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C Yugandhar
Assistant Professor (Contractual), Department of Veterinary Pathology, College of Veterinary Science, SVVU, Proddatur, Andhra Pradesh, India

RV Ramanamurty
Associate Professor and Head, Department of Veterinary Pathology, College of Veterinary Science, SVVU, Garividi, Andhra Pradesh, India

K Sujatha
Professor, Department of Veterinary Pathology, College of Veterinary Science, S.V.V.U, Tirupati, Andhra Pradesh, India

N Vinod Kumar
Professor and Head, Department of Microbiology, College of Veterinary Science, S.V.V.U., Proddatur, Andhra Pradesh, India

TNVKV Prasad
Senior Scientist, Institute of Frontier Technologies, R.A.R.S, S. V. Agricultural College, Tirupati, Andhra Pradesh, India

U Vinod
Assistant Professor, Department of Animal Genetics and Breeding, College of Veterinary Science, SVVU, Tirupati, Andhra Pradesh, India

Corresponding Author:
C Yugandhar
Assistant Professor (Contractual), Department of Veterinary Pathology, College of Veterinary Science, SVVU, Proddatur, Andhra Pradesh, India

Histopathological study on monosodium glutamate salt (Ajinomoto) induced toxicity in male wistar albino rats and its amelioration with zinc oxide (ZnO) nanoparticles

C Yugandhar, RV Ramanamurty, K Sujatha, N Vinod Kumar, TNVKV Prasad and U Vinod

Abstract
Monosodium glutamate (MSG) is a widely used flavor enhancer and food additive in meat, fish, milk, and cheese or vegetable origins. A total of 48 healthy adult male albino Wistar rats of 6-7 weeks of age were used for the study. These rats were divided randomly into four groups having 12 animals in each group. Rats were clinically monitored throughout the experimental period of 6 weeks. Six rats from each group were randomly sacrificed at every three weeks interval after starting the experiment i.e., 3rd and 6th week. It was observed that MSG @ 5 g/ kg b.wt / day orally for 6 weeks was toxic to rats and caused induced adverse effects of histopathological changes in various visceral organs by increasing the production of reactive oxygen species (ROS) and lipid peroxidation and decreased levels of antioxidants. Histopathologically the liver of Group II showed a microvesicular fatty change of hepatocytes, karyomegaly and binucleated hepatocytes, and bile ductular hyperplasia was observed. Whereas kidney sections showed degenerated and desquamated renal tubular epithelium, congested, atrophied and cystic glomeruli, and pockets of hemorrhages in intertubular space. Testes revealed interstitial edema with MNCs infiltration, degenerative and desquamative changes of seminiferous tubules, and necrosis of Leydig cells. Brain sections showed neuronal degeneration and sub meningial haemorrhages and gliosis. The lung showed thickened interstitial space and thickened blood vessels, severe lymphoid hyperplasia in the peribronchial area. The treatment of ZnO NPs and rats concurrently with the MSG was shown to have ameliorating effect on different pathological manifestations. The ameliorating effect of ZnO NPs was found to be relatively better than that of most of the parameters.

Keywords: MSG, ZnO NPs, gross, histopathology, male wistar albino rats

1. Introduction
Monosodium Glutamate (MSG) or Ajinomoto is a food additive (E621) that is widely used around the world (Husarova and Ostatnikova, 2013) [18]. It is a sodium salt of glutamic acid that produces a distinct taste different from the four classical sensations (sweet, salty, sour, and bitter) known as the fifth taste "umami" (Ninomiya, 1998) [25]. It increases the quality of food intake by enhancing chemosensory perception (Kulkarni *et al*., 2014) [23]. The average MSG intake in European and Asian countries is 0.3-0.5 g/day and 1.2-1.7 g/day, respectively. MSG intake of 16.0 mg/kg body weight is considered safe (Beyreuther *et al*., 2007) [8].

MSG is neither a nutrient, vitamin or mineral, and it has no health benefits. It is, however, a slow toxin. Milk, vegetables, seafood, poultry, meats, traditional seasonings like soups or sauces (canned, packed), prepared meals, frozen foods, marinated meats, fresh sausages, chips and snacks, bottled soy and stuffed or seasoned chicken, manufactured meats, some hams, luncheon chicken and turkey, flavoured tuna, vegetarian burgers and sausages (Bojanic *et al*., 2009) [9].

The Food and Drug Administration (FDA) declared it safe for limited use. Excess MSG consumption can cause cardiac, circulatory, gastrointestinal, muscular, and neurological disorders (Zehra Kazmi *et al*., 2017) [41] and it affects the hypothalamus-pituitary axis of the brain, resulting in neuro-excitatory/neuroendocrine effects, obesity induction and increased body weight (Egbuonu *et al*. 2010) [12]. MSG consumption may have an adverse effect on the Sertoli cells and Leydig cells of the testes and may have a role in male infertility due to its negative impact on testes functioning (Reham and Mohammad, 2014) [31].

Nanotechnology is an important area of study in the twenty-first century. Nanotechnology is an exciting field for investigators. Green zinc oxide nanoparticles (ZnO NPs) with *Camellia sinensis* extract used in the treatment of the toxicity of monosodium glutamate (MSG) in the liver, kidney, and testis of rats (Hamza *et al*., 2021) [14]. Zinc oxide nanoparticles are the most important and widely used metal nanoparticles (Bedi and Kaur, 2015) [7]. Zinc is a powerful antioxidant with important properties such as anti-inflammatory activity (Costa *et al*., 2012) [10], free radical scavenging or detoxification (Hassan *et al*., 2016) [15], and it protects cell membrane integrity against oxidative damage and improves antioxidant enzyme levels by reducing ROS production (Hassan *et al*., 2016) [15].

Hence present research work was carried out to study the Pathology of MSG on various organs of rats and its Amelioration with ZnO nanoparticles.

2. Materials and Methods

The present research work was planned to study the pathology of monosodium glutamate (Ajinomoto) and the ameliorative effect of ZnO NPs in male Wistar albino rats. The experiment was carried out in the Department of Veterinary Pathology, College of Veterinary Science, Tirupati during the period of April 2018 to June 2018.

2.1 Procurement and Maintenance of Experimental Animals

Male Wistar albino rats weighing 150 to 170 g (procured from Sri Venkateswara Agencies in Bangalore) were used in the present study. The rats were acclimatized in laboratory conditions for two weeks prior to the investigation. Clean and dry rice husk was used as bedding, and it was changed every other day. The rats were grouped and housed in normal polypropylene rat cages (four rats in one cage) during the experiment after two weeks of acclimatization. They were kept at 25 °C±10 °C and a 12:12 hour interval light / dark cycle for 6 weeks by taking essential care and ensuring standard laboratory sanitary conditions. There was ad libitum laboratory animal feed (pellet diet) and clean drinking water provided. The approval of the Institutional Animal Ethical Committee (IAEC) was obtained prior to commencement of the experiment.

2.2 Chemicals

i. Monosodium glutamate salt

The Monosodium glutamate salt was purchased from Lobachemie Pvt. Ltd, Palghar, Maharashtra, product code No. 0395600500 with 99% extra purity.

ii. Zinc oxide nanoparticles

Zinc oxide nanoparticles (ZnONPs) powder was obtained from the Nanotechnology laboratory, Institute of Frontier Technology, Regional Agricultural Research Station (RARS), Tirupati. ZnO nanoparticles of mean size of 45 nm diameter (fig. 1) were used in the study. The prepared zinc oxide nanoparticles were characterized by using techniques such as UV-Vis spectrophotometer, FT-IR (Frontier transform infra red) spectrophotometry, dynamic light scattering and Scanning electron microscopy (SEM). This work was done at Indian Institute of Technology (IIT), Hyderabad.

2.3 Experimental design

A total of 48 healthy adult male albino Wistar rats of 6-7 weeks of age were used for the study. These rats were divided randomly into four groups having 12 rats in each group. The groups and the doses employed in the present study are shown in the Table 1.

Table 1: Various experimental groups and the dose details

Groups	Number of Rats/Group	Doses
1. Control. (Group-I)	12	Adlibitum feed and water
2. Monosodiumglutamate (MSG) control (Group-II)	12	Monosodium glutamate orally in distilled water @ 5 g/kg body weight (daily).
3. Zinc oxide nanoparticle control (Group-III)	12	Zinc oxide nanoparticles orally in distilled water @ 10 mg/kg body weight (daily).
4. Monosodium glutamate (MSG) + Zinc oxide nanoparticles (Group-IV)	12	Monosodium glutamate orally in normal saline @ 5 g/kg body weight + Zinc oxide nanoparticles orally in distilled water @ 10 mg/kg body weight (daily).
Total number of animals	48	

MSG was administered orally using distilled water as a vehicle. The rats were clinically monitored throughout the experimental period of 6 weeks and their body weights were measured at weekly intervals. All the rats from each group were sacrificed at 6th-week after the experiment started.

2.4 Gross and histopathology

In each sacrifice, a detailed postmortem examination was conducted on rats of all the experimental groups and recorded the gross lesions, and representative tissue pieces from the liver, kidney, testes, brain and lungs were collected and preserved in 10% neutral buffered formalin for histopathological studies. All these formalin-fixed tissues were processed by routine paraffin embedding technique. Sections of 5-6 microns thickness were cut and stained with routine Haematoxylin and Eosin method (H&E) (Culling, 1974) [12].

3. Results and Discussion

3.1 Gross Lesions

In the present study, conspicuous gross and histopathological lesions were noticed in the liver followed by kidney, testes, brain and lungs.

Grossly MSG treated (Group II) rats showed paleness of the liver (Fig. 1A) Whereas kidneys showed severe congestion (Fig. 1B), small and atrophied testes (Fig. 1C), congested brain (Fig. 1D) and lung (Fig. 1E) was observed throughout the experimental period.

Whereas grossly ZnO NPs ameliorated group (Group IV) rats showed, slight paleness of liver (Fig. 1A), mild reduction in

the testes size (Fig. 1C),mild congestion of brain (Fig. 1D), kidneys (Fig. 1B) and lungs (Fig. 1E) were noticed by the end of the experimental period. The appearance of other organs remained normal. The less severe changes or in all organs might be due to antioxidant property of ZnO NPs (Costa *et al*., 2012) [10], free radical scavenging property of ZnO NPs (Wang *et al*., 2006) [29].

3.2 Histopathology

3.2.1 Liver

Histopathologically liver of MSG treated (Group II) rats showed, severe degenerative changes, loss of cell membrane, disruption of hepatocytes and hepatocytes with binuclei and karyomegaly (Fig. 3A), dilated and congested sinusoids, at places pockets of hemorrhages and microvesicular fatty change of hepatocytes (Fig. 3B) were evident by the end of 6th week of the experiment. Similar findings were observed by Yaqub *et al*., (2008) [31], Thomas *et al*. (2009) [26], Eweka *et al*. (2011) [13], Afeefy *et al*. (2012) [1], AL-Mosaibihb *et al*. (2013) [4], Nagata *et al*. (2006) [20] and Egbuonu *et al*. (2010) [12]. Chronic venous congestion, diffuse degeneration, and necrosis of hepatocytes of para-cortical and mid-zonal areas of the liver were observed by Thomas *et al*. (2009) [26]. Dilated, congested central vein and loss of architecture of the liver were observed by Yaqub *et al*. (2008) [31]. These changes were in the liver might be due to hepatotoxic behaviour of MSG.

Whereas during the 3rdweek of the experiment, the liver of ZnO NPs ameliorated (Group IV) rats showed mild dilation of sinusoidal space with mild infiltration of MNCs, mild degenerative changes, and by the end of the experiment, the liver regained its near normal appearance in the majority of animals. The less severe changes or in the liver might be due to antioxidant property of ZnO NPs (Costa *et al*., 2012) [10], free radical scavenging property of ZnONPs (Wang *et al*., 2006) [29].

3.2.2 Kidney

By the end of 6th week, histopathologically kidneys of MSG treated (Group II) rats showed, thickened blood vessels, perivascular MNCs infiltration, and pockets of inter tubular hemorrhages, in some places severe degenerative and desquamative changes in the renal tubules and some places renal tubules contain hyaline-like casts (Fig.3C) vacuolated, cystic glomerulus (Fig.3D) and atrophied (Fig. 3E) were more conspicuous at the end of the experiment. Similar findings were observed by Thomas *et al*. (2009) [26], Afeefy *et al*. (2012) [1], AL-Agha (2009), Ortiz *et al*. (2006) [23], Osman *et al*. (2012) [29], (Eweka, 2007) [13]. The changes in the present study might be due to prolonged administration of MSG leads to different degrees of architectural destruction of the kidney and reduction in the number of renal corpuscles (Ortiz *et al*. 2006) [23].

Whereas the kidney of ZnO NPs ameliorated (Group IV) rats showed mild degenerative changes in renal tubules and glomeruli. The kidney regained its near to normal appearance by the end of 6th week due to the antioxidant property and protection of cell membrane integrity of ZnO NPs (Costa *et al*., 2012 and Badkoobeh *et al*., 2013) [10, 6].

3.2.3 Testes

By the end of 6th week, histopathologically kidneys of MSG treated (Group II) rats showed, severe desquamation of germinal epithelium, atrophied seminiferous tubules, shrinkage of seminiferous tubules and thickened tunica albugenia (Fig. 3F) and presence of giant cells in few severely degenerated seminiferous tubules (Fig. 3G). In some places basement membrane of seminiferous tubules lined with single layer of spermatogonia (Fig. 3H) and the rest of the cells were degenerated. Bared appearance of seminiferous tubules were also observed in few rats and were observed by the end of 6th week. The findings in this study were agreement with (Das and Ghosh 2010) [11], (Igwebuike *et al.*, 2011) [16], **(**Ochiogu *et al.*, 2015) [21], **(**Ismail *et al.*, 2012) [17], (Sakr and Badawy 2013) [25], Aisha (2013) [3]. MSG consumption might have some deleterious effects on the sertoli cells and leydig cells of testes at higher doses and by prolonged usage might contribute to the causes of male infertility Eweka and Om' Iniabohs (2011) [13]. Whereas Histopathologically, testes of ZnO NPs ameliorated (Group IV) rats showed, mild degeneration of germinal epithelium and by the end of 6th week regained almost it normal structure. This might be due to the antioxidant property and protection of cell membrane integrity of ZnO NOs (Costa *et al*., 2012 and Badkoobeh *et al*., 2013) [10, 6].

3.2.4 Brain

The microscopic examination of brain of MSG group animals showed thickened meninges with infiltration of few MNCs and fibroblasts, severe congestion of blood vessels and capillary proliferation, severe demyelinating and spongiosis, gliosis (Fig. 3I) and shrinkage of neuron in the cerebral cortex. Severe neuronal degeneration with central chromatolysis (Fig. 3J), satellitosis, neurophagia and severe capillary proliferation in the cerebral cortex and pockets of hemorrhages in focal areas of cerebral cortex, and spongiosis, rounding and loss of Purkinje cells in the cerebellum. These results were in accordance with Khadiga *et al*. (2009) [19], Ramanathan *et al*. (2007) [25], Xu *et al*. (2005) [30]. The changes in the present study might be due to neurotoxic effect of MSG and might have led to oxidative stress as glutamate crosses the blood-brain barrier quite readily or excessive activation of Glu receptors and the overloading of intracellular Ca++ induced by MSG finally lead to neuronal death. Histopathologically brains of Group IV animals revealed mild capillary proliferation, and mild neuronal degenerative changes, normal Purkinje cell layer in the cerebellum were observed by the end of 6th week of experiment. This might be due to ZnO NPs that promotes elimination of reactive oxygen species (ROS), thereby helping to reduce oxidative stress (Wang *et al*. 2006 and Hassan *et al*. 2016) [29, 15].

3.2.5 Lung

lungs of Group II rats revealed, perivascular edema and infiltration of macrophages, plasma cells, and eosinophils, degenerated and hyperplastic changes in bronchial epithelium and MNCs infiltration in the lumen, severe thickening of interstitial spaces along with hemorrhages in the interstitium, perivascular infiltration of MNCs, eosinophils were more prominent, along with hemorrhages and MNCs in interstitial space, hyalinization of blood vessels (Fig.3K) and severe lymphoid hyperplasia in the peribronchial area, desquamation of bronchial epithelium, fat vacuoles were also noticed in peri

bronchial space (Fig. 3L). These changes were in accordance with Yonedaa *et al*. (2011) [32]. The changes in the present study might be due to the effect of MSG on endothelial cells of blood vessels or due to the release of ROS during MSG toxicity (Youssef *et al*., 2010) [33].Histopathologically brains of Group IV animals revealed, mild infiltration of MNCs in perivascular spaces with mild lymphoid hyperplasia was noticed by the end of experiment. This might be due to effect of MSG on endothelial cells of blood vessels or due to release of ROS during MSG toxicity (Youssef *et al*., 2010) [33].

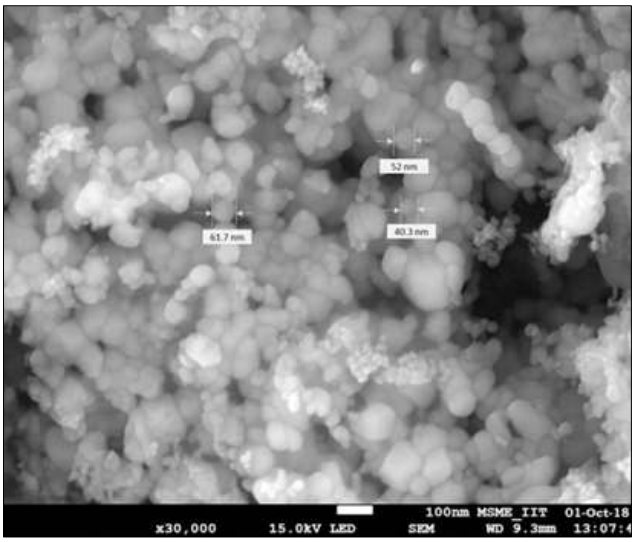

Fig 1: HR-SEM with EDS analysis showing ZnO nanoparticles of mean size of 45 nm diameter.

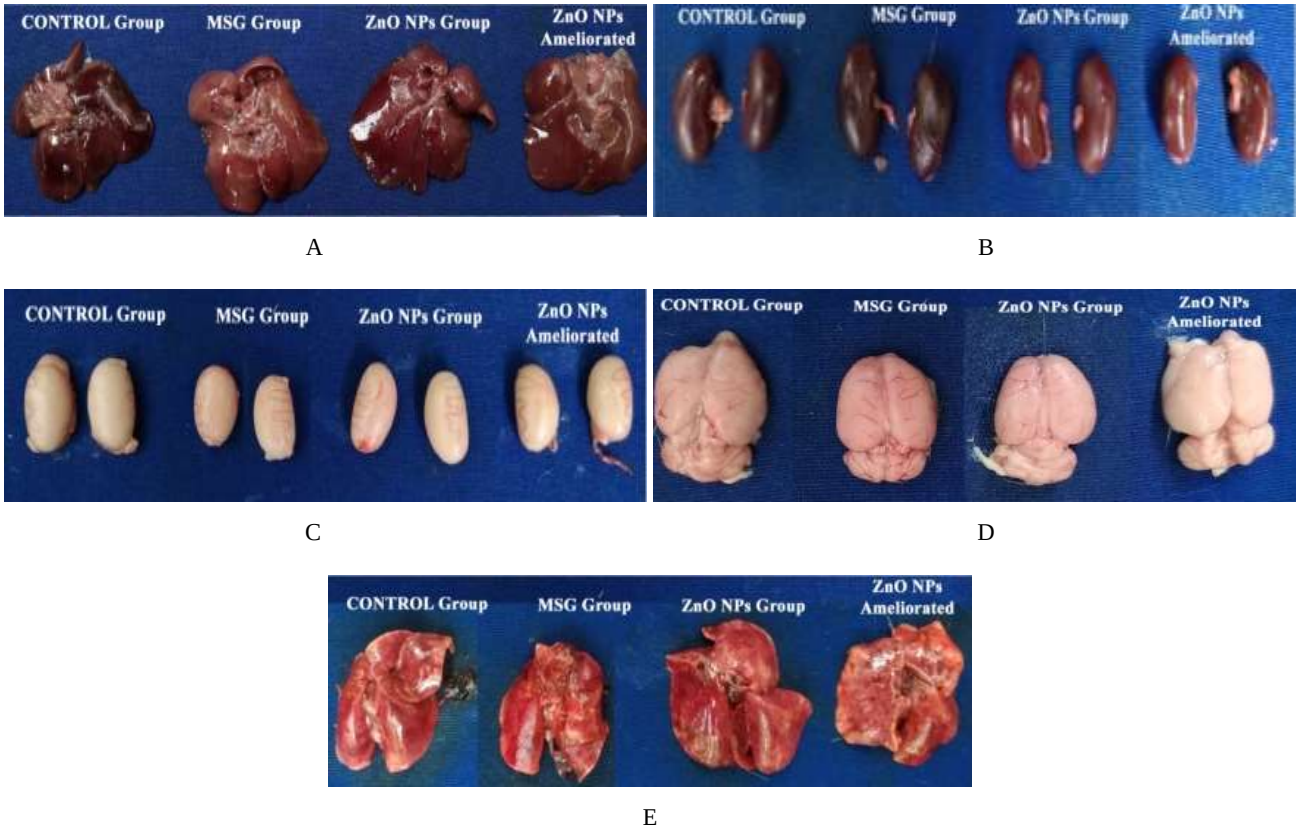

Fig 2: Gross lesions were noticed in various organs of control, MSG treated, ZnO NPs and comination of (MSG+ZnO NPs) treated groups of male rats. (A) Liver (B) Kidney (C) Testes (D) Brain (E) Lungs.

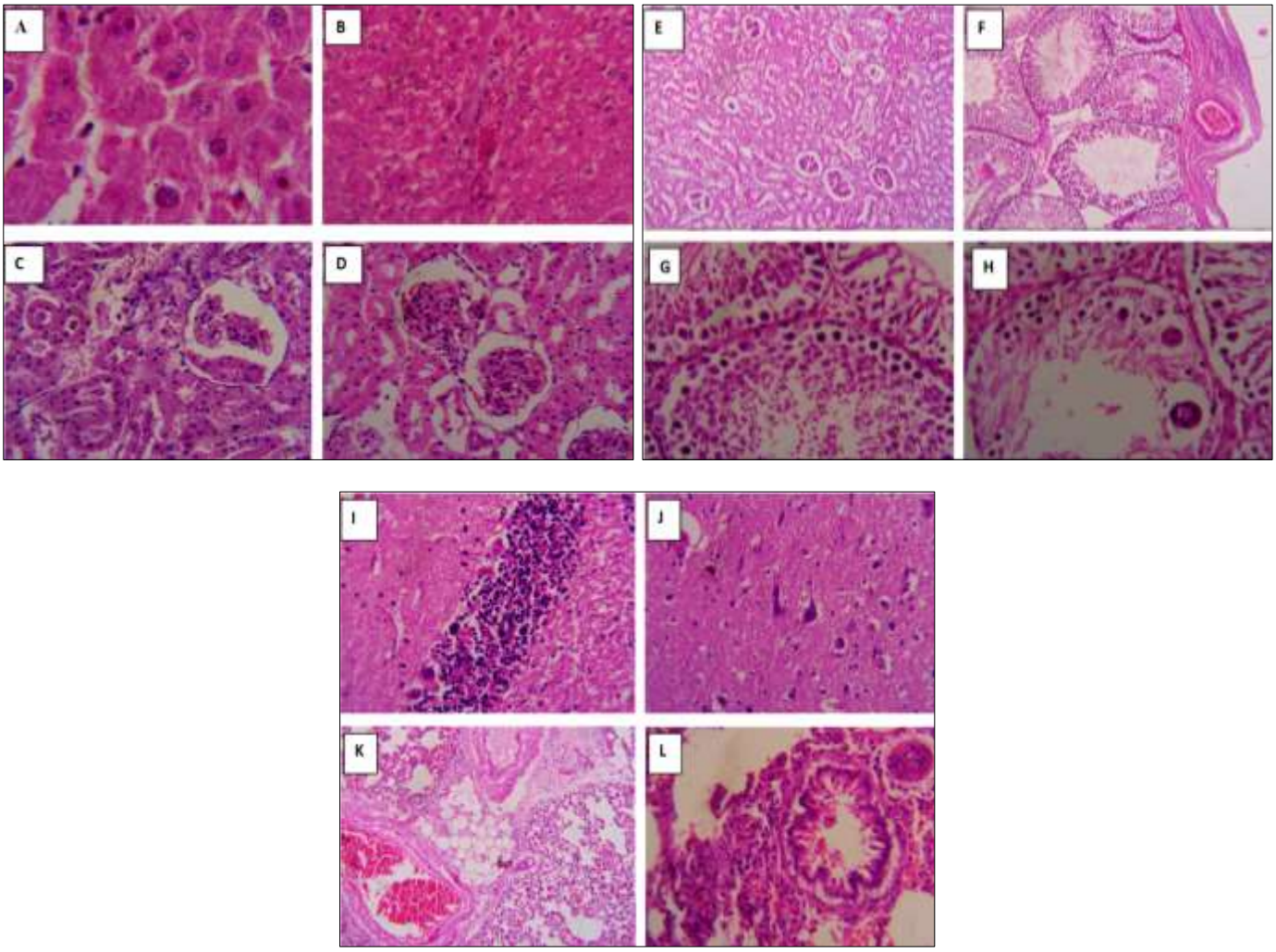

Fig 3: (A) Liver: Group II: section showing degenerated hepatocytes with binucleated and karyomegaly. H&E: x 100. (B) Liver: Group II: section showing microvesicular fatty change of hepatocytes H&E: x 40. (C) Kidney: Group II: section showing hyaline like casts in renal tubules. H&E: x 40. (D) Kidney: Group II: section showing vacuolated glomerulus along with degenerated renal tubules. H&E: x 40. (E) Kidney: Group II: section showing atrophied glomerulus. H&E: x 10. (F) Testes: Group II: section showing thickened tunica albugenia. H&E: x 10. (G) Testes: Group II: section showing single layer of spermatogonia. H&E: x 40. (H) Testes: Group II: section showing gaint cells in lumen of tubules. H&E: x 40. (I) Brain: Group II: section showing degeneration, rounding of purkinje cells and demyelination of cerebellus H&E: x 40. (J) Brain: Group II: section showing Chromatolysis. H&E: x 40. (K) Brain: Group II: section showing perivascular accumulation of fat vacuoles. H&E: x 10. (L) Brain: Group II: section showing hyalinised blood vessels and hemorrhages in bronchioles. H&E: x 40.

4. Conclusion

The results of our current investigation showed that oral administration of Monosodium glutamate caused histopathological lesions in the hepatic, renal, nervous, and lung tissues, as observed by gross and microscopic examination. MSG at 5 g/kg b.wt/day orally for 6 weeks was harmful to rats and produced numerous histopathological abnormalities by increasing the formation of reactive oxygen species (ROS) and lipid peroxidation and decreasing antioxidant levels. Concurrent administration of ZnO NPs and MSG to rats was proven to improve a variety of pathological alterations. The ameliorating effect of ZnO NPs was found to be relatively better than that of the majority of the parameters. The results of this investigation suggest that using ZnO NPs on a regular basis in human and veterinary medicine may be effective in protecting against the harmful and toxic effects of MSG.

5. References

1. Afeefy AA, Marwa MS, Arafa MAA. Effect of honey on monosodium glutamate induced nephrotoxicity (Histological and Electron Microscopic Studies). Journal of American Science. 2012;8(1):146-156.
2. Afifi M, Aaser MA. Ameliorating effect of zinc oxide and silver nanoparticles on antioxidant system in the brain of diabetic rats. Asian Pacific Journal of Tropical Biomedicine. 2015;5(10):874-877.
3. Aisha DA. Monosodium glutamate induced testicular lesions in rats (histological study). Middle East Fertility Society Journal. 2013;19:274-280.
4. AL-Mosaibih MA Effects of monosodium glutamate and acrylamide on the liver tissue of adult wistar rats. Life Science Journal. 2013, 10(2).
5. Anonymus. Monosodium glutamate a safety assessment technical report series no. 2. Food Standards Australia new Zealand; c2003.
6. Badkoobeh P, Parivar K, Kalantar SM, Hosseini SD, Salabat AR. Effect of nano-zinc oxide on doxorubicin-induced oxidative stress and sperm disorders in adult male Wistar rats. Iranian Journal of Reproductive Medicine. 2013;11(5):355-364.
7. Bedi PS, Kaur A. An overview on uses of zinc oxide nanoparticles. World Journal of Pharmacy and Pharmaceutical Sciences. 2015;4(12):1177-1196.

8. Beyreuther K, Bresalski JD, Fernstrom P, Grimm W, Hammes P, Heinemann U, *et al*. Consensus meeting monosodium glutamate: An update. European Journal of Clinical Nutrition; c2006. p. 1-10.
9. Bojanic V, Bojanic Z, Najman S, Savic T, Jakovljevic V. Diltiazem prevention of toxic effects of monosodium glutamate on ovaries in rats. Gen Physiol Biophys. 2009;28:149-154.
10. Ciric M, Cekic S, Pavlovic V, Jovic Z, Tasic G. Histopathological changes in spleen of rats treated with monosodium glutamate. Acta Fac. Med. Naiss. 2005;22(4):191-194.
11. Costa C, Brazao V, Kuehn C, Oliveira L, Junior J, Sala M, *et al*. Zinc and pregnancy: marked changes on the immune response following zinc therapy for pregnant female challenged with trypanosome Cruzi. Clin. Nutr. In press; c2012.
12. Culling CFA. Hand book of histopathological and histochemical techniques (Including museum techniques). 1974;3:361.
13. Das RS, Ghosh SK. Long term effect of monosodium glutamate on spermatogenesis following neonatal exposure in albino mice. A histological study. Nepal Medical College Journal. 2010;12(3):149-153.
14. Egbuonu ACC, Ejikeme P, Madus, Obasi L, Namdi N. Influence of sub-chronic oral exposure to high monosodium glutamate on some serum markers of the renal functions in male wistar rats. African Journal of Biochemistry Research. 2010;4(9):225-228.
15. Eweka AO, Igbigbi PS, Ucheya RE. Histochemical studies of the effects of monosodium glutamate on the liver of adult wistar rats annals of medical and health sciences research. 2011, 1(1).
16. Reham HZ, Al-Salmi, Fawziah A, El-Shenawy, Nahla S. Zinc oxide nanoparticles with green tea extract complex in the pancreas of rats against monosodium glutamate toxicity. Journal of Basic and Clinical Physiology and Pharmacology. 2021;32(5):979-985. https://doi.org/10.1515/jbcpp-2020-0164
17. Hassan AA, Mogda KM, Essam M, Ibrahim, Rasha MH, El-Ahl S, *et al*. Efficacy of zinc oxide nanoparticles and curcumin in amelioration the toxic effects in aflatoxicated rabbits. International Journal of Current Microbiology and Applied Sciences. 2016;5(12):795-818.
18. Husarova V, Ostatnikova D. Monosodium glutamate toxic effects and their implications for human intake: A Review JMED Research; c2013. p. 1-12.
19. Igwebuike UM, Ochiogu IS, Blessing IC, Ikokide JE, Idika IK. The effects of oral administration of monosodium glutamate (MSG) on the testicular morphology and cauda epididymal sperm reserves of young and adult male rats. Veterinarski Arhiv. 2011;81(4):525-534.
20. Ismail NH. Assessment of DNA damage in testes from young wistar male rat treated with monosodium glutamate. Life Science Journal. 2012, 9(1)
21. Jacobson EL, Shieh WM, Huang AC. Mapping the role of NAD metabolism in prevention and treatment of carcinogenesis. Mol. Cell. Biochem. 1999;193:69-74.
22. Khadiga A, Mohammed S, Saad A, Mohamed H. Response of broiler chicks to dietary monosodium glutamate. Pakisthan vet. J. 2009;29(4):xxx
23. Kulkarni AD, Sundaresan A, Rashi MJ, Yamamoto S Karkow F. Application of diet-derived taste active components for clinical nutrition: Perspectives from ancient ayurvedic medical science. Space Medicine and Modern Clinical Nutrition. Current Pharmaceutical Design. 2014;20: 2791-2796.
24. Nagata M, Suzuki W, Iizuka S, Tabuchi M, Maruyama H, Takeda S, *et al*. Type 2 diabetes mellitus in obese mouse model induced by monosodium glutamate. Experimental Animal. 2006;55(2):109-115.
25. Ninomiya K. Natural occurrence. Food Review International. 1998;14:177-212.
26. Ochiogu IS, Ogwu D, Uchendu CN, Okoye CN, Ihedioha JI, Mbegbu EC. Serum luteinising hormone, testosterone and total cholesterol levels, libido and testicular histomorphology of male West African Dwarf goats orally or subcutaneously treated with monosodium l-glutamate. Veterinarni Medicina. 2015;60(5):253-260
27. Olney JW. Brain damage and oral intake of certain aminoacids. In: Levi, G., Battistin, L., Lajtha, A., (eds). Transport Phenomena in the Nervous System: Physiological and Pathological Aspects. Plenum: New York; c1976.
28. Ortiz GG, Bitzer-Quintero OK, Zárate BC, Rodríguez-Reynoso C, Larios-Arceo F, Velázquez-Brizuela IE, *et al*. Monosodium glutamate-induced damage in liver and kidney: A morphological and biochemical approach. Biomedicine & Pharmacotherapy. 2006;60:86-91.
29. Osman HEH, Elshama SS, El-Meghawry EA. Assessment of nephrotoxicity of repeated use of monosodium glutamate in adult albino rats. Ain Shams Journal of Forensic Medicine and Clinical Toxicology. 2012;19:88-96.
30. Ramanathan M, Sivakumar S, Anandvijaykumar P, Saravanababu C, Pandian P. Neuroprotective evaluation of standardized extract of *Centella asiatica* in monosodium glutamate treated rats. Indian Journal of Experimental Biology. 2007;45:425-431.
31. Reham ZH, Mohammad S. AL-Harbib. Monosodium glutamate induced testicular toxicity and the possible ameliorative role of vitamin E or selenium in male rats. Toxicology Reports. 2014;1:1037-1045.
32. Sakr SA, Badawy GM. Protective effect of curcumin on monosodium glutamate-induced reproductive toxicity in male albino rats. Global J Pharmacol. 2013;7(4):416-22.
33. Thomas M, Sujatha KS, Sisilamma G. Protective effect of *piper longum* Linn. on sodium glutamate induced oxidative stress in rats. Indian Journal of Experimental Biology. 2009;47:186-192.
34. Toyomasu Y, Mochiki E, Yanai M, Ogata K, Tabe Y, Ando H, *et al*. Intragastric monosodium L-glutamate stimulates motility of upper gut via vagus nerve in conscious dogs. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology. 2010 Apr;298(4):R1125-35.
35. Wafa M, Ibrahim SS, Oda A, Khafaga F. Pathological evaluation of the effect of zinc oxide nanoparticles on chromium-induced reproductive toxicity in male albino rats. A. J. V. S. 2017;53(2):24-32.
36. Wang Q, Heimberg H, Pipeleers D, Ling Z. Glibenclamide activates translation in rat pancreatic β cells through calcium-dependent mTOR, PKA and MEK signalling pathways. Diabetologia. 2008;51:1202-1212.
37. Xu L, Sun J, Lu R, Ji Q, Xu JG. Effect of glutamate on inflammatory responses of intestine and brain after focal cerebral ischemia. World journal of gastroenterology:

WJG. 2005 Feb 2;11(5):733.
38. Yaqub H, Baky ANA, Attia HA, Faddah L. Hepatoprotective effect of N-acetyl cysteine and/or β-carotene on monosodium glutamate-induced toxicity in rats. Res J Med Med Sci. 2008;3(2):206-215.
39. Yoneda J, Chin K, Torii K, Sakai R. Effects of oral monosodium glutamate in mouse models of asthma. Food and Chemical Toxicology. 2011 Jan 1;49(1):299-304.
40. Youssef MH, Saleh NK, Mohamed AE, Khatib YA. Enhanced platelet aggregation, hyperinsulinemia and low testosterone level in monosodium glutamate obese rats. Australian Journal of Basic and Applied Sciences. 2010;4(10):4532-4539.
41. Kazmi Z, Fatima I, Perveen S, Malik SS. Monosodium glutamate: Review on clinical reports, International Journal of Food Properties. 2017;20(2):1807-1815