Published in final edited form as:
JOM (1989). 2008 March 1; 60(3): 33–37. doi:10.1007/s11837-008-0029-8.

Nanoceria as Antioxidant: Synthesis and Biomedical Applications

A.S. Karakoti, **N.A. Monteiro-Riviere**, **R. Aggarwal**, **J.P. Davis**, **R.J. Narayan**, **W.T. Self**, **J. McGinnis**, and **S. Seal**

A.S. Karakoti is with the Surface Engineering and Nanotechnology Facility, Advanced Materials Processing and Analysis Center, Department of Mechanical Materials and Aerospace Engineering, University of Central Florida, Orlando, Florida. N.A. Monteiro-Riviere is with the Joint Department of Biomedical Engineering, University of North Carolina and North Carolina State University, and the Center for Chemical Toxicology Research and Pharmacokinetics, North Carolina State University, Raleigh, North Carolina. R. Aggarwal and R.J. Narayan are with the Joint Department of Biomedical Engineering, University of North Carolina and North Carolina State University. J.P. Davis is with the USDA ARS Market Quality and Handling Research Unit, Department of food, Bioprocessing and Nutrition Sciences, North Carolina State University, Raleigh, North Carolina. W.T. Self is with the Department of Molecular Biology and Microbiology, Burnett College of Biomedical Sciences, University of Central Florida. J. McGinnis is with the Department of Ophthalmology, Dean A. McGee Eye Institute, University of Oklahoma, Oklahoma City, Oklahoma. S. Seal is with the Surface Engineering and Nanotechnology Facility, Advanced Materials Processing and Analysis Center, Department of Mechanical Materials and Aerospace Engineering, University of Central Florida; and also with the Nanoscience and Technology Center, University of Central Florida. Dr. Narayan can be reached at e-mail: roger_narayan@unc.edu

Abstract

The therapeutic application of nanomaterials has been a focus of numerous studies in the past decade. Due to its unique redox properties, cerium oxide (ceria) is finding widespread use in the treatment of medical disorders caused by the reactive oxygen intermediates (ROI). The radical-scavenging role of ceria nanoparticles (nanoceria) have been established, as well as the autocatalytic ability of nanoceria to regenerate under various environmental conditions. The synthesis of nanoceria in biocompatible media has also been reported along with cell viability in order to determine the potential use of nanoceria in biomedical applications.

INTRODUCTION

In recent years cerium oxide has been used prolifically in various engineering and biological applications.[1–10] Ceria nanoparticles (nanoceria), as opposed to their coarser counterparts, have a large number of surface defects. These defects, which are primarily surface oxygen vacancies, cause a change in the local electronic and valence arrangement that stabilizes the trivalent oxidation state (III).[11–13] Ceria and nanoceria can be found in several high-end research technologies, such as solid-oxide fuel cells,[14] high-temperature oxidation protection materials,[15] catalytic materials,[16,17] and more recently, solar cells.[18] Recently, ceria nanoparticles have emerged as a fascinating and lucrative material in biomedical science due to their unique ability to switch oxidation states between III and IV based on environmental conditions.[19]

The ability of nanoceria to switch between oxidation states is comparable to that of biological antioxidants.[2] This capability imparts nanoceria with the very important

biological property of radical scavenging. A sustained and collaborative effort has demonstrated the capability of nanoceria to protect against cellular damage caused by various radicals in different tissues and organ systems as well as biomedical applications. Nanoceria has been shown to impart protection against the reactive oxygen species (ROS)[1] and against radiation damage.3

Lung cancer, colon cancer, breast cancer, pancreatic cancer, and prostate cancer are common causes of morbidity and mortality in the United States, with approximately 100 new cases diagnosed each day. Recently, ROS have been implicated in the development of cancer, including the initiation, promotion, and progression phases.[20] For example, ROS may interfere with cytoplasmic and nuclear signal transduction pathways, cause structural alterations in DNA, and modulate genes related to cell proliferation, apoptosis, and differentiation processes.[21]

McGinnis et al. have shown ceria nanoparticles can prevent retinal degeneration induced by intracellular peroxide molecules.[1] The application of ceria nanoparticles in the treatment of spinal cord injury and other central nervous system-based neuron degenerative diseases[4] has proven the biological importance of nanoceria beyond doubt. A molecular mechanism to explain the antioxidant properties of nanoceria has been established using a superoxide dismutase mimetic activity-based model.[2] In the wake of several reports that describe the potential toxicity of certain nanophase materials, the unique biomedical properties of nanoceria suggest that it may be an ideal nanophase material.[22,23]

In order to develop medical applications for nanoceria, it is important to synthesize nanoceria in biologically relevant media so that it is compatible with organism physiology. Synthesis of stable aqueous media of nanoceria requires the understanding of colloidal chemistry (zeta potential, particle size, dispersant, pH of solution, etc.)[24] as well as reduction/oxidation behavior. It must be noted that the synthesis of nanoceria in biocompatible media is a challenging task as the synthesis should not interfere with the redox ability of nanoceria and the nanoparticles so formed should not be toxic to cells. A host of biologically relevant media, including ethylene glycol (EG), polyethylene glycol (PEG), glucose, or dextran, can serve as media for synthesizing and/or dispersing the nanoceria particles. 25›26 While nanoceria particles can be synthesized and then re-dispersed in biological media, our experience with precipitation and redispersion has been limited with respect to biological efficacy. Thus this paper will discuss the direct synthesis of nanoceria in various aqueous biocompatible media and the cell viability of these materials. A brief overview of biological importance of nanoceria and its relation to the unique chemistry of nanoceria is paramount to this discussion.

$$Ce^{4+} + e^{-} \rightarrow Ce^{3+} \quad (1)$$

$$Ce^{4+} + e^{-} \leftrightarrow Ce^{3+} \quad (2)$$

$$Ce^{3+} + OH^{\bullet} \rightarrow Ce^{4+} + OH^{-} \quad (3)$$

$$Ce^{4+} + O_2^{\bullet -} \leftrightarrow Ce^{3+} + O_2 \quad (4)$$

$$t \xrightarrow{\lim} \infty \left\langle \Delta r^2(t) \geq 6D_0^t = \frac{kTt}{\prod \mu a} \right. \tag{5}$$

$$W_{EL} = \frac{q_1 q_2}{4\varepsilon_0 \varepsilon_r \prod R_{12}} = \frac{\sigma_1 A_1 \sigma_2 A_2}{4\varepsilon_0 \varepsilon_r \prod R_{12}} \tag{6}$$

$$Ce^{+4} + 4OH^- \rightarrow Ce(OH)_4 \tag{7}$$

$$Ce^{+3} + 3OH^- \rightarrow Ce(OH)_3 \tag{8}$$

How would you…

…describe the overall significance of this paper?

Due to its unique redox properties, cerium oxide (ceria) is finding widespread use in the treatment of medical disorders caused by reactive oxygen intermediates. The synthesis of nanoceria in biocompatible media has also been reported along with cell viability.

…describe this work to a materials science and engineering professional with no experience in your technical specialty?

Reactive oxygen species have been recently implicated in the initiation, promotion, and progression phases of tumor development. The unique valence and oxygen defect structure of cerium oxide nanoparticles can be optimized to promote scavenging of reactive oxygen species.

…describe this work to a layperson?

Cerium oxide nanoparticles exhibit unique capabilities for quenching free radicals. In this paper, the synthesis and biological properties of these materials were examined. These materials could find widespread use in the treatment of free radical-mediated medical disorders.

REVERSIBLE REDOX CHEMISTRY OF CERIA

The neuroprotective, radical scavenging, and autocatalytic properties of nanoceria stem from redox chemistry. The standard reduction potential for Equation 1 changes with pH and is found to be above −1.58 V for values greather than 1.67.[19] (Note: all equations are shown in the table.) The redox value is sensitive to pH; however, it can be catalyzed in either direction by most radical species, making it a reversible process. This process imparts nanoceria with antioxidant properties as shown in Equation 1.

Thus, ceria can be reversibly oxidized from a +3 state to a naturally stable +4 oxidation state and back by radical species such as peroxides and superoxides. The overall redox reactions can now be listed as Equation 2–Equation 4.[1]

It must be noted that Equation 4 may not be the only mechanism for the regeneration of +3 oxidation state of nanoceria. As indicated by the redox potential, the reverse of Equation 1 can occur at the surface of the nanoceria depending upon the environment (surface and electrochemical potential) and vacancies present on the nanoceria surface. It is imperative to note that an initial concentration of cerium (+3) oxidation state is required for redox cycling as well as activity in biological media.[2] The auto-regenerative property of nanoceria is susceptible to an initial concentration of trivalent cerium; this phenomenon is currently being investigated. See the sidebar for biological applications of nanoceria.

COLLOIDAL STABILITY OF NANOCERIA

Synthesis of a stable nanoceria suspension is necessary in order to develop medical and biological applications. For example, agglomeration may deteriorate the chemical and biological properties of nanoceria. The physiochemical properties can be altered by an increase in nanoceria particle size, making it difficult for nanoceria to enter and/or protect cells. Moreover, the medical use of nanomaterials requires synthesis of nanomaterials in biocompatible media as stable dispersions. Stability can be provided in a number of ways that may involve altering the surface charge (electrostatic) of the nanoparticles, modifying the surface chemistry of the nanoparticles, or imparting steric stability to the nanoparticles by surface modification.[24] To stabilize a nanomaterial by manipulating the electrostatic surface charge, a thorough understanding of the Stern layer, iso-electric point, zeta potential, electric double layer, and potential-determining ion is necessary. 27 These parameters are generally dependent on the polarizability of the nanomaterial. For example, knowledge of zeta potential, which is the potential at the interface between the Stern layer and the diffuse layer, is crucial for determining colloidal stability. To achieve the most stable colloid system, a maximum electrostatic potential between the two adjacent particles is desired. In general, Equation 5 can be used to determine the minimum and maximum interaction potentials between nanoparticles and establish the general distribution of nanoparticles through a diffusion model.[27]

In Equation 5, D_o is the Stokes–Einstein diffusivity, k is Boltzmann's constant, T is the temperature, t is time, a is the particle size, Δr^2 is the mean square displacement, and μ is the solvent viscosity. Electrostatic interaction between the two point charges at a distance of R_{12} can be quantified using the electrostatic potential, W_{EL} (Equation 6).

In this equation, q1, q2 are the products of the charge densities (σ1, σ2) and the contact areas at the interface (A1, A2), and ε_r is the dielectric constant of water. Nanoparticle stability can be achieved by incorporating the appropriate conditions in this equation.[28] This information can be further tailored to obtain stable dispersions by electrostatic stabilization of nanoparticles.

Another mechanism for achieving stable suspensions involves surface modification of nanoparticles. The modification of an inorganic oxide nanoparticle can be accomplished using both inorganic and organic materials. As most of the biocompatible media that can act as delivery media are organic in nature, it is more common to achieve surface modification using organic compounds. Inorganic oxide nanoparticles when modified with biocompatible agents such as polymers can either form core-shell type structures or structures in which several nanoparticles can cluster together on the polymer backbone. In either case, the nature of bonding between the nanoparticles and the polymeric species governs the stability and the dynamics of inter-particle agglomeration. However, selecting an ideal organic polymer that can trap nanoparticles without interfering with nanoparticle chemistry is critical to this type of synthesis. This in turn depends on the molecular weight of the functional groups, the chemical reactivity of the polymer at fixed molar concentrations, and solvent pH. Recent

advances in colloid stability using both electrostatic and surface modifications have significantly contributed to the target-oriented drug delivery and other medical applications for nanomaterials.

BIOLOGICAL APPLICATIONS OF NANOCERIA

The unique redox property of nanoceria can protect against diseases caused by the reactive oxygen species (ROS) or intermediates (ROI). Since nanoceria can interact with a number of reactive oxygen intermediates, it has potential uses in numerous biological applications. McGinnis et al. demonstrated that nanoceria can prevent an increase in intracellular ROI concentration in primary cells of the rat retina.[1] These in-vivo investigations established the role of nanoceria in preventing vision loss due to light-induced degeneration of photoreceptor cells; this degeneration process is caused primarily by ROI production upon direct exposure to light. The reversibility and auto-regenerative properties of nanoceria suggest that this material could be provided in a single dose and could exhibit an apparent pseudo-infinite shelf life. Another study recently demonstrated the potential role of nanoceria in spinal cord repair and other diseases related to the central nervous system (CNS).4 This in-vitro study indicated that nanoceria can increase the survival of the neurons in the spinal cord and CNS against oxidative stress-related damage. Moreover, the neuroprotective effect was observed with just a single dose of nanoceria.

It was also established that nanoceria can protect the normal cells against radiation damage as opposed to tumor cells.[3] While radiation therapy is a widely accepted technique for treatment of cancer, it can cause severe damage to normal cells that are in close proximity to the treatment site. The cause of this damage is attributed to the free radicals that are produced during the treatment process. An in-vitro study has shown that nanoceria can provide radioprotection to normal human breast cells but not to human breast tumor cells (human breast tumor cell line MCF-7). While it was established that the cellular uptake of nanoceria was identical for both tumor cells and normal cells, the fact that normal cells were protected against free radical damage suggests the selective nature of nanoceria in conferring protection.

More direct proof of the capability of nanoceria to react with ROI was confirmed using a classical superoxide dismutase (SOD) model, in which nanoceria competed with cytochrome C for reduction by superoxide.[2] It was found that nanoceria did compete with cytochrome C for reduction by superoxide, and SOD mimetic activity was dependent upon the concentration of the +3 oxidation state. This study suggested that there was a positive correlation between the trivalent oxidation state of nanoceria and superoxide dismutase-mimetic activity. It was shown that a single ceria nanoparticle was more efficient as an SOD catalyst than the natural superoxide dismutase enzyme. These experiments also confirmed that surface oxygen vacancies in nanoceria play an indirect role in the radical scavenging properties. The authors' group has shown that nanoceria contain higher oxygen vacancies than their coarser counterparts. A large number of vacancies is responsible for stabilizing the +3 oxidation state and retaining a higher concentration of the +3 oxidation state in nanoceria.12,13

These studies suggest that nanoceria can be used in treatment of various medical conditions caused by reactive oxygen intermediates. However, in most cases either in-vitro studies or in-vivo studies involving intravenous delivery were conducted. For most medical applications, nanoceria needs to be stabilized in aqueous dispersions.

SYNTHESIS OF CERIA IN BIOLOGICALLY RELEVANT MEDIA

The authors' group has been successful in synthesizing ceria in different biocompatible media utilizing both electrostatic stabilization as well as steric stabilization by modifying the nanoparticle surface. It is known that Ce(IV) is stable as transparent yellow-colored solution below pH=3.5. It can be precipitated above this pH following Equation 7. Similarly, Ce(III) also exists as a stable clear solution below pH 6.0 and can be precipitated as the pH increases (Equation 8)[29]. This limits the stability of ceria nanoparticles ($CeO_2 \cdot 2H_2O$) to highly acidic solutions (pH 2.0–3.5) that are not suitable for biological applications.

Ceria has been systematically synthesized in pure water, ethylene glycol, polyethylene glycol, glucose, and dextran. By synthesizing ceria in media such as glucose and dextran, the extended stability of nanoceria was demonstrated through a pH range of 2.0–8.0. Table I lists the synthesis of nanoceria using several media and the range of pH over which these nanoparticle solutions are stable.[19] This process involves direct synthesis of nanoceria in aqueous suspensions and does not involve precipitation and redispersion. The important parameters in direct synthesis are the choice of precursors, concentration of precursors, and utilization of cerium redox chemistry. High-resolution transmission-electron micrographs (Philips 300, Tecnai, Hillsboro, Oregon) of ceria synthesized in various media are shown in Figure 1. A clear distinction can be seen in the agglomeration behavior of the ceria nanoparticles. It can be observed from Figure 1a and 1b that modifying the oxidizing agent and the pH of the medium can alter the agglomeration behavior of ceria nanoparticles synthesized in dextran. The high-magnification image (Figure 1c) shows that the agglomerated nanoceria in dextran contain individual 3–5 nm particles. Figure 1d and 1e contain low- and high-magnification images of the nanoceria particles synthesized in polyethylene glycol, respectively. Nanoceria particles stabilized in acidic medium have a minimum agglomerate size of 10–15 nm. On the other hand, samples stabilized in a neutral to alkaline medium are less agglomerated.[19] The individual particle size remains ~3–5 nm despite the variation in the synthesis parameters. A further analysis was done using ultraviolet-visible spectroscopy (not shown here) to establish reversibility and switching of nanoceria oxidation states during synthesis. It was observed that the synthesis medium modifies the rate of reversibility of oxidation state to a small extent.[19] Thus, the choice of media should not hinder the radical-quenching capability of nanoceria.

TOXICITY ANALYSIS OF NANOCERIA SYNTHESIZED IN VARIOUS MEDIA

Nanoceria particles synthesized in polymeric media (dextran and polyethylene glycol) along with water-based nanoceria were assessed to determine the potential of toxicity. Cell viability utilizing the MTT assay was examined using cryopreserved neonatal human epidermal keratinocytes (HEK) (Lonza, Walkersfield, Maryland). The HEK were plated in two 96-well plates at a density of approximately 8,000 HEK per 200 μL of keratinocyte growth media (KGM-2), consisting of serum-free keratinocyte basal media supplemented with human epidermal growth factor, insulin, bovine pituitary extract, hydrocortisone, transferrin, epinephrine, and GA-1000 (gentamicin-amphotericin). Cells were allowed to proliferate until approximately 70% confluent prior to dosing with nanoceria. All nanoceria and control samples were vortexed prior to dosing.

Ceria (CeO_2) stock doses with different vehicles and concentrations were used: CeO_2 in water (5 μM); CeO_2 in dextran (5 μM); and CeO_2 in polyethylene glycol (30 μM) vehicle controls. CeO_2 in polyethylene glycol was diluted to 5 μM using a 1:6 dilution of 20 μL of CeO_2 in PEG stock into 100 μL PEG vehicle. Serial dilutions were used to create 5 μM, 0.5 μM, and 0.05 μM CeO_2 concentrations in media. Vehicle controls were diluted to 0.1% with media for the experiment to examine any inhibition at the highest concentration. [22] All doses

were run in quadruplicate and CeO_2 dilutions remained in the wells for 24 h. After 24 h, an MTT (3-[4,5-dimethyl-2-thiazol]-2,5-diphenyl-2H-tetrazolium bromide) viability assay was conducted.[30] The MTT assay is based on reduction of a yellow tetrazolium salt (MTT) to a purple formazan dye by succinnic dehydrogenase within mitochondria. Human epidermal keratinocyte viability (normalized to control) was statistically compared using ANOVA (SAS 9.1 for Windows, Cary, North Carolina). Multiple comparisons were made between different treatments using the student's t-test at $p<0.05$.

The percent viability of cells using the MTT assay is shown in Figure 2. It can be observed that the nanoceria synthesized in media such as dextran and polyethylene glycol did not show a statistically significant decrease in viability. On the other hand, the nanoceria synthesized in pure water exhibited a statistically significant decrease in viability compared to the nanoceria synthesized in polyethylene glycol or dextran. Thus, it is established that synthesis of nanoceria in polyethylene glycol and dextran tends to increase or enhance cell viability rather than decrease cell viability. A higher concentration of ceria nanoparticles in +3 oxidation state, less agglomeration, and a uniform distribution of the particles may be some of the reasons for this observation. In addition, biocompatible coatings of dextran and/or polyethylene glycol could strengthen the possible medical applications of nanoceria.

CONCLUSION

Vacancy-engineered ceria nanoparticles exhibit unique capabilities for quenching reactive oxygen intermediates, and could find widespread use in the treatment of ROI-mediated medical disorders. Controlled synthesis of nanoceria in a variety of biologically relevant media is a challenging task as the medium should not interfere with the physicochemical properties of the nanoceria particles. Nanoceria were successfully synthesized in several biocompatible media including water, polyethylene glycol, ethylene glycol, glucose, and dextran. Synthesis of a stable suspension requires consideration of the chemistry of nanoceria along with the physical and chemical parameters involved in colloidal stability. The nanoceria synthesized in media such as polyethylene glycol and dextran did not show a decrease in viability; however, nanoceria synthesized in water did exhibit a decrease in viability. The effects of medically relevant media and medically relevant environmental conditions on the biological activity of nanoceria are presently under investigation.

Acknowledgments

The authors acknowledge the National Science Foundation (NSF) Chemical, Bioengineering, Environmental and Transport Systems Division (CBET): 0711239 (Title: Surface Chemistry in Metal Oxide Nanoparticle Cytotoxicity); NSF Nanoscale Interdisciplinary Research Team CBET: 0708172; National Institutes of Health (NIH): R21EY018306; and NIH: 5R21EB003090 for funding.

References

1. Chen J, et al. Nature Nanotechnology 2006;1:142–150.
2. Korsvik C, et al. Chemical Communications. 2007 accepted.
3. Tarnuzzer RW, et al. Nano Letters 2005;5:2573–2577. [PubMed: 16351218]
4. Das M, et al. Biomaterials 2006;28:1918–1925. [PubMed: 17222903]
5. Patil S, Kuiry SC, Seal S. Proceedings of the Royal Society A: Mathematical, Physical & Engineering Sciences 2004;460:3569–3587.
6. Chen J, et al. Investigative Ophthalmology & Visual Science 2005;46:186.
7. Ellison A, et al. Journal of Neurotrauma 2003;20:1105–1105.
8. Limbach LK, et al. Environmental Science and Technology 2005;39:9370–9376. [PubMed: 16382966]

9. Niu JL, et al. Cardiovascular Research 2007;73:549–559. [PubMed: 17207782]
10. Tsai YY, et al. Nanomedicine 2007;2:325–332. [PubMed: 17716177]
11. Campbell CT, Peden CHF. Science 2005;309:713–714. [PubMed: 16051777]
12. Deshpande S, et al. Applied Physics Letters 2005;87:133113.
13. Patil S, et al. Applied Physics Letters 2006;88:243110.
14. Stambouli AB, Traversa E. Renewable and Sustainable Energy Reviews 2002;6:433–455.
15. Patil S, et al. Journal of Nanoparticle Research 2002;4:433–438.
16. Li FB, et al. Applied Catalysis A 2005;285:181–189.
17. Jobbagy M, et al. Chemistry of Materials 2006;18:1945–1950.
18. Lira-Cantu M, Krebs FC. Solar Energy Materials & Solar Cells 2006;90:2076–2086.
19. Karakoti AS, et al. Journal of Physical Chemistry C 2007;111:17232–17240.
20. Mates JM, Sanchez-Jimenez FM. International Journal of Biochemistry and Cell Biology 2000;32:157–170. [PubMed: 10687951]
21. Senturker S, et al. FEBS Letters 1997;416:286–290. [PubMed: 9373171]
22. Lin WS, et al. International Journal of Toxicology 2006;25:451–457. [PubMed: 17132603]
23. Karakoti AS, Hench LL, Seal S. JOM 2006;58(7):77–82.
24. Kuchibhatla S, Karakoti AS, Seal S. JOM 2005;57(12):52–56.
25. Maia J, et al. Polymer 2005;46:9604–9614.
26. Mehvar R. Journal of Controlled Release 2000;69:1–25. [PubMed: 11018543]
27. Hunter, RJ. Introduction to Modern Colloidal Science. New York: Oxford University Press; 1993.
28. Hiramatsu H, Osterloh FE. Langmuir 2003;19:7003–7011.
29. Hayes SA, et al. Journal of the Electrochemical Society 2002;149:C623–C630.
30. Mosmann T. Journal of Immunological Methods 1983;65:55–63. [PubMed: 6606682]

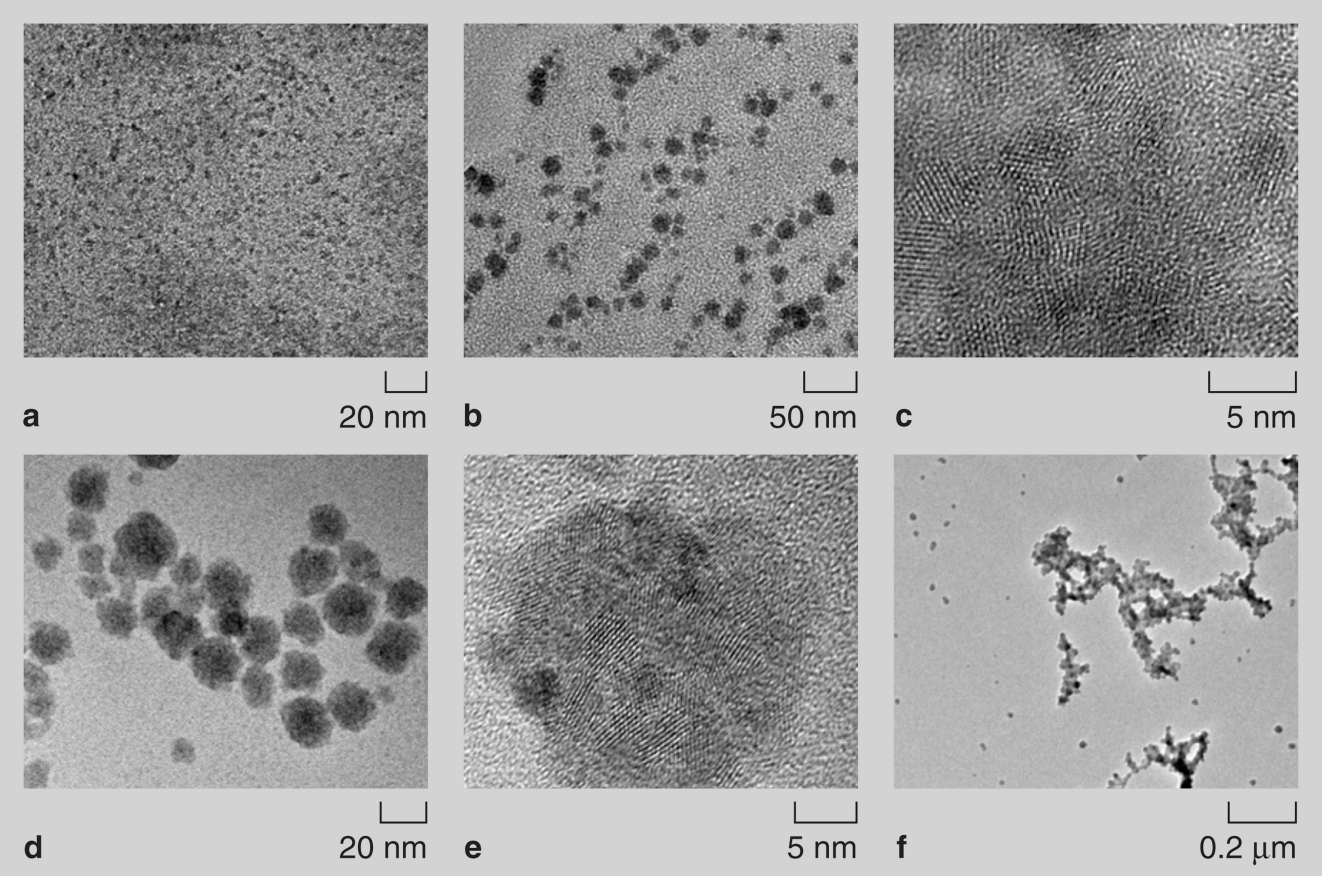

Figure 1.
High-resolution transmission-electron micrographs of nanoceria samples prepared in different biocompatible media. (a) Nanoceria in dextran (alkaline conditions). (b) Nanoceria in dextran (acidic conditions). (c) High-magnification image of nanoceria synthesized in dextran (acidic conditions) confirming the crystalline nature of the material as well as individual 3–5 nm particle size. (d) Nanoceria in polyethylene glycol. (e) High-magnification image of nanoceria synthesized in polyethylene glycol showing 3–5 nm particle size. (f) Nanoceria in water. A clear distinction in agglomeration can be seen by varying the medium as well as the pH.

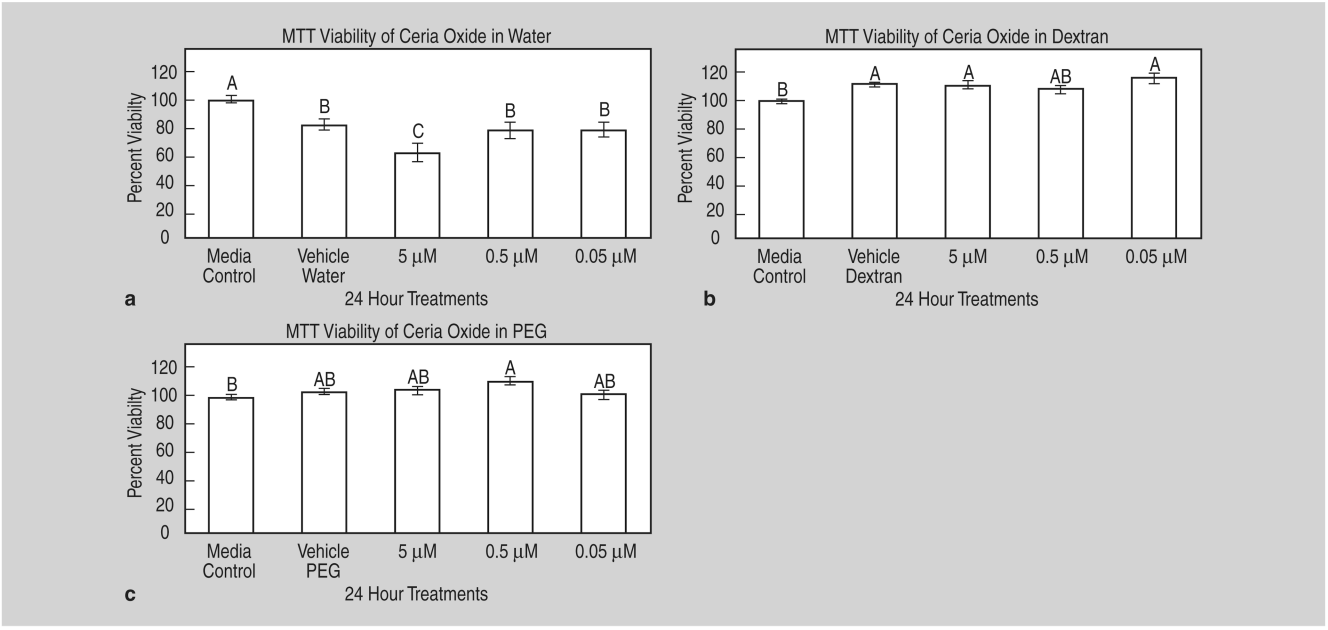

Figure 2.

Percent viability of human epidermal keratinocyte (HEK) cells treated with nanoceria in (a) water, (b) dextran, and (c) PEG after 24 hours of treatment. Histogram with different letters (a, b, c) denote mean values that are statistically different at $p<0.05$.

Table I

Synthesis of Nanoceria in Biocompatible Media*

Precursors	Medium	Oxidizer	pH	Particle Size (nm)
Cerium Nitrate	Aqueous water (18.2 MΩ)	Hydrogen peroxide	3.4	3–5 15–20 (agg)
Cerium Nitrate poly(ethylene glycol) (mol. wt. 600)	20% (vol.) polyethylene glycol solution	Hydrogen peroxide	3.15	3–5 10–15 (agg)
Cerium Nitrate Dextran (mol. wt. 1000)	0.5 mM and 5 mM dextran solution	Hydrogen peroxide	3.1	3–5 13–17 (agg)
Cerium Nitrate Dextran (mol. wt. 1000)	5mM dextran solution	Ammonia	7.6	3–5

* The particle size values mentioned are the individual particle size (from transmission electron microscopy [TEM] and x-ray diffraction) as well as the agglomerate (agg) particle size (from TEM).