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Metal oxide nanoparticles with low toxicity

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ABSTRACT

A number of different nanomaterials produced and incorporated into various products are rising. However, their environmental hazards are frequently unknown. Here we consider three different metal oxide compounds (SnO_2, In_2O_3, and Al_2O_3), which have not been extensively studied and are expected to have low toxicity. This study aimed to comprehensively characterize the physicochemical properties of these nanomaterials and investigate their toxicity on bacteria (*Escherichia coli*) under UV illumination and in the dark, as well as on a marine diatom (*Skeletonema costatum*) under ambient illumination/dark (16–8 h) cycles. The material properties responsible for their low toxicity have been identified based on comprehensive experimental characterizations and comparison to a metal oxide exhibiting significant toxicity under illumination (anatase TiO_2). The metal oxide materials investigated exhibited significant difference in surface properties and interaction with the living organisms. In order for a material to exhibit significant toxicity, it needs to be able to both form a stable suspension in the culture medium and to interact with the cell walls of the test organism. Our results indicated that the observed low toxicities of the three nanomaterials could be attributed to the limited interaction between the nanoparticles and cell walls of the test organisms. This could occur either due to the lack of significant attachment between nanoparticles and cell walls, or due to their tendency to aggregate in solution.

1. Introduction

Toxicity of nanomaterials has been a rising concern with the increase of the production of various nanomaterials [1–8]. In particular, there is interest in elucidating the relationship between the structural properties and the activity of a nanomaterial [1], and developing predictive toxicological approaches to establish toxicity screening priorities [2]. Such predictive approaches can include prediction of oxidative stress (for example, the ability of a nanomaterial to generate reactive oxygen species (ROS) [2] or their chemical stability [2,5]. They can be semi-empirical approaches such as quantitative structure–activity relationship (QSAR) [2,5,6] or purely theoretical approaches based on fundamental properties of the nanomaterials.

In spite of enormous interest in predictive toxicology of nanomaterials, to date there has been very limited progress on this issue. Furthermore, there is limited understanding of the mechanisms of toxicity of metal oxides and a large number of studies in the literature report incomplete characterization of the nanomaterials studied [9]. Different toxicity mechanisms, such as ROS production followed by oxidative stress/lipid peroxidation/cell wall damage, metal ion release, and interaction between the nanomaterial and cells, have been proposed by different research groups but as yet no conclusive and unambiguous identification of the mechanism of toxicity has been made [9]. This has an obvious implication on trying to understand and predict toxicity of nanomaterials. Due to the complexity of biological systems, it is difficult to theoretically predict the nanomaterial behavior in the environment, especially considering the fact that experimental studies often report contradictory results and the actual toxicity mechanism is unclear [9]. Thus, comprehensive experimental studies which would establish distinguishing features of interaction between toxic and non-toxic nanoparticles and living organisms are of significant interest in establishing the toxicity mechanisms

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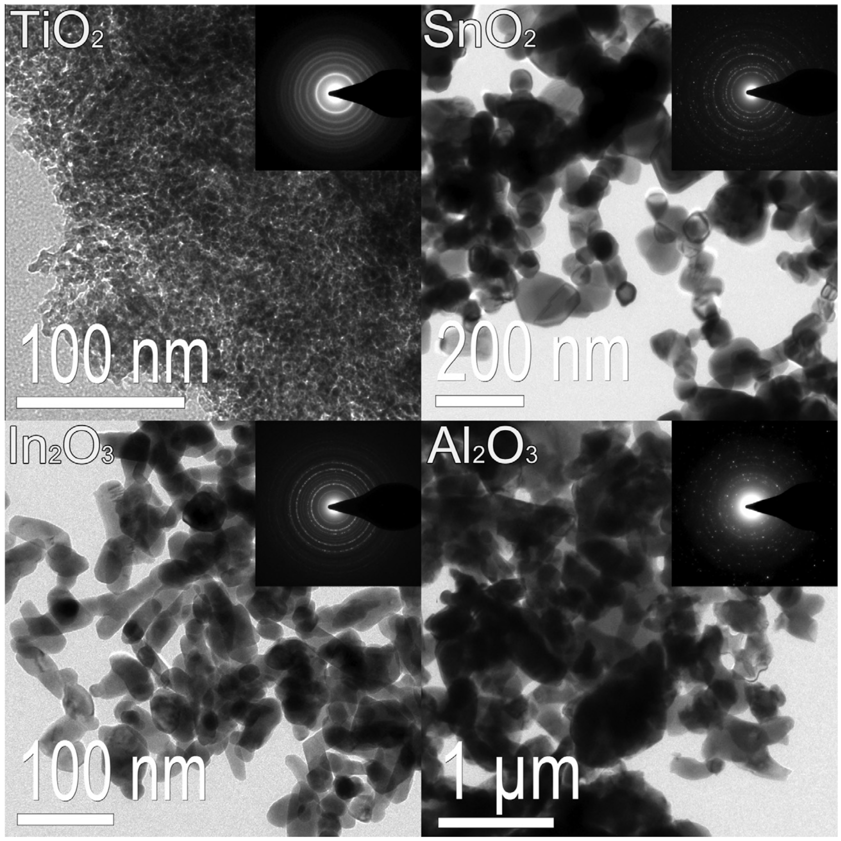

Fig. 1. TEM images of different nanoparticles. The insets show corresponding selected area electron diffraction patterns.

and possibly enable future predictions once more realistic models are developed. We have selected to study the following metal oxides: α-Al_2O_3, In_2O_3, and SnO_2, which have not been extensively studied but are expected to result in low to moderate toxicity [10–20]. The majority of studies was performed on alumina which exhibited low to moderate toxicity according to literature reports [12,14,16–18,20], while there have been very few studies on tin oxide [18] and indium oxide [15]. On the other hand, anatase TiO_2 is well studied and known to exhibit toxicity to various organisms under different illumination conditions [9]. Therefore, a comprehensive comparative study of anatase TiO_2 compared to low toxicity metal oxides is expected to reveal distinguishing characteristics of nanomaterial/organism interactions resulting in toxicity.

2. Methods

2.1. Materials and characterization

TiO_2 (99%, average particle size APS 15 nm), SnO_2 (99.5%, APS 55 nm), In_2O_3 (99.99%, APS 30–50 nm), and Al_2O_3 (99%, APS 30–40 nm) nanoparticles were obtained from Nanostructured & Amorphous Materials Inc. The particle morphology and structure was investigated by transmission electron microscopy (TEM) and selected area electron diffraction (SAED) using a Phillips Tecnai G2 20 S-TWIN TEM. Absorption measurements were performed using a Cary 50 Bio UV–Vis spectrophotometer. Aggregation sizes of the nanoparticles in 0.9% w/v sodium chloride solution were determined using ZETASIZER 3000HSA (Malvern Instruments Ltd.). For aggregate size determination in artificial seawater, nanoparticles at a concentration 100 mg/L were dispersed in filtered artificial seawater (salinity, 30 ± 0.5‰; pH, 8.0 ± 0.1; sea salt: Tropic Marine, Germany; filtered through 0.45 μm membrane filter). The aggregate size (average of three replicates) was determined using laser diffractometry (LD; LS 13 320 Series, Beckman Coulter Inc., Fullerton, USA).

The reactive oxygen species generated by the nanoparticles were detected using electron spin resonance (ESR) spectroscopy at room temperature with the addition of a spin trap molecule [21]. Spin trap 5,5-Dimethyl-1-pyrroline N-oxide (DMPO) was purchased from Sigma–Aldrich Co., and the solution was prepared by adding 0.02 M DMPO to 1 mg/ml metal oxide nanoparticle

Table 1
Summary of nanoparticle characteristics and toxicity testing results in 0.9% w/v NaCl (SC) and artificial seawater (ASW), respectively, and toxicity testing results on the marine diatom in ASW. The toxicity endpoint is median inhibition concentration (IC_{50}) after 72 h of exposure to the nanomaterial, and the IC_{50} values sharing with the same superscripted letter are statistically indifferent (based on overlapping of the 95% confidence intervals). IC_{50} values are given as mean value (n = 3), with confidence interval indicated in brackets.

Nanoparticle	Aggregation size in SC (μm), metal content (μg/L)	Aggregation size in ASW (μm), metal content (μg/L)	72-h IC_{50} (mg L^{-1}) *Skeletonema costatum*
Control	–, <10 (Sn, In, Ti), <100 (Al)	–, <10 (Sn, In, Ti), <100 (Al)	–
TiO_2	0.6, <10 (Ti)	0.69, <10 (Ti)	353.3 (322.8–386.8)[a]
SnO_2	1.1, <10 (Sn)	0.42 and 1.8, <10 (Sn)	5200.0 (1389.0–19472.0)[b]
In_2O_3	0.1–0.5, <10 (In)	0.45 and 1.6, <10 (In)	739.8 (580.0–943.7)[c]
Al_2O_3	0.35 and 1.6, <100 (Al)	0.67, <100 (Al)	2101.0 (1671.0–2642.0)[b]