Copper oxide nanoparticles induces oxidative stress and liver toxicity in rats following oral exposure

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ABSTRACT

The present study aimed to evaluate the effect of Copper Oxide (CuO) Nanoparticles (NP) on liver following oral exposure in rats. A total of 18 male wister rats were used in the experiments including a control group (6 rats). NP were given to the rats with a doses (5, 50 mg/kg b.w./day) via oral gavage and a control group (received only 200 μl PBS). The treatment was continued for 14 days. The supernatants of rat Liver tissue homogenates were used to analyze for glutathione levels (GSH), Catalase, superoxide dismutase (SOD), the extent of lipid peroxidation products (Malondialdehyde, MDA). Oral administration of NP to rats caused a significant (P < 0.05) dose dependent alterations in antioxidant enzyme activities. Data results clearly showed the significant decrease (p < 0.05) in GSH, Catalase (CAT) and SOD activity, whereas the lipid peroxidation product (MDA) levels were increased (p < 0.05). In conclusion, oral exposure of CuO nanoparticles to rats causes significant toxicity to the liver and it might be due to oxidative stress.

1. Introduction

Nanoparticles (NP) with < 100 nm size, are widely used nanotechnology [1,2]. Metal-oxide NP contain heavy metal ions and other organic and inorganic groups which make them unique in their functional groups, electronic properties, shape, surface structure and aggregation behavior. Because of these particular characteristics make the nanoparticles suitable for various applications in modern industries [3]. However, widespread use of nanomaterials may lead to environmental contamination and human exposure by inhalation, dermal and oral routes, raising concerns about their potential toxicity [4]. The extreme usage of these NP brings challenges to the environment and to humans. With sizes smaller than cellular organelles, nanoparticles can easily penetrate through basic biological structures [5]. Administration routes (oral, inhalation, subcutaneous, injection etc.) of NPs are also known to have significant effects on their toxicities in mammals [6].

Copper oxide nanoparticles (CuO NPs) have attracted attention and used in industrial, commercial fields like medicine, engineering for their photovoltaic and photoconductive properties [7]. Copper oxide is a semiconductor metal with unique optical, electrical and magnetic properties and it has been used for various applications, such as the development of supercapacitors, near-infrared filters, in magnetic storage media, sensors, catalysis, semiconductors, etc. [7]. Particularly, CuO NPs useful in the pharmaceutical industry especially in the production of anti-microbial fabric treatments or prevention of infections caused by E.coli and methicillin-resistant S.aureus. [8]. In this study, we aimed at investigating the effects of oral exposure of CuO NP on the antioxidant enzyme activities in the liver in Wistar rats.

2. Materials and methods

2.1. Nanoparticles

CuO NPs (size < 50 nm, surface area 29 m²/g, crystalline shape, diameter < 50 nm, length < 50 nm) purchased from Sigma Aldrich, USA. Suspension of CuO NPs was prepared using Phosphate Buffer Saline (PBS) and subsequently sonicated and mixed vigorously with a sonicator (20 min).

2.2. Animals and treatment

Male wistar albino rats (Mahaveer Enterprises, Hyderabad, India) of 8 weeks old at study start (180–200 g) were selected. A total of 18 rats were used in the experiments as each experimental group consisted of 6 rats, including a control group (6 rats). NPs were given to the rats with a doses (5, 50 mg/kg b.w./day) via oral gavage and a control group

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nanoparticles induces toxicity and oxidative stress both in vivo as well as in vitro. Recently, Assadian et al., [8] also reported the in vitro cytotoxicity of CuO-NP, which was associated with significant increase at intracellular ROS level with effective induction of oxidative stress. The capability of NP to produce free radicals is one of the primary mechanisms of NPs toxicity [19–21]. It may result in oxidative stress, inflammation, and consequent damage to proteins, membranes, and DNA [22,23]. In conclusion, oral exposure of CuO nanoparticles to rats causes significant toxicity to the liver and it might be due to oxidative stress. More extensive studies would be needed to verify the safety issues related to increased usage of CuO NPs by consumers.

Conflict of interest

No conflicts of interest.

References

[1] S. Linic, U. Aslam, C. Boerigter, M. Morabito, Photochemical transformations on plasmonic metal nanoparticles, Nat. Mater. 14 (2015) 567–576.

[2] A. Ucles, S.H. Lopez, M.D. Hernando, R. Rosal, A.R. Fernandez-Alba, Application of zirconium dioxide nanoparticle sorbent for the clean-up step in post-harvest pesticide residue analysis, Talanta 144 (2015) 51–61.

[3] H.P. Misra, I. Fridowich, Superoxide dismutase, a photochemical augmentation of hydrogen peroxide by catalase, J. Biol. Chem. 195 (1952) 133–140.

[4] G. Oberdörster, Safety assessment for nanotechnology and nanomedicine: concepts of nanotoxicology, J. Intern. Med. 267 (1) (2010) 89–105.

[5] R. Lei, B. Yang, C. Wu, M. Liao, R. Ding, Q. Wang, Mitochondrial dysfunction and oxidative damage in the liver and kidney of rats following exposure to copper nanoparticles for five consecutive days, Toxicol. Res. 4 (2) (2018) 351–364.

[6] R. Shrivastava, S. Raza, A. Yadav, P. Kushwaha, S.J.S. Flora, Effects of sub-acute exposure to TiO2, ZnO and Al2O3 nanoparticles on oxidative stress and histological changes in mouse liver and brain, Drug Chem. Toxicol. 37 (2014) 336–347.

[7] D.H. Jo, J.H. Kim, T.G. Lee, J.H. Kim, Size, surface shape, and shape determine therapeutic effects of nanoparticles on brain and retinal diseases, Nanomedicine 11 (2015) 1663–1671.

[8] E. Assadian, M.Z. Zarei, A.G. Gilani, M. Farshin, H. Degampanah, J. Pourrahmad, Toxicity of Copper Oxide (CuO) Nanoparticles on Human Blood Lymphocytes, Biol. Trace Element Res. 184 (2) (2018) 350–357.

[9] D.V. Beaulier, O. Durm, B.M. Kelly, Improved method for the determination of blood glutathione, J. Lab Chem. Med. 61 (5) (1965) 882–888.

[10] R.F. Beers, I.W. Sizer, A spectrophotometer method of measuring the breakdown of hydrogen peroxide by catalase, J. Biol. Chem. 195 (1952) 133–140.

[11] X.S. Ran, A.K. Kumar, Ch P. Kumar, A.R.N. Reddy, Palynomen Toxicity of Copper Oxide (CuO) Nanoparticles in Rats, J. Medical Sciences 13 (2015) 571–577.

[12] A.R.N. Reddy, L. Srividya, Evaluation of In Vitro Cytotoxicity of Zinc Oxide (ZnO) Nanoparticles Using Human Cell Lines, Toxicol. In Vitro 23 (2009) 1365–1371.

[13] B. Fahmy, A.C. Stephanina, Copper nanoparticles induce oxidative stress and cytotoxicity in airway epithelial cells, Toxicol. Ind. Health 32 (5) (2016) 809–821.

[14] X. Fu, Oxidative stress induced by CuO nanoparticles (CuO NPs) to human hepatocarcinoma (HeptG2) cells, J. Cancer Ther. 6 (2015) 889–895.

[15] W.S. Lin, Y. Xu, C.C. Huang, Y.F. Ma, K.B. Shannon, D.R. Chen, Y.W. Huang, Toxicity of nano- and micro-sized ZnO particles in human lung epithelial cells, J. Nanopart. Res. 11 (2009) 285–299.

[16] R.N.R. Anreddy, Y.N. Reddy, R.K. Krishna, V. Himabindu, Multi wall carbon nanofibers induce oxidative stress and cytotoxicity in human embryonic kidney (HEK293) cells, Toxicology 272 (2010) 11–16.

[17] R.J. Griffith, R. Weil, K.A. Hyndman, N.D. Denlow, K. Powers, Exposure to copper nanoparticles causes gill injury and acute lethality in zebrafish (Danio rerio), Environ. Sci. Technol. 41 (2007) 8178–8186.

[18] B. Fahmy, A.C. Stephanina, Copper nanoparticles induce oxidative stress and cytotoxicity in airway epithelial cells, Toxicol. In Vitro 23 (2009) 1365–1371.

[19] X. Fu, Oxidative stress induced by CuO nanoparticles (CuO NPs) to human hepatocarcinoma (HeptG2) cells, J. Cancer Ther. 6 (2015) 889–895.

[20] Y.X. Deng, Q.X. Luan, W.T. Chen, Y.L. Wang, M.H. Wu, H.J. Zhang, Z. Jiao, Nanosized zinc oxide particles induce neural stem apoptosis, Nanotechnology 20 (2009) 115101.

[21] H. Yang, C. Liu, D.F. Yang, H.S. Zhang, Z.G. Xi, Comparative study of cytotoxicity, oxidative stress and genotoxicity induced by four typical nanomaterials: the role of particle size, shape and composition, J. Appl. Toxicol. 29 (2009) 69–78.

[22] M.J. Akhtar, S. Kumar, H.A. Alhadjag, S.A. Alrokayan, K.M. Abu-Salah, M. Ahmed, Dose-dependent genotoxicity of CuO nanoparticles stimulated by reactive oxygen species in human lung epithelial cells, Toxicol. Ind. Health 32 (5) (2016) 809–821.

[23] X.K. Hu, S. Cook, P. Wang, H.M. Huang, In vitro evaluation of cytotoxicity of engineered metal oxide nanoparticles, Total Environ 407 (2009) 3070–3072.