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The amelioration of vitamin E on histological changes of rabbit's brain treated with zinc oxide nanoparticles

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Abstract

Zinc-oxide in nanoparticles is suggested to be one of the crucial nanoparticles due to its expanse implementation in many industries, like electrons, food supplements, and maquillage and makeup. This led to more individual exposure to ZnO NPs through inspiration and skin penetration. This study objected to estimating the toxic impact of ZnO NPs on the cerebral cortex, hippocampus, and cerebellum in male rabbits by studying the gross and histological changes. Twenty-four adult male rabbits were divided randomly into four groups, comprising six animals. The first group was considered as the control group left without treatment; the second group was treated with 100 mg/kg BW of vitamin e orally, the third group was treated intraperitoneally with ZnO NPs 600 mg/kg BW, and the fourth group was treated with I/P 600 mg/kg BW of ZnO NPs in addition to 100 mg/kg BW orally of vitamin e twice weekly for twenty-one days. The histological results showed degenerative, necrotic changes in neurons with a vascular and inflammatory response in the cerebral cortex, hippocampus, and cerebellum in the second group of rabbits treated with ZnO NPs. In contrast, the treated rabbits with ZnO NPs and vitamin E revealed slight improvement in the histological picture of brain sections. Also, there was an alteration in acetylcholine levels in all groups compared with the control group.

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Introduction

The ZnO NPs are substances about 1-100 nm (1,2). Nanotechnology in veterinary medicine is a progressively growing technology that has a considerable role in numerous specialties of therapeutic implementation (3,4). On the other hand, long-term exposure to such considerable amounts of these compounds showed a life-threatening condition (5,6). Because of the tiny size of nanoparticles, the surface area is increased, leading to inducing single and a specific physiochemical characterization like reaction, resistance with high conduction comparison to the bulk material (7,8). ZnO NPs have enticed attentiveness due to their unrivaled lineaments. Also, there is a considerable potential implementation of ZnO NPs in veterinary medicine because of their antibacterial, antineoplastic, the healing of wounds, and angiogenic properties (9,10). Animals in several areas are primarily prone to ZnO NPs rather than other areas because they are considered terrestrial, such situations may intend in acute shock, and high levels can be enhanced exposure that leads to progressive, irreversible lesions (11). Considerable changes are observed in blood with pathological lesions in the stomach, liver, and kidney of affected animals after short-term exposure to ZnO NPs in mice, rats, fish, and rabbits (12-14). Recently many researchers have proved that nanoparticles can arrive brain through the blood-brain barrier then these are causing lesions by inducement the oxidative stress, inflammatory reaction, and cytotoxicity as a result of their toxic impacts on the blood and brain (15,16). Acetylcholine is a chief transmitter of nerve signals within the central and peripheral nervous systems. ACH activities within the autonomic nervous system cause vasodilation, decreased cardiac muscle contraction, and decreased heart rate, affect the

gastrointestinal tract and urinary system and affect CNS (17). Vitamins C and E are considered major antioxidant additives commonly used in the food industry and have lower oxidative stress in animals (18). Researchers have recently focused on determining how to use antioxidant substance mechanisms, enhancing the antioxidant system efficiency (19). Vitamins, notably vitamin E, are widely used in many organisms for ameliorative aims (20-22).

Upon all the above, we aimed in the current study to investigate the histopathological impacts of ZnO NPs on male rabbits' brains and the ameliorative effects of vitamin E in reducing the effects of zinc oxide nanoparticles.

Materials and methods

Ethical approval

The scientific committee has approved this study of the department of pathology and poultry diseases of collage of veterinary medicine- University of Mosul at the first congress dated 13/9/2021, that the concurrent conducting experiment did not violent the laws of animal rights and the euthanasia is applied in accordance of this guidelines.

Animals

This study was set on 24 adult male rabbits (obtained from a rabbit breeding farm in Gogjali quarter in Mosul city), weighing 1.5 to 2 kg. They were kept in clean, well-ventilated cages throughout the experiment, with unrestricted access to food and water.

Chemicals

Zinc oxide nanoparticle (>100nm) the powder was obtained from Sigma-Aldrich chemicals (color: white, form: rod-shape, x-ray diffraction: conforms, particle size: ≤50nm.Vitamin E from Poland- Pharmacy laboratories.

Experimental design

the rabbits were randomly divided into four groups, each containing 6 rabbits. Group 1; kept without treatment. Group 2; treated with vitamin E orally at 100 mg/kg B. W. twice weekly for 3 weeks (23). Group 3; treated with ZnO NPs Intraperitoneally 600 mg/kg B. W. two times weekly for 3 weeks. Group 4; treated with ZnO NPs intraperitoneally 600 mg/kg B. W. two times weekly in addition to vitamin E orally 100 mg/kg B. W. two times weekly for 3 weeks.

Blood sampling

On the 21st day, the rabbits' blood was obtained aseptically using disposable syringes. Afterward, the blood was transferred to a clean tube containing gelatin to be separated at room temperature by centrifugation at 3600 RPM for 15 minutes. A Pasteur pipette aspirated the serum to Eppendorf tubes, then stored in a freezer at -20ºC for estimation of acetylcholine level (24).

Tissue sampling

Rabbits were euthanized for 21 days from the beginning of the experiment, and brains were obtained from them. Then swilled with saline and fixed in 10% neutral buffered formalin for 72 h. then the brain was processed by dehydrating in ethyl alcohol, clearing in xylol, then infiltrating and embedding in paraffin wax. The wax blocks have been trimmed at 25µ and then sectioned at 5µ thick with a complete rotary microtome. Then the slides were stained with hematoxylin and eosin for routine staining (25,26).

Laboratory analysis

According to the manufacturer's instructions, the concentration of ACH in serum has been calculated using an ELISA kit (SunLong Biotech Co., LTD, Shanghai, China). Elisa Reader has read the microplate at 450nm wavelength. These were performing at 25°C.

Statistical analysis

Analysis of variance has been done using the SPSS program Ver.26 (SPSS Inc., Chicago, IL, USA) and using ANOVA (one-way analysis of variance), and the Duncan test has been used in data analysis. The P-value has been estimated at $P \leq 0.05$ whether there was a significant difference between groups (27).

Results

Clinical symptoms

Some clinical symptoms are observed in treated animals with ZnO NPs 600mg/kg BW, such as abnormal movement and behavior like paralysis of the legs and crawling either by using front legs or hind legs. Also, the animals suffered from diarrhea, frequent urination, and abnormal feeding behavior.

Macroscopic observation

Macroscopic appearance of the brain of animals treated with 600mg/kg BW of ZnO NPs showed severe congestion of blood vessels and flattened the dorsal surface of the brain with an absence of the groove on the surface of the brain (Figure 1) in comparing to control group and group treated with vitamin E only (Figure 2). The brain of treated animals with both 600mg/kg BW and vitamin E revealed a slight improvement compared to the treated group with 600mg/kg BW only (Figure 3).

Acetylcholine concentration by using ELISA

The results of the analysis show a significant difference in the concentration of ACH levels where it was a higher concentration of ACH in the third group treated with ZnO NPs Intraperitoneally 600 mg/kg B. W. two times weekly and the treated group with ZnO NPs intraperitoneally 600 mg/kg B. W. and then the fourth group treated with nano ZnO particles intraperitoneally 600 mg/kg B. W. two times weekly in addition to vitamin E orally 100 mg/kg B. W. two

times weekly compared with the first and second control groups (Table 1).

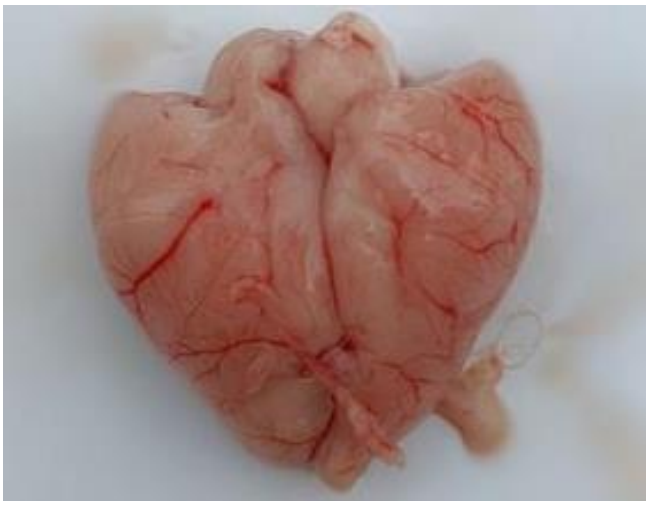

Figure 1: Gross view of the brain of adult male rabbits treated with Zinc oxide nanoparticles showing severe congestion and flattening of the dorsal surface.

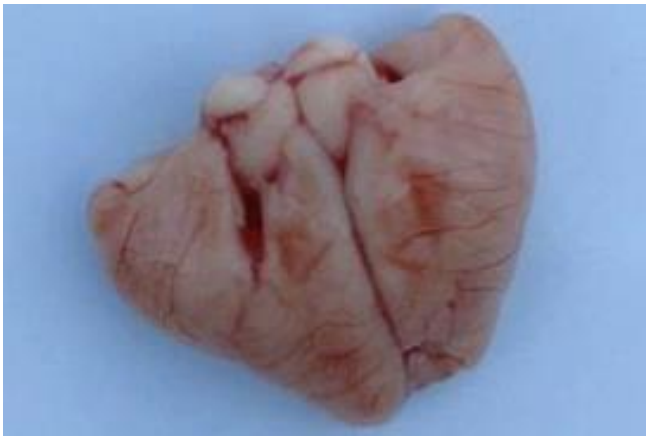

Figure 2: Gross view of the brain of adult male rabbits treated with vitamin E only showing typical appearance of the brain.

Cerebral cortex portion

The histological examination of the microscopic section of the cerebral cortex portion of the control group showed normal architecture of the cortex portion (Figure 4). In contrast, the histological examination of the H&E section of the ZnO NPs treated group showed histological alteration of cerebral cortex architecture, characterized by multiple necrotic foci infiltrated microglial cells proliferation (Figure 5). Severe diffused leptomeningitis (Figure 6). Perivascular mononuclear cells are cuffing (Figure 7). Also, foci of granulomatous inflammation are characterized by necrotic center infiltrated with chronic inflammatory cells and giant cells (Figure 8). Another section showed multifocal gliosis and severe congestion of blood capillaries (Figure 9). Degeneration and necrosis of pyramidal cells were also observed (Figure 10). As for the histological finding of the cerebral cortex portion of the treated animals with ZnO NPs with co-administration of vitamin E showed a slight improvement in the histological alteration, characterized by vasogenic edema and congestion of blood capillaries, vacuolar degeneration, and necrosis of neuronal and pyramidal cells (Figures 11 and 12). However, the group of treated animals with vitamin E only showed no histological alterations, and the histological examination appeared similar to the control group (Figure 13).

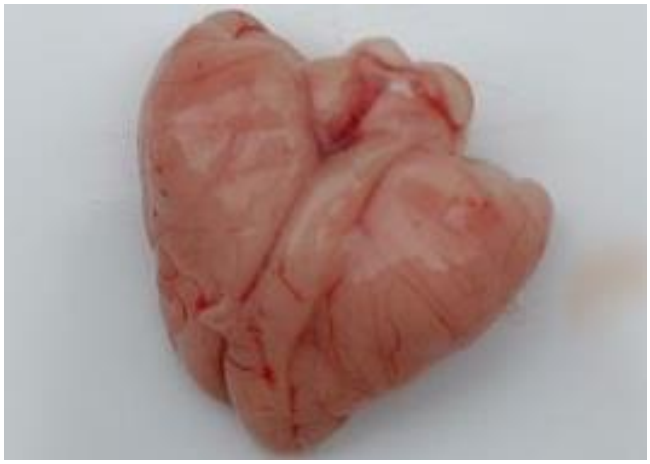

Figure 3: Gross view of the brain of adult male rabbits treated with Zinc oxide nanoparticles and Vitamin E showing slight improvement in the brain.

Table 1: ZnO NPs and vitamin E effects on the concentration of Acetylcholine (ACH) in blood serum

Groups	ACH concentration (pg/ml)
First group	27.73±1.28c
Second group	25.29±0.39c
Third group	254.53±3.68a
Fourth group	186.29±2.70b

(a-c) the letters are different vertically, indicating a significant difference at level P≤0.05. a means higher value followed by b then c.

Hippocampus portion

The histological examination of the microscopic section of the hippocampus portion of the control group showed normal cellular architecture (Figure 14). as well as the group of vitamin E-treated animals showed normal architecture of the hippocampus layer appeared similar to the control group (Figure 15). The treated group with ZnO NPSs alone showed abnormal shape and size due to degenerative and necrotic changes mainly in the pyramidal cells, and neuronal cells,

congestion of blood capillaries of the molecular layer, and vasogenic edema also observed, and vacuolation of neuronal cells of polymorphic cells layer also observed. Additionally, diminution of pyramidal cells was also noticed (Figures 16 and 17). However, the histological examination of the hippocampus portion of treated animals with ZnO NPs with co-administration of vitamin E showed a slight improvement in the histological appearance of histological changes, which means a small degree of neuronal and pyramidal cell damage (Figure 18).

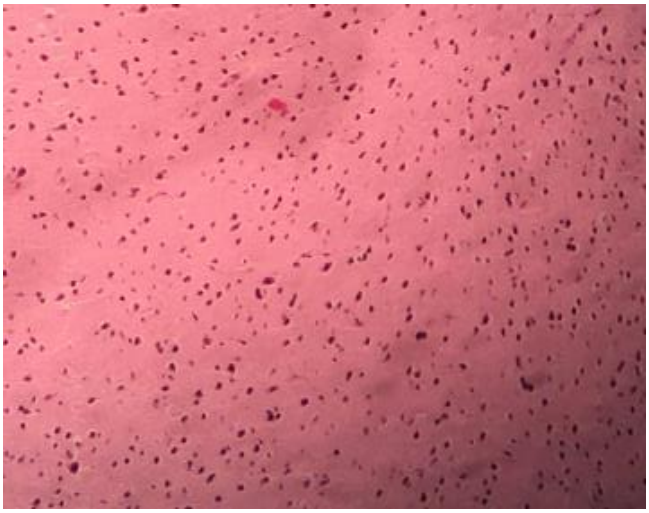

Figure 4: Micrograph of rabbit cerebral cortex of control group showed normal architecture. H&E, 10X.

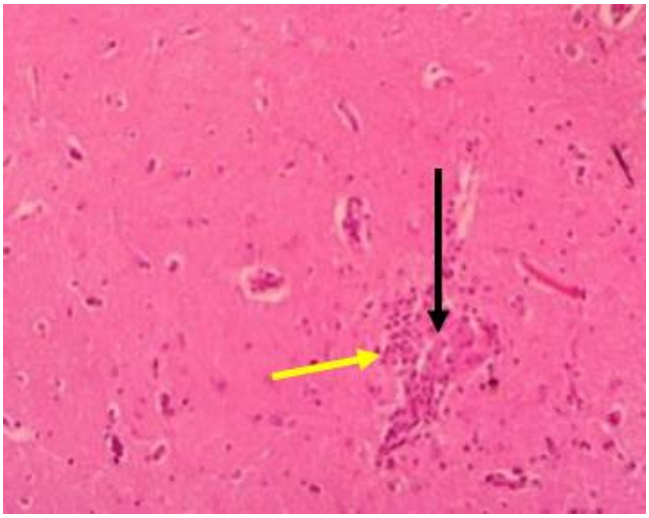

Figure 5: Micrograph of rabbit cerebral cortex showing necrotic foci (black arrow), inflammatory cells (yellow arrow). H&E, 10X.

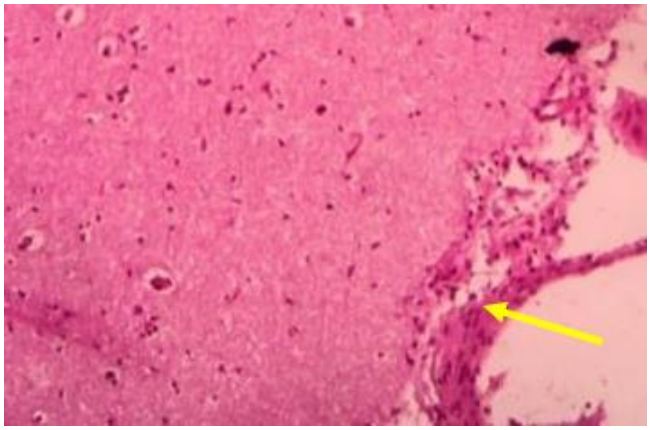

Figure 6: Micrograph of rabbit cerebral cortex showing Leptomeningitis (yellow arrow). H&E, 10X.

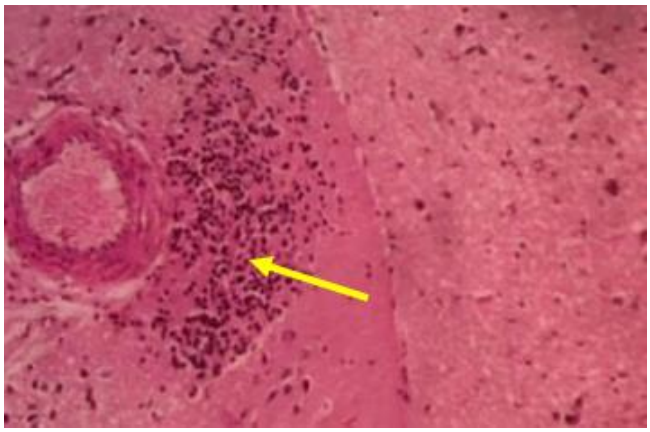

Figure 7: Micrograph of rabbit cerebral cortex showing perivascular mononuclear cells cuffing (yellow arrow). H&E, 10X.

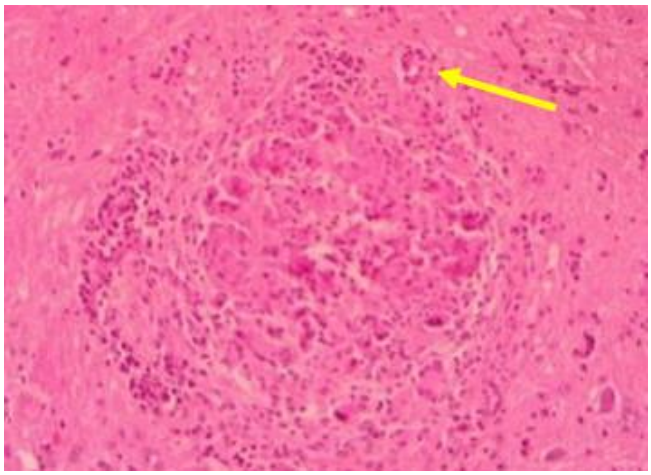

Figure 8: Micrograph of rabbit cerebral cortex showing giant cell (yellow arrow). H&E, 10X.

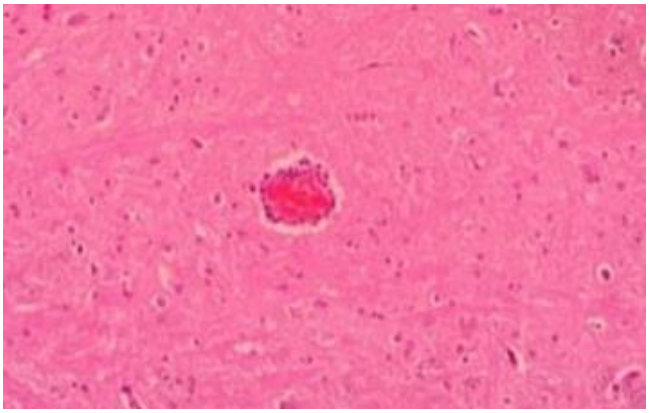

Figure 9: Micrograph of rabbit cerebral cortex showing severe congestion of blood capillaries. H&E, 10X.

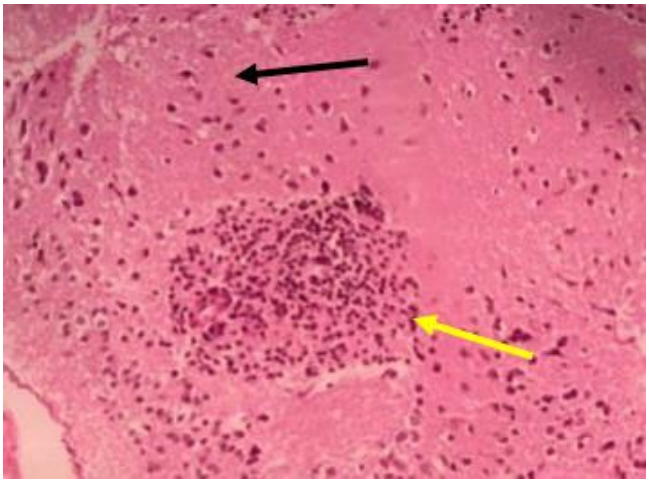

Figure 10: Micrograph of rabbit cerebral cortex showing multifocal gliosis (yellow arrow) and necrosis of pyramidal cells (black arrow). H&E, 10X.

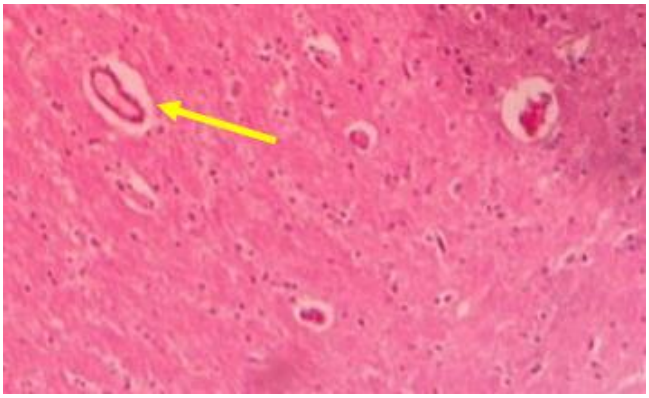

Figure 11: Micrograph of rabbit cerebral cortex showing the treated group with ZnO NPs and vitamin E show vasogenic edema (yellow arrow). H&E, 10X.

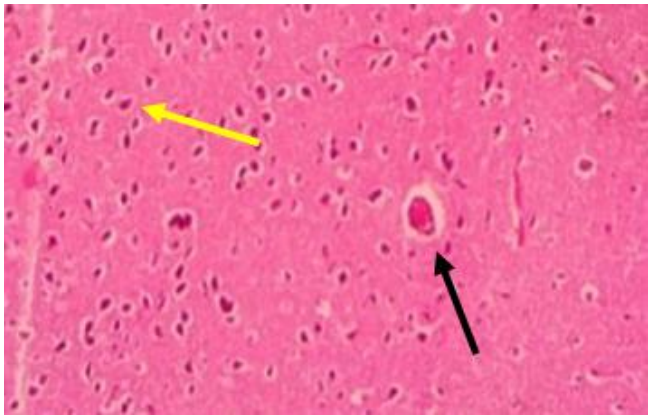

Figure 12: Micrograph of rabbit cerebral cortex showing degeneration of pyramidal cells (yellow arrow), edema, and congestion of blood vessels (black arrow). H&E, 10X.

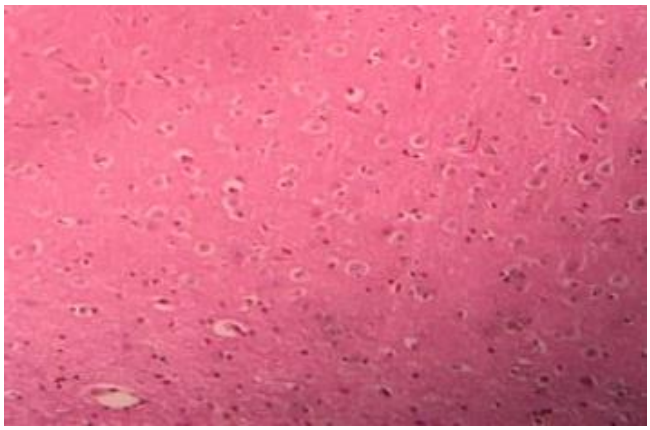

Figure 13: Micrograph of rabbit cerebral cortex of treated group with vitamin E only shows normal architecture. H&E, 10X.

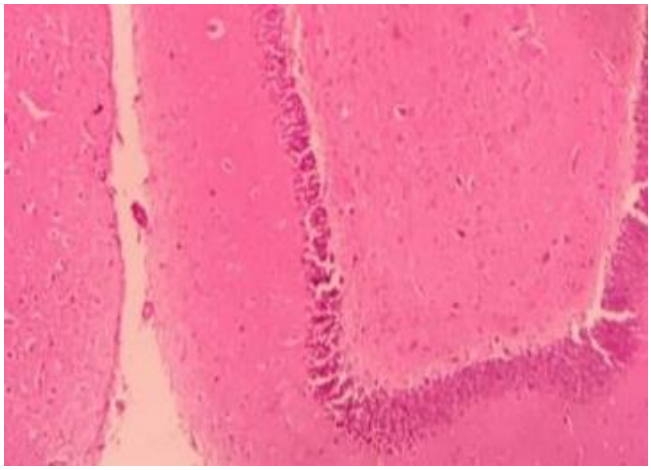

Figure 14: Micrograph of rabbit hippocampus of control group showed normal architecture. H&E, 10X.

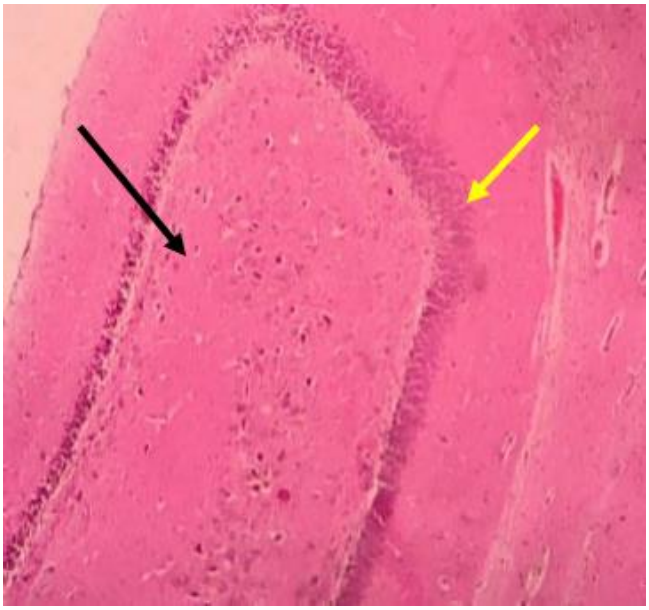

Figure 15: Micrograph of rabbit hippocampus of the group of vitamin E showed normal architecture of hippocampus layer appeared similar to control group, polymorphic layer (yellow arrow) and molecular layer (black arrow). H&E, 10X.

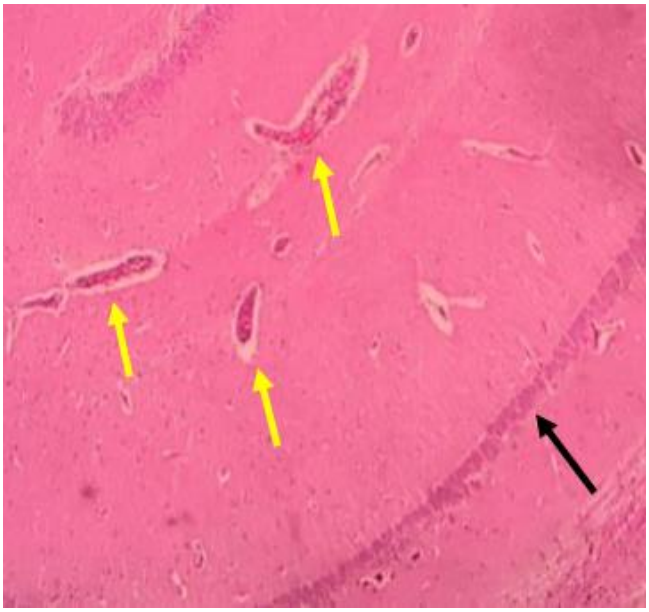

Figure 16: Micrograph of rabbit hippocampus of treated group with ZnO NPs showed congestion and vasogenic edema (yellow arrow), diminution, and necrosis of pyramidal cells (black arrow). H&E, 10X.

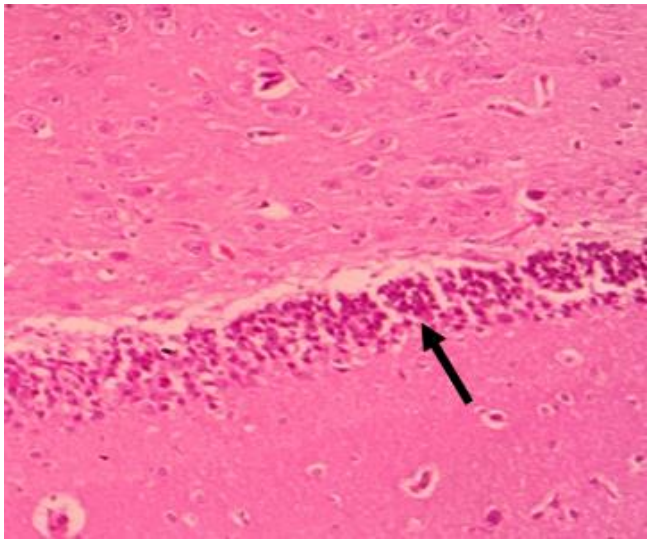

Figure 17: Micrograph of rabbit hippocampus of treated group with ZnO NPs showed diminution and necrosis of pyramidal cells (black arrow). H&E, 40X.

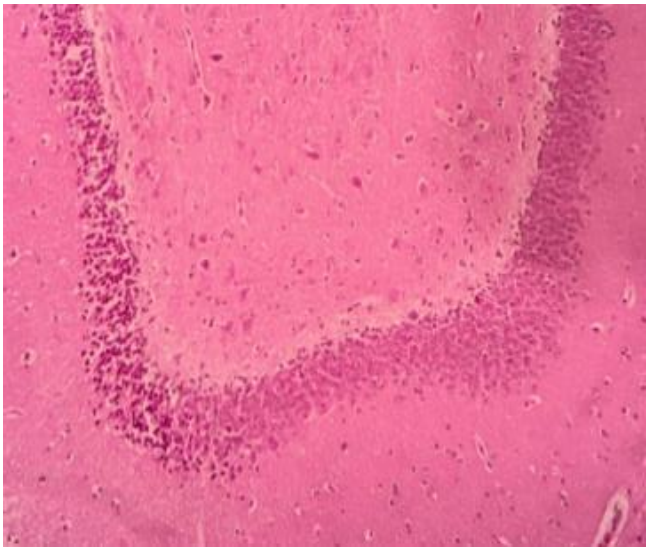

Figure 18: Micrograph of rabbit hippocampus of treated group with ZnO NPs and vitamin E showing slight improvement. H&E, 10X.

Cerebellum portion

The histological examination of the cerebellum portion of the control group revealed the normal architecture of all cerebellar layers (Figure 19). The histological section cerebellum portion of vitamin E of treated group showed no histological changes (Figure 20). Animals treated with ZnO NPs revealed histological changes characterized by diminution with degeneration and necrosis of Purkinje cells and degeneration and necrosis of satellite of basket cells of the molecular layer (Figure 21). Congestion of blood

capillaries (Figure 22). degeneration, necrosis, and hemorrhage were observed in the granular layer (Figure 23). At the same time, the histological alteration of the animal group treated with ZnO NPs with co-administration of vitamin E showed a slight improvement of histological changes characterized by degeneration and necrosis of Purkinje cells and degeneration of granular cells layer (Figure 24).

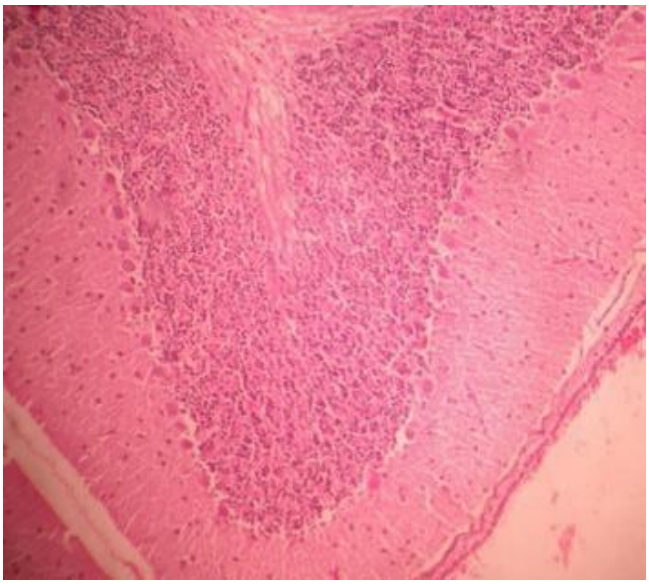

Figure 19: Micrograph of rabbit brain of control group showed normal architecture. H&E, 10X.

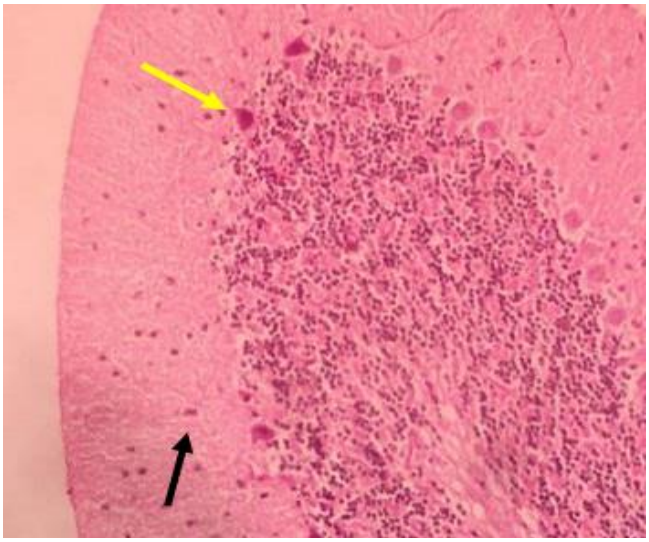

Figure 20: Micrograph of rabbit brain of treated group with ZnO NPs showing diminution with degenerative and necrotic changes of Purkinje cells (yellow arrow), degeneration and necrosis of satellite of basket cells of the molecular layer (black arrow). H&E, 10X.

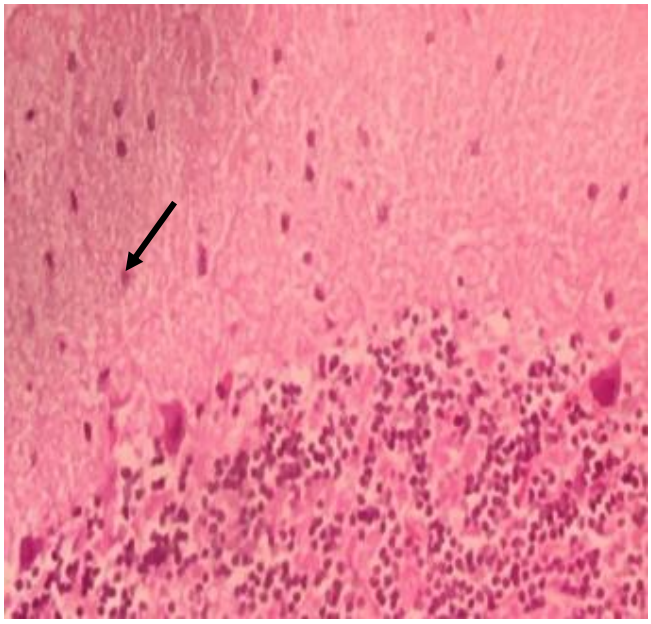

Figure 21: Micrograph of rabbit brain of treated group with ZnO NPs showing diminution of Purkinje cells (black arrow). H&E, 40X.

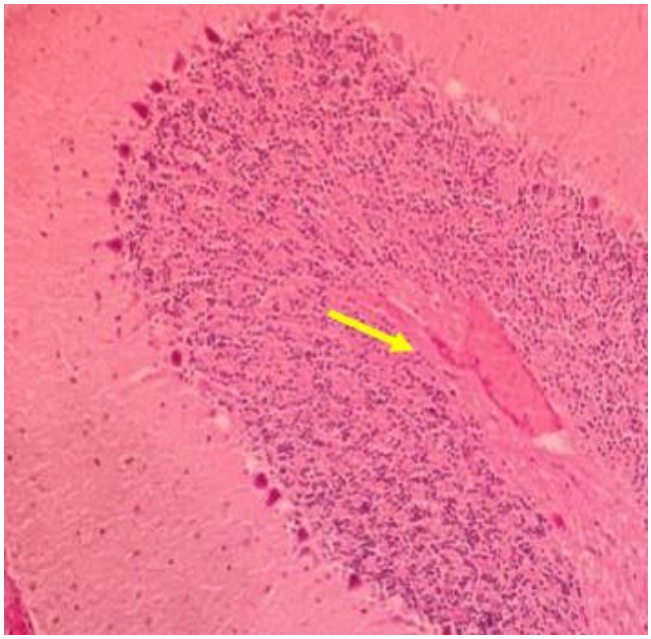

Figure 22: Micrograph of rabbit brain of treated group with ZnO NPs showing a hemorrhage in the granular layer (yellow arrow). H&E, 10X.

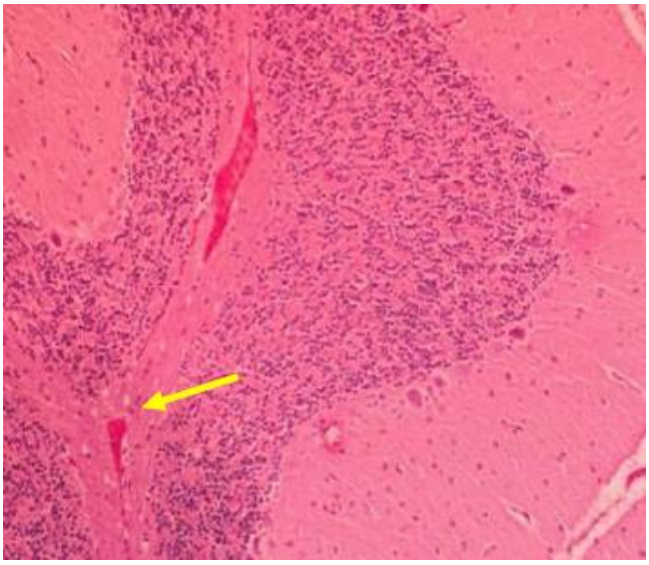

Figure 23: Micrograph of rabbit brain of treated group with ZnO NPs showing congestion of blood capillaries (yellow arrow). H&E, 10X.

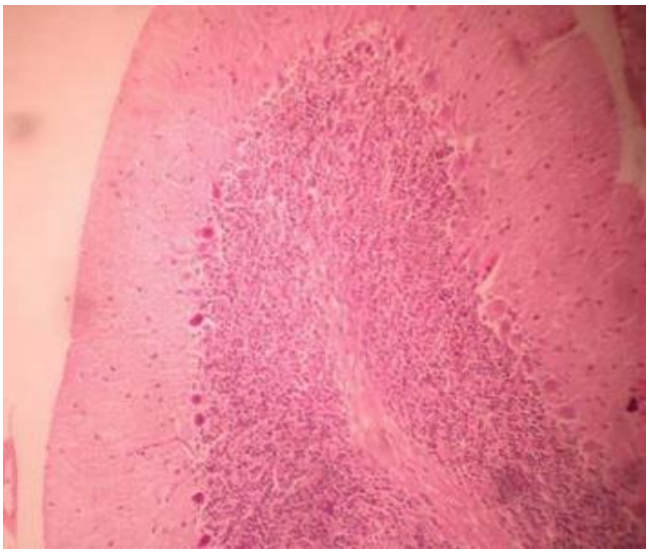

Figure 24: Micrograph of rabbit brain of treated group with ZnO NPs and vitamin E showed slight improvement of histological changes characterized by degeneration and necrosis of Purkinje cells, degeneration of granular cells layer. H&E, 10X.

Discussion

In recent times much research has proved that nanoparticles can reach the brain through the blood brain barrier. This will lead to damage to the brain due to ROS production (reactive oxygen species) and cause oxidative stress (15). This study showed macroscopic and microscopic alterations of the brain due to the desolation of blood brain barrier integrity. The histological alteration in the cerebral cortex, hippocampus and cerebellum could occur due to oxidative stress and the variance between the production of ROS and the capability of the antioxidant mechanisms to deactivate them (28). Many ROS mediators led to the injury of cell organelles which led to the production of other toxic substances (29).

The free radicals cause the triggering of the nuclear kappa B-factor (NF-KB), a redox-sensitive transcription factor that excites the inflammation gene and produces the chemical mediators of inflammation (16,30). Exposure to ZnO NPs causes nervous signs like abnormal movement and behavior. Also, the animals suffered from diarrhea, urination, and feeding behavior. These results agreed with Kim (31), Han (16). this occurs due to the histological changes in the hippocampus (32,33). The formation of Zn ions could partially lead to toxic effects of ZnO NPs in vital organs, especially in the brain of animals and human beings (34). The microscopic alteration in all regions of the brain is in agreement with Sawicki (35), Amara (36), and Liang (37). In comparison, the results of animals treated with ZnO NPs with vitamin E showed a slight improvement in histological alteration. This may be the dose of vitamin E used may be insufficient to improve the histological alteration.

The histological alteration in the cerebellar cortex is characterized by degenerative and necrotic vascular changes with inflammatory responses that occur due to cytotoxic effects of ZnO NPs. Because ZnO NPs cause an increase in the serum inflammatory mediators like IL1 and IL6 levels (38,39). The result is proportionate to (40). The high level of acetylcholine occurs due to ZnO NPs increasing ACh synthesis, upregulating the vesicular ACH transporter, and the action of the ACh hydrolysis enzyme (AChE) is suppressed, possibly through direct Zn/AChE interactivity or the process of transcriptional down-regulation (41).

Conclusions

It is concluded that ZnO NPs induce histological changes in all brain regions in adult male rabbits, and the dose of vitamin E used is insufficient to improve histological changes; so, in the future, the study must use a higher dose more extended period of vitamin E.

Acknowledgments

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Conflict of interest

No conflict of interest.

References

1. Patel M, Mishra S, Verma R, Shikha D. Synthesis of ZnO and CuO nanoparticles via Sol gel method and its characterization by using various technique. Discov Mater. 2022;2(1):1-1. DOI: 10.1007/s43939-022-00022-6
2. Dhanshree K, Elangovan T. Synthesis and characterization of ZnO and Mn-doped ZnO nanoparticles. Int J Sci Res. 2015;4(11):1816-1820. DOI: 10.21275/v4i11.nov151529
3. El-Oksh AS, Elmasry DM, Ibrahim GA. Effect of garlic oil nanoemulsion against multidrug resistant Pseudomonas aeruginosa isolated from broiler. Iraqi J Vet Sci. 2022;36(4):877-88. DOI: 10.33899/ijvs.2022.132430.2094
4. Ali MR, Bayati SM, Mahmood MB, Mohammed AA. In vitro study of curcumin calcium carbonate phosphate nanoparticles (Curcumin-NPs) impacts on the meriz goat's coccidian oocysts. Iraqi J Vet Sci. 2022;36(3):809-14. DOI: 10.33899/ijvs.2022.132196.2067
5. Youssef FS, El-Banna HA, Elzorba HY, Galal AM. Application of some nanoparticles in the field of veterinary medicine. Int J Vet Sci Med. 2019;7(1):78-93. DOI: 10.1080/23144599.2019.1691379
6. Mohammadpour R, Dobrovolskaia MA, Cheney DL, Greish KF, Ghandehari H. Subchronic and chronic toxicity evaluation of inorganic nanoparticles for delivery applications. Adv Drug Deliv Rev. 2019;144:112-132. DOI: 10.1016/j.addr.2019.07.006
7. Saleh TA. Nanomaterials: classification, properties, and environmental toxicities. Environ Technol Innov. 2020;20:101067. DOI: 10.1016/j.eti.2020.101067
8. Nel A, Xia T, Madler L, Li N. Toxic potential of materials at the nanolevel. Sci. 2006;311(5761):622-627. DOI: 10.1126/science.1114397
9. Raguvaran R, Manuja A, Manuja BK. Zinc oxide nanoparticles: opportunities and challenges in veterinary sciences. Immunome Res. 2015;11(2):1. DOI: 10.4172/1745-7580.1000095
10. Metwally A, Abdel-Hady AN, Ebnalwaled K, Morad SA, Soliman AA. Wound-healing activity of green and chemical zinc oxide nanoparticles (ZnO-NPs) gels in equine wounds: a clinical study. SVU-Int J Vet Sci. 2020;3(1):66-79. DOI: 10.21608/svu.2020.21254.1040
11. Srivastav AK, Kumar M, Ansari NG, Jain AK, Shankar J, Arjaria N, Jagdale P, Singh D. A comprehensive toxicity study of zinc oxide nanoparticles versus their bulk in Wistar rats: toxicity study of zinc oxide nanoparticles. Human Exp Toxicol. 2016;35(12):1286-1304. DOI: 10.1177/0960327116629530
12. Zahra J, Iqbal S, Zahra K, Javed Z, Shad MA, Akbar A, Ashiq MN, Iqbal F. Effect of variable doses of zinc oxide nanoparticles on male albino mice behavior. Neurochem Res. 2017;42(2):439-445. DOI: 10.1007/s11064-016-2090-y
13. Zhao X, Ren X, Zhu R, Luo Z, Ren B. Zinc oxide nanoparticles induce oxidative DNA damage and ROS-triggered mitochondria-mediated apoptosis in zebrafish embryos. Aquat Toxicol. 2016;180:56-70. DOI: 10.1016/j.aquatox.2016.09.013
14. Chun HS, Park D, Lim SE, Jeong KH, Park JS, Park HJ, Kang S, Kang KS, Park HG, An HR, Huh YS. Two zinc-aminoclays' in-vitro cytotoxicity assessment in HeLa cells and in-vivo embryotoxicity assay in zebrafish. Ecotoxicol Environ Saf. 2017;137:103-112. DOI: 10.1016/j.ecoenv.2016.11.022
15. Hu YL, Gao JQ. Potential neurotoxicity of nanoparticles. Int J pharm. 2010;394(1-2):115-21. DOI: 10.1016/j.ijpharm.2010.04.026
16. Han D, Tian Y, Zhang T, Ren G, Yang Z. Nano-zinc oxide damages spatial cognition capability via over-enhanced long-term potentiation in hippocampus of Wistar rats. Int J Nanomed. 2011;6:1453-1461. DOI: 10.2147/ijn.s18507
17. Gordan R, Gwathmey JK, Xie LH. Autonomic and endocrine control of cardiovascular function. World J Cardiol. 2015;7(4):204. DOI: 10.4330/wjc.v7.i4.204
18. Baker RT, Davies SJ. Muscle and hepatic fatty acid profiles and α-tocopherol status in African catfish (*Clarias gariepinus*) given diets varying in oxidative state and vitamin E inclusion level. Anim Sci. 1997;64(1):187-195. DOI: 10.1017/S1357729800015708
19. Sahiti H, Bislimi K, Bajgora A, Rexhepi A, Dalo E. Protective effect of vitamin C against oxidative stress in common carp (*Cyprinus carpio*) induced by heavy metals. Int J Agric Biosci. 2018;7(2):71-75. [available at]
20. Alkaladi A, El-Deen NA, Afifi M, Zinadah OA. Hematological and biochemical investigations on the effect of vitamin E and C on *Oreochromis niloticus* exposed to zinc oxide nanoparticles. Saudi J Biol Sci. 2015;22(5):556-563. DOI: 10.1016/j.sjbs.2015.02.012
21. Dahdouh FA, Salah A, Mohamed RD, Zine K. Effect of the joint supplementation of vitamin c and vitamin e on nickel heamatotoxicity and nephrotoxicity in male swiss albino mice. Int J Pharm Pharm Sci. 2016;8(6):234-239. [available at]
22. Alkaladi A. Vitamins E and C ameliorate the oxidative stresses induced by zinc oxide nanoparticles on liver and gills of *Oreochromis niloticus*. Saudi J Biol Sci. 2019;26(2):357-362. DOI: 10.1016/j.sjbs.2018.07.001
23. Abd Elmonem HA, Mahmoud AH, Abbas MM. Ameliorative effect of zinc oxide nanoparticles and vitamin e on some biochemical and histological changes in irradiated albino rats. J Radiat Res Appl Sci. 2021;34(1):1-10. DOI: 10.21608/ejrsa.2021.63788.1116
24. Salah BA. Effect of boron on some organs of pregnant BALB/c mice. Iraqi J Vet Sci. 2021;35(4):633-42. DOI: 10.33899/ijvs.2020.127549.1509
25. Luna L. Manual of histological staining methods of the armed forces institute of pathology. 3rd ed. New York: McGraw-Hill; 1968. 1-35 p.
26. Fadel MA, Abdullah MA, Al-Mahmood SS, Thanoon IA. Protective effect of propolis on liver and kidney injury caused by methotrexate in chicks. Iraqi J Vet Sci, 2022;36(4):1067-1061. DOI: 10.33899/ijvs.2022.133021.2162
27. Petrie A, Watson P. Statistics for veterinary and animal science. 3rd ed. UK: Wiley-Blackwell; 2013.
28. Setyawati MI, Tay CY, Leong DT. Effect of zinc oxide nanomaterials-induced oxidative stress on the p53 pathway. Biomater. 2013;34(38):10133-10142. DOI: 10.1016/j.biomaterials.2013.09.024
29. Roy R, Tripathi A, Das M, Dwivedi P. Cytotoxicity and uptake of zinc oxide nanoparticles leading to enhanced inflammatory cytokines levels in murine macrophages: comparison with bulk zinc oxide. J Biomed Nanotechnol. 2011;7(1):110-111. DOI: 10.1166/jbn.2011.1226
30. Wang J, Deng X, Zhang F, Chen D, Ding W. ZnO nanoparticle-induced oxidative stress triggers apoptosis by activating JNK signaling pathway in cultured primary astrocytes. Nanoscale Res Lett. 2014;9(1). DOI: 10.1186/1556-276x-9-117
31. Kim MH, Seo JH, Kim HM, Jeong HJ. Zinc oxide nanoparticles a novel candidate for the treatment of allergic inflammatory diseases. Eur J Pharmacol. 2014;738:31-39. DOI: 10.1016/j.ejphar.2014.05.030
32. Xie Y, Wang Y, Zhang T, Ren G, Yang Z. Effects of nanoparticle zinc oxide on spatial cognition and synaptic plasticity in mice with depressive-like behaviors. J Biomed Sci. 2012;19(1). DOI: 10.1186/1423-0127-19-14
33. Akintunde JK, Farai TI, Arogundade MR, Adeleke JT. Biogenic zinc-oxide nanoparticles of Moringa oleifera leaves abrogates rotenone-induced neuroendocrine toxicity by regulation of oxidative stress and acetylcholinesterase activity. Biochem Biophys Rep. 2021;26:100999. DOI: 10.1016/j.bbrep.2021.100999
34. Zhao F, Zhao Y, Liu Y, Chang X, Chen C, Zhao Y. Cellular uptake, intracellular trafficking, and cytotoxicity of nanomaterials. Small. 2011;7(10):1322-1337. DOI: 10.1002/smll.201100001
35. Sawicki K, Czajka M, Matysiak-Kucharek M, Fal B, Drop B, Męczyńska-Wielgosz S, Sikorska K, Kruszewski M, Kapka-Skrzypczak L. Toxicity of metallic nanoparticles in the central nervous system. Nanotechnol Rev. 2019;8(1):175-200. DOI: 10.1515/ntrev-2019-0017
36. Amara S, Slama IB, Omri K, Ghoul JE, Mir LE, Rhouma KB, Abdelmelek H, Sakly M. Effects of nanoparticle zinc oxide on emotional behavior and trace elements homeostasis in rat brain. Toxicol Ind Health. 2013;31(12):1202-1209. DOI: 10.1177/0748233713491802
37. Liang H, Chen A, Lai X, Liu J, Wu J, Kang Y, Wang X, Shao L. Neuroinflammation is induced by tongue-instilled ZnO nanoparticles

التأثيرات المحسنة لفيتامين هـ على التغيرات النسجية المحدثة بوساطة جزيئات أوكسيد الخارصين في أدمغة الأرانب

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الخلاصة

تعد جزيئات أوكسيد الزنك النانوية من الجسيمات النانوية المهمة نظرًا لتطبيقاتها الواسعة في العديد من الصناعات، مثل الإلكترونيات والمكملات الغذائية والمواد التجميل. أدى ذلك إلى زيادة التعرض الفردي لها من خلال الاستنشاق وعن طريق اختراق الجلد. اظهرت الدراسة الحالية التأثير السام لـجزيئات أوكسيد الخارصين النانوية على القشرة الدماغية وقرن آمون والمخيخ في ذكور الأرانب من خلال دراسة التغيرات العيانية والنسيجية. تم تقسيم أربعة وعشرين ذكرًا بالغًا بشكل عشوائي إلى أربع مجموعات، تضم ست حيوانات لكل مجموعة. اعتبرت المجموعة الأولى هي مجموعة السيطرة التي تركت دون معاملة. المجموعة الثانية عوملت بجرعة ١٠٠ ملغم / كغم من وزن الجسم من فيتامين هـ عن طريق الفم، المجموعة الثالثة عوملت بالحقن داخل غشاء الخلب بجرعة ٦٠٠ ملغم / كغم من وزن الجسم من جزيئات أوكسيد الخارصين النانوية، والمجموعة الرابعة عوملت بالحقن داخل غشاء الخلب بجرعة ٦٠٠ ملغم / كغم من وزن الجسم من جزيئات أوكسيد الخارصين النانوية بالإضافة إلى ١٠٠ ملغم / كغم من وزن الجسم فيتامين هـ عن طريق الفم مرتين أسبوعياً لمدة واحد وعشرين يوماً. أظهرت نتائج الدراسة النسيجية وجود تغيرات تنكسية ونخرية في الخلايا العصبية مع استجابة وعائية والتهابات في القشرة الدماغية وقرن آمون والمخيخ في المجموعة الثانية من الأرانب المعالجة بـجزيئات أوكسيد الخارصين النانوية. في المقابل، أظهرت الأرانب المعالجة بـجزيئات أوكسيد الخارصين النانوية وفيتامين هـ تحسنًا طفيفًا في الصورة النسيجية لأقسام الدماغ. وكذلك كان هناك تغيير في مستويات أستيل كولين في جميع المجموعات مقارنة مع مجموعة التحكم.

via the Ca2+-dependent NF-κB and MAPK pathways. Part Fibre Toxicol. 2018;15(1). DOI: 10.1186/s12989-018-0274-0

38. Lockman PR, Koziara JM, Mumper RJ, Allen DD. Nanoparticle surface charges alter blood-brain barrier integrity and permeability. J Drug Target. 2004;12(9-10):635-641. DOI: 10.1080/10611860400015936
39. Lockman PR, Oyewumi MO, Koziara JM, Roder KE, Mumper RJ, Allen DD. Brain uptake of thiamine-coated nanoparticles. J Control Release. 2003;93(3):271-282. DOI: 10.1016/j.jconrel.2003.08.006
40. Win-Shwe TT, Fujimaki H. Nanoparticles and neurotoxicity. Int J Mol Sci. 2011;12(9):6267-6280. DOI: 10.3390/ijms12096267
41. Guo Z, Zhang P, Luo Y, Xie HQ, Chakraborty S, Monikh FA, Bu L, Liu Y, Ma Y, Zhang Z, Valsami-Jones E, Zhao B, Lynch I. Intranasal exposure to ZnO nanoparticles induces alterations in cholinergic neurotransmission in rat brain. Nano Today. 2020;35:100977. DOI: 10.1016/j.nantod.2020.100977