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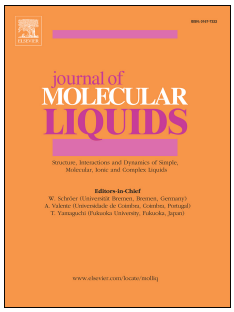

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Antioxidant Properties of Gold Nanozyme: A review

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Abstract

AuNPs with enzyme-like features have received strong attention in different areas, although limited data is available in literature on their biological/industrial functions. NPs especially Au counterparts have been shown to functionally mimic the activity of antioxidant enzyme. Indeed, due to low cytotoxicity and SPR characteristics of AuNPs, there are a great number of reports in which Au nanozymes yield promising responses in biomedical applications. In this review, we aim to overview the enzymatic activity of Au nanozymes along with their regulatory and controlling mechanisms. We have reviewed the effect of various factors such as dimension, morphology, functionalization and presence of hybrid materials on the catalytic activity of Au nanozymes as well as a detail survey on the oxidase, peroxidase, SOD, and CAT-like activities of Au nanozyme. Finally, the significance of Au nanozymes in mitigating oxidative stress followed by conclusion and challenges were reported. Based on this paper, we envision that Au nanozymes can be used as a promising material to prevent oxidative stress-stimulated disorders.

Keywords: Au nanozymes, enzymatic mimic, physicochemical properties, oxidase-like activity, peroxidase-like activity, superoxide dismutase-like activity, catalase-like activity.

Abbreviation: Catalase (CAT); Cerium oxide (CeO_2); Copper oxide (CuO); Glucose oxidase (GOD); Gold nanoparticle (AuNPs); Gold nanocluster (AuNCs); Graphene oxide (GO); Horseradish peroxidase (HRP); Iron (Fe); Limit of detection (LOD); Platinum (Pt); Palladium (Pd); Silver (Ag); Single-wall carbon nanotubes (SWCNT); Superoxide dismutase (SOD);

Reactive oxygen species (ROS); Surface-enhanced Raman scattering (SERS); Surface plasmon resonance (SPR)

Contents

1. Introduction

Enzymes are protein biocatalysts that have been expanded to RNA by the discovery of ribosomes since the early 1980s [1]. Generally, catalytic processes by enzymes always take place under very specific conditions such as temperature, pressure and physiological pH. Therefore, the industrial use of enzymes is associated with constraints due to fluctuations in environmental

conditions [2]. Hence, based on catalytic concepts, researchers are interested in producing compounds with an enzyme-like behavior that, in addition to the high sustainability and easy separation of products, have a massive and inexpensive production capacity compared to enzymes [3]. With the first discovery of the catalytic activity of NPs in 2007 [4] (Fig. 1) that stated similar activity of Fe NPs with HRP, it was provided new opportunities and hopes in this regard. To date, various kinds of NPs have been introduced that show intrinsic enzymatic activity. The most important of these are Pt NPs [5, 6], CeO_2 NPs [7], AuNPs, CuO NPs [8], Fe-based hybrid NPs like bismuth ferrite ($BiFeO_3$), Cobalt ferrite ($CoFe_2O_4$), Fe sulfide (Fe-S), and Fe selenide (Fe-Se) NPs [9-11], and carbon compounds, such as GO and SWCNT [12, 13]. NPs have also been used in numerous other applications including biomedical application (1), tissue engineering (2, 3), cellular differentiation (4), and wound healing (5) [14-18]. Despite the extensive enzymatic activity of nanomaterials as catalysts, their main activity is focused on oxidases.

AuNPs have been used as a catalyst for some chemical reactions in recent years. For example, Haruta, et al. [19] exhibited that AuNPs are capable of oxidizing CO at room temperature. Based on the reported results, the catalytic activity of AuNPs can be described either according to the multivalent cooperative catalytic activity of AuNCs [20, 21] or on the basis of the intrinsic activity of the small NPs with constant level [22, 23]. In both cases, AuNPs, as artificial enzyme (named as nanozyme), can be involved in the catalytic activity of nuclease, esterase, oxidase and peroxidase. ROS are produced as a consequence of cellular activities. At lower doses, ROS act as crucial second messengers in different signaling pathways [24] whereas at higher doses, ROS display damaging impacts on the cell through oxidative injury to biomacromolecules and switching on apoptotic pathways [24, 25]. Thus, regulation of ROS is crucial for the maintenance

of cellular homeostasis [24, 26]. Although, cells produce a number of antioxidant enzymes, the excessive production of ROS through stress highlights the significant need of antioxidant agents. Recently, NPs having enzyme-like activities have attracted substantial attention in biosensor and medical applications [27-30]. AuNPs with intrinsic oxidase, peroxidase, SOD, and CAT-like activities entice notable current attentiveness due to their capability to replace targeted enzymes in enzyme-based implementations.

1.1. Facts

- Although Au nanozymes are more stable and recyclable than natural enzymes, natural enzymes exhibit higher catalytic activity due to the unique catalytic position.
- Unlike natural enzymes that typically work in a specific area, Au nanozymes have multi-purposes and cascading catalytic reactions.

1.2. Opening questions

- Can Au nanozymes show high performance similar to the native enzyme in the physiological conditions?
- Which parameters may affect the enzyme-like activity of Au nanozymes?
- Do multienzyme complexes provide advantageous over processes catalyzed by individual nanozymes?
- Can Au nanozymes show outstanding ROS scavenging activity?

2. Tuning gold-nanozyme activity

In addition to controlling the activity of Au nanozymes by pH, temperature, surrounding environment, and metallic ions similar to those of natural enzymes, they can be regulated by the

properties of Au nanozymes such as particle size, composition, shape, surface coating and other factors. In summary, some of the factors controlling the activity of Au nanozymes are discussed below.

2.1. Size

Since many properties of nanomaterials depend on the particles size, their catalytic performance can be adjusted by resizing NPs [31]. Experiments revealed that with increasing surface to volume ratio, the catalytic activity of nanozymes increases. In this line, GOD activity (Fig. 2A). Likewise, it was demonstrated that by decreasing the size of the Au nanozymes (up to 3-5 nm), the oxidase activity as well as the stability of Au nanozymes increased [33]. Also, Han, Choi and Kwon [23] revealed that despite the higher catalytic activity of Au nanozymes at dimensions below 10 nm, the Au nanozymes of 20 nm exhibited a higher tendency to detect and remove Hg^{2+} from the environment.

2.2. Shape and morphology

Based on the results of other metallic nanozymes such as changing Pd nanozymes from octahedrons to cubic form which reduce their peroxidase activity due to reduced surface energy (Fig. 2B) [34], the shape and morphology of Au nanozymes may be effective on their catalytic activity. In this regard, Li, Liu, Wu and Gao [33] showed improved peroxidase activity of Au nanozymes in the presence of H_2O_2 in both acidic and basic conditions by changing the morphology of Au nanosheets from the corrugated (Au: 110 and 211) to flat (Au: 111) state, and by increasing the surface energy for the reaction.

2.3. Surface coating and modification

In addition to the size and shape, several experiments show that the modification of the surface of the Au nanozymes results in changing their catalytic activity. In this regard, Lin, et al. [35] revealed that the modification of Au nanozymes from citrate to cysteamine changed their catalytic activity from GOD to peroxidase. Also, the surface modification of AuNPs by melamine, in addition to increasing LOD of melamine in compounds such as milk and dietary supplements up to 0.2 nM, enhanced the peroxidase-like activity of AuNPs compared to the bare AuNPs [36]. In this regard, Shah, et al. [37] showed that the modification of the surface of AuNPs with ATP not only increased the catalytic activity of the NPs in comparison to natural enzyme, but also preserved the activity of nanozyme in the presence of compounds such as carbonate and sulfate. Moreover, Wu, et al. [38] showed that the modification of Au nanozymes with purine, as compared with pyrimidine, can enhance the activity of Au nanozymes peroxidase. At the same time, it was found that modifying the level of AuNCs nanozymes with heparin not only enhanced the activity of peroxidase in physiological pH, but also decreased the LOD of heparinase to 0.06 μg/mL with a range of 0.1 to 3 μg/mL [39]. However, a group of compounds can reduce the catalytic properties of AuNPs. For example, McVey, et al. [40] demonstrated that modifying the level of AuNPs by casein protein, reduced the peroxidase activity of AuNPs down to 77.1% (Fig. 2C). Thus, modifying the surface of AuNPs with various coatings like a protein, enhanced the catalytic activities as well as regulated the type and range of catalytic activity.

2.4. Composition and hybrid nanomaterials

The catalytic activity of AuNPs, in addition to the size and surface of the NPs, is significantly increased by changing the ratio of the components in the nanomaterials [41]. The combination of two or more nanomaterials to adjust catalytic activity relative to surface modification by other compounds is very economical [42]. In this regard, it was determined that Au-Pt alloy as core-shell NPs could improve the activity of Au nanorod oxidase [33, 43]. Analogously, Wu, et al. [44] showed that by increasing the ratio of Pt to Au it could be possible to improve the SERS activities of Au-Pt NPs in addition to increasing their catalytic properties. Likewise, Dehghani, et al. [45] revealed that modifying the surface of AuNPs with Pt (Au/Pt NCs) not only enhanced the activity of their peroxidase compared to bare Au nanozyme in detection of lead (Pb) in milk, but also increased the LOD to 16 nM with detection range 25 nM to 1 μM. Recently, it was found that the modification of the AuNP composition with CuO not only resulted in nanozymes stability of up to 2 months, but also enhanced the activity of the Au-Cu nanozymes oxidase [46]. Because of the fact that nanocomposites exhibit a good performance in biological activities, researchers have applied this composite structure to control catalytic activity of nanozymes. For instance, the Fe_3O_4-Au alloy exhibits better peroxidase activity compared to bare Fe_3O_4 and AuNPs, due to the change in the specific structure resulting from the accumulation of Fe_3O_4 and AuNPs [47]. Moreover, Tao, et al. [48] with the design of Au clusters-GO nanocomposites, were able to maintain the catalytic activities of Au nanozymes in a wide range of pH compared to natural peroxidase. Whereas, it has been determined that pH changes of the environment can greatly limit the activity of the Au nanozyme peroxidases [33]. It has also been shown that Au-Pt alloy exhibits higher levels of peroxidase activity compared to AuNPs and Pt NPs [49]. In addition, in this research, He, Han, Jia, Cai, Zhou and Zheng [49] revealed that the changing the

Au/Pt ratio is highly effective in the catalytic activity of nanozymes, and with increasing the amount of Pt NPs, its catalytic level is also improved (Fig. 2D). Besides, Ma, et al. [50] showed that increasing the peroxidase activity of molybdenum disulfide-Au nanocomposites is due to the increase in the large surface of nanozymes and the synergistic catalytic effect of molybdenum disulfide and AuNPs.

2.5. Other factors

Similar to the activity of natural enzymes, the activity of nanozymes, in particular Au nanozymes, also depends on the pH of the environment, temperature and presence of ions [23, 33, 41, 51]. In this regard, Li, Liu, Wu and Gao [33] revealed that Au nanozymes exhibit oxidative-like activities under acidic conditions and, in basic conditions, peroxidase-like activities. Likewise, it was determined that a change in the pH of the environment could change the catalytic activities of AuNPs, and the optimum activity of oxidase occurs at pH of 6 [52]. Various studies have shown that the oxidase-like activity of Au nanozymes is prominent in the neutral and basic state, whereas, their peroxidase-like activity is leading in poorly acidic conditions [35, 53, 54]. In addition, Xu, Bing, Wang, Ren and Qu [52] showed that increasing or decreasing temperatures from the optimum point (61 ºC) reduces the catalytic activity of Au nanozymes. On the other hand, the temperature, the pH of the environment and the ions around Au nanozymes can further inhibit or increase their activity. For instance, Long, et al. [55] described that Hg^{2+} could enhance peroxidase-like activity of Au nanozymes coated with citrate. Likewise, it was determined that Pb^{2+} and Hg^{2+} in the presence of bismuth (Bi^{3+}) ion and Pt^{4+} increase the peroxidase-like activity of the Au nanozymes [56]. In this line, Han, Choi and Kwon

[23] have been able to detect Hg^{2+} in water by changing the peroxidase-like activity of Au nanozymes due to the high tendency of reduced metal on the surface of Au.

3. Enzymatic activities by gold-nanozymes

As shown, AuNPs provide a distinguished catalytic activity concerning the size, shape and distribution effects. AuNPs Also possess a high extinction coefficient and strong SPR [57]. The unique optical features of AuNPs have also been addressed as a potential sensitive detection system as well as catalytic activity. These properties can be coupled with enzyme assays and/or with metal deposition for signal amplification called nanozyme. Nanozymes have shown great interest owing to the potential of easy fabrication, simple, and cost-effective production and detection. However, artificial nanozymes are applicable to passivate in complex biotechnological and medical areas (e.g., serum), which may destroy the catalytic activity and consequently reduce the application in biosciences analysis. For this purpose, despite the large catalytic activity of AuNPs coated with monolayer organic compounds such as nuclease [58] and esterase [59], in order to reduce possible disturbances in the occurrence of the enzymatic activity of bare AuNPs, their catalytic activity was classified into 4 general categories including oxidase, peroxidase, SOD and CAT. Some catalytic activity of AuNPs coupled with enzyme assays, were summarized in Table 1.

3.1. Oxidase mimic

Similar to the activity of natural enzymes, NPs can catalyze the conversion of analytes to oxidized compounds. Today, due to the importance of oxidase reaction in biosensors, pharmaceutical compounds, food, chemotherapy, and biotechnology a wide range of attentions have been devoted to this subject [41, 60, 61]. Despite the well-known oxidase activity of metals,

unexpectedly, Comotti, et al. [62] discovered that bare AuNPs could oxidize glucose with O_2 and lead to the formation of gluconic acid and H_2O_2. Subsequent studies have confirmed the oxidase-like activity of Au nanozymes, based on the mechanism of generating a negative charged AuNPs by glucose [63-65]. In this line, Li, et al. [66] monitored the glucose oxidation reaction using plasmonic imaging techniques (Fig. 3A). It has also been shown in this study that with decreasing the size of AuNPs, the catalytic activity also increases. However, due to the instability of AuNPs, the catalytic activity of Au nanozymes is extremely short [54]. Therefore, the use of Au nanozymes in the oxidase activity depends on the preparation of NPs by stabilizers.

3.2. Peroxidase mimic

Peroxides (especially HRP and cytochrome C peroxidase) are enzymes that generically catalyze the oxidation product with peroxide. For the first time in 2007, it was found that Fe_3O_4 NPs, show peroxidase-like activity [4]. The catalytic mechanism is based on the peroxide bonding on the surface of Au nanozymes and the formation of two hydroxyl radicals [67]. Radicals produced by AuNPs are stabilized through a sectorial electron exchange interaction, which could also contribute to the catalytic capability of Au nanozymes. In this regard, AuNPs with a positive or negative charge easily show peroxidase-like activity (Fig. 3B) [68]. By modifying the surface of the AuNPs, their peroxidase activity can be altered by controlling their surface dependence on the substrate [61].

3.3. Superoxide dismutase mimic

Metal nanozymes such as Fe, Pt, and Au similar to those of natural enzymes eliminate $O_2^{\bullet-}$ by the dismutation of $O_2^{\bullet-}$ to H_2O_2 and O_2 [69]. Some nanozymes can eliminate not only $O_2^{\bullet-}$, but also other free radicals to protect the ROS-associated inflammation and damage. However, He, et al. [70] exhibited that the dismutase activity of AuNPs in physiological pH can easily destroy $O_2^{\bullet-}$ (Fig. 3C), while, their SOD-like catalytic activity in acidic conditions is reduced [71].

3.4. Catalase mimic

Generally, CAT can break down H_2O_2 into water and oxygen. Several NPs can provide a similar activity to CAT, which results have shown that Pt and Pd demonstrate CAT activity better than Au and Ag (Fig. 3D) [33]. Also, similar with SOD-like activity, the CAT-like activity of Au and Pt nanozymes increases in alkaline conditions and decreases with the acidic condition [51].

4. Significance of Au nanozymes in mitigating oxidative stress

ROS results in the induction of oxidative stress and subsequent pathogenesis of many hallmark disorders. Therefore, using nanozymes with outstanding enzyme-like activity against oxidative stress can be considered as a useful replacement of native enzymes. Wang, et al. [72] reported a simple and unique route for fabricating activity-adjustable nanozymes (Fig. 4A). They used the light-driven isomerization of azobenzene (Azo) and host–guest reaction to control the function of nanozyme by irradiation. AuNP as a representative CAT -mimic nanozyme were encapsulated and dispersed with Azo-modified mesoporous silica combined with cyclodextrin (CD) as an inhibitor [72]. The data showed that the Au nanozyme could reversibly control ROS production for several cycles and reduce the cell mortality [72].

In biological media, multienzyme systems play vital roles in catalyzing crucial processes of key metabolic reactions such as oxidative phosphorylation and protein synthesis. It is well documented that metabolic reactions associated with multienzyme systems provide a number of positive points over processes catalyzed by individual catalyzers. A promising nanozyme representing multienzyme like features has evaded the scientists in the nanoscience group for several years. In the recent year, some functional multienzyme in terms of AuNPs has been designing. For example, Bhagat, et al. [73] reported that Au (core)-CeO_2 (shell) NPs (Au/CeO_2 CSNPs) working as an exceptional multienzyme complex that are manipulated easily by varying the pH of the medium (Fig. 4B). The kinetic parameters indicated that the peroxidase-like activity of Au/CeO_2 CSNPs is close to natural HRP. Dissimilar to peroxidase-like activity revealed by other NPs, Au/CeO_2 CSNPs demonstrated a reduction in OH^o generation, indicating that the biocatalytic processes are carried out by potential electron transfers. An excellent enzyme-like function of Au/CeO_2 CSNPs was preserved over a pH range and temperatures, understandably proposing the advantage over natural enzymes [73]. Furthermore, Dashtestani, et al. [74] reported that riApoferritin-Au-Ag nanoconjugate (Au-Ag-AFT) as a nanozyme could show significant antioxidant activity (Fig. 4C). They showed that Au-Ag-AFT nanohybrid have remarkable SOD, CAT and peroxidase-like activities. With corresponding k_{cat} values of 1.4×10^{6}, 1×10^{-1} and $9\times10^{3}s^{-1}$, respectively, indicating that Au-Ag-AFT nanozyme can serve as a potential ROS scavenger. Moreover, they showed that Au-Ag-AFT nanozyme provided a protective effect against oxidative stress human sperm [74].

5. Conclusion and challenges

In this article, we reviewed the enzymatic activity of Au nanozymes along with their regulatory and control mechanisms, the effect of various factors such as dimension, morphology, functionalization and presence of hybrid materials on the catalytic activity of Au nanozymes, as well as their oxidase, peroxidase, SOD, and CAT-like activities. The review indicated that physicochemical properties of AuNPs can influence their catalytic activity. The utility of oxidase, peroxidase, SOD, and CAT-like activities of AuNPs can be exploited for mitigating the oxidative stress induced by ROS. Also, it was revealed that multi-enzyme complexes give more interesting data regarding catalyzing crucial processes like antioxidant reaction relative to reaction accelerated by individual nanozymes. Although it was determined that AuNPs as nanozyme have important advantages over natural enzymes as well as other synthetic enzymes, they are still confronted with limitations. These restrictions will be vital for use in biomedical activities. For example, despite the controlling the physicochemical and optoelectronic properties of AuNPs based on size, shape, composition, and surface modification using target ligands are often encountered by loss of catalytic activity or the presence of uncontrolled activity in medical and biological activities [75, 76]. For this purpose, some researchers have focused on preventing the active positions of Au nanozymes and releasing some of them for catalytic activities [77, 78]. Also, in order to prevent the removal of enzymatic activity of AuNPs, the use of coatings and multi-agent linker dependent on environmental conditions, such as pH and heat, is recommended and implemented [79]. The next major challenge in the use of Au nanozymes is the lack of catalytic efficiency similar to that of natural enzymes, in which the use of auxiliary compounds on the surface of AuNPs as hot-spots can appropriately reduce this drawback. In addition, in biological processes, natural enzymes have higher and more selectable power than Au nanozymes because of their specificity. While in this paper, it was shown that AuNPs with

peroxidase-like activities can be used to detect glucose. Further, the lack of uniformity in the shape and size of AuNPs produced in the industrial sector, and even the possibility of their changes during the implementation in biological activities, has caused their physical and chemical properties to be constantly fluctuated even with minimal variations. Ultimately, the toxicity/cytotoxicity of AuNPs in biotechnology and biomedical applications should be vigorously addressed which is still confronted with many uncertainties. Despite the use of a variety of polymers and proteins coatings to reduce the toxicity/cytotoxicity of Au nanozymes, many of them are still unlikely to be used due to unknown hazards. Therefore, critical efforts to investigate the possible changes in the activity of AuNPs will be critical.

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Conflict of interest

The authors declare no conflict of interest

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491 **Table 1.** Some catalytic activity of AuNPs as nanozyme

Nanozyme	catalytic activity	Ref.
Chiral Nanozymes-AuNP	Nanozymes-based transphosphorylation catalysts capable of enantiomeric discrimination	[80]
Amphiphilic protein/AuNP hybrid	Peroxidase-like activity and Ag-mediated inhibition	[81]
Palladium-Au	Excellent peroxidase mimetic activity with O-phenylenediamine in the presence of hydrogen peroxide	[82]
Triazacyclonane-functionalized thiols – AuNP/ ZnII	Cleavage of phosphate esters	[83]
β-cyclodextrin-modified AuNP	Esterase mimic.	[84]
AuNP	Intrinsic peroxidase-like activity	[85]
AuNP	Glucose oxidation	[62, 86]
Bismuth–AuNP	Peroxidase-like activity	[87]
Unmodified, Amino-Modified, and Citrate-Capped AuNP	Peroxidase-like activity	[68]
55-atom Au clusters	Selective oxidation of styrene by dioxygen	[88]
Polymer-Stabilized Au Nanoclusters	Aerobic Alcohol Oxidation in Water	[89]
Mesoporous Silica-Supported AuNPs	Intrinsic oxidase and peroxidase catalytic activities	[90]
AuNP	Enhancing the catalytic activity of manganese oxides	[91]
AuNP	Reduction of 4-nitrophenol to 4-aminophenol by excess $NaBH_4$	[92]
Zone-activated Ag- Au alloys	Selective alcohol oxidation	[93]
Fe_2O_3@AuNP anchored nitrogen	Methanol oxidation	[94]
AuNPs supported on Fe_2O_3	Co oxidation	[95]
AuNP	4-nitrophenol into 4-aminophenol	[96]
Bio-organic AuNP	Degradation of the organic pollutants, Methylene blue, Methyl orange, Eosin yellowish and 4-Nitrophenol.	[97]
AuNP/GO nanocomposite	Oxygen reduction reaction	[98]
Biosynthesized AuNP	Reduction of 4-nitrophenol	[99]
Biosynthesized AuNP	Dye reductions	[100]
AuNP	Reduction of 4-nitrophenol	[101]
Biosynthesized AuNP	Reduction of 3-nitrophenol	[102]

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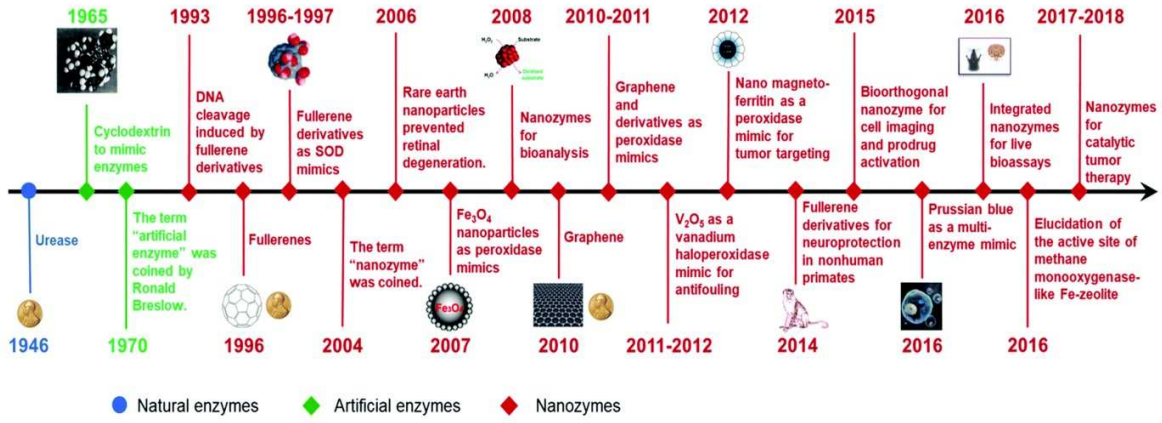

Figure 1. A brief timeline for the development of artificial enzymes (natural enzymes are also listed for comparison). Reproduced with permission from Ref. [41].

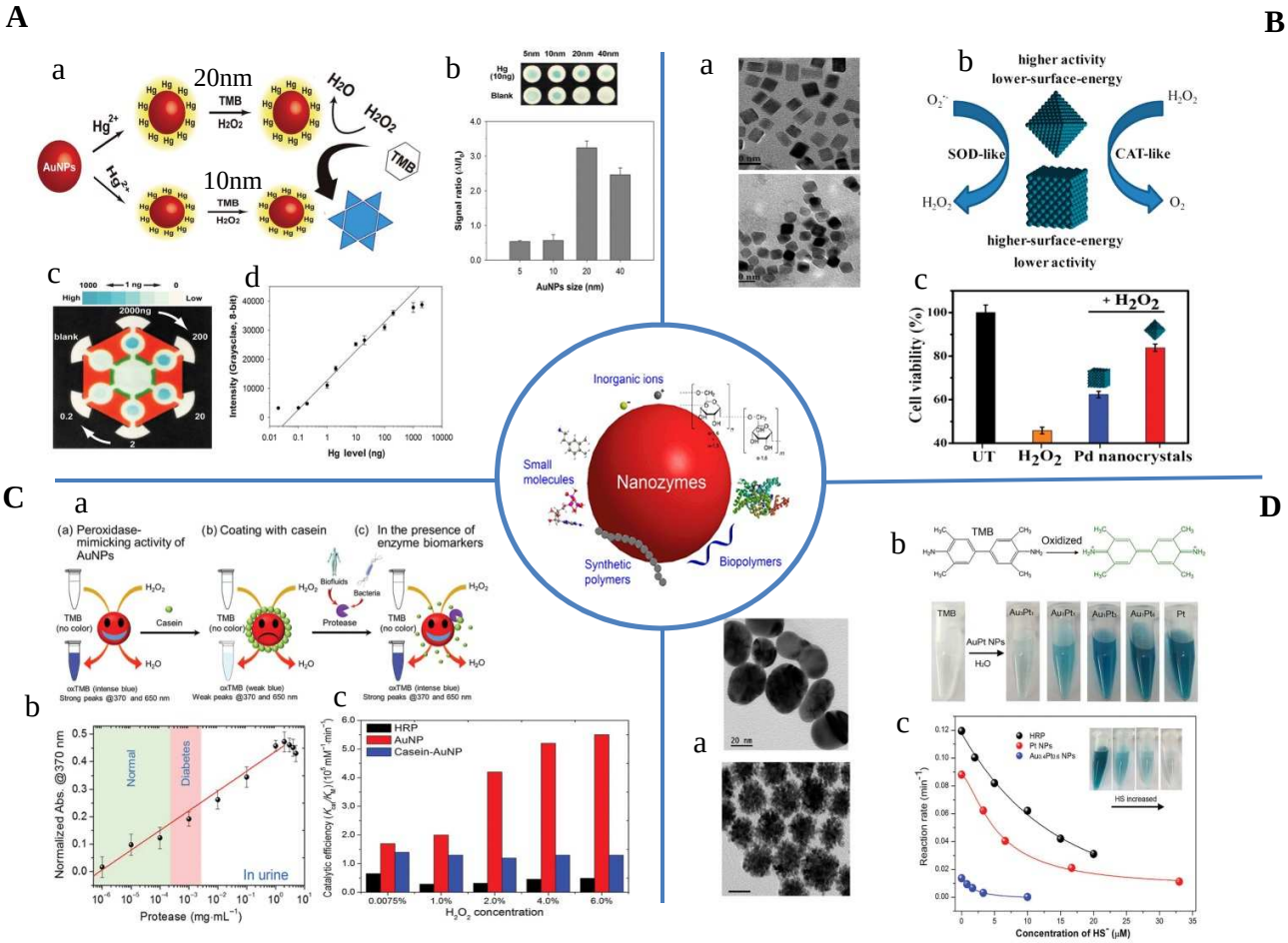

Figure 2. Tuning AuNPs for catalytic activities. **(A)** Effect of size on catalytic activity AuNPs, (a): Schematic illustration of the AuNZ-PAD colorimetric sensing mechanism for Hg^{2+} ions based on the Hg-promoted nanozyme activity of AuNPs, (b): effect of the size of AuNPs, on the colorimetric response in the absence and presence of Hg^{2+} ions, (c): photographic image of an AuNZ-PAD used to simultaneously test samples with Hg levels ranging from 0.2 to 2000 ng, (d): calibration plot of colorimetric responses for Hg levels in the range of 0.02–2000 ng [32]. **(B)** Influence of NP shape on catalytic activity, (a): TEM images of NPs, (b): schematic image of the enzymatic activity changes during NP deformation, (c): the quantification of oxygen production from superoxide turnover by Pd nanocrystals [34]. **(C)** Peroxidase-mimicking AuNPs coated by casein, (a): overall scheme demonstrating the switching of peroxidase-mimicking activity of casein coated AuNPs for the detection of enzyme biomarkers, (b): relationship between normalized absorbance at 370 nm and increasing protease concentration spiked into urine (R^2 = 0.97), demonstrating potential applications of the biosensor in food safety analysis and clinical and veterinary diagnosis of bacterial infections, (c): comparison of catalytic efficiency of HRP, uncoated AuNPs and casein-AuNPs [40]. **(D)** CAT-like activities of Au (a): TEM images of pure AuNPs (top) and AuPt bimetallic nanostructures (down), (b): color evolution of TMB oxidation in the absence of H_2O_2 catalyzed by different NPs, (c): concentration dependent effect of HS^- on inhibiting the activities of enzyme HRP, and Pt or $Au_{0.4}Pt_{0.6}$ alloy NPs [49]. Reproduced with permission from Ref. [32, 34, 40, 49]

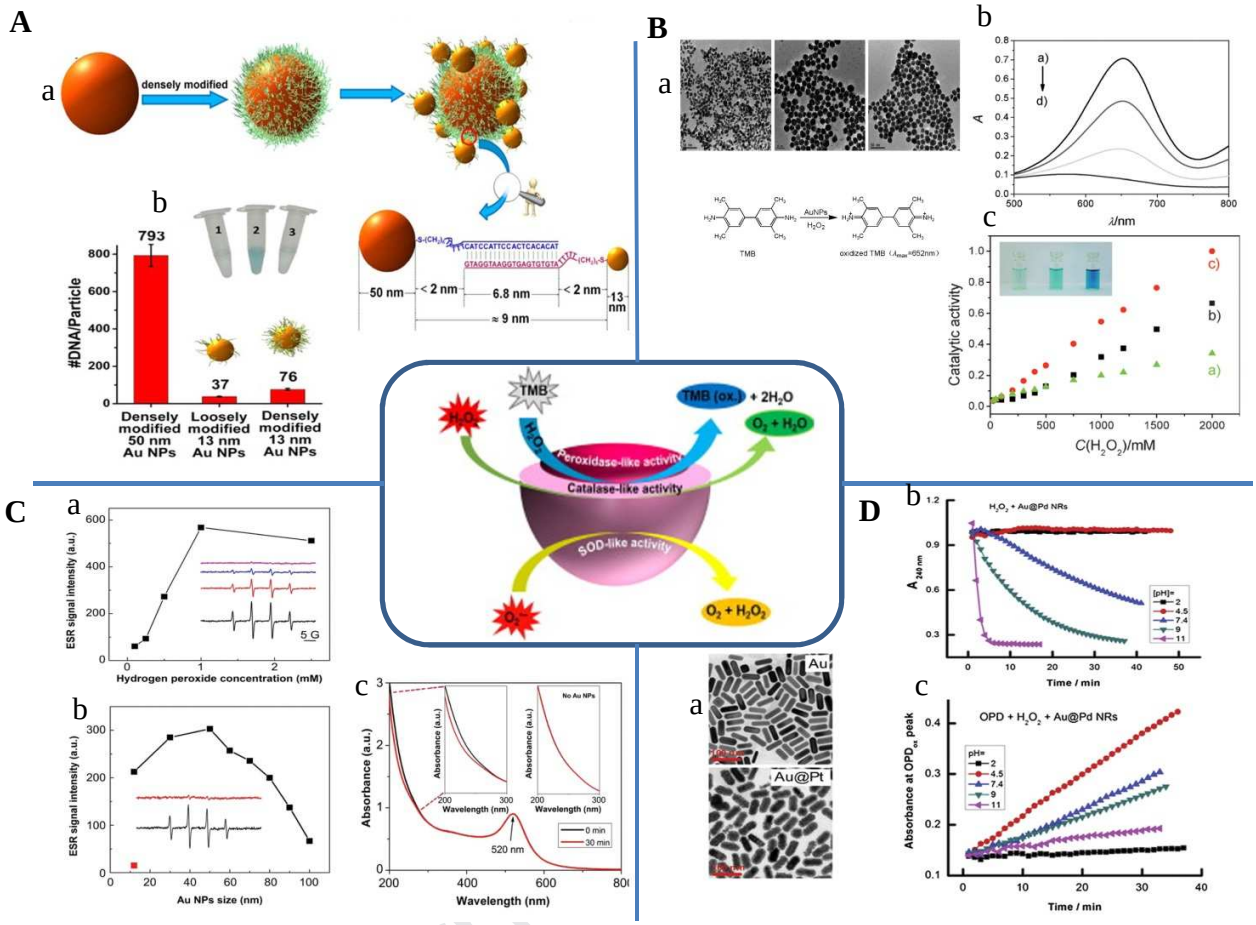

Figure 3. Enzymatic activity by AuNPs. (A) Au nanohalo for catalysis, (a): synthetic scheme for the preparation of Au nanohalo through the self-assembly of AuNPs of different diameters modified with complementary oligonucleotides, (b): number of oligonucleotides per particle of different kinds of L- and S-AuNPs. Inset shows the colored product catalyzed by L- and S-AuNPs that loaded different amounts of oligonucleotides, respectively, as tested by a HRP-cascaded colorimetric reaction [66]. **(B)** Au core/ceria shell-based redox active nanozyme mimicking, (a): TEM images of unmodified (left), amino-modified (middle), and citrate-capped (right) AuNPs, (b): influence of citrate ions on the peroxidase-like activity of unmodified AuNPs; concentration of sodium citrate: a) 0, b) 0.5, c) 0.75, d) 1.25 mm (c): comparison of the peroxidase-like activity of (a) amino-modified, (b) citrate-capped, and (c) unmodified AuNPs toward TMB as peroxidase substrate [68]. **(C)** Intrinsic catalytic activity of AuNPs with respect to H_2O_2, (a): effect of H_2O_2 concentration on the generation of OH induced by AuNPs, (b): effect of AuNPs size on the generation of hydroxyl radicals induced by AuNPs (Conditions: 50 mM DMPO, 1.0 mM H_2O_2, 10 mM pH 1.2 buffer 0.1 mg/mL PVP coated AuNPs having different sizes), the red square dot represents the control and inset shows the ESR spectra obtained in absence and presence of 0.1 mg/mL PVP coated AuNPs (10 nm), (c): UV-vis spectra of AuNPs in the presence of 10 mM H_2O_2 at pH 1.2 before and after 30 min reaction. Insets show the absorption in 200-300 nm range in the presence and absence of AuNPs [70]. **(D)** CAT-like activities of Au (a): TEM images of the NRs, (b): 20 mM H_2O_2, 0.4 mM OPD and for CAT with 20 mm H_2O_2, (c): 20 mM H_2O_2 0.4 mM OPD and for CAT [33]. Reproduced with permission from Ref. [33, 66, 68, 70]

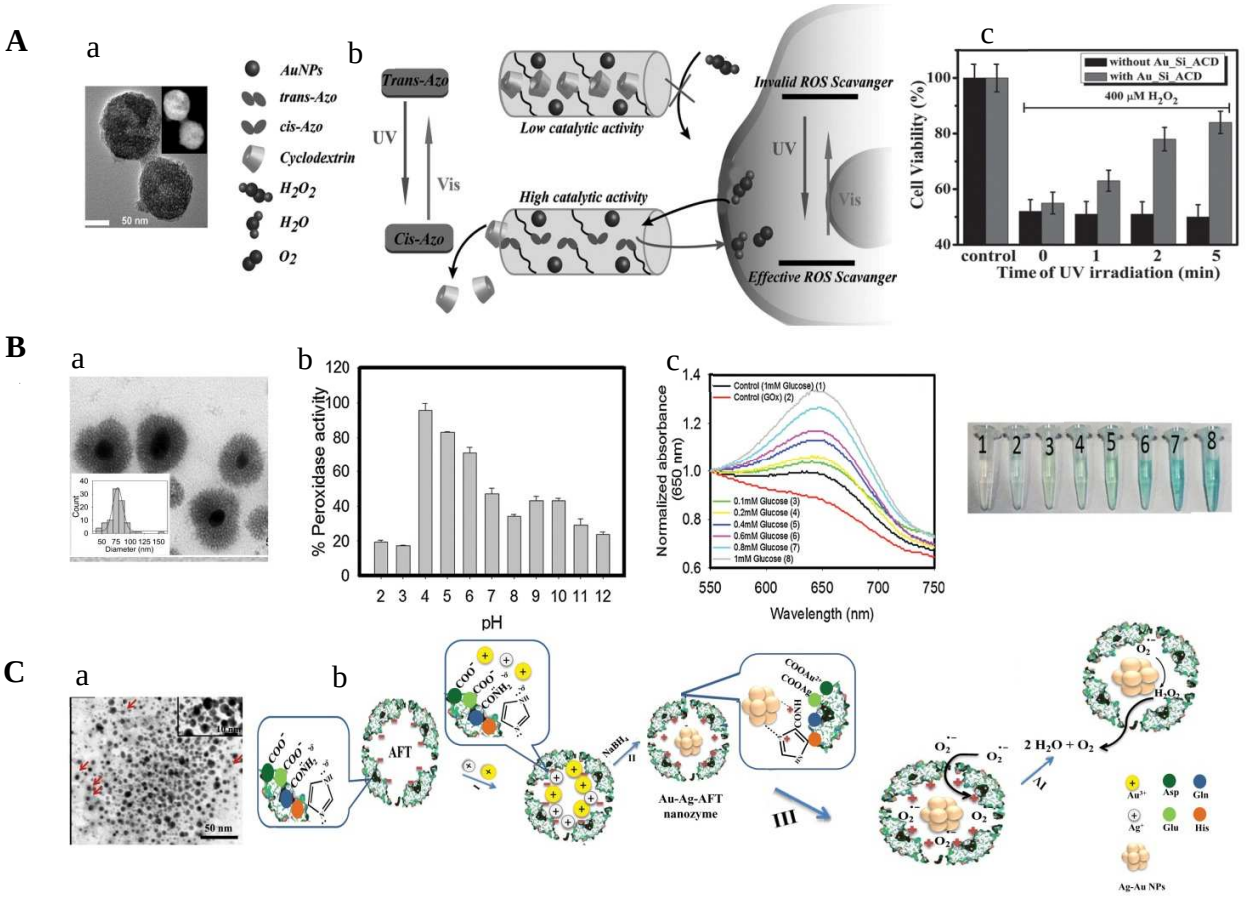

Figure 4. **Oxidative stress. (A)** Light-mediated reversible modulation of ROS level, (a): TEM images of Au_Si_ACD, (b): the UV and visible light reversibly regulate the catalytic activity of Au_Si_ACD by using the *trans–cis* photoisomerization of Azo molecules to control the host–guest interaction between Azo and CD. The new nanozyme can act as a controllable ROS scavenger in cells with different catalytic activity, (c): the changes of the ROS level in MCF-7 cells along with the different irradiation time under the condition of exogenous [72]. **(B)** Au core/ceria shell-based redox active nanozyme mimicking, (a): average particle size distribution, (b): peroxidase-like activity monitoring by change of pH, (c): detection of different concentrations of glucose using the peroxidase-like activity of Au/CeO_2 NPs. Inset tubes 3, 4, 5, 6, 7 and 8 respectively represent the color of oxidized TMB generated in presence of different glucose concentration (0, 0.1, 0.2, 0.4, 0.6, 0.8, 1 mM) and TMB and H_2O_2 and GOD. Tube 1 and 2 contain only glucose and GOD, respectively in similar reaction conditions as above [73]. **(C)** Ag-Au-apoferritin nanozyme, (a): TEM images of Au-Ag-AFT nanozyme, (b): the illustration for the synthesis of Au-Ag-AFT nanozyme and its triple-enzyme like activity for $O2^{\bullet-}$ scavenging and H_2O_2 reduction. (I) Electrostatic absorption of cations by negative charge residues in AFT active site, (II) formation of nanozyme via reduction of metallic cations to NPs or changing the charges in active site to positive, (III) electrostatic absorption of superoxide negative ions by positive charges in nanozyme active site, (IV) Functions of nanozyme [74]. Reproduced with permission [72-74]

Highlights

- Antioxidant-like activities of Au nanozymes
- Oxidase-like activity of Au nanozymes
- Peroxidase-like activity of Au nanozymes
- Superoxide dismutase-like activity of Au nanozymes
- Catalase-like activity of Au nanozymes

Conflict of interest

The authors declare no conflict of interest