Nano Today 29 (2019) 100775

Contents lists available at ScienceDirect

Nano Today

journal homepage: www.elsevier.com/locate/nanotoday

News and opinions

Nanozyme antioxidants as emerging alternatives for natural antioxidants: Achievements and challenges in perspective

Milad Ghorbani[a], Hossein Derakhshankhah[b,c,*], Samira Jafari[b,c,*], Sara Salatin[d,e], Mojtaba Dehghanian[f,g], Mojtaba Falahati[h], Ali Ansari[i]

[a] Department of Chemical Engineering, College of Engineering, University of Tehran, Tehran, Iran
[b] Pharmaceutical Sciences Research Center, Health Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran
[c] Zistmavad Pharmed Co., Tehran, Iran
[d] Department of Pharmaceutical Nanotechnology, Faculty of Pharmacy, Tabriz University of Medical Science, Tabriz, Iran
[e] Student Research Committee, Tabriz University of Medical Science, Tabriz, Iran
[f] Department of Biotechnology, Shahr-e Kord Branch, Islamic Azad University, Shahr-e Kord, Iran
[g] Blood Transfusion Research Center, Semnan Regional Blood Transfusion Center, Semnan, Iran
[h] Department of Nanotechnology, Faculty of Advance Science and Technology, Pharmaceutical Sciences Branch, Islamic Azad University (IAUPS), Tehran, Iran
[i] Department of Civil & Environmental Engineering, University of Houston, Houston, TX 77004, United States

ARTICLE INFO

Article history:
Received 2 June 2019
Received in revised form
14 September 2019
Accepted 16 September 2019
Available online 27 September 2019

Keywords:
Reactive oxygen species
Oxidative stress
Antioxidants
Nanozymes

ABSTRACT

Nanozymes are nanoparticulated structures with the inherent enzymatic activities, which their advances in bio/nanomedicine field are progressively growing regarding their exceptional properties, such as nano-size, irregular shape, rich surface chemistry, low cost production, *etc.* These features enable nanostructures to mimic the cellular antioxidant enzymes as novel candidates for treatment of oxidative stress-induced disorders. Oxidative stress reflects principally an imbalance between generation of reactive oxygen species (ROS), such as hydroxyl and superoxide radicals, and the level of antioxidant defense system, so that this imbalance can lead to harsh pathological conditions. Here we present prevalent nanozyme antioxidants as well as their therapeutic concerns from diverse points of view including bio/cytocompatibility and cellular uptake, biomolecular corona, effect of pH and temperature on enzymatic function, and *in vivo* analysis, which are of paramount importance for reducing the bench-to-clinic gap.

© 2019 Elsevier Ltd. All rights reserved.

Introduction

In the case of augmentation of reactive oxygen species (ROS) concentration to reach the levels beyond normal, they produce detrimental effects to cellular components, such as proteins, lipids, and DNA resulting in severe clinical conditions including cancer, diabetes, neurological disorders, atherosclerosis, hypertension, acute respiratory distress syndrome, asthma, *etc.* (Supplementary Information (SI), Fig. S1) [1–3]. Overall, oxidative stress is referred to a condition in which the balance between the production of ROS and antioxidant defense system of the body is disrupted [4].

A broad spectrum of antioxidants have been commonly used to curb and combat oxidative stress related pathological conditions which fall into two main categories of non-enzymatic and enzymatic antioxidants [5,6]. Non-enzymatic antioxidants include dietary and non-dietary antioxidants (SI, Table S1) [4]. Superoxide dismutase (SOD), glutathione peroxidase (GPx), catalase (CAT), and glutathione S-Transferase (GST) are examples of enzymatic antioxidants, and N-acetylcysteine (NAC) is recognized as an enzyme-related antioxidant (SI, Fig. S2) [5,7]. Despite the widespread applications of the conventional antioxidants, there are still some serious constraints, such as prooxidant function of dietary antioxidants [8], low bioavailability of flavonoids [9], incapability of passing blood brain barrier [10], and being neutralized in cell culture media [11].

Contrary to conventional antioxidants, nanozyme antioxidants, as nanomaterial-based enzyme mimetics, possess excellent properties including inexpensiveness, flexibility for manipulation, high stability, large-scale production, *etc.* [12]. According to the literature reviews, several *in vitro* and *in vivo* studies have been

* Corresponding authors at: Pharmaceutical Sciences Research Center, Health Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran.
E-mail addresses: Derakhshankhah.hossein@gmail.com, h-derakhshankhah@alumnus.tums.ac.ir (H. Derakhshankhah), Samiraa.jafari1362@gmail.com (S. Jafari).

https://doi.org/10.1016/j.nantod.2019.100775
1748-0132/© 2019 Elsevier Ltd. All rights reserved.

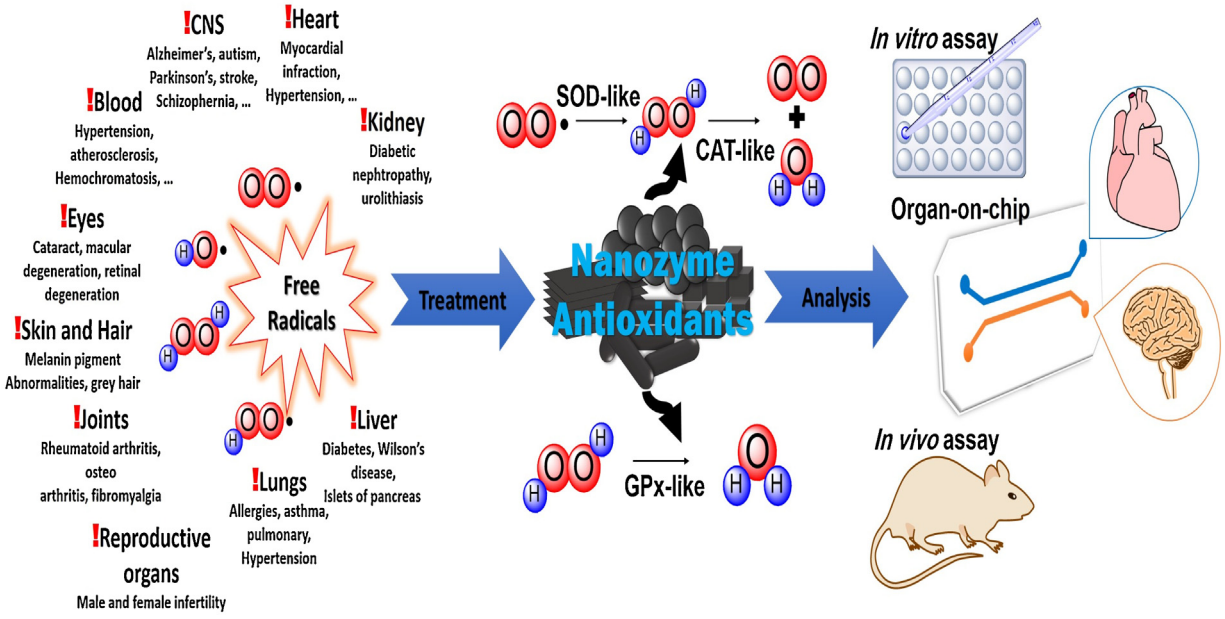

Fig. 1. Nanomaterials showing enzyme-mimetic features, known as Nanozymes, with various structures, such as nanoparticles, nanowires, nanorods, hollow spheres, *etc.* have been evaluated *in vitro*/*in vivo* and introduced as a new generation of antioxidants with SOD-, CAT-, GPx-like activities, mostly, for cytoprotection applications.

conducted to evaluate nanozymes [13–15]; nevertheless, many aspects concerning the specific characteristics of nanozymes as nanobiomaterials and their behavior in biological media are still unknown owing to lack of characterization analysis from different biological points of view. To address these challenges, herein we have reviewed some of the recent research with the focus on four major factors, *i.e.*, bio/cytocompatibility and cellular uptake, biomolecular corona, the effect of pH and temperature on enzymatic function, and *in vivo* analysis to draw a big picture of the current status of surveys in this field which may be profitable for the scientists to ameliorate their research (Fig. 1).

Nanozymes as antioxidants

Nanozymes have drawn a lot of attention owing to their above-mentioned merits and also their wide range of applications from combined diagnostic and therapy (*i.e.*, theranostics) and environmental safety to biomedical analysis and imaging [12,16]. Table S2 presents some of the recent published reports (since 2009) on nanozyme antioxidants, which are generally categorized according to their catalytic function, *e.g.*, CAT-, SOD-, GPx-, NAC-, or peroxidase-like activity and •OH-, •DPPH-, or •NO-scavenging activity. Fig. 2 depicts some common features among the studied antioxidant nanozymes in terms of elemental content, size, shape, and surface charge which impact key factors, such as cellular uptake, biomolecular corona, cytotoxicity, clearance, *etc.* [17,18]. Also, it is noteworthy that size and morphology of nanozymes have profound impact on their enzyme-mimetic function [19–22]. For instance, Hao et al. reported that 65 nm spherical phenylalanine-conjugated Cu_xO nanoparticle clusters (NCs) (Cu_xO-Phe) showed the highest activity (≈88%) in comparison with ellipsoids, *i.e.*, 186 nm tyrosine (Tyr)-conjugated and 105 nm aspartate (Asp)-conjugated Cu_xO (≈43% and ≈70%) and rods, 212 nm glutamate (Glu)-conjugated Cu_xO (≈73%). It was also concluded that the porous structure of Cu_xO-Phe (61 $m^2.g^{-1}$) was favorable for its catalytic function as compared to Cu_xO-Tyr (70 $m^2.g^{-1}$), Cu_xO-Asp (37 $m^2.g^{-1}$), and Cu_xO-Glu (34 $m^2.g^{-1}$). Lower activity of Cu_xO-Tyr was ascribed to the effect of Tyr on enzymatic function of Cu_xO, though its larger size and surface area were considered in favor of enzymatic activity [19].

Bio/cytocompatibility and cellular uptake

While recent research depict the potential application of nanomaterials against cellular oxidative stress, it is much more interesting to hinder sudden oxidative damage to normal cells [23]. Since increased levels of ROS are commonly observed upon endocytic internalization of nanoparticles (NPs) into a cell, professional knowledge creation is important for improving the biocompatibility of nanomaterials by introducing anti-oxidative properties [24]. Table S3 presents some of the investigated nanozymes regarding cellular uptake mechanisms.

For instance, intracellular tracking of Pt NPs demonstrated that they possess strong antioxidant properties and high cellular uptake with compartmentalization within the endo/lysosomal vesicles in size and cell type dependent manners. Authors reported that Pt NPs were resistant to the acidic environment of late endosome/lysosome hybrids and the primary size of NPs was not altered by cellular uptake in these organelles after 24 h. The cytocompatibility of Pt NPs could also be attributed to their resistance to the acidic corrosion within lysosomes as compared to other metal containing NPs which release ions that enhance the amount of cell death [25].

Unlike the traditional use of "inert" coating, the novel approach of "active" modification holds high promise of designing long-term biocompatible materials with unique versatility. Biocompatible Ceria NPs (CNPs) encapsulated in albumin NPs (BCNPs) were developed as potential candidates against ROS induced diseases. The cellular uptake results depicted that the encapsulation of CNPs inside the albumin NPs increased the cellular uptake of CNPs and thereby BCNPs pretreatment markedly protects cells against cytotoxicity induced by H_2O_2 (SI, Fig. S3) [26].

Biomolecular corona

It is of paramount importance to appraise the formation of biomolecular corona on the surface of nanomaterials *in vitro* and *in vivo* and study the consequent impacts on the desired function of nanomaterials, such as antioxidant activity [27]. Among the thirty one papers we reviewed, only two had discussed protein corona. Moglianetti et al. incubated Pt NPs in a culture medium

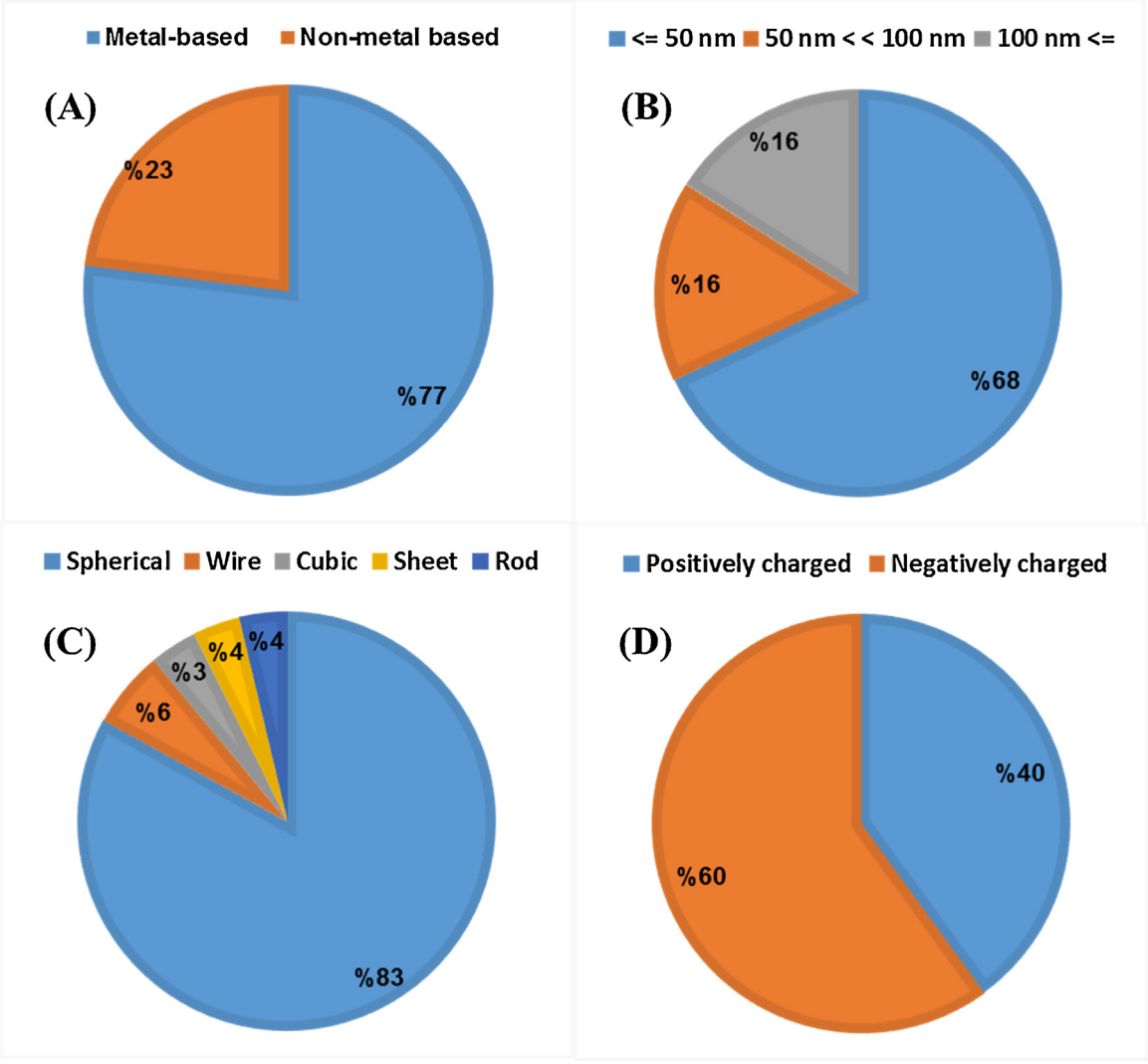

Fig. 2. Common features among studied antioxidant nanozymes in terms of (A) elemental content, (B) size, (C) shape, and (D) surface charge.

and observed the conspicuous agglomeration of NPs resulted from protein corona formation using small angle X-ray scattering (SAXS) analysis [25]. Clark et al. incubated $CeTiO_2$ NPs in a culture medium and observed no noticeable change in their CAT-like activity in comparison with the NPs not exposed to culture medium [28]. Hence, there is a vivid lack of biomolecular corona assessments for nanozymes which would definitely lead to a yawning gap between laboratory and clinical studies, so more research are needed to focus on *in vitro* and *in vivo* investigations regarding the impact of biomolecular corona on the factors concerning antioxidant activity of nanozymes, *e.g.*, clearance, cellular uptake, stability, *etc.*

Effect of pH and temperature on enzymatic function

Several studies have shown the tangible impact of pH and temperature alterations on enzymatic activity of antioxidants [29–31]. However, there is not a particular guideline which could be applied for most of the antioxidant enzymes to explain the pH and temperature effects on their activity. Therefore, it is of paramount importance that every antioxidant nanozyme should be appraised carefully from this viewpoint. In this regard, we reviewed all of the discussed papers and realized that only six of them have investigated the effect of pH on antioxidant activity of the introduced nanozymes, and merely one of them has discussed the impact of temperature. Thus, it is of great importance to meticulously examine the effect of pH and temperature changes on the activity of every synthesized nanozyme distinctly. For instance, Su et al. assessed the impact of pH and temperature on the antioxidant function of Polyvinylpyrrolidone-stabilized iridium NPs (PVP-Ir NPs) (SI, Fig. S4), so that it was revealed that CAT-like activity of PVP-Ir NPs increased with a rise in pH and temperature values [32].

In vivo *analysis*

Albeit *in vitro* studies provide salutary information about the biocompatibility of nanomaterials, *in vivo* analysis are yet momentous to learn about bio distribution, clearance, hematology, serum chemistry, and histopathology features associated with nanozymes [33]. Also, *in vivo* assessments are of crucial importance to understand absorption, distribution, metabolism, and excretion of nanomaterials before conducting clinical trials. Among the reviewed papers, only five had carried out *in vivo* analysis [34–38]; hence, it goes without saying that studies on nanozymes noticeably suffer from lack of *in vivo* assessments leading to a widening bench-to-clinic gap. For example, Ju et al. prepared a novel nanozyme through the integration of ZnO NPs and CeOx NPs into hollow microspheres (ZnO/CeOx HMS) with the ability of scavenging ROS induced by UV irradiation on skin tissue [34]. They appraised the

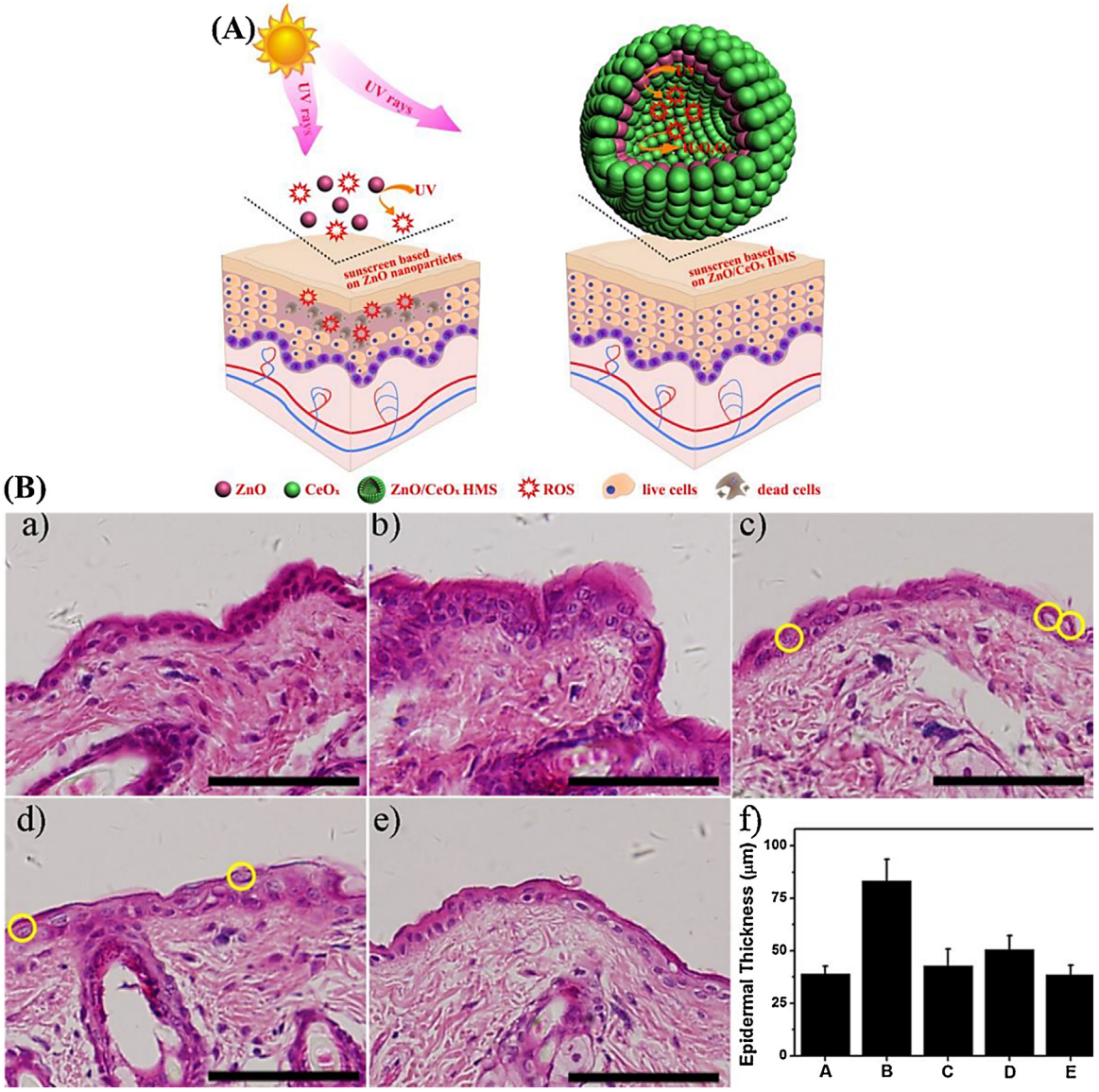

Fig. 3. (A) Schematic representation of ZnO/CeOx HMS function as ROS scavenging nanozymes on the surface of skin upon UV irradiation. ZnO/CeOx HMS, in their void space, could catalyze UV-induced ROS into safe molecules, while ZnO NPs alone induce ROS production. (B) Histological examination of dorsal mouse skin upon diverse treatment conditions. (a) normal skin, (b) skin exposed to UV, (c) skin treated by ZnO NPs sunscreen with UV exposure, (d) skin treated by sunscreen based on ZnO and CeOx NPs' mixture with UV exposure, and (e) skin treated by ZnO/CeOx HMS sunscreen with UV exposure. Yellow circles indicate obvious nuclear fragments. (f) Epidermal thickness of the dorsal skin in corresponding (a–e) pictures. Reprinted with permission from Ref. [34]. Copyright (2017), John Wiley and Sons.

potential ability of ZnO/CeOx HMS to protect the skin tissue against UV-induced ROS on mouse dorsal skin, so that ZnO/CeOx HMS treated skin was comparable to normal skin control (Fig. 3). It is noteworthy that in an *ex vivo* study, dextran coated iron oxide magnetic nanoparticles (MNPs) were applied to study a new histochemical approach to picture unlabeled MNPs in mice organs, *i.e.*, liver, spleen, lung, kidney, lymph node, and thymus, *via* their innate peroxidase-like activity which leads to generation of a color reaction at the location of MNPs. Hence, through this approach, it was possible to determine bio-distribution and clearance of MNPs in the organs both qualitatively and quantitatively, which demonstrated higher sensitivity as compared to traditional Prussian blue assay (Fig. S5) [39].

It is worth mentioning that only Onizawa et al. [38] have investigated the bio-distribution of their prepared nanozyme and also its access and associated probable toxic impacts to important organs of the body *in vivo*. And merely Ju et al. [34] have performed stability study and reported that their nanozyme was able to keep its integrity and avoid leaching of metal ions. None of these five studies have assessed the momentous terms of clearance, hematology, serum chemistry, and excretion *in vivo*.

Conclusion and perspective

There are an adequate number of research which have focused on design and development of novel antioxidant agents based on nanozymes. Reviewing thirty one published studies since 2009, we gathered that several nanozyme antioxidants with diverse structural features and SOD-, CAT-, GPx-, or NAC-like activities have been designed and evaluated mostly *in vitro* and less *in vivo*. Diverse pathological conditions, such as smoke induced oxidative stress, Alzheimer's disease, UV induced skin damage, *etc.* have been addressed. Nevertheless, albeit the performed analysis concerning bio/cytocompatibility and antioxidant activity of nanozymes are kind of sufficient, some serious points, such as biomolecular corona, stability in biological media, impact of pH and tempera-

ture alterations on the function of nanozymes, and precise behavior of the nanozymes in the body including antioxidant activity, biodistribution, adsorption, metabolism, clearance, excretion, *etc.* have been missed in most of the papers. Therefore, the following concerns are to be addressed: (1) the impact of nanozyme structure on its catalytic mechanism needs to be evaluated, and in this regard, an optimized synthesis methodology should be designed and developed *via* both experimental and computational methods to reach the highest possible efficacy. (2) Selectivity and efficacy of conventional enzymes are dependent to their native microenvironment (*e.g.*, lipid membrane), so the effect of this factor should be also studied for nanozymes. (3) There are several routs for detoxification of ROS, yet most of the studied nanozymes function in one or two of them (see Table S2); thus, there is a need to develop multifunctional nanozymes to achieve an enhanced antioxidant activity. (4) Detailed biological analysis concerning the aforementioned momentous factors, *e.g.*, pharmacodynamics, pharmacokinetics, immunogenicity, clinical toxicity, analysis of conjugates on both cytotoxicity and catalytic activity, *etc.* need to be conducted *in vitro and in vivo* to improve the research and thus lessen the bench-to-clinic gap. (5) Standardized analysis are to be developed to measure antioxidant activity of nanozymes, which will lead to far more reliable results and noticeably facilitate research in this field. In sum, nanozymes are likely to play a key role as promising antioxidants for clinical applications, such as treatment of stress-mediated diseases like Alzheimer's disease (AD), Parkinson's disease, pulmonary inflammation caused by cigarette smoke, *etc.* in a foreseeable future.

Declaration of Competing Interest

The authors declare no conflict of interest.

Acknowledgements

This work was supported by Kermanshah University of Medical Sciences, Kermanshah, Iran.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.nantod.2019.100775.

References

[1] E. Birben, U.M. Sahiner, C. Sackesen, S. Erzurum, O. Kalayci, World Allergy Organ. J. 5 (2012) 9.
[2] H. Derakhshankhah, A. Saboury, A. Divsalar, H. Mansouri-Torshizi, I. Bamery, D. Ajloo, A. Moosavi-Movahedi, R. Hosseinzadeh, M. Ganjali, H. Ilkhani, J. Iran. Chem. Soc. 11 (2014) 1381–1390.
[3] H. Derakhshankhah, A.A. Saboury, A. Divsalar, H. Mansouri-Torshizi, Biophys. J. 100 (2011) 217a.
[4] M. Hepel, S. Andreescu, Oxidative Stress: Diagnostics, Prevention, and Therapy, American Chemical Society, 2015.
[5] J. Morry, W. Ngamcherdtrakul, W. Yantasee, Redox Biol. 11 (2017) 240–253.
[6] M. Hakiman, M. Maziah, J. Med. Plants Res. 3 (2009) 120–131.
[7] E.M. Conner, M.B. Grisham, Nutrition 12 (1996) 274–277.
[8] C. Villanueva, R.D. Kross, Int. J. Mol. Sci. 13 (2012) 2091–2109.
[9] K.E. Heim, A.R. Tagliaferro, D.J. Bobilya, J. Nutr. Biochem. 13 (2002) 572–584.
[10] Y. Gilgun-Sherki, E. Melamed, D. Offen, Neuropharmacology 40 (2001) 959–975.
[11] M. Carocho, I.C. Ferreira, Food Chem. Toxicol. 51 (2013) 15–25.
[12] J. Wu, X. Wang, Q. Wang, Z. Lou, S. Li, Y. Zhu, L. Qin, H. Wei, Chem. Soc. Rev. 48 (2019) 1004–1076.
[13] H. Cheng, L. Zhang, J. He, W. Guo, Z. Zhou, X. Zhang, S. Nie, H. Wei, Anal. Chem. 88 (2016) 5489–5497.
[14] J. Yao, Y. Cheng, M. Zhou, S. Zhao, S. Lin, X. Wang, J. Wu, S. Li, H. Wei, Chem. Sci. 9 (2018) 2927–2933.
[15] K. Fan, J. Xi, L. Fan, P. Wang, C. Zhu, Y. Tang, X. Xu, M. Liang, B. Jiang, X. Yan, Nat. Commun. 9 (2018) 1440.
[16] X. Wang, Y. Hu, H. Wei, Inorg. Chem. Front. 3 (2016) 41–60.
[17] A. Sen Gupta, Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology, vol. 8, 2016, pp. 255–270.
[18] S. Honary, F. Zahir, Trop. J. Pharm. Res. 12 (2013) 255–264.
[19] C. Hao, A. Qu, L. Xu, M. Sun, H. Zhang, X. C. H, H. Kuang, J. Am. Chem. Soc. 141 (2018).
[20] N. Singh, M.A. Savanur, S. Srivastava, P. D'Silva, G. Mugesh, Angew. Chem. Int. Ed. 56 (2017) 14267–14271.
[21] Y. Li, X. He, J.J. Yin, Y. Ma, P. Zhang, J. Li, Y. Ding, J. Zhang, Y. Zhao, Z. Chai, Angew. Chem. Int. Ed. 54 (2015) 1832–1835.
[22] X. Shen, W. Liu, X. Gao, Z. Lu, X. Wu, X. Gao, J. Am. Chem. Soc. 137 (2015) 15882–15891.
[23] N.H. Alsharif, C.E. Berger, S.S. Varanasi, Y. Chao, B.R. Horrocks, H.K. Datta, Small 5 (2009) 221–228.
[24] L. Wang, Z. Wang, X. Li, Y. Zhang, M. Yin, J. Li, H. Song, J. Shi, D. Ling, L. Wang, Nano Res. 11 (2018) 2746–2755.
[25] M. Moglianetti, E. De Luca, D. Pedone, R. Marotta, T. Catelani, B. Sartori, H. Amenitsch, S.F. Retta, P.P. Pompa, Nanoscale 8 (2016) 3739–3752.
[26] B. Bhushan, P. Gopinath, J. Mater. Chem. B 3 (2015) 4843–4852.
[27] M. Mahmoudi, Trends Biotechnol. 36 (2018) 755–769.
[28] A. Clark, A. Zhu, H.R. Petty, J. Nanoparticle Res. 15 (2013) 2126.
[29] G. Shu, B. Zhang, Q. Zhang, H. Wan, H. Li, Acta Universitatis Cibiniensis. Ser. E: Food Technol. 20 (2016) 29–38.
[30] M. Hu, L. Li, Y. Sui, J. Li, Y. Wang, W. Lu, S. Dupont, Fish Shellfish Immunol. 46 (2015) 573–583.
[31] I. Thomson, Asian J. Anim. Sci. 12 (2018) 9–15.
[32] H. Su, D.-D. Liu, M. Zhao, W.-L. Hu, S.-S. Xue, Q. Cao, X.-Y. Le, L.-N. Ji, Z.-W. Mao, ACS Appl. Mater. Interfaces 7 (2015) 8233–8242.
[33] V. Kumar, N. Sharma, S. Maitra, Int. Nano Lett. 7 (2017) 243–256.
[34] E. Ju, K. Dong, Z. Wang, Y. Zhang, F. Cao, Z. Chen, F. Pu, J. Ren, X. Qu, Chem. Eur. J. 23 (2017) 13518–13524.
[35] Y. Huang, Z. Liu, C. Liu, E. Ju, Y. Zhang, J. Ren, X. Qu, Angew. Chem. Int. Ed. 55 (2016) 6646–6650.
[36] M.R. Khaksar, M. Rahimifard, M. Baeeri, F. Maqbool, M. Navaei-Nigjeh, S. Hassani, S. Moeini-Nodeh, A. Kebriaeezadeh, M. Abdollahi, J. Trace Elem. Med. Biol. 41 (2017) 79–90.
[37] Y. Huang, Z. Liu, C. Liu, Y. Zhang, J. Ren, X. Qu, Chem. Eur. J. 24 (2018) 10224–10230.
[38] S. Onizawa, K. Aoshiba, M. Kajita, Y. Miyamoto, A. Nagai, Pulm. Pharmacol. Ther. 22 (2009) 340–349.
[39] J. Zhuang, K. Fan, L. Gao, D. Lu, J. Feng, D. Yang, N. Gu, Y. Zhang, M. Liang, X. Yan, Mol. Pharm. 9 (2012) 1983–1989.

Milad Ghorbani holds a Master's degree in Chemical Engineering- Biotechnology from the University of Tehran, Iran. His research interests cover a variety of interdisciplinary fields, such as "surface chemistry", "nano- and nanobiotechnology", "synthesis, characterization, and evaluation of materials for novel industry-oriented applications", "nanobiomaterials", and "to study materials interactions in various media from chemical and biological points of view".

Dr. Hossein Derakhshankhah is an Assistant Professor at the Pharmaceutical Science Research Center (PSRC) of the Kermanshah University of Medical Sciences (KUMS). He obtained his Ph.D. in 2017 from Tehran University of Medical Sciences (TUMS), under supervision of Professor Morteza Mahmoudi, on earning deep understanding of "hidden" factors in neurodegenerative disease with focus on Alzheimer disease. His current research area is in development/design of Nano/Bio materials for treatment of Neurodegenerative Diseases (Alzheimer, Parkinson, etc.) in collaboration with Prof. Mahmoudi's laboratory. Also Derakhshankhah is currently Chief Executive Officer (CEO) of Zistmavad Pharmed knowledge based company. Hossein Derakhshankhah dedicates this paper to Professor Morteza Mahmoudi.

Samira Jafari is an Assistant Professor of Pharmaceutical Nanotechnology at Kermanshah University of Medical Sciences. She is Ph. D graduated from Tabriz University of Medical Sciences (TUMS) in 2017, she also holds a postdoctoral degree from Tehran University of Medical Sciences. The most of her research is on field of nanomedicine, drug delivery systems, tissue engineering and cell penetrating peptides with emphasis on biomedical applications.

Sara Salatin earned Bachelors of Science degree in pure chemistry from the University of Urmia in 2009. She continued her master of science in analytical chemistry at the University of Urmia in 2010 under supervision of Prof. Bahram. She completed her Ph.D in pharmaceutical nanotechnology at the University of Tabriz in 2018 under supervision of Prof. Jelvehgari and Prof. Barar. Her thesis focused on the developing of thermosensitive nanohydrogel systems based on the polymeric nanoparticles for brain drug delivery. During her research opportunity as MSc and PhD student, she got enough skills in the nano-materials technology toward target drug delivery systems.

Mojtaba Dehghanian received his Master's degree in the department of Biotechnology from Islamic Azad University (Damghan Branch) in 2017 with a focus on detection of bacterial contamination of blood and blood products. Currently, he is a Ph.D. student in department of Microbial Biotechnology (Islamic Azad University, Shahr-e Kord Branch), and his current research interests lie in rapid and specific detection of bacterial contamination of blood and blood product by nanosensors to prevent transfusion-related sepsis. These days he is holding a work position at Iranian Blood Transfusion Organization (IBTO) for near eight years.

Dr. Mojtaba Falahati has completed his Bachelor Curriculum in the field of Biology majored in Zoology at Ferdowsi University in 2004 (Mashhad, Iran). Due to his high interests in Biophysical mechanisms related to diseases and pathological disorders, he performed his master thesis in Biophysics in the area of nerve membrane with focusing on medicinal polymers for the treatment of spinal cord injury at the Institute of Biochemistry and Biophysics (IBB) between 2005-2007 at the University of Tehran, Iran. Dr. Mojtaba Falahati received his PhD in Biophysics from the University of Tehran, Iran in 2011. During his PhD thesis he had a visit from Bremen University, Jacob University, Göttingen University, and Tübingen University in Germany. His main research area during the PhD was the immobilization of enzyme into the nanoporous materials and uncovering of the factors influencing the activity and stability of enzyme after interaction with nanoparticles. Since 2012, Dr. Falahati is an assistant professor at the Department of Nanotechnology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran. He has published several papers in well-prestigious journals such as *BBA*, *Scientific Reports*, *Controlled release*, *Biosensors and Bioelectronics*, *Cleaner Production*. Dr. Falahati has recently received several national and international funding for the investigating the interaction of nanomaterials with proteins and cells, development of nanozymes, and nanomaterials-mediated tissue engineering.

Ali Ansari is a doctoral student at the University of Houston Cullen College of Engineering studying environmental engineering. His research interests are wastewater treatment and seawater/brackish water desalination using nanomaterials. He has worked with various nanomaterials for environmental applications, e.g., magnetic nanoparticles with different coatings for contaminant removal from wastewater and graphene oxide to reduce scaling and biofouling on reverse osmosis membranes.