



# Antioxidant Activities of Green Tea Extract/Zinc Oxide Nanoparticles Against Monosodium Glutamate in Different Organs

Reham Z. Hamza<sup>1,2</sup>, Fawzeh A. Al-Salmi<sup>1</sup>, Nahla S. El-Shenawy<sup>3\*</sup>

<sup>1</sup>Biology Department, Faculty of Science, Taif University, Taif, Saudi Arabia.

<sup>2</sup>Zoology Department, Faculty of Science, Zagazig University, Zagazig, Egypt.

<sup>3</sup>Zoology Department, Faculty of Science, Suez Canal University, Ismailia, 41522, Egypt.

**\*Corresponding author:**

Nahla S El-Shenawy,  
Zoology Department, Faculty  
of Science, Suez Canal  
University, Ismailia 41522,  
Egypt.  
Tel: 002/01008660620;  
Email: elshenawy\_nahla@  
hotmail.com.  
nahla.el-shenawy@scuegypt.  
edu.eg.

Received: 8 June 2020

Accepted: 18 June 2020

ePublished: 29 June 2020



## Abstract

This brief review provided evidence for the role of green tea extract (GTE)/zinc oxide nanoparticles (ZnO NPs) in a variety of biomedical applications against the toxic effect of monosodium glutamate (MSG). MSG is used to enhance the taste, however it causes oxidative stress in the long-term. Many effects of MSG consumption on the brain, obesity, sex organs, and metabolism have been verified. This review covered the effect of GTE/ZnO NPs on many different organs including the liver, kidney, heart, spleen, testis, brain, and pancreas after being exposed to MSG. The review indicated that the toxicity induced by MSG could be restored by GTE/ZnO NPs in different organs. Accordingly, the green nanoparticles could be attended as a futuristic approach to be used against any toxic substance.

**Keywords:** Nanoparticles, Cytokine, Antioxidant, Organ, Monosodium glutamate

## Introduction

Nanotechnology is named in the case of science and technology as a consequence of the development, discovery, and evaluation of nano-scale structures. In the last few years, zinc oxide nanoparticles (ZnO NPs) have been applied as important components in various sectors of manufacturing as medicine and textile, as well as automotive markets. Several chemical and physical techniques have been used in the preparation of ZnO NPs, and biomaterials applied using various substrates (e.g. bacteria, microorganisms, plant extracts, and enzymes) are theoretically guided as eco-friendly alternatives compared with chemical ones (1).

Different plant parts were used for the formation of NPs because their extracts are rich in phytochemicals that function like a reducing and a stabilizing agent (2-9). Leaf is the most widely utilized plant component, washed in distilled water, which is used for the development of ZnO NPs. The new tea leaf is abundant in the group of polyphenol flavonols called catechins (30%). Flavonoids and their glycosides including gallic acid, coumaroylquinic acid, chlorogenic acid, and theogallin are other polyphenols that are present in the green tea. To prevent the oxidation of polyphenols in the green leaves, green tea is produced without fermentation (10). The chemical composition of

fresh leaves is very similar to that of dry green tea except for a slight enzymatically catalyzed shift that occurs with extremities after fast plucking. During drying, fresh, volatile substances are formed: (i) phenolic compounds (30%), (ii) proteins (15%), (iii) amino acids (4%), (iv) carbohydrates (7%), and (v) lipids (7%), as well as (vi) vitamins C and E are the normally-measured compositions of green tea leaves (10-12).

Monosodium glutamate (MSG) is used as a flavor enhancer, however it causes oxidative stress in the long-term (13,14). MSG is used to improve the meatiness and savory aroma and taste of many dried types of meat, soups, stews, and many other foods. Many effects of MSG consumption on the brain, obesity, sex organs, and metabolism have been proved (15). MSG is known as a non-essential amino acid discovered as sodium salt; it is found to enhance food flavor as abovementioned (16). Glutamate is a neurotransmitter of amino acids in the brain, and glutamate-responsive tissues are also found in other organs of the body. Some diseases such as Alzheimer's disease and Huntington's chorea have been associated with abnormal glutamate receptor activity. Headaches, severe allergic reactions, sickness, heart attack-like signs, fatigue, and so on are the adverse effects of MSG. In both

## Archive of SID

women and men, the use of MSG raises the possibility of reproductive disorder (17). The median lethal dose ( $LD_{50}$ ) of MSG in rats and mice is 15 and 18 g/kg body weight, respectively, which is five times the  $LD_{50}$  of NaCl (3 g/kg in rats). The findings of both animal and human tests have shown that even the minimum dose of MSG exerts harmful effects. It is believed that the total MSG consumption per day should be 0.3-1.0 g (18).

Phenolic compounds hold a greater antioxidant capacity, and antioxidants are metal ion reducing agents; thus, the synthesis of plant-mediated NPs is preferred. The synthesis of NPs, which inhibit particle agglomeration, is supported by more modest amounts of proteins, lipids, and amino acids. The aim of this mini-review was the synthesis of ZnO NPs mediated by green tea extract (GTE) and determination of its activity against MSG in different organs.

### Liver

In a study by Al-Salmi et al, following 28 days of exposure, oxidative stress and inflammation were caused by MSG in the liver. Histological research was conducted and the transmission of hepatic parenchyma was observed. GTE/ZnO NPs exerted partial hepato-protective effect against MSG at aqueous solution of 0.001 M (13).

MSG is dose-dependently affected by all the antioxidants [lipid peroxidation (LPO), catalase (CAT), superoxide dismutase (SOD), xanthine oxidase (XO), myeloperoxidase (MPO), and glutathione (GSH)]. It also affects the inflammatory markers such as interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor-alpha (TNF- $\alpha$ ). Such parameters have been taken as indicators of oxidative stress. Moreover, the inadequate molecular mechanism of antioxidants may cause liver injury. The study of Al-Salmi et al (13) clarified that ZnO NPs/GTE gave hepatic safety through restoring the antioxidant enzyme activities, decreasing LPO, and increasing GSH concentrations, as well as enhancing pro-inflammatory biomarkers. Moreover, Hamza et al (16) reported that ZnO NPs/GTE had a beneficial effect on MSG-induced hyperlipidemia. The anti-hyperlipidemic effect of GTE/ZnO NPs was improved by a decrease in the triglyceride, total cholesterol, and low-density lipoprotein levels, as well as an elevation in high-density lipoprotein. The rectitude of hepatocytes was also refined, as seen by reducing the enzyme activity.

### Kidney

A previous study showed that MSG would cause renal dysfunction due to the peroxidation imbalance and its levels of antioxidants. The histopathological changes of rat kidney tissue are specifically sufficient for the dose of MSG and biochemical variations. GTE/ZnO NPs complex proved the maintenance and restoration of kidney capacity by inhibiting oxidative damage through a mere way. The

study indicated that the therapeutic impact of ZnO NPs on MSG-fed rats could be antioxidant-dependent (19). No unusual findings have been obtained and its biochemical parameters included levels of urea, uric acid, and creatinine in the rats treated with ZnO NPs and ZnO NPs/GTE. Data of unvaried creatinine and uric acid levels within the ZnO NPs/GTE-exposed rats have suggested normal renal functions.

### Heart

The impact of MSG on oxidative stress by modifying the factors such as LPO, CAT, SOD, GPx, and GSH in the cardiac tissue of adult rats with a standard dose for the bodyweight of 17.5 mg/g was investigated (20). MSG may lead to cardiac disorder. Consequently, all results indicated that the continuous usage of MSG could dramatically increase the health hazard and result in cardiac hypertrophy and oxidative stress. Treatment with GTE/ZnO NPs and MSG decreased LPO, increased antioxidants, and reduced oxidative damage. The effectiveness requires GTE/ZnO NPs to scavenge free radicals, as well as architectural improvement (20). The antioxidant property of the green GTE/ZnO NPs can be attributed to their ingredients from GTE phenol compounds (21), which give hydrogen ions to free radicals to prevent oxidation reactions in the cells. It could get rid of free radicals that are the fundamental causes of antioxidant and cardiac tissue damage caused by LPO and disturbance.

### Spleen

MSG had a dose-dependent effect on spleen tissue and caused an improvement in hypertrophy of the white spleen pulp. Due to its strong antioxidant properties and reduced ZnO, the ZnO NPs/GTE complex may have a defensive advantage against splenomegaly that is excited against MSG (22).

### Testis

The limited toxicity of ZnO NPs administration to the testicular tissue was recorded. The treatment of adult male rat with MSG decreased the levels of testosterone, along with interaction with testicular histology, indicating dose-dependence of MSG. Testicular dysfunction was also caused by ZnO NPs by interfering with the balance of antioxidants/oxidants, suppressing testosterone levels, and causing damage to the cellular testis (23). The interaction of ZnO NPs with the GTE complex strongly prevented the MSG or ZnO NPs toxic effects by decreasing DNA damage and lipid peroxidation, and improving both the antioxidant and architecture structure of the testis.

### Brain

MSG was orally administered (6.0 and 17.5 mg/kg body weight). The larger dose was characterized by a reduction of SOD, CAT, and GPx activities, as well as a decrease

*Archive of SID*

in GSH and brain neurotrophic factor levels in cerebral cortex of rats (24). ZnO NPs/GTE complex conferred an advantage on the cerebral cortex rather than ZnO NPs or GTE separately. Compared to control animals, a substantial decrease was observed in noradrenaline, adrenaline, dopamine, and serotonin levels at higher doses (17.5 mg/kg) of MSG. Furthermore, important variations in acetylcholinesterase activity and thiol levels were recorded at the same dose of MSG. The findings of cyclooxygenase 2 declared that it is an important mechanism by which large doses of MSG can correspond to cellular oxidative status in the brain. The levels of CAT, SOD, GPx, and GSH, and the effect of ZnO NPs/GTE on MSG-induced brain toxicity could be enhanced and the other parameters of neural biomarkers can be restored because of their effect on different neurotransmitters or their antioxidant properties.

**Pancreas**

Degenerative histopathological changes in the pancreatic acini with a significant increase in acinar cell nuclei were recorded in the animals treated with MSG.

The results of anti-diabetic and antioxidant research showed that the synthesized GTE/ZnO NPs could be used to lower sugar levels, stimulate insulin, and boost pancreatic architecture against MSG. Biosynthesized preparation of ZnO NPs/GTE was expected to be important in biomedical applications against diabetic complications induced by MSG (25).

**Conclusion**

To conclude, people must limit their national use of foods containing the taste enhancer, namely MSG, and caution should be taken as regards its industrial use. To reduce the toxicity of ZnO NPs and MSG to the liver, kidney, heart, spleen, testis, pancreas, and brain at cellular and oxidative stress levels, the use of GTE / ZnO NPs complex is strongly recommended.

**Authors' Contributions**

All authors are equal in contribution.

**Conflict of Interest Disclosures**

There is no conflict of interests.

**Ethical Issues**

Not applicable.

**Funding**

None.

**References**

- Mirzaei H, Darroudi M. Zinc oxide nanoparticles: biological synthesis and biomedical applications. *Ceram Int.* 2017;43(1 Pt B):907-14. doi: [10.1016/j.ceramint.2016.10.051](https://doi.org/10.1016/j.ceramint.2016.10.051).
- Zong Y, Li Z, Wang X, Ma J, Men Y. Synthesis and high photocatalytic activity of Eu-doped ZnO nanoparticles. *Ceram Int.* 2014;40(7 Pt B):10375-82. doi: [10.1016/j.ceramint.2014.02.123](https://doi.org/10.1016/j.ceramint.2014.02.123).
- Nachiyar V, Sunkar S, Pandurangan P. Biological synthesis of gold nanoparticles using endophytic fungi. *Der Pharma Chem.* 2015;7(2):31-8.
- Ramesh M, Anbuvaran M, Viruthagiri G. Green synthesis of ZnO nanoparticles using *Solanum nigrum* leaf extract and their antibacterial activity. *Spectrochim Acta A Mol Biomol Spectrosc.* 2015;136 Pt B:864-70. doi: [10.1016/j.saa.2014.09.105](https://doi.org/10.1016/j.saa.2014.09.105).
- Xiao L, Liu C, Chen X, Yang Z. Zinc oxide nanoparticles induce renal toxicity through reactive oxygen species. *Food Chem Toxicol.* 2016;90:76-83. doi: [10.1016/j.fct.2016.02.002](https://doi.org/10.1016/j.fct.2016.02.002).
- Rajeshkumar S. Anticancer activity of eco-friendly gold nanoparticles against lung and liver cancer cells. *J Genet Eng Biotechnol.* 2016;14(1):195-202. doi: [10.1016/j.jgeb.2016.05.007](https://doi.org/10.1016/j.jgeb.2016.05.007).
- Nagajyothi PC, Minh An TN, Sreekanth TVM, Lee JI, Lee DJ, Lee KD. Green route biosynthesis: characterization and catalytic activity of ZnO nanoparticles. *Mater Lett.* 2013;108:160-3. doi: [10.1016/j.matlet.2013.06.095](https://doi.org/10.1016/j.matlet.2013.06.095).
- Gnanajobitha G, Paulkumar K, Vanaja M, Rajeshkumar S, Malarkodi C, Annadurai G, et al. Fruit-mediated synthesis of silver nanoparticles using *Vitis vinifera* and evaluation of their antimicrobial efficacy. *J Nanostructure Chem.* 2013;3(1):67. doi: [10.1186/2193-8865-3-67](https://doi.org/10.1186/2193-8865-3-67).
- Dobrucka R, Długaszewska J. Biosynthesis and antibacterial activity of ZnO nanoparticles using *Trifolium pratense* flower extract. *Saudi J Biol Sci.* 2016;23(4):517-23. doi: [10.1016/j.sjbs.2015.05.016](https://doi.org/10.1016/j.sjbs.2015.05.016).
- Bancirova M. Comparison of the antioxidant capacity and the antimicrobial activity of black and green tea. *Food Res Int.* 2010;43(5):1379-82. doi: [10.1016/j.foodres.2010.04.020](https://doi.org/10.1016/j.foodres.2010.04.020).
- Cabrera C, Artacho R, Giménez R. Beneficial effects of green tea--a review. *J Am Coll Nutr.* 2006;25(2):79-99. doi: [10.1080/07315724.2006.10719518](https://doi.org/10.1080/07315724.2006.10719518).
- Lin YS, Tsai YJ, Tsay JS, Lin JK. Factors affecting the levels of tea polyphenols and caffeine in tea leaves. *J Agric Food Chem.* 2003;51(7):1864-73. doi: [10.1021/jf021066b](https://doi.org/10.1021/jf021066b).
- Al-Salmi FA, Hamza RZ, El-Shenawy NS. The interaction of zinc oxide/green tea extract complex nanoparticles and its effect on monosodium glutamate toxicity in liver of rats. *Curr Pharm Biotechnol.* 2019;20(6):465-75. doi: [10.2174/1389201020666190408120532](https://doi.org/10.2174/1389201020666190408120532).
- Diniz YS, Fernandes AA, Campos KE, Mani F, Ribas BO, Novelli EL. Toxicity of hypercaloric diet and monosodium glutamate: oxidative stress and metabolic shifting in hepatic tissue. *Food Chem Toxicol.* 2004;42(2):313-19. doi: [10.1016/j.fct.2003.09.006](https://doi.org/10.1016/j.fct.2003.09.006).
- Husarova V, Ostatnikova D. Monosodium glutamate toxic effects and their implications for human intake: a review. *JMED Res.* 2013;2013:608765. doi: [10.5171/2013.608765](https://doi.org/10.5171/2013.608765).
- Hamza RZ, Al-Salmi FA, El-Shenawy NS. Nanoparticles effects on zinc oxide/green tea complex on the lipid profile and liver functions of rats after monosodium glutamate treatment. *J Appl Sci.* 2018;18(2):65-70. doi: [10.3923/jas.2018.65.70](https://doi.org/10.3923/jas.2018.65.70).
- Ramesh M, Muthuraman A. Flavoring and coloring agents: Health risks and potential problems. In: Grumezescu AM, Holban AM, eds. *Natural and Artificial Flavoring Agents and Food Dyes.* Academic Press; 2018. p. 1-28. doi: [10.1016/b978-0-12-811518-3.00001-6](https://doi.org/10.1016/b978-0-12-811518-3.00001-6).
- Umukoro S, Oluwole GO, Olamijowon HE, Omogbiya AI, Eduviere AT. Effect of monosodium glutamate on behavioral phenotypes, biomarkers of oxidative stress in brain tissues and liver enzymes in mice. *World J Neurosci.* 2015;5(5):339-49. doi: [10.4236/wjns.2015.55033](https://doi.org/10.4236/wjns.2015.55033).
- El-Shenawy NS, Hamza RZ, Al-Salmi FA, Al-Eisa RA. Evaluation of the effect of nanoparticles zinc oxide/*Camellia sinensis*

- complex on the kidney of rats treated with monosodium glutamate: antioxidant and histological approaches. *Curr Pharm Biotechnol.* 2019;20(7):542-50. doi: [10.2174/1389201020666190522075928](https://doi.org/10.2174/1389201020666190522075928).
20. El-Shenawy NS, Hamza RZ, Al-Salmi FA. Cardioprotective effect of zinc oxide nanoparticles/green tea extract complex on monosodium glutamate toxicity. *J Biol Eng Med.* 2019;1(1):1-5. doi: [10.31487/j.jbem.2019.01.03](https://doi.org/10.31487/j.jbem.2019.01.03).
  21. Srivastava RC, Husain MM, Hasan SK, Athar M. Green tea polyphenols and tannic acid act as potent inhibitors of phorbol ester-induced nitric oxide generation in rat hepatocytes independent of their antioxidant properties. *Cancer Lett.* 2000;153(1-2):1-5. doi: [10.1016/s0304-3835\(99\)00400-0](https://doi.org/10.1016/s0304-3835(99)00400-0).
  22. Al-Salmi FA, Hamza RZ, El-Shenawy NS. Effect of a green nanoparticles complex on histopathology of spleen in rat induced by monosodium glutamate. *Instant J Hematol Oncol.* 2019;2:4-11. doi: [10.36811/ijho.2019.110002](https://doi.org/10.36811/ijho.2019.110002).
  23. Hamza RZ, Al-Salmi FA, Laban H, El-Shenawy NS. Ameliorative role of green tea and zinc oxide nanoparticles complex against monosodium glutamate-induced testicular toxicity in male rats. *Curr Pharm Biotechnol.* 2020;21(6):488-501. doi: [10.2174/1389201020666191203095036](https://doi.org/10.2174/1389201020666191203095036).
  24. Hamza RZ, Al-Salmi FA, El-Shenawy NS. Evaluation of the effects of the green nanoparticles zinc oxide on monosodium glutamate-induced toxicity in the brain of rats. *PeerJ.* 2019;7:e7460. doi: [10.7717/peerj.7460](https://doi.org/10.7717/peerj.7460).
  25. Hamza RZ, Al-Salmi FA, El-Shenawy NS. Zinc oxide nanoparticles with green tea extract complex in the pancreas of rats against monosodium glutamate toxicity. *J Basic Clin Physiol Pharmacol.* 2020. doi: [10.1515/jbcpp-2020-0164](https://doi.org/10.1515/jbcpp-2020-0164).