines including IF-gamma and, IL-6 showed a dramatic rise ($P \leq 0.05$) in the levels of tested cytokines levels in male and female rats treated by a high dose of MSG for long time relative to control. While, the assessment of the concentrations of anti-inflammatory cytokines including IL-4 showed a significant reduction ($P \leq 0.05$) in the levels of tested cytokine level in male and female rats treated by a high dose of MSG for long time relative to control as depicted in (Fig. 3 A-C).

On the other hand, evaluation of sodium and potassium concentrations revealed a slight elevation in sodium levels as well as dramatic rise ($P \leq 0.05$) in potassium concentrations in male and female rats treated by a high dose of MSG for long time relative to control as depicted in (Fig. 4 A & B).

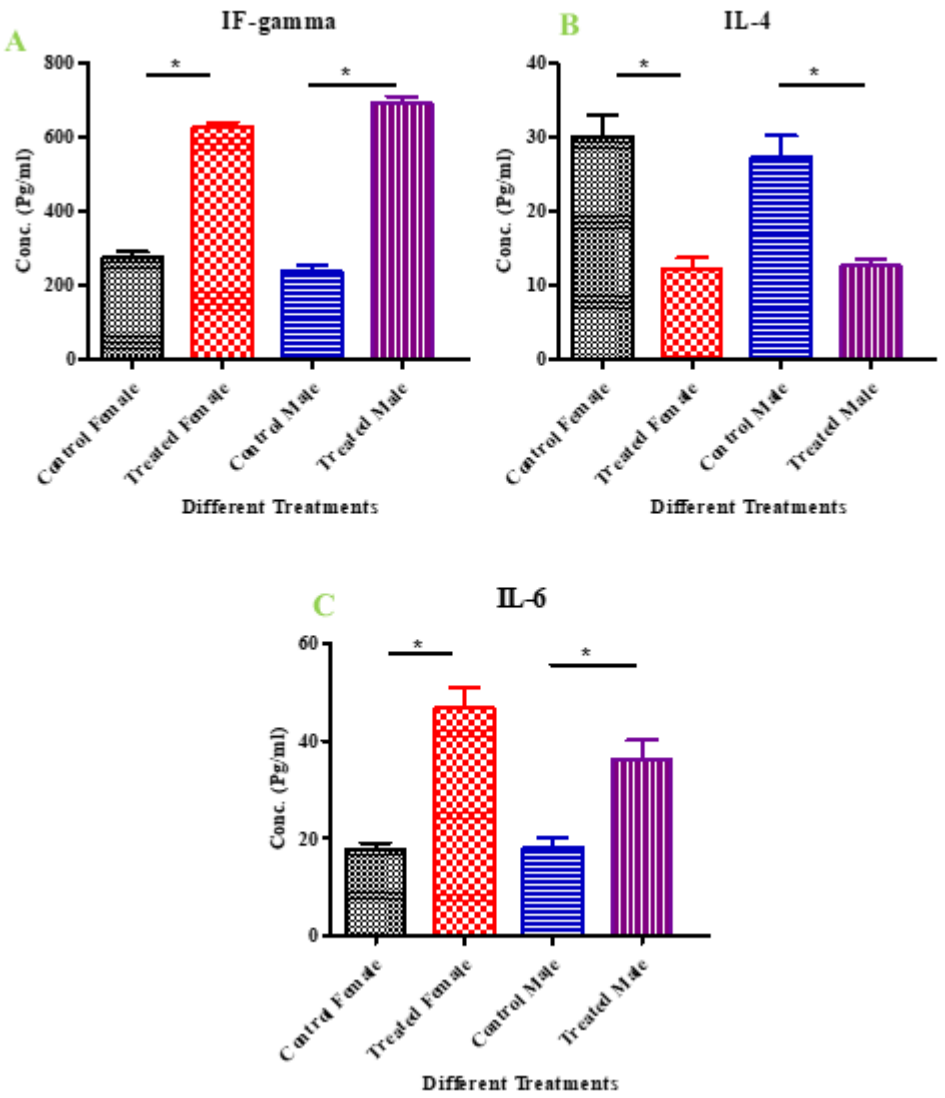

Fig. 3: Determination of pro-and anti-inflammatory mediators' levels in various tested groups (A) IF-gamma; (B) IL-4 and (C) IL-6. Results are represented as means ± SD, where (*) refer to significant difference where $P \leq 0.05$.

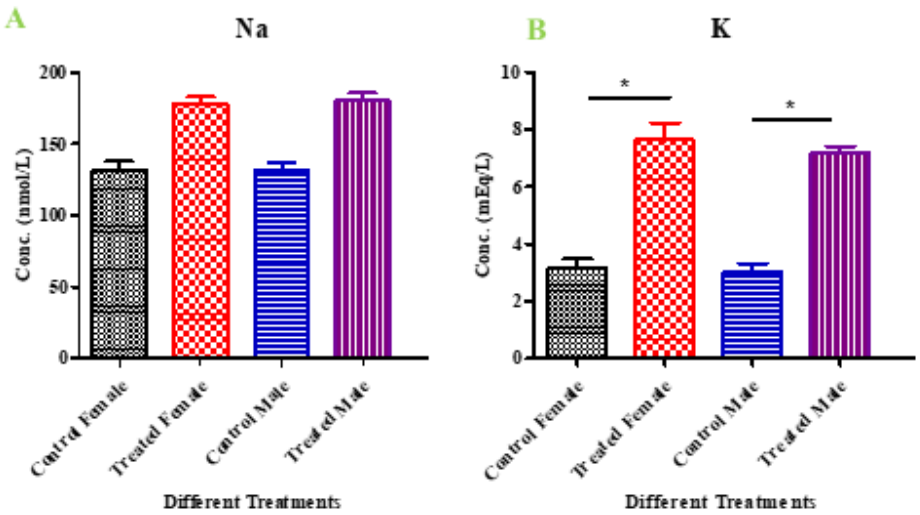

Fig. 4: Determination of sodium (Na) and potassium (K) levels in various tested groups (A) Na; and (B) K. Results are represented as means ± SD, where (*) refer to significant difference where $P \leq 0.05$.

Evaluation of the Concentrations of Biochemical Markers:

In the present work**,** testing the renal function marker level (creatinine) as well as the liver function enzyme level (ALT) showed a dramatic rise ($P \leq 0.05$) in the levels of tested renal and liver functions markers in in male and female rats treated by a high dose of MSG for long time relative to control as illustrated in as illustrated in (Fig. 5 A, B).

Furthermore, measurement of catalase as an oxidative marker showed a significant reduction ($P \leq 0.05$) in the levels of tested renal and liver functions markers in in male and female rats treated by a high dose of MSG for long time relative to control as illustrated in (Fig. 5C). While testing MDA as peroxide enzyme showed a significant reduction ($P \leq 0.05$) in the levels of tested renal and liver functions markers in in male and female rats treated by a high dose of MSG for long time relative to control as illustrated in (Fig. 5D).

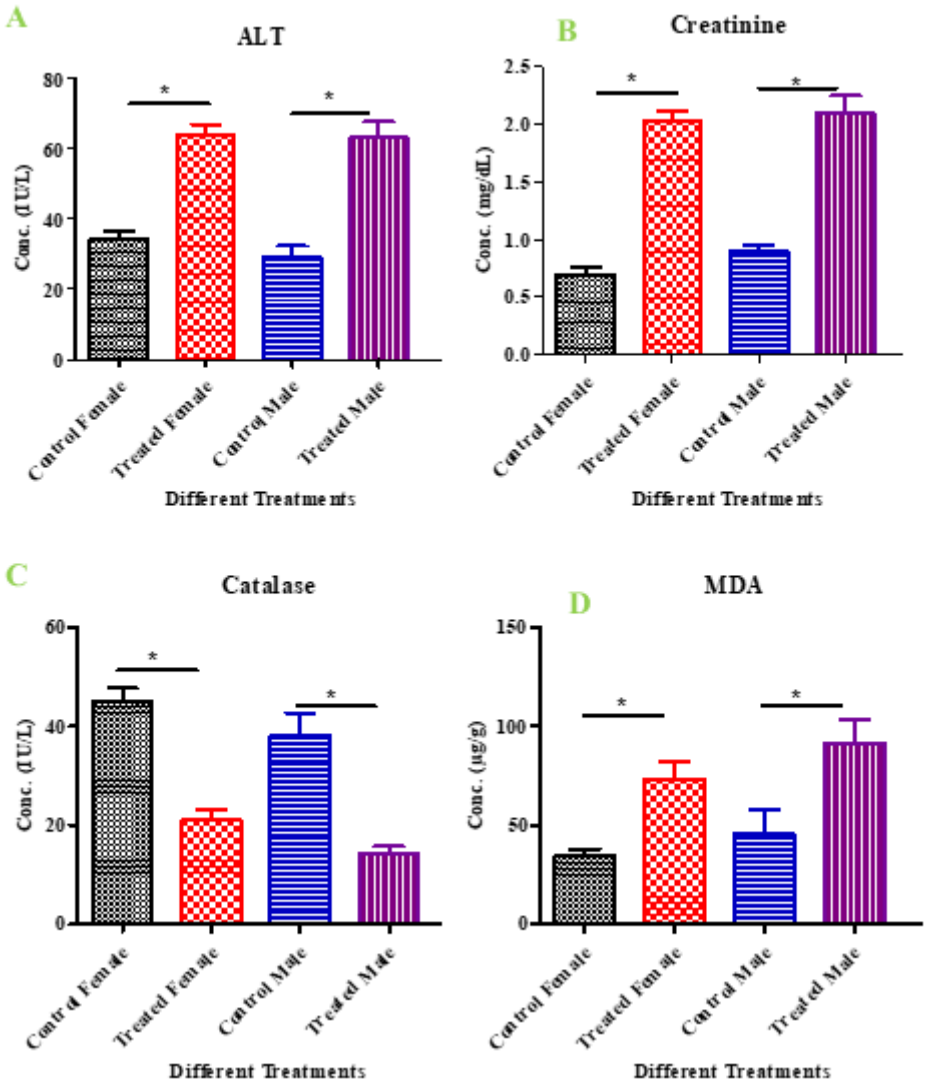

Fig. 5: Testing biochemical levels in various tested groups (A) ALT; (B) Creatinine; (C) Catalase and; (D) MDA. Results are represented as means ± SD, where (*) refer to significant difference where $P \leq 0.05$.

DISCUSSION

In recent years, there has been controversy around the security and poisoning of MSG due to reports of negative reactions ingestion of MSG-containing foods. Such unfavorable effects have been demonstrated by Shosha *et al.,* (2023).

According to Hall *et al.* (1996), MSG has been linked to migraines, nausea, diarrhea, bowel dysfunction, and anxiety disorders. Furthermore, studies have demonstrated that MSG has negative impacts on a variety of bodily systems. Specifically, diets containing nutritional additives have been found to impact consciousness, behavior, and brain neural

communication (Umukoro *et al.*, 2015, Akataobi, 2020). In the current investigation, young male and female albino rats were orally given a high dose of MSG every day for three months to determine what would happen on the joints of rats as well as screening of some representative markers.

In cartilage, extracellular matrix components such collagen, and proteoglycans are combined with chondrocytes to form connective tissue (Sundaram *et al.,* 2015). The human articular cartilage's chondrocytes release reactive oxygen species that cause apoptosis in the chondrocytes, including nitric oxide, and H_2O_2 (Carlo and Loeser, 2003). Apoptotic cell death, proteoglycan degradation, and lipid peroxidation occur when various doses of H_2O_2 are applied to articular cartilage (Khan *et al.,* 2008).

In this work a clear alteration in the histological structures of chondrocytes in treated animals could be seen. By blocking inflammatory signalling and immune cell access into tissue, pro-inflammatory and inflammatory cytokines and chemokines accumulated in tissue would be crucial (Navarro and Boveris, 2004). The current study revealed a notably elevated level of IL-6 and IF-gamma in MSG. Excessive use in MSG causes the body's inflammatory response to be promoted, which in turn causes chondrocyte derangements and joint damage. MSG dysregulates the levels of inflammatory cytokines. The immune response is therefore related to variations in the amounts of specific chondrocyte forms. Furthermore, increased ROS generation, which triggers the release of pro-inflammatory cytokines including IF-gamma and IL-6, is indicative of MSG's pro-oxidative characteristics (Das *et al.,* 2022).

Many studies assessed the toxicity of MSG reveal a considerable degree of variation in the dosage and duration of administration (Banerjee *et al.,* 2020; Kassab *et al.,* 2022). According to this study, which was done on rats, consuming large doses of MSG raised the levels of creatinine, AST, and catalase and decreased the level of MDA. The modified biological reactions could be explained by oxidative stress (Pruett *et al.,* 2009). Oxidative stress-mediated damage occurs within the body when redox-equilibrium is altered by raising lipid peroxidation, NO generation, and CAT and GSH levels. Animals that experience immune suppression due to chemicals may experience oxidative stress, immune cell death, and pathological changes in several organs (Gao *et al.,* 2008).

In this study, eating MSG significantly raised the levels of potassium and sodium. In same line with (El-Meghawry *et al.,* 2013) who reported that blood lactate levels rise upon consuming high doses of MSG. Besides, Phosphate is moved from the intracellular to the extracellular pool more readily during acidosis (Walwadkar *et al.,* 2006). Furthermore, when taking a high and recurrent dose of MSG orally, the effects of sex may be shown in all evaluated parameters. In the treated female group, the majority of the examined markers were greater than in the male group in the present work. (Katalinic *et al.,* 2005) linked the higher level of oxidative injury in males compared to females to the higher level of radical degradation of DNA in males Gonad hormones are the impacted factor. Additionally, according to (Kataranovski *et al.,* 2009) investigation into gender variations in the inflammatory reaction as a result of cadmium in rats, as estrogen can reduce the synthesis of interleukin-6 in mice.

The current report suggests that consuming MSG led to harmful impact in joints which confirmed by various biochemical and inflammatory markers.

Declarations:

Ethical Approval: The study has been approval by ethical committee in Ain Shams University, Faculty of Women for Arts Science and Education, Code: sci1332411001.

Competing interests: The author states that there are no competing interests to declare.

Author's Contributions: HMA and NKM conceived and carried out the experiments, wrote the draft of the manuscript, and analyzed the data. HMA and NKM organized the data, supervised, and reviewed the manuscript. The final manuscript was read and approved by both Authors.

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Availability of Data and Materials: The datasets utilized and analyzed during this investigation are available upon reasonable request from the corresponding author.

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REFERENCES

Abd-Elkareem, M.; El-Rahman, A.; Mokhless, A.; Khalil, N.S.A.; Amer, A.S. (2021). Antioxidant and cytoprotective effects of Nigella sativa L. seeds on the testis of monosodium glutamate challenged rats. *Scientific Reports,* 11, 13519. doi: 10. 1038/s41598-021-92977-4.

Al-Ghamdi, F.A. (2021). Microscopic study of potential toxic effects of monosodium glutamate on liver of chicken embryos aged 16 days. *Egyptian liver Journal,* 11, 38. https://doi.org/10.1186/s43066-021-00109-4

Alsalmi, F.; Hamza, R.; El-Shenawy, N. (2019). Effect of Green Tea and Zinc Oxide Nanoparticles Complex on Histopathology of Spleen of Male Rats Induced by Monosodium Glutamate. *Instant Journal of Hematology and Oncology,* 1, 4–11.

Ajibade, A.; Fakunle, P.; Adetunji, M. (2015). Some effects of monosodium glutamate administration on the histo-architecture of the spleen and pancreas of adult Wistar rats. *Journal of Pharmaceutical and Biological Science,* 3, 39.

Akataobi US (2020). Effect of monosodium glutamate (MSG) on behavior, body and brain weights of exposed rats. *Environmental Disease* ;5(1):3–8. doi: 10.4103/ed. ed_31_19.

Araujo, T.R.; Freitas, I.N.; Vettorazzi, J.F.; Batista, T.M.; Santos-Silva, J.C.; Bonfleur, M.L.; Balbo, S.L.; Boschero, A.C.; Carneiro, E.M.; Ribeiro, R.A. (2017). Benefits of L-alanine or L-arginine supplementation against adiposity and glucose intolerance in monosodium glutamate-induced obesity. *European Jornal of Nutrition,* 56, 2069–2080.

Anbarkeh, F.R.; Baradaran, R.; Ghandy, N.; Jalali, M.; Nikravesh, M.R.; Soukhtanloo, M. (2019). Effects of monosodium glutamate on apoptosis of germ cells in testicular tissue of adult rat: An experimental study. *International Journal of Reproductive. Biomedicine,* 17, 261.

Banerjee, A.; Mukherjee, S.; Maji, B.K. (2021). Worldwide flavor enhancer monosodium glutamate combined with high lipid diet provokes metabolic alterations and systemic anomalies: An overview. *Toxicological Reports,* 8, 938–961.

Banerjee, A.; Das, D.; Paul, R.; Roy, S.; Das, U.; Saha, S.; Dey, S.; Adhikary, A.; Mukherjee, S.; Maji B.K. (2020). Mechanistic Study of Attenuation of Monosodium Glutamate Mixed High Lipid Diet Induced Systemic Damage in Rats by *Coccinia Grandis*. *Science Reports,* 10:15443. doi: 10.1038/s41598-020-72076-6.

Beyreuther, K.; Biesalski, H.K.; Fernstrom, J.D.; Grimm, P.; Hammes, W.P.; Heinemann, U.; Kempski, O.; Stehle, P.; Steinhart, H.; Walker, R. (2007). Consensus meeting: Monosodium glutamate An update. *European Journal of Clinical Nutrition,* 61, 304–313.

Carlo, M.D.; Loeser, R.F. (2003). Increased oxidative stress with aging reduces chondrocyte survival: correlation with intracellular glutathione levels. *Arthritis & Rheumatism*, 48(12): 3419-3430.

Chakraborty, S.P. (2019). Patho-physiological and toxicological aspects of monosodium glutamate. *Toxicology Mechanisms and Methods,* 29, 389–396.

Collins, K. H.; Paul, H. A.; Reimer, R. A.; Seerattan, R. A.; Hart, D. A.; Herzog W. (2015). Relationship between inflammation, the gut microbiota, and metabolic osteoarthritis development: studies in a rat model. Osteoarthritis and Cartilage ;23(11):1989–1998. doi: 10.1016/j.joca.2015.03.014.

Conti, V.; Corbi, G.; Costantino, M.; De Bellis, E.; Manzo, V.; Sellitto, C.; Stefanelli, B.; Colucci, F.; Filippelli, A. (2020). Biomarkers to Personalize the Treatment of Rheumatoid Arthritis: Focus on Autoantibodies and Pharmacogenetics. Biomolecules,10, 1672.

Das, D.; Banerjee, A.; Bhattacharjee, A.; Mukherjee, S.; Maji, B. K. (2022). Dietary food additive monosodium glutamate with or without high-lipid diet induces spleen anomaly: A mechanistic approach on rat model. Open Life Sciences, 17(1), pp. 22-31. https://doi.org/10.1515/biol-2022-0004

Eid, R.A.; Al-Shraim, M.; Zaki, M.S.; Kamar, S.S.; Abdel Latif, N.S.; Negm, S.; Al-Ani, B.; Haidara, M.A (2019). Vitamin E protects against monosodium glutamate-induced acute liver injury and hepatocyte ultrastructural alterations in rats. Ultrastructure.

Pathology, 43, 199–208.
El-Meghawry, E. A.; Osman; H.E., Daghestani, MH. (2013). The effect of vitamin C administration on monosodium glutamate induced liver injury. An experimental study. *Experimental Toxicology and Pathology;*65(5):513-21. doi: 10.1016/j. etp. 2012.02.007.
Eweka, A.; Igbigbi, P.; Ucheya, R. (2011). Histochemical studies of the effects of monosodium glutamate on the liver of adult Wistar rats. *Annals in Medical Health Science Research*, 1, 21–30.
Flood, S.; Parri, R.; Williams, A.; Duance, V.; Mason, D. (2007). Modulation of interleukin-6 and matrix metalloproteinase 2 expression in human fibroblast-like synoviocytes by functional ionotropic glutamate receptors. *Arthritis & Rheumology;*56(8):2523-34. doi: 10.1002/art.22829.
Gao, S.; Wang, Y.; Zhang, P.; Dong, Y.; Li, B. (2008). Subacute oral exposure to dibromoacetic acid induced immunotoxicity and apoptosis in the spleen and thymus of the mice. *Taxological Science,*105(2):331–41.doi:10.1093/toxsci/kfn139
García-González, A.; Gaxiola-Robles, R.; Zenteno-Savín, T. (2015). Oxidative stress in patients with rheumatoid arthritis. *Revista de Investigación Clínica,* 67, 46–53.
Hall, J.E.; Guyton, A.C.; Brands, MW. (1993). Pressure-volume regulation in hypertension. *Kidney International Supplements,* 55: S35–S41.
Hinoi, E.; Takarada, T.; Ueshima, T.; Tsuchihashi, Y.; Yoneda Y. (2004). Glutamate signaling in peripheral tissues. *European Journal of Biochemistry,* 271, 1–13 10.1046/j.1432-1033.2003. 03907.x
Ioannidou, S.; Tsiakalidou, A.; Kazeli, K.; Ginoudis, A.; Fouza, A.; Daoudaki, M.; Lymperaki, E. (2024). Evaluation of Biochemical and Oxidative Stress Markers in the Early Stages of Rheumatoid Arthritis in a Comparative Study of Two Different Therapeutic Approaches. Oxygen*,* 4, 253-265. https://doi.org/10.3390/oxygen 4030014
Kassab, R.B.; Theyab, A.; Al-Ghamdy, A.O.; Algahtani, M.; Mufti, A.H.; Alsharif, K.F.; Abdella, E.M.; Habotta, O.A.; Omran, M.M.; Lokman, M.S.; et al. (2022). Protocatechuic Acid Abrogates Oxidative Insults, Inflammation, and Apoptosis in Liver and Kidney Associated with Monosodium Glutamate Intoxication in Rats. *Environmental Science and Pollution Research,* 29:12208–12221. doi: 10.1007/s11356-021-16578-4.
Katalinic, V.; Modun, D.; Music, I.; Boban, M. (2005). Gender differences in antioxidant capacity of rat tissues determined by 2,2'-azinobis (3-ethylbenzothiazoline 6-sulfonate; ABTS) and ferric reducing antioxidant power (FRAP) assays. *Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology,* 140(1):47-52. doi: 10.1016/j.cca.2005.01.005.
Kataranovski, M.; Janković, S.; Kataranovski, D.; Stosić, J.; Bogojević, D. (2009). Gender differences in acute cadmium-induced systemic inflammation in rats. *Biomedical and Environmental Sciences;*22(1):1-7. doi: 10.1016/s0895-3988(09)60014-3.
Khan, I.M.; Gilbert, S.J.; Caterson, B.; Sandell, L.J.; Archer, CW. (2008). Oxidative stress induces expression of osteoarthritis markers procollagen IIA and 3B3(-) in adult bovine articular cartilage. Osteoarthritis Cartilage,16(6):698-707. doi: 10.1016/j. joca.2007.10.004.
Mateen, S.; Moin, S.; Khan, A.Q.; Zafar, A.; Fatima, N. (2016). Increased Reactive Oxygen Species Formation and Oxidative Stress in Rheumatoid Arthritis. *PLoS ONE,* 11, e0152925.
Navarro, A.; Boveris, A. (2004). Rat brain and liver mitochondria develop oxidative stress and lose enzymatic activities on aging. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology,* 287(5):R1244–9.10.1152/ajpregu. 00226. 2004
Nguyen, L.; Salanta, L.-C.; Socaci, S.; Tofana, M.; Fărcaș, A.; Pop, C. (2020). A Mini Review About Monosodium Glutamate. Bull. Univ. Agric. Sci. Vet. Med. Cluj-Napoca. *Food Science Technology,* 77, 2020.
Nnadozie, J.O.; Chijioke, U.O.; Okafor, O.C.; Olusina, D.B.; Oli, A.N.; Nwonu, P.C.; Mbagwu, H.O.; Chijioke, C.P. (2019). Chronic toxicity of low dose monosodium glutamate in albino Wistar rats. *BMC Research Notes,* 12, 593.

Pavlovic, V.; Pavlovic, D.; Kocic, G.; Sokolovic, D.; Jevtovic-Stoimenov, T.; Cekic, S.; Velickovic, D. (2007). Effect of monosodium glutamate on oxidative stress and apoptosis in rat thymus. *Molecular and Cellular Biochemistry,* 303, 161–166.

Pavlovic, V.; Pavlovic, D.; Kocic, G.; Sokolovic, D.; Sarac, M.; Jovic, Z. (2009). Ascorbic acid modulates monosodium glutamate induced cytotoxicity in rat thymus. *Bratislavske lekarske listy,* 110, 205–209.

Piepoli, T.; Mennuni, L.; Zerbi, S.; Lanza, M.; Rovati, L.C.; Casell,i G. (2009). Glutamate signaling in chondrocytes and the potential involvement of NMDA receptors in cell proliferation and inflammatory gene expression. Osteoarthritis Cartilage; 17(8):1076-83. doi: 10.1016/j.joca.2009.02.002.

Pruett, S.B.; Fan, R.; Zheng, Q.; Schwab, C. (2009). Patterns of immunotoxicity associated with chronic as compared with acute exposure to chemical or physical stressors and their relevance with regard to the role of stress and with regard to immunotoxicity testing. *Toxicological Sciences;*109(2):265–75.doi:10.1093/toxsci/kfp073

Rohmawati, W.; Istiananingsih, Y.; Nurdiana, N.; Barlianto, W.; Dwijayasa, P.M. (2014). Vitamin CE ve Monosodyum Glutamata Bağlı Ovaryan Toksisite. *Cukurova Medical Journal,* 39, 517–524.

Sedlak, T.W.; Paul, B.D.; Parker, G.M.; Hester, L.D.; Snowman, A.M.; Taniguchi, Y.; Kamiya, A.; Snyder, S.H.; Sawa, A. (2019). The glutathione cycle shapes synaptic glutamate activity. *Proceedings of the National Academy of Sciences of the United States of America,* 116, 2701–2706.

Shosha, H.M.; Ebaid, H.M.; Toraih, E.A.; Abdelrazek, H.M.A.; Elrayess, RA. (2023). Effect of monosodium glutamate on fetal development and progesterone level in pregnant Wistar Albino rats. *Environmental Science and Pollution Research,* 30(17):49779-49797. doi: 10.1007/s11356-023-25661-x.

Spencer, G. J.; McGrath, C. J.; Genever, P. G. (2007). Current perspectives on NMDA-type glutamate signalling in bone. *The International Journal of Biochemistry & Cell Biology,* 39, 1089–1104 10.1016/j.biocel.2006.11.002

Špolcová, A.; Mikulášková, B.; Holubová, M.; Nagelová, V.; Pirnik, Z.; Zemenová, J.; Haluzík, M.; Železná, B.; Galas, M.-C.; Maletínská, L. (2015). Anorexigenic lipopeptides ameliorate central insulin signaling and attenuate tau phosphorylation in hippocampi of mice with monosodium glutamate-induced obesity. *Journal of Alzheimer's Disease, 45*, 823–835.

Sundaram, M.S.; Hemshekhar, M.; Santhosh, M.S.; Paul, M.; Sunitha, K.; Thushara, R.M.; Naveen Kumar, S.K.; Naveen, S.; Devaraja, S.; Rangappa, K.S.; Kemparaju, K.; Girish, K.S. (2015). Tamarind Seed (*Tamarindus indica*) Extract Ameliorates Adjuvant-Induced Arthritis via Regulating the Mediators of Cartilage/Bone Degeneration, Inflammation and Oxidative Stress. *Scientific Reports,* 10; 5:11117. doi: 10.1038/srep11117.

Thomas, M.; Sujatha, K.; George, S. (2009). Protective effect of Piper longum Linn. on monosodium glutamate induced oxidative stress in rats. *Indian journal of experimental biology*, 47(3): p. 18-25.

Umukoro, S.; Oluwole, G.O.; Olamijowon, H.E.; Omogbiya, A.I.; Eduviere, A.T. (2015) Effect of monosodium glutamate on behavioral phenotypes, biomarkers of oxidative stress in brain tissues and liver enzymes in mice. *World Journal of Neuroscience,* 5:339–349. doi: 10.4236/wjns.2015.55033.

Walwadkar, S.D.; Suryakar, A.N.; Katkam, R.V., Kumbar, K.M.; Ankush RD. (2006). Oxidative stress and calcium-phosphorus levels in Rheumatoid arthritis. *Indian Journal of Clinical Biochemistry,* 21(2):134-7. doi: 10.1007/BF02912928.

Yosri, M.; Elaasser, M.M.; Abdel-Aziz, M.M.; Hassan, M.M.; Alqhtani, A.H.; Al-Gabri, N.; Ali, A.B.A.; Pokoo-Aikins, A.; Amin, B.H. (2022). Determination of Therapeutic and Safety Effects of *Zygophyllum coccineum* Extract in Induced Inflammation in Rats. *Biomedicine Research International,* 7513155. doi: 10.1155/2022/7513155.

Zanfirescu, A.; Ungurianu, A.; Tsatsakis, A.M.; Nițulescu, G.M.; Kouretas, D.; Veskoukis, A.; Tsoukalas, D.; Engin, A.B.; Aschner, M.; Margină, D. (2019). A Review of the Alleged Health Hazards of Monosodium Glutamate. *Comprehensive Reviews in Food Science and Food Safety,* 18, 1111–1134.