INTERNATIONAL JOURNAL OF CURRENT ADVANCED RESEARCH
ISSN: O: 2319-6475, ISSN: P: 2319-6505, Impact Factor: 6.614
Available Online at www.journalijcar.org
Volume 13; Issue 04; April 2024; Page No.3014-3016
DOI: http://dx.doi.org/10.24327/ijcar.2024.3016.1653

Research Article

NANOZYMES– A NEW HORIZON IN PERIODONTICS

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ARTICLE INFO

Article History:
Received 19th February, 2024
Received in revised form 24th February, 2024
Accepted 18th March, 2024
Published online 28th April, 2024

Key words:

Nanozymes, Metal- and metal oxide-based nanozymes, nano particles, anti bacterial therapy.

ABSTRACT

Nanozymes are nanomaterials with inherent enzyme-like properties that have been more popular over the past ten years due to their capacity to overcome the limitations of natural enzymes, such as their limited stability, high cost, and challenging storage. Nanozymes, which replicate and further design the active centers of natural enzymes, have the potential to operate as direct substitutes for conventional enzymes as a result of the rapid development and ongoing advances in nanoscience and nanotechnology. Nanozymes have drawn significant interest in a variety of biomedical applications as a class of nanomaterials with good catalytic efficiency, exceptional substrate specificity, and high recovery efficiency by utilizing their multi enzyme-like properties, inexpensive, and great stability, a number of nanozyme-assisted techniques have been successfully created for the theranostic of various diseases. Periodontitis, an inflammatory illness caused by oxidative stress, develops as a result of reactive oxygen speciescausing cell and tissue damage, which leads to alveolar bone resorption as well as the destruction of other periodontal supporting tissues. Due to their inherent antibacterial, antioxidants, osteogenic, anti-corrosive and bio-compatible capacity, nanozymes have contributed significantly on research in periodontal health and improve the success rate of implants. Thus, we provide a brief review that focus on classification and advancements in nanozymes.

INTRODUCTION

Enzymes are biocatalysts that facilitate a majority of biological reactions that occur in living systems. However, the intrinsic drawbacks of natural enzymes, such as ease of denaturation, high cost, laborious preparation, and difficulties in recycling, greatly limit their practical applications (Garcia-Viloca *et al* 2004). To overcome these limitations, artificial enzymes have been developed as stable, low-cost alternatives to natural enzymes since the 1950s (Lin, Y*et al* 2014). Nanozymes, as a new type of promising artificial enzyme, have attracted considerable interest over the past decade owing to their obvious advantages over natural enzymes and conventional artificial enzymes, such as high and tunable catalytic activities, low cost, easy large-scale production, and high stability (Breslow, R *et al* 2005).

In very recent years, along with significant advances in nanotechnology, biotechnology, and nanomaterial science, great progress has been achieved in the field of nanozymes(Gao, L *et al* 2007),(Kotov *et al* 2010).

ADVANTAGES

1. High catalytic activity
2. Tunable catalytic activity and types
3. Multienzyme mimetic activity
4. High stability
5. Recyclable utilization
6. Easy to mass produce
7. Low cost
8. Long-term storage
9. Robustness to harsh environments
10. Easy to multi-functionalize (large surface area for bioconjugation)
11. Controllable catalytic activity and types via external stimuli (such as light, ultrasound, heat, magnetic field, etc.)
12. Unique physicochemical properties (such as fluorescence, electricity, paramagnetic properties, etc.)

CLASSIFICATION

Nanozymes have been classified in different ways. According to Huang *et al*. (2019), these are classified into two families:

- (i) Oxidoreductase (oxidase, peroxidase, catalase, superoxide dismutase, and nitrate reductase) and
- (ii) Hydrolase (nuclease, esterase, phosphatase, protease, and silicatein).

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(Wang *et al*., 2020) classifies nanozymes depending on the material from which they are made into three categories.

(i) Metal-based nanozymes,
(ii) Metal-oxide or sulfide-based nanozymes.
(iii) Carbon-based nanozyme

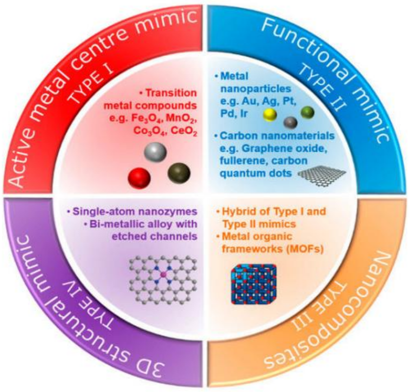

Fig. 1 Types of nanozymes based on their mode of natural enzyme-mimicking behaviour

CLINICAL INCORPORATION

NANOZYMES AS AN ANTIBACTERIAL AGENT

Researchers have made significant advances in developing innovative, consistent, and effective oral antibacterial medications that promote enzymes. Nanozymes aid in the prevention of root canal biofilm infection. According to Koo's findings, activating H2 O2 can significantly eliminate biofilm plaque from the surface of a root canal and dentinal tubules. They developed two types of antibacterial catalytic robots. When put in a limited environment, the threedimensional catalytic antibacterial automaton is a soft robot that allows precise effects ($P < 0.0005$). According to their findings, dual catalytic magnetic iron oxide nanoparticle-equipped catalytic antibacterial robots in magnetic fields may generate free radicals, break down exopolysaccharide matrix, and clear biofilm particles. When put in a limited environment, the threedimensional catalytic antibacterial automaton is a soft robot that allows precise effects. The leaf-shaped catalytic antibacterial robot removes exopolysaccharide matrix and biofilm buildup from intricate dentinal tubules while also killing microorganisms. The study discovered that catalytic antibacterial robots might be used to treat the severely limited anatomical surfaces of human teeth. By removing biofilms and eradicating germs, these catalytic antibacterial robot systems can endure persistent biofilm-associated diseases and prevent cross-contamination of medical equipment and other surfaces.

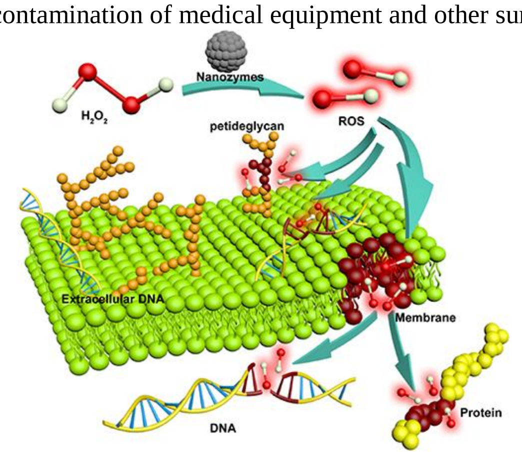

Fig. 2 Mechanism of nanozyme-based catalytic antibacterial therapy

ROLE OF NANOZYMES IN TISSUE REGENERATION

Many studies have shown the prospects of nanozymes in biomedical regeneration application, including healing of soft tissue injuries, bone regeneration and nerve regeneration, providing new ideas for the repair of oral soft and hard tissue defects. The regeneration mechanism of nanozymes in soft and hard tissues is different. Generally, the enzyme-like activity of nanozymes buffers H2O2 and O2 in cells, acts as an antioxidant, and activates ion channels or cell cycles protein, increase the level of certain factors (the specific factors in each study are different, such as vascular endothelial growth factor), promote cell attachment, proliferation and differentiation. At the same time, the antibacterial properties of nanozymes can provide a good sterile environment for tissue regeneration and accelerate healing tissue (D.Yu*et al* 2020).

ROLE OF NANOZYMES IN BONE REGENERATION

In bone regeneration, nanoceria is currently studied mostly, its antioxidant properties can buffer H2O2 and O2 levels in cells, promote osteogenic differentiation of stem cells and collagen production, and different valence cerium also affecting cell adhesion and proliferation. Fe3O4 nanozymes promoting osteogenic proliferation may be due to lysosomal degradation of free iron accelerates the cell cycle process (Xiaohang Chen *et al* 2013).

In the regeneration of soft tissues, the antioxidant properties of nanozymes can provide a good sterile environment, as well as reduce the oxidation of cell membranes and proteins to enhance the migration and proliferation of fibroblasts, keratinocytes and vascular endothelial cells, and accelerate healing tissue.

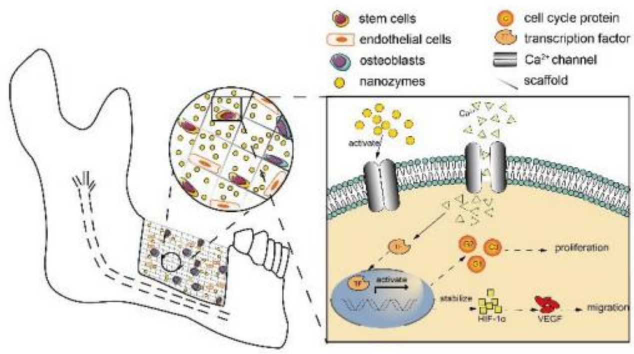

Fig.3 The role of nanozymes in bone regeneration

NANOZYMES IN OSTEOGENESIS

The key point for the application of bone regeneration is based on enhancing proliferation, migration and osteogenic differentiation of stem cells, and many studies are still working on solving this problem. In previous studies, intermittent supply of cytokines was usually used to promote cell proliferation and differentiation (C. Deng *et al* 2019). Scientists are also looking for the possibility of a long-term promotion effect by adding some substances during the synthesis of biological scaffolds. The biological scaffold containing nanozymes is promising. In 2009, Huang *et al*. firstly found that the peroxidase-like activity of super paramagnetic iron oxide nanoparticles could reduce intracellular H2O2, while regulated cell cycle proteins to promote the growth of human mesenchymal stem cells(X.Wang 2019). In addition, Naganuma *et al*. pointed out that metal ions of different valences affected the adhesion, growth and proliferation of mesenchymal stem cells. $Ce3+$ and $Ce4+$ played a role in promoting and inhibiting osteogenesis respectively, due to different metal charges and hydrophilicity or hydrophobicity, which provides a more comprehensive perspective for the next step of research (H.Xing 2020).

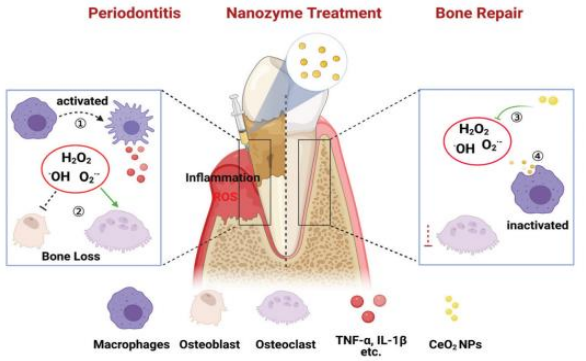

Fig. 4: The effect of CeO2 NPs on periodontitis treatment.

In the periodontitis microenvironment, ROS induced the activation of macrophages, leading to the release of pro-inflammatory cytokines such as TNF-α, IL-1β and so on. ROS inhibited the survival and differentiation of osteoblasts, while promoted the activity of osteoclast, and consequently resulted in the bone loss. With the treatment of CeO2 NPs, ROS was scavenged by CeO2 NPs, and inflammation could be restrained by the inhibition of the NFκBsignalling pathway in macrophages. Therefore, there would appear bone repair in periodontal destruction.

ROLE OF NANOZYMES IN SOFT TISSUE REGENERATION

Scientists still face major challenges in repairing or replacing soft tissues such as skin, nerves and cartilage. Oral and maxillofacial soft tissue regeneration and healing require a good sterile environment (B.R.Freedman *et al* 2019). Traditional antibacterial strategies such as H2O2 will delay the healing rate and affect healthy tissues. The application of nanozymes can decline the effective concentration of H2O2 and coordinate cells as an antioxidant. The cooperation between them promotes healing of soft tissues (Z.Guo *et al* 2020). Chigurupati *et al*. reported that the topical application of watersoluble nanoceria promoted the proliferation and migration of fibroblasts, keratinocytes and vascular endothelial cells, reduced the oxidation of cell membranes and proteins in the environment, and accelerated the full-thickness dermal healing. Qu's research group synthesized gold nanoparticles and ultra-thin graphite carbonitride (g-C3N4) system with good peroxidase activity that could effectively catalyze H2O2 (S.Chigurupati 2013). Hematoxylin-Eosin staining showed that compared with other control groups, after treatment with g-C3N4 + H2O2 (100µM), complete and thickened epidermis was observed, indicating that the system could significantly prevent bacterial infections and accelerate wounds healing. Subsequently, other scholars proposed vanadium oxide nanodots with dual-enzyme-like properties of peroxidase and oxidase. H2O2 (50 µM) companied with this nanozymes can build an effective antibacterial system, and the soft tissue regenerates quickly (Z.Wang *et al* 2017).

NANOZYMES AND ROS

A concise answer is that nanozymes are intimately related to ROS because of the need for oxygen to preserve life on Earth. Interestingly,"hyperactivated" polymorphonuclear neutrophils, characterized by the overproduction of reactive oxygen species (ROS), appear to be associated with periodontal diseases (J.F.Turrens *et al* 2003). ROS include hydrogen peroxide (H2O2), superoxide (O2 •−), hydroxyl radical (• OH), and singlet oxygen (1 O2). Importantly, ROS can be considered as a double-edged sword, as they help destroy pathogens to keep health, while contribute to oxidative stress when their levels are excessive. Although ROS play an important role in cell signalling, an excess of ROS results in direct cell and tissue damage including lipid peroxidation, protein oxidation, and mitochondrial depolarization (Y.J.Taverne *et al* 2018). Furthermore, ROS activate NFκ Bsignalling and thereby promotes inflammation. Interestingly, ROS-mediated intracellular signalling induces osteoclastogenesis and this eventually results in bone tissue damage around teeth. Data from a systematic review revealed plasma, serum and salivary total antioxidant concentrations to be decreased in periodontitis patients as compared with healthy controls (R.Gerschman *et al* 1954). Taken into consideration the detrimental effects exerted by excess ROS levels, a therapeutic strategy targeted to scavenge ROS and thus alleviate inflammation could be an effective therapeutic approach for the management of periodontitis (M. C.W. Oswald*et al* 2018).

COMPLICATIONS OF NANOZYMES

However despite nanozymes being promising materials for the development of biosensors they currently have the following disadvantages,

(1) Efficiency of nanozymesare lower than natural enzymes,
(2) The 3D complexity of the natural enzymes cannot be mimicked by nanozymes.

Currently, one of the main disadvantages associated with nanomaterials is considered to be inhalation exposure. This concern arises from animal studies, the results of which suggested that nanomaterials such as carbon nanotubes and nanofibers may cause detrimental pulmonary effects, such as pulmonary fibrosis.

FUTURE OF NANOZYMES

Undoubtedly nanodentistry confers numerous advantages over conventional systems, such as higher bio-regeneration, a notable antimicrobial effect due to anti-biofilm properties, but at the same time, its precise placement, associated toxicity, costly development, and international regulations limit the clinical exploration.

Nanozymes are less costly, easy to synthesize, more stable, and highly efficient compared to their natural counterparts. They are vastly used for their theranostic applications. Zhang *et al*. developed DNA nanozymes for biosensing the presence of dental bacteria. Similarly, Huang *et al*. presented bifunctional nanozymes that specifically inhibit the pathogenic Streptococcus mutans (pathogen) but not the commensal, Streptococcus oralis using iron oxide nanozymes having oxidase kind activity.

CONCLUSION

Although nanozymes have shown great success in treating bacteria-related diseases in many in vitro or in vivo models, they still have a long, long way to go before clinical translation due to the rather limited studies at the current stage. The emergence of nanozymes uncovers the biological effects of inorganic nanomaterials. Nanozymes thus can be used as an alternative of natural enzymes because of their capability to address the limitations of natural enzymes such as low stability, high cost, and difficult storage. Over the past decade, nanozyme-based probes have been widely developed for disease imaging and diagnosis from in vitro to in vivo. In this review, we summarized the progress of nanozymes in disease detection and imaging, and discussed the current challenges and future directions of nanozyme development in clinical treatment.

References

1. Garcia-Viloca, M., Gao, J., Karplus, M., & Truhlar, D. G. (2004). How enzymes work: analysis by modern rate theory and computer simulations. *Science, 303,* 186−195.
2. Lin, Y., Ren, J., & Qu, X. (2014). Catalytically active nanomaterials: A promising candidate for artificial enzymes. *Accounts of Chemical Research, 47,* 1097−1105.
3. Breslow, R. (2005). *Artificial Enzymes.* Weinheim: Wiley-VCH.
4. Gao, L., Zhuang, J., Nie, L., Zhang, J., Zhang, Y., Gu, N., & Yan, X. (2007). Intrinsic peroxidase-like activity of ferromagnetic nanoparticles. *Nature Nanotechnology, 2,* 577−583.
5. Kotov, N. A. (2010). Inorganic nanoparticles as protein mimics. *Science, 330,* 188−189.
6. Yu, D., Ma, M., Liu, Z., Pi, Z., Du, X., Ren, J., & Qu, X. (2020). *Biomaterials, 255,* 120160.
7. Chen, X., Xing, H., & Zhou, Z. (20xx). Nanozymes Go Oral: Nanocatalytic Medicine Facilitates Dental Health. *Journal Name, 00,* 1-3.
8. Deng, C., Xu, C., Zhou, Q., & Cheng, Y. (2019). Wires Nanomed,Nanobi, 11, e1576.
9. Wang, X., Wu, X., Xing, H., Zhang, G., Shi, Q., E, L., & Liu, H. (2017). *ACS Applied Materials & Interfaces, 9,* 11380-11391.
10. Xing, H., Wang, X., Xiao, G., Zhao, Z., Zou, S., Li, M., & Guo, J. (2020). *Biomaterials, 235,* 119784.
11. Freedman, B. R., & Mooney, D. J. (2019). *Advanced Materials, 31,* e1806695.
12. Guo, Z., Liu, Y., Zhang, Y., Sun, X., Li, F., Bu, T., ... Wang, L. (2020). *Biomaterials Science, 8,* 4266-4274.
13. Chigurupati, S., Mughal, M. R., Okun, E., Das, S., Kumar, A., McCaffery, M., & Mattson, M. P. (2013). *Biomaterials, 34,* 2194-2201.
14. Wang, Z., Dong, K., Liu, Z., Zhang, Y., Chen, Z., Sun, H., & Qu, X. (2017). *Biomaterials, 113,* 145-157.
15. Turrens, J. F. (2003). *Journal of Physiology, 552*(2), 335–344.
16. Taverne, Y. J., Merkus, D., Bogers, A. J., Halliwell, B., Duncker, D. J., & Lyons, T. W. (2018). *Bioessays, 40*(3), 1700158.
17. Gerschman, R., Gilbert, D. L., Nye, S. W., Dwyer, P., & Fenn, W. O. (1954). *Science, 119*(3097), 623–626.
18. Oswald, M. C. W., Garnham, N., Sweeney, S. T., & Landgraf, M. (2018). *FEBS Letters, 592*(5), 679–691.

How to cite this article:

M.V.NoblinShyma*., C. S Prabhahar ., M. Umayal ., T. B. Meenalochani ., M. Tamilarasan and S. S. Vijayalakshmi . (2024). Nanozymes- a new horizon in periodontics. *International Journal of Current Advanced Research.*13 (04), pp.3014-3016.

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