1D Ceria Nanomaterials: Versatile Synthesis and Bio-application

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Ceria has emerged as a fascinating and lucrative material in bio-application, for instance, disease treatment, bioimaging and drug delivery due to its abilities of transforming oxidation states between Ce3+ and Ce4+ and scavenging free radicals, which can produce biological effect, such as being potentially antioxidant towards reactive oxygen species. Recently, many studies about one dimension (1D) CeO2 nanomaterials have received much attention because of the unique properties of their length and aspect ratio. We highlight here current research activities focused on the bio-application of 1D ceria nanomaterials. The synthesis methods of 1D cerium oxide nanomaterials were introduced. Several synthesis routes, including template, hydrothermal, sonochemical and other methods, were then discussed with examples developed by recent research. The differences among these methods were also analyzed. This review provides a comprehensive introduction to the synthesis of 1D ceria, its potential applications in biological fields and perspectives on this exciting realm.

1. Introduction

Ceria nanomaterials are one of the most widely used materials as catalysts and supports, and have been paid much attention to be employed in fuel cells [1–3], optical films [4], polishing materials [5], gas sensors [6] and biological antioxidants [7], because of the nature of the 4f orbits, which are “buried” inside the atom and are shielded from the atom’s environment by the 4d and 5p electrons [8,9]. Ce exists in two oxidation states: Ce3+ (electronic configuration: [Xe] 4f1) and Ce4+ (electronic configuration: [Xe]) [10]. The ability of ceria nanomaterials to exhibit free radical scavenging activity by reversibly binding oxygen and shifting between the Ce3+ and Ce4+ formed at the nanomaterial surface can make it act as an antioxidant in bio-application. Especially ceria nanomaterials can be used to cure some diseases induced by the reactive oxygen species (ROS) [11–13].

Ever since Mattson et al. [14] reported the first application of carbon nanotube technology to neuroscience research, the bio-application of one dimension (1D) nanomaterials has attracted widespread attention. Many studies on 1D nanomaterials, such as nanorods, nanotubes, and nanowires, are mainly focused on their length and aspect ratio in biological reactivity. Longer 1D nanomaterials tending to bundle together, contact with the cellular surface easily or even pierce the surface membrane [15,16]. 1D CeO2 nanomaterials with finely tuned aspect ratios are frequently inert at biological level, or even may act as an antioxidant [6,17–19]. It allows an appropriate comparison in toxicity upon the change in its length and aspect ratio. So it is necessary to assess the safety of 1D CeO2 nanomaterials and understand their behavior in biological systems when 1D CeO2 nanomaterials act as the commercial products [15].

Due to their unique application, well-defined 1D ceria nanostructures with various morphologies such as nanorods, nanowires, nanotubes, etc., have been successfully fabricated by a variety of methods [20–26]. In this perspective, our review provides a brief summary of the synthesis methods of 1D cerium oxide nanomaterials including template method, hydrothermal method, sonochemical method and other methods. Among these reported approaches, templating strategies hold a well-defined size, shape and configuration, which usually benefit from the directing effect of the templates [27]. Additionally, the hydrothermal approach has attracted significant interest on preparing nanostructure with controllable morphology due to its unique advantages. What’s more, the sonochemical synthesis has been proved to be a useful method to obtain novel materials and prepare materials with novel morphologies. Then, there is a particular focus to amplify bio-

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application of 1D cerium oxide nanomaterials. Recently, CeO2 has been reported to have multi-enzyme, including superoxide oxidase, catalase and oxidase, mimetic properties, and has emerged as a fascinating material in biological fields[28–32]. This review provides a comprehensive introduction to potential application in biological fields, and the recent studies of 1D CeO2 is highlighted. Finally, a near future is prospected briefly in this article.

2. Synthesis of 1D Ceria Nanomaterials

1D ceria nanomaterial research has focused on the physical treatment, based on the controlling of the reaction time, temperature, pressure etc. In this perspective, the preparation of ceria nanomaterials generally divides into four basic steps: synthesis of precursors, treatment of precursors before conversion to oxides, conversion of precursors to mixed oxides, and post treatment of mixed oxide material. Through these steps, there are many preparation methods of 1D cerium oxide nanomaterials which have been reported, such as hydrothermal method, template method, gas phase method, etc[33,34].

2.1. Template method

Template synthesis is derived from the host-guest chemistry. The inner structure of the host molecular or material has an ability to form 1D spatial structure, and while the growth of the guest molecular or material in this structure would be 1D nanomaterial. The general route for templated synthesis of nanostructured materials includes the following steps: (1) template preparation, (2) direct synthesis of target materials using the template, and (3) template removal[27]. Template methods have attracted enormous attention in preparing 1D inorganic nanomaterials in recent years due to the formation of 1D inorganic nanomaterials array. There are two kinds of techniques about template methods: one is soft-template techniques, the other is hard-template techniques.

2.1.1. Soft-template technique

Surfactant plays an effective role in the preparation of 1D nanophase compounds and has been adversely observed in the past decades[34,39]. The surfactant or anion is commonly used as templates, which can induce self-assembly of 1D nanomaterials. Mitsunori and his coworkers[36] described the synthesis of rare earth oxide nanotubes templated by dodecylsulfate assemblies, realized by homogeneous precipitation with urea and their conversion into a hollow nanotube with an inner diameter of 3 nm after anionic exchange of the surfactant with acetate ions. Yang and his coworkers[37] used a simple method to synthesize single crystal cubic CeO2 nanowires employing octadecylamine (C18H37NH2) as the structure-directing agent, nitrate cerium as the cerium source, and ammonia as the precipitating agent. The octadecyl ammonium cations (C18H37NH+3) in aqueous solution could form claviform micelles by self-assembly. The cerium hydroxide, which combined by the hydrated Ce4+ ions with H2O molecules or OH– ions[38], polymerized at the micelles—solution interface and formed the nanowire structure cluster. During this process, they grew into the linear structure and finally had lengths up to several hundreds of nanometers and diameters ranging between 10 and 25 nm, the length of the nanowire after 8 h reaction is presented in Fig. 1(c). Aurelien and his coworkers[35] used cationic surfactant cetyltrimethylammonium bromide (CTMABr) to direct the growth and aggregation of crystallizing nanostructures in order to obtain single crystalline and uniform CeO2 nanorods with quite thin diameters of 10–25 nm. In order to investigate the role of the surfactant CTMABr in the formation of nanorod, the preparation of CeO2 particles without CTMABr was also carried out. In this experiment, not rod-shaped but granular particles closely packed together were observed. In conclusion, the synthesis was performed at a low content of surfactant, in which only a small quantity of nanorods with a shorter length were obtained.

Pan et al[39] also synthesized the CeO2 nanoplates by hydrothermal reaction with CTAB and then controlled the conversion of nanorods into nanotubes and nanorods by changing CTAB/Ce3+ ratio, reaction time, temperature, and ammonia solution. In their experiment, higher temperature and higher concentration of CTAB as a surfactant were controlled by the synthesis of Ce nanotubes (Ce-NT) in two step procedure. In the first step, a higher concentration of the CTAB led to the increase in the absorption force between the CTA+ and Ce3+/4+ ion pairs and accelerate the formation of lamellar sheet. In the second step, Ce-NT formed by rolling up the lamellar sheets. In addition, the lower concentration of CTAB can

Fig. 1. (a) Possible formation mechanism of CeO2 nanorods[34] (Copyright 2007, American Chemical Society). (b) HRTEM images of the cubic ceria nanowires calcined at air-dried temperature; (c) TEM image of the sample obtained at a molar ratio of 1.0 Ce(NO3)3·10H2O:2.0 C38H72NH2· 40.0 NH4OH with 8 h growth period[38] (Copyright 2005, Springer). (d) Possible formation mechanism of CeO2 nanostructures[39] (Copyright 2008, Elsevier).
lead to the formation of cubic plate-like structure, where reaction temperature and time control the conversion of the cubic plate-like structure to nanoplate, hexagon, and nanorod, respectively (Fig. 1(d)). Vantomme et al.[23] and Yan et al.[40] carried out the preparation of the ceria nanowires with easily available CTAB by precipitation method. Furthermore, Zhang et al.[34] prepared 1D ceria nanorods at room temperature in one step process through polyethylene glycol (PEG) surfactant and alkali solution. They confirmed that vigorous agitation without ultrasound at various temperatures (25, 40, and 60 °C) would form only nanoparticles as the sole products, even with a longer reaction time. Concentration of the surfactant (e.g. PEG or CTAB) significantly affects the formation of 1D nanostructure because the transformation from one structure to the next is caused by intermolecular interactions between surfactant monomers. Fig. 1(a) shows the formation of the CeO2 nanorods. PEG was weakly absorbed onto the surfaces of CeO2 nanocrystals and could play the bridge-linking role since PEG has a linear structure and multiple coordinating sites. And with the high velocity of liquid jets, the chance of collision between two PEG-absorbed nanoparticles increased so that more nanocrystals fused in an oriented manner, and then CeO2 nanorods formed.

2.1.2. Hard-template technique

The ordered CeO2 nanowire arrays were fabricated in anodic alumina membranes (AAM), which is also a novel technique. La et al.[20] and Wu et al.[41] fabricated CeO2 nanowires with a diameter of 60–70 nm using AAM as templates. Anions and cations conversely migrated into the hexagonally ordered nanochannel so that AAM and reacted inside the channels to form 1D nanostructures. In Fig. 2(a), the TEM images show that the diameter of CeO2 nanowires with smooth surface is about 60 nm, which is approximately equal to that of the nanochannels. Wu et al.[41] indicted that traditional sol−gel templates were usually dipped into the relevant sols directly, and the only driving force of this technique is capillary action. When a higher concentration sol is filling the pores will be difficult, especially small pore diameter templates. However, low concentration leads to nanomaterials without the presence of surfactant. They observed that acidic precipitant H2O2 with 0.1 mol/L Ce(NO3)3 produces the nanowires and nanocubes, whereas only nanowires with diameters of 20–70 nm and lengths up to 40 μm formed in the presence of lower concentration of the precursor (0.05 M Ce(NO3)3) at 250 °C for 3 h. Furthermore, aggregated nanoneedles have been formed without the oxidizing agent H2O2 and thus acted as a template agent in this experiment. The interplane distance in this research material[42–46]. Carbon nanotube (CNT) as a template plays a significant role in the formation of 1D ceria nanostructures. It was reported that the surface of the template was covered with ceria nanomaterials and possessed Ce-NT whose formation depended on a homogeneous and continuous layer of ceria nanoparticles on CNTs in the presence of pyridine. It should be noted that it is impossible to fabricate Ce-NT if the pyridine is replaced by dimethyl formamide (DMF). In addition, higher-temperature treatment was carried out for the removal of the templates[39,45,47,48]. Yu et al.[49] synthesized Ce-NT through an AAM template.

Metal ion doping is a promising technique to control the properties of material. Laha and Ryoo[50] prepared the mesoporous cerium oxide using the hexagonal p6mm and cubic Ia3d symmetries of the silica templates. Later on, Shen et al.[51] used the similar types of ordered mesoporous silica KIT-6 as a hard template for the formation of mesoporous ceria oxide and doped CuO structure by wet impregnation technique.

2.2. Solvothermal/hydrothermal method

The hydrothermal treatment in highly alkaline condition is the method that provide highly anisotropic cerium oxide nanomaterial[52]. In the hydrothermal method, water is used as not only the solvent but also the mineralizer, which is a chemical constituent to enter into a reaction in order to fabricate the various morphologies. Li and his coworkers[53] reported the synthesis of lanthanide hydroxide nanowires (La(OH)3, Pr(OH)3, Nd(OH)3, Sm(OH)3, Eu(OH)3, Gd(OH)3, Dy(OH)3, Tb(OH)3, Ho(OH)3, Er(OH)3, and Yb(OH)3) through a facile solution-based hydrothermal synthetic pathway. The synthesis of Ln(OH)3 nanowires was based on the preparation of colloidal Ln(OH)3 at room temperature, with subsequent hydrothermal treatment at 180 °C for about 12 h. This study is the basic foundation of the preparation of 1D rare earth nanomaterial using hydrothermal method.

Tang et al.[54] simply used the hydrothermal method to achieve nanowires without the presence of surfactant. They observed that acidic precipitant H2O2 with 0.1 mol/L Ce(NO3)3 produces the nanowires and nanocubes, whereas only nanowires with diameters of 20–70 nm and lengths up to 40 μm formed in the presence of lower concentration of the precursor (0.05 M Ce(NO3)3) at 250 °C for 3 h. Furthermore, aggregated nanoneedles have been formed without the oxidizing agent H2O2 and thus acted as a template agent in this experiment. The interplane distance in this research.
was 0.28 nm, corresponding to the (200) lattice planes of cubic CeO2. However, this method either was time-consuming or required special equipment, moreover the cavities of the obtained ceria nanotubes were quite small, and there were also a great deal of rod-like concomitant in the products (Fig. 3(a, b)). So Zhou and his coworker[55] reported a facile rational synthesis of CeO2 nanotubes with large cavities and thin walls by a simple oxidation-coordination-assisted dissolution process of the Ce(OH)3 nanotubes/nanorods. Cerium hydroxide could be synthesized by hydrothermal treatment of Ce2(SO4)3·9H2O with a 10 mol/L NaOH solution at 130 °C. The formation mechanism was explored in detail and an oxidation-coordination-assisted dissolution was involved in whole process in Fig. 3(d), where the partially oxidized Ce(OH)3 was used as the starting materials. Since most of the outer wall has been oxidized into ceria, the oxidation-coordination-assisted dissolution process was limited inside the 1D nanomaterials. Thus, the ceria nanotubes with extended cavities were formed finally.

Then, Huang et al.[21] reported Au/CeO2 nanorods with the wet chemical reducing system in the presence of NaBH4 solution as a reducing agent and also observed that hydrothermal temperatures influence the nucleation and crystal growth of the CeO2 nanorods. Because morphological transformation of the nanorods was not completed below 150 °C at 5 or 10 mol/L KOH solution, the thicker nanorod structures was only provided by higher alkaline concentration. Therefore, it would be considered that higher alkaline concentration was involved in increasing the width of the nanostructure rather than the nucleation of length of the sample. Similar to this, it was also confirmed for the formation of different shape of ceria 1D nanostructure with different concentration of alkali[56].

2.3. Sonochemical method

In the previous reports, the synthesis methods of CeO2 nanorods were relatively complicated and always needed high-temperature, high-pressure or long-time treatment[45,57–59]. In this case, ultrasound irradiation has been extensively used to generate novel material with unusual properties. Sonochemical method is based on acoustic cavitation resulting from the continuous formation, growth and implosive collapse of the bubbles in a liquid[60]. Qi and his coworkers[61] synthesized the thicker CeO2 microrod (200–250 nm in diameter and 600–1200 nm in length) by an ultrasonication process followed with a surfactant assisted hydrothermal method. Miao and his coworkers[62] reported the ultrasonic-induced synthesis of CeO2 nanotubes. During the reaction, the spherical CeO2 nanoparticles can be transformed into nanotubes in alkali aqueous solution without any templates. They successfully synthesized CeO2 nanotubes with diameters of 10–15 nm and lengths of 150–200 nm. Later on, Zhang et al.[63] reported the synthesis of the rhombic Ce(OH)CO3 nanostructure by a sonochemical method using surfactant/Ce3+ molar ratio 1:10. Finally rhombic ceria nanostructure is obtained by calcination at
500 °C in air for 0.5 h to remove the CTAB. They found that the mixture of nanoparticles, nanorods and irregular microrods can be formed below 100 °C. Therefore, reaction temperature and time also play an important role in the formation of rhombic microrods.

2.4. Other methods

Compared with a conventional hydrothermal method, the microwave-assisted hydrothermal method has a lot of benefits, such as rapidity, convenience, cost-effectiveness. Recently, Gao et al.[64] approached the microwave-hydrothermal method for the facile, rapid synthesis of higher yields of 1D CeO2 with average sizes of 1.6 nm–20 nm. After that, Riccardi et al.[58] synthesized the cerium carbonate hydroxide (orthorhombic Ce(OH)CO3) hexagonal-shaped microplates with a domestic microwave (2.45 GHz maximum power of 800 W) at 150 °C for 30 min at a fixed heating rate of 10 °C/min and then converted into ceria cubic/rhombus shape after a thermal decomposition oxidation process at 500 °C for 1 h. They concluded that the microwave method increases the kinetics of crystallization by one or two orders of magnitude compared to the convention hydrothermal method.

Yang et al.[65] found a novel method to produce inorganic nanofibers using electrospun fibers of polymer/inorganic composite as a precursor. This processing involves the following steps: (1) prepare a sol with suitable inorganic precursor and polymer content, and achieve the right rheology for electrospinning; (2) spin the solution to obtain polymer/inorganic fibers; and (3) calcinate the composite fibers to obtain final oxide nanofibers (Fig. 4).

3. Bio-application of Ceria Oxide Nanomaterial

With the development of the nanotechnology, nanomaterials have been widely used in catalysts, storage capacity, optics, magnetism, electricity and other applications due to their unique properties, such as small size effect, surface effect etc. In recent years, the bio-application of nano CeO2 has attracted much more attention. The ability of ceria nanoparticles to switch between oxidation states and scavenge free radicals is comparable to biological antioxidants. It can be used to cure chronic inflammation, ischemic stroke, nervous system disease and other diseases induced by active oxygen species[66]. Furthermore, CeO2 nanomaterials are widely used in immunodetection, drug delivery and other bio-application[67,68].

3.1. Biological antioxidants

Nanoceria are known to exhibit free radical scavenging activity by reversibly binding oxygen and shifting between the Ce3+ (reduced) and Ce4+ (oxidized) forms at the particle surface[30]. From the crystal structure of nanoceria, cerium ions mostly exist in the valence state of Ce4+; however, reduction in particle size results in oxygen vacancies from the particle surface, which allows the coexistence of Ce3+[69]. Kim and his coworkers[70] reported that

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**Fig. 4.** SEM micrographs for (a) as-prepared and (b) calcined (500 °C) PVA/cerium nitrate composite fibers; (c) Scheme of the electrospinning process[65] (Copyright 2005, Elsevier).
Ceria nanoparticles can protect against ischemic stroke in an in vivo animal model since ceria nanoparticles can reduce apoptotic cell death by decreasing reactive oxygen species (ROS). They synthesized CeO$_2$ nanomaterials encapsulated with phospholipid-polyethylene glycol to enable longer circulation in the bloodstream by reducing non-specific binding and uptake by organs. They concluded that the optimal doses of ceria nanoparticles (0.5 and 0.7 mg/kg), which reduced ischemic brain damage, targeted the damaged area by disruption of the blood–brain barrier after ischemia. They further demonstrated this protective effect in living animal model (rats) with ischemic stroke. Their study offered hope that an alternative treatment modality is for patients with ischemic stroke (Fig. 5).

ROS is unstable and highly reactive compounds that can strip electrons from cellular macromolecules and render them dysfunctional[12]. And ROS is a major constituent of inflammation that can affect normal cellular function and have pathogenic consequences. Quenching ROS production can decrease inflammation and subsequent tissue damage. Hirst and his coworkers[71] observed the quenching of ROS and the enzyme-inducible nitric oxide synthase (iNOS) inflammatory mediator in immune cells by the unique scavenging ability of nanoceria. They showed that nanoceria decreased NO production in J774A.1 macrophages and was deposited in tissue of C57BL/6 mice following intravenous injections without overt pathology. This ability may have the potential to serve as a treatment for a broad spectrum of inflammatory. They observed a decrease in fluorescence (directly proportional to ROS level) between 10 μM pretreated and untreated cells both with and without stimulation (Fig. 6(a)).

Recently, CeO$_2$ nanomaterials have presented an ability in protecting neurons from free-radical-mediated damage initiated by UV light, H$_2$O$_2$, irradiation and excitotoxicity[19,72–74]. Schubert et al.[73]...
demonstrated protection from exogenous oxidants in a neuronal cell line (HT22) in the presence of ceria and yttrium oxide nanomaterials. Perez and his coworkers[19] reported a facile synthesis of monodisperse, water-soluble, and highly crystal-line dextran-coated nanoceria (DNC), whose improved water solubility showed an unique pH-dependent antioxidant activity which would be of vital importance in the design of improved therapeutics and in tailoring its antioxidant properties (Fig. 6(b)). CeO2 nanomaterials can also prolong the lifespan of healthy cortical brain cells by about up to sixfold. Because of these neutron-protective effects, the application of CeO2 nanomaterials for treatment of neurodegenerative disorder-related disease is promising (Fig. 6(c)).

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia and insufficient secretion or action of endogenous insulin[12]. Abdollahi and his coworkers[75] reported that the combination of CeO2 nanomaterials and sodium selenium was beneficial to diabetic rats. The weight of diabetic rats decreased significantly and blood glucose increased compared with that in control rats. After treatment with the combination of sodium selenite and CeO2 nanomaterials, a significant increase in weight and a significant decrease in blood glucose was shown. An improvement in biomarkers of diabetes, including oxidative stress, energy compensation (ADP/ATP), lipid profile and hepatic ROS levels, was also observed.

The ROS that damage the sensitive cells in the retina are thought to have a central role in retina disease, including inherited retinal degeneration, diabetic retinopathy, macular degeneration and retinal detachment, which could lead to partial or complete loss of vision. Abdollahi and his coworkers[75] reported that the combination of CeO2 nanomaterials and sodium selenium was beneficial to diabetic rats. The weight of diabetic rats decreased significantly and blood glucose increased compared with that in control rats. After treatment with the combination of sodium selenite and CeO2 nanomaterials, a significant increase in weight and a significant decrease in blood glucose was shown. An improvement in biomarkers of diabetes, including oxidative stress, energy compensation (ADP/ATP), lipid profile and hepatic ROS levels, was also observed.

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**Fig. 7.** (a) Physicochemical characterization of CeO2 nanospheres and nanorods. Representative TEM images show the primary size, shape, and AR of CeO2 (C1, C2, C3, C4, and C5). (b) Subchronic pulmonary effect of CeO2 nanoparticles at 44 days. TGF-β1 levels in BALF and total collagen content of the lungs of mice receiving 4 mg/kg CeO2 nanoparticles. The picture shows lung sectioning and staining with Masson’s trichrome. Areas of concentrated blue staining represent collagen deposition sites. QTZ at 5.0 mg/kg served as a positive control. (c) Use of the number of calcified vertebrae as assessed by calcein staining. The representative fluorescence images show that control or larvae exposed to C1 and C3 exhibit 25 calcified vertebrae at 14 dpf. By contrast, larvae exposed to C5 and AgNPs showed 17 and 9 calcified vertebrae[78] (Copyright 2014, Royal Society of Chemistry).
vision\textsuperscript{76}. McGinnis and his coworkers\textsuperscript{30} demonstrated for the first time that CeO\textsubscript{2} nanomaterials could prevent retinal degeneration induced by intracellular peroxides and thus preserve retinal morphology and prevent loss of retinal function by using in vitro cell culture system and an in vivo albino rat light-damage model. Moreover, they explored the mechanism further by using the homozgyous tubby mouse as a model, which exhibits inherited early progressive cochlear and retinal degeneration\textsuperscript{15,77}.

In addition, more attention is paid to one-dimensional CeO\textsubscript{2} nanostructures such as nanorods, nanowires, and nanotubes due to their high redox and catalytic activities. In a recent study, 1D ceria nanostructure exhibited the highest oxygen-storage capacity. Recently, Zhou and his coworkers\textsuperscript{55} demonstrated the superior reduction capabilities of CeO\textsubscript{2} nanotube compared to the conventional nanoparticles. Lin and his coworkers\textsuperscript{56} showed that there was a relationship between the aspect ratio (AR) of CeO\textsubscript{2} nanoparticles in vitro hazard potential. A library of CeO\textsubscript{2} nanoparticles that included nanospheres (AR = 1, C1) and nanorods showing ARs of 8 (C2), 22(C3), 52(C4), and >100 (C5) were prepared by hydrothermal method (Fig. 7(a)). They also compared the mouse lung and gastrointestinal tract (GIT) of zebrafish larvae to study whether this toxicological paradigm for long aspect ratio CeO\textsubscript{2} is also relevant in vivo. They found only the nanorods with the highest AR (C5) induced significant IL-1\textbeta and TGF-\beta1 production in the bronchoalveolar lavage fluid at 21 days but did not induce pulmonary fibrosis. However, after a long duration (44 days) exposure to 4 mg/kg of the C5 nanorods, more collagen production was seen with the C5 nanorods contrast to nanospheres after correcting for Ce lung burden (Fig. 7(b)). The same result was shown in zebrafish larvae (Fig. 7(c)). In contrast, CeO\textsubscript{2} nanospheres and shorter nanorods had no effects.

3.2. Other applications

Except for biological antioxidants, CeO\textsubscript{2} nanomaterials can be used in bioimaging and drug delivery\textsuperscript{67,68}. Co-doped cerium oxide nanoparticles exhibited strong conversion properties and can be used as therapeutic agents for treatment of cancer, demonstrating the potential to be applied in clinical contrast agents for imaging. Babu and his coworkers\textsuperscript{71} synthesized rare earth co-doped CNPs with a sensitizer (Yb\textsuperscript{3+}) and an emitter (primarily Er\textsuperscript{3+}) having near-infrared (NIR)-to-visible upconversion fluorescence and changed the dopant chemistry in order to demonstrate the tunability of emission wavelength. They chose primary human umbilical vein endothelial cell (HUVEC) as well secondary cell line which is human lung fibroblasts cell line (WI-38) to be used in their experiment. They assessed toxicity by the metabolic reduction of a tetrazolium dye (MTT) and by the release of lactate dehydrogenase (LDH). No significant toxicity was observed in WI-38 cells with upconversion phosphors and some toxicity was observed in HUVeCs in a dose dependent manner when viability was determined by MTT assay, however no significant release of LDH occurred, suggesting the material caused a decrease in cellular metabolic rate without lysis of the cell membrane (Fig. 8a).

Patil and his coworkers\textsuperscript{69} used cerium oxide nanoparticles (nanoceria) as a potential delivery device for human carbonic anhydrase (hCAII) inhibitors. HCAII is a metalloenzyme that catalyzes the reversible hydration of carbon dioxide to bicarbonate and is associated with glaucoma which is a major cause of blindness. Carboxybenzenesulfonamide, an inhibitor of the hCAII enzyme, was attached to nanoceria particles using epichlorohydrin as an intermediate linkage. This nanoceria is an effective treatment of glaucoma (Fig. 8(c)). Asati and his coworkers\textsuperscript{67} designed an immunoassay in which folate-conjugated cerium oxide nanoparticles provided dual functionality by binding to folate-expressing cancer cells and facilitating detection by catalytic oxidation of sensitive colorimetric substrates. They found that dextran-coated nanoceria behaved an oxidation catalyst in a pH-dependent manner and performs optimally at acidic pH values through dye experiment. And contrast to traditional ELISA which is a horseradish peroxidase (HRP)-labeled secondary antibody, a nanoceria-based detection approach would be more robust that current HRP-based assays, as no enzyme or hydrogen peroxide would be needed for detection (Fig. 8(b)).

4. Conclusion and Outlook

Due to various preparation procedures, different 1D ceria nanostructures can be accomplished. To improve the properties of the ceria nanomaterials in terms of environmental and other issues, an enormous amount of reaction preparation procedures have been developed. Therefore, an overview of several syntheses
of 1D ceria nanomaterials and the bio-application of nanoceria is provided in the present work. So far, the bio-application of 1D nanoceria has seldom been reported. Considering the advantages of nanoceria in bio-application, we summarized the bio-application of ceria nanostructure with all morphologies. In addition, there are few reports about the toxic effects of 1D CeO₂ nanomaterials. Thus, the toxic mechanism about 1D CeO₂ should be carefully used in the above investigations did consist in preparation, aspect ratio, length or surface characteristic, even though these features could have an important role in 1D CeO₂ bio-application. Unluckily, the information about the relationship between the properties of 1D CeO₂ was fragmented. Nanoscale ceria materials of 1D structure are represented with special characteristics, such as high porosity and oxygen-storage capacity and reducibility allowing applications in catalytic reactions. Except for these properties, the aspect ratio, length and tip of 1D CeO₂ could be intelligent to embody the features of 1D structure. According to the modeling work by Shi et al.[16], they showed experimentally and theoretically that cylindrical one-dimensional nanomaterials enter cells through the tip first. Then, taking account of this special characteristic, intelligent bio-modification of 1D nanoceria may provide new approaches in the future for engine 1D nanomaterials for cell delivery in bio-application or to avoid frustrated uptake and achieve materials safety by design. Thus, combining the catalytic features of 1D CeO₂ with its aspect ratio and tip modification could achieve wide bio-application, such as drug delivery and drug therapy. In the future, we believe that 1D nanoceria will have various applications due to its unique properties. 1D ceria nanostructures will reach numerous applications owing to their size, shapes and crystallographic behaviors. While there are still some unresolved issues and challenges, the unique physical and chemical properties and the achieved significant advances clearly indicate that 1D CeO₂ is a fascinating and versatile material that is promising for numerous bio-application.

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References


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