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Nanozymes: A Novel Strategy in Theranostics and Biomedical Sensing

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Pournami Mohan*, Subodh S Satheesh

1. Pharm D Student, Sreekrishna College of Pharmacy and Research Centre, India.*

2. Assistant professor, Sreekrishna College of Pharmacy and Research Centre, India.

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ABSTRACT

Our human body consists of an enormous number of natural enzymes that play a vital role in biological reactions. The practical applications of natural enzymes are limited to some extent due to some intrinsic drawbacks. To overcome this problem, an innovation was made into launch called Artificial enzyme and has attained complete attention on the researcher. In the field of environmental science and technology, they have shown increasingly wide interest. Along with rapid development and an ever-deepening understanding of Nanoscience and nanotechnology, nanozymes hold promise to serve as direct surrogates of traditional enzymes by mimicking and further engineering the active centers of natural enzymes. As a novel type of artificial enzyme, nanozymes, along with their enzyme-like catalytic activity also exhibits the unique physicochemical properties of nanomaterials, such as photothermal properties, super-paramagnetism, and fluorescence. By combining the unique physicochemical properties and enzyme-like catalytic activities, nanozymes have been widely developed for in vitro detection and in vivo disease monitoring and treatment. The challenges and future directions of computational research in the field of Nanozymes are also discussed. Scientists mainly focus on our progress in systematic design and construction of functionally specific Nanozymes, the standardization of Nanozymes research, and exploration of their application for replacing natural enzymes in living systems.

INTRODUCTION:

Nanozymes are said to be inorganic nanoparticles that show enzyme-like characteristics. The term Nanozymes was coined by Pasquato, Scrimin, and their coworkers in 2004. By 2013, Wei and Wang defined Nanozymes as the nanomaterials with enzyme-like functions. Nanomaterials are linked to the biological system via Nanozymes. Nanozymes can be designed with a range of catalytic activity by simply varying shape, structure, and composition. A new type of artificial enzymes, Nanozymes not only have enzyme-like catalytic activity but also exhibit unique physicochemical properties of Nanomaterials such as photothermal properties, superparamagnetism, and fluorescence(1). The atomic composition of Nanozymes is the most important factor in determining their catalytic activity. These artificial enzymes have a wide range of advantages when compared to natural enzymes(2). Nanozymes are less expensive and recyclable and can be easily manufactured and stored for a very long period. Nanozymes can work in an environment closer to physiological conditions and respond to a range of external stimuli. This invention of Nanozymes creates a multimodal platform interfacing biological complex.

Nanozymes open novel avenues for monitoring the initiation and progress of diseases by combining the unique physiochemical properties and enzyme-like catalytically of Nanozymes. Nanozymes hold promise to achieve quantitative analysis for pathological diseases staining diagnosisNanozymes also have been broadly developed for *in-vivo* monitoring and imaging of disease. Besides tumor pathological diagnosis, Nanozymes have also been used for the identification of human high risk and ruptured atherosclerotic plaques(3). For practical applications, reliable methods for bioconjugation of Nanozymes with affinity ligands need to be achieved, but not at the cost of losing the activity of Nanozymes.Finally, fundamental mechanistic studies are needed to rationally design Nanozymes and to obtain key insight into a few model systems. The thorough understanding of experimental phenomena and the mechanisms beneath practical applications of Nanozymes limits their rapid development(4). Targeting antibody conjugated ferromagnetic Nanozymes simultaneously provide three functions: target capture, magnetic separation, and Nanozymes color development for target detection. We finally will address the prospect of Nanozymes research to become Nanozymology.

Surface modification and Nanozymes design can be processed by combining experimental and computational studies. Thus in recent years, researchers have focused on utilizing the catalytic powers of chemical molecules such as cyclodextrins, metal complexes, porphyrin, polymeric, and supramolesculecules, as alternatives to natural enzymes(5). However, the catalytic efficiency and biocompatibility were some of the harboring concerns with these molecules. The toxicity of Nanozymes to humans and the ecosystem is also an essential issue to be solved regarding environmental and therapeutic applications(6). Efforts have been made to develop such multifunctional Nanozymes. The artificial enzymes could one day be used in the fight against infections and to keep high-risk public spaces like hospitals free of bacteria like E.coli and Golden Staph.

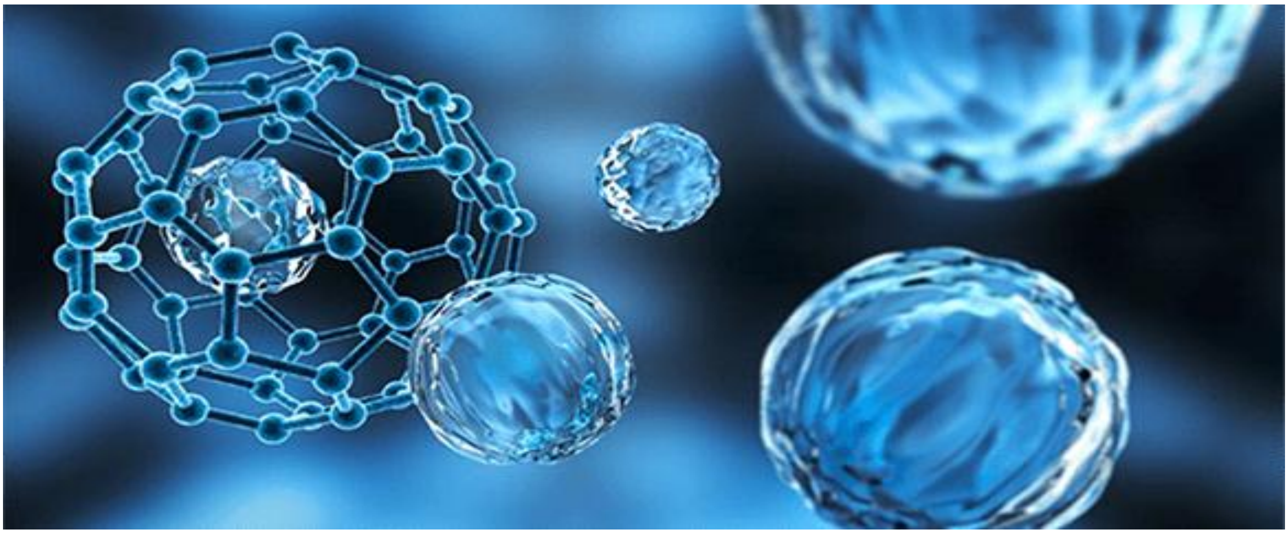

Figure No. 1: Structure of Nanozymes

CLASSIFICATION

More and more Nanozymes have emerged one after another the peroxidase Nanozymes were reported. (7). Nanozymes are mainly classified into three;

1. Fe based Nanozymes.

2. Non- Fe metal-based Nanozymes.

3. Non- metal-based Nanozymes.

1. Fe –based Nanozymes

The initial study was based on the ferromagnetic nanomaterials whether they have peroxidase catalytic activity or not.

Subsequently, the iron may forms oxides and peroxidase-like catalytic activity showing nanomaterials such as Fe-Mn oxide nanoparticles, Fe-Co oxide nanoparticles, and Fe-Bi oxide nanoparticles.

2. Non –Fe metal-based Nanozymes

Metal-based Nanozymes were also found showing peroxidase catalytic activity. eg: Cerium dioxide nanoparticles, Manganese dioxide nanoparticles. Copper sulfide nanoparticles and Cadmium sulfide nanoparticles also have similar catalytic activity.

3. Non –metal-based Nanozymes.

There are also some non-metal based Nanozymes that shows catalytic activity such as carbon nanotubes, graphene oxide, and Carbon Nanodots.

Catalase mimetic can protect hepatic cells from cytotoxicity and genetic damage induced from the increased concentration of hydrogen peroxidase. There are various types of mimetic nanoparticles, they are as follows:

A. Catalase mimetic nanoparticles.

B. Pro –oxidant Nanozymes.

C. Peroxidase mimetic nanoparticles.

D. Oxidase mimetic nanoparticles.

A. Catalase mimetic nanoparticles.

With the help of Nanozymes like cerium oxide, iron oxides it helps to convert hydrogen peroxidase to hydroxyl radicals.

B. Pro –oxidant Nanozymes.

Free radicals are produced by induced oxidative stress by the action of Nanozymes in mammalian cells or inhibiting these antioxidant systems.

C. Peroxidase mimetic nanoparticles.

Peroxidase enzyme-like activity is shown by iron –oxides. FeS nanoneedles are also shown to have better peroxidase activity than spherical FeS nanoparticles.

D. Oxidase mimetic nanoparticles.

With the help of molecular oxygen, the oxidase enzyme involves oxidation of the substrate converts into hydrogen peroxide and water.

APPLICATIONS AND RECENT TRENDS OF NANOZYMES

PH, Hydrogen peroxide, and glutathione concentration regulate catalytic activities of the nanozyme. Heat, ultrasound, light magnetic field remotely control the Nanozymes. To improve clinical outcomes, Nanozymes are used in the early stages to detect disease.

Elisa test

Elisa is said to be a biochemical assay used for biomedical diagnosis, food safety, environmental monitoring. In Elisa, the function of horseradish peroxidase can be replaced by Nanozymes using as a signal tag, it forms a nanozyme based NELISA ASSAY. The temperature resistance of Nanozymes is also much better than Horseradish peroxidase. In a typical sandwich ELISA assay, the target analyte to be measured is first recognized through a specific reaction of antigen (analyte) and the capture antibodies immobilized in an ELISA plate(8). Then, binding of the captured analytes to detection antibodies conjugated with horseradish peroxidase (HRP) makes access for a color reaction of HRP and the substrate after washing steps.

There is also another immunodetection technique called lateral flow immunoassay [LFIA], In addition to ELISA. It is an important choice to integrate Nanozymes as a signal tag with detection systems to construct a Nanozymes based FLIA assay.

USE OF NANOZYMES AS BACTERICIDES

Nanozymes make use of visible light to create highly reactive oxygen species that rapidly break down and kill bacteria efficiently. Nanozymes combines light with moisture to cause a biochemical reaction that produces OH radicals and break down bacteria. Nanozymes shined upon with a flash of white light, the activity of Nanozymes increases 20 times and it forms holes in bacterial cells and killing them efficiently.

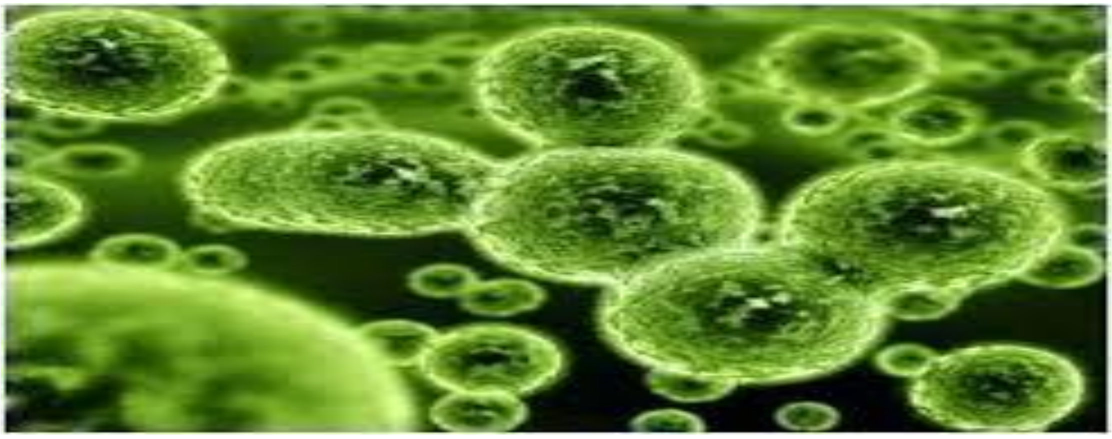

Figure No. 2: Use of Nanozymes as a bactericide

USE OF NANOZYMES IN SEWAGE TREATMENT:

Nanozyme-based methods are a powerful, cost-effective, and simple method for degradation and mineralization of organic dyes from industrial processes. Most prominently, MNPs such as peroxidase have been investigated for the degradation of organic pollutants, such as methylene blue, phenol, and rhodamine B(9). Phenol is a harmful carcinogen that is commonly seen in the sewage. To remove phenol, peroxidase. Nanozymes can be used to catalyze hydrogen peroxide and that produces a large number of free radicals That can degrade phenol in sewage to produce carbon dioxide, water, and small molecular organic acids. A MNP-based degradation method offers distinct advantages over existing degradation methods that use HRP, such as lower cost, high stability, and reusability.

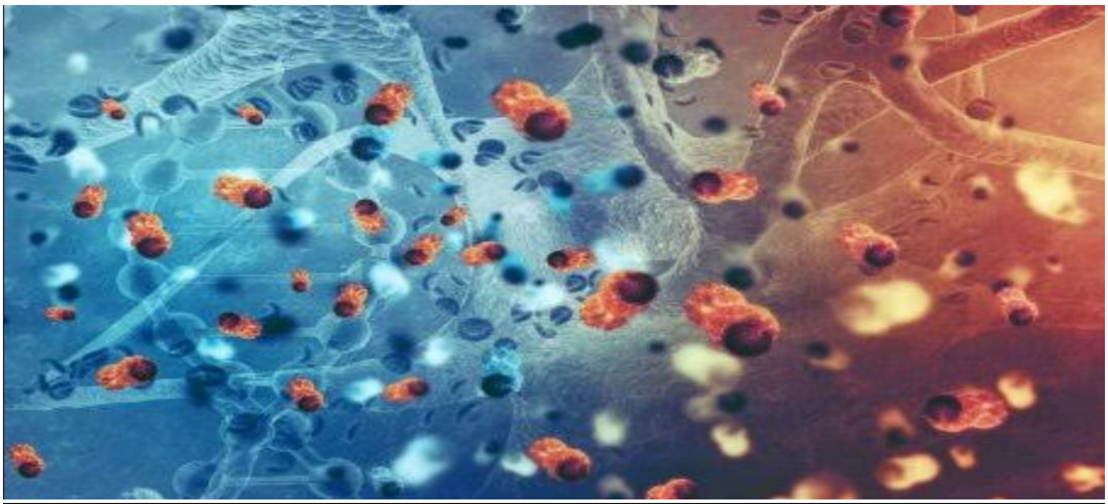

Figure No. 3: Use of Nanozymes in sewage treatment

USE OF NANOZYMES IN FOOD QUALITY

Nanozymes based detection techniques can be applied for inspection of both endogenous and exogenous contaminants [hydrogen peroxide, toxic ions, and antibiotics] in foods and agricultural products. It is essential to develop techniques for the analysis of acetylcholine or choline in functional foods. These are essential for brain development. They have shown highly sensitive detection approaches to compounds like **pesticides** especially organophosphate pesticides. These are a type of prevalent contaminants in fruits and vegetables. Although a necessary nutrient for human bodies, glucose is also a biomarker that concerns the induction or exacerbation of diabetes. Accurate quantification of glucose in foods can guide dietary recommendations for diabetic patients. Therefore, novel detection methods using nanozymes have been established for detecting glucose in food samples, with the majority of the studies being accomplished by collaborative work of natural GOX and a POD-mimicking nanozyme(10).

Mycotoxins are of ultrahigh toxicity to a living organism and pose a long term safety risk to agrifood products even worse than that of OP residues OXD-like activity of MnCO2O4 microspheres could be regulated by reversible attachment of aptamer on a MnCO2O4 microsphere surface mediated by target recognition.

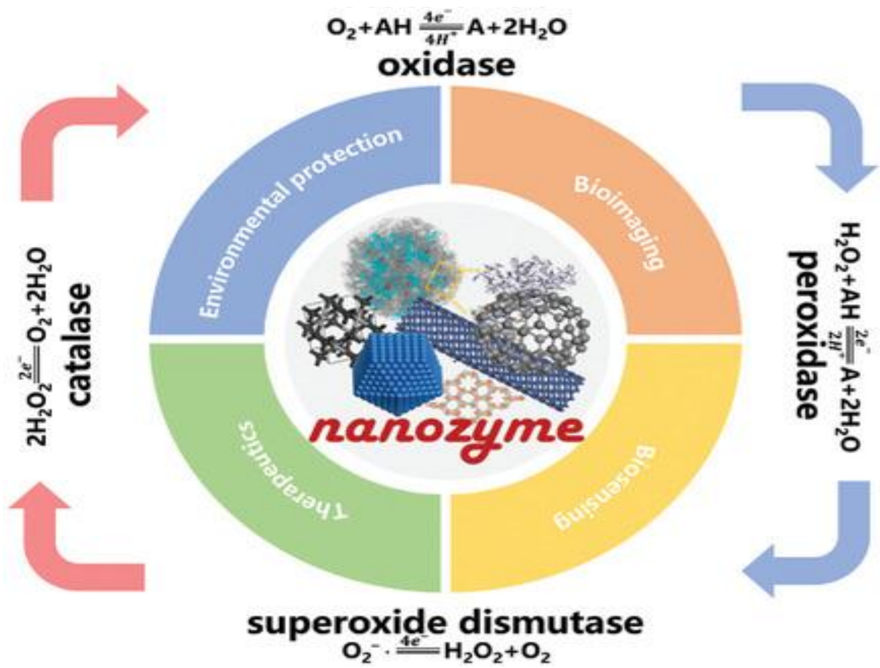

Figure No. 4: Use of nanozumes in food quality

USE OF NANOZYMES IN DIAGNOSING TUMOR.

Without any targeted ligands or contrast agents to target and visualize tumor tissues, magnetic ferritin Nanozymes can be used. In presence of hydrogen peroxide, iron oxide Nanozymes catalyze the oxidation of peroxidase substrates to produce a chromogenic reaction to diagnose the tumor. This diagnostic method detects tumor tissue with 98% sensitivity and 95%specificity.this test can be done within 1 hour. It is very simple, rapid, and economic. Ultra small gold Nanoclusters have been used as a sensitive probe for in vivo imaging due to their excellent tumor enrichment and kidney clearance. When the nanoparticles were conjugated with folic acid, they bound to folate receptors on the tumor cell (A-549 lung cancer cells), due to the high expression of folate receptors on the tumor cell surface.

Polymer-coated nanoceria as an oxidase mimic made detection of tumor cells easier than with traditional immunoassay because it directly oxidized a colorimetric substrate to a colored product without H_2O_2 and additional steps to introduce an enzyme-conjugated secondary antibody. The iron oxide cores catalyzed the oxidation of peroxidase substrates in the presence of H_2O_2 to produce the colorimetric signal that was used to visualize tumor tissues. Through this strategy, nine types of cancer were successfully verified with enough specificity and sensitivity.

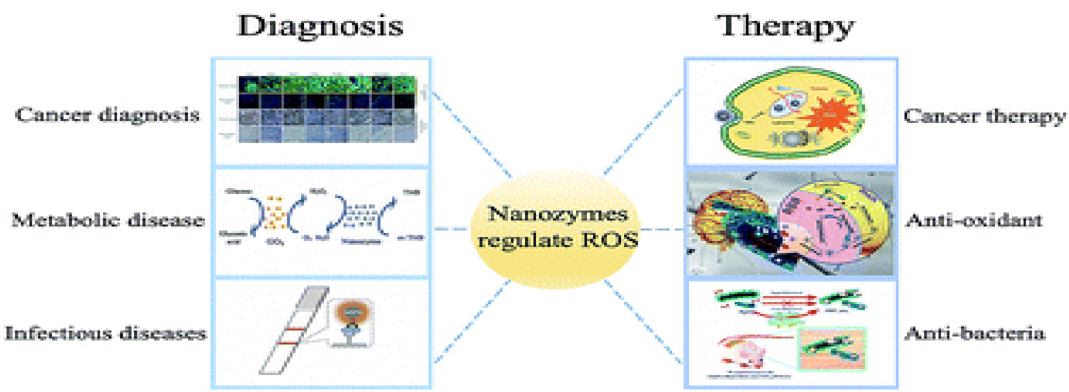

Figure No. 5: Use of nanozymes in diagnosing tumor

USE OF NANOZYMES IN POLLUTANT DETECTION

A simple and rapid colorimetric method for detecting melamine, an organic nitrogenous compound that is toxic when swallowed and has been illegally added to dairy products. The principle of this method is as follows. Melamine inhibits the catalytic oxidation of colorimetric substrates (ABTS) by MNPs in the presence of H_2O_2, because it competitively reacts with H_2O_2, forming an additional compound. Consequently, the intensity of the ABTS color signal was dependent on the concentration of melamine. Based on this reaction, a colorimetric system using MNPs could enable easy detection by the naked eye of concentrations of melamine above safety limits in dairy products. Nanocomposite-entrapping MNPs and oxidase in mesoporous carbon were used to detect several phenol compounds amperometrically, such as phenol, cresol, and catechol (11). These phenol compounds produced a concentration-dependent increase of cathodic current in this system, which may have great potential in the field of environmental monitoring.

USE OF NANOZYMES IN DIAGNOSING VIRAL INFECTIONS

Nanozymes strips can be used to detect Ebola. The colloidal gold in a traditional test strip is replaced by Fe_3O_4 magnetic nanoparticle Nanozymes. This can be used to detect viruses and toxins at customs ports by switching types of antibodies on probes. The aptamer-nanozyme system has wider utility and has shown its value to detect a variety of analytes ranging from small molecules to the whole cell. Further, the adaptation of this system on to an electrochemical sensing platform has increased the sensitivity and low-end detection limit. The aforementioned advances in this field have given a strong foundation to develop a robust, rapid, sensitive, and cost-effective point-of-care device similar to lateral flow shortly that can be used as a Target Product Profile 1 (TPP-1) diagnostics.

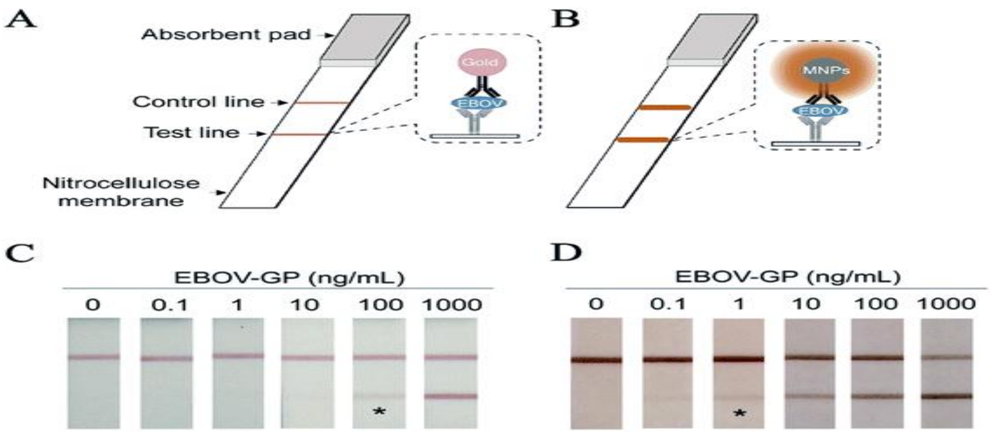

Figure No. 6: Use of nanozymes in diagnosis of viral infection

ROLE OF NANOZYMES IN OTHER DISEASES

Nanozymes can also be used in cases of degenerative diseases like **Parkinson's disease**. Nanozymes can alleviate the damage caused by oxidative stress. First, carbon-based Nanozymes called Fullerene, also known as free radical sponge has been found to have SOD activity. Nanozymes are currently being used to fight **inflammation.** Inflammation is our body's defense responses to stimuli.Mn3O4 nanoparticles had superoxide dismutase activity, catalase activity, and free radical scavenging functions. Copper tannic acid coordination Nanozymes reduces oxidative stress pulmonary inflammation which can result in acute lung injury. Nanozymes is also used in detecting **the acid present in rain.** Nitrogen-containing and sulfur-containing compounds in the rainwater will be oxidized by hydrogen peroxide, this increases the acidity and forming acid rain. Using catalytically activity of peroxidase Nanozymes, the scientist can quickly detect the content of hydrogen peroxide in rainwater and this helps us in realizing the monitoring of acid rain.

In the agricultural field, these Nanozymes were used in a modified form called **Nanozymes 2.0**and this helped balance the soil ph. and assist in increasing nutrient and fertilizer uptake for healthier plant growth. Thomas Kent, Neurologist in Texas A and M health science center has said that "while speculative that these Nanozymes will be helpful in COVID-19, if the administration is timed correctly, they could reduce the damaging radicals that accompany the cytokine storm and could be further chemically modified to reduce other injury-causing features of this disease"(12).

CONCLUSION

Nanozymes can create huge miracles and innovations in the field of medicine using nanotechnology. Nanozymes are considered to have enormous potential for biomedical applications. Reseachers must take innovative steps to promote the use of Nanozymes and it can create promising new horizons for diagnosis, treatment, and theranostics. Despite the remarkable advantages of nanozymes, there remains plenty of limitations while putting nanozymes into practical clinical applications, such as poor dispersibility, easy sedimentation after surface modification, limited catalytic types, poor substrate selectivity, and potential nanotoxicity. Nanozymes also have low selectivity to targets, owing to the absence of active sites where a substrate molecule binds and undergoes a chemical reaction in a natural enzyme. Although researchers have designed various types of surface-modified nanozymes with polymers, nucleic acids, and antibodies to provide selectivity mimicking natural enzymes, this is still insufficient for use in practical applications. We address the current challenges facing Nanozymes research as well as possible directions to fulfill their great potential in the future. Undoubtedly in the coming years, research on Nanozymes will continue to expand at the interface of nanomedicine, animal biotechnology, and enzymology and material science.

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