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Review Article

Using a holistic approach to assess the impact of engineered nanomaterials inducing toxicity in aquatic systems

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ABSTRACT

In this report, we critically reviewed selected intrinsic physicochemical properties of engineered nanomaterials (ENMs) and their role in the interaction of the ENMs with the immediate surroundings in representative aquatic environments. The behavior of ENMs with respect to dynamic microenvironments at the nano–bio–eco interface level, and the resulting impact on their toxicity, fate, and exposure potential are elaborated. Based on this literature review, we conclude that a holistic approach is urgently needed to fulfill our knowledge gap regarding the safety of discharged ENMs. This comparative approach affords the capability to recognize and understand the potential hazards of ENMs and their toxicity mechanisms, and ultimately to establish a quantitative and reliable system to predict such outcomes.

1. Introduction

Along with the rapid growth of nanotechnology, there arises the need for a definition of engineered nanomaterials (ENMs) for regulatory purposes. Definitions help to avoid misunderstandings and to ensure efficient communication. For regulatory purposes, a definition should be as clear and simple as possible, but at the same time unambiguous and comprehensive [1]. The European Commission's Joint Research Center Reference Reports of 2010 recommended that a definition for regulatory purposes should only concern particulate nanomaterials, be broadly applicable in European Union (EU) legislation and in line with other approaches worldwide, and use size as the only defining property [1]. The definition of the term nanoscale as recently given by International Organization for Standardization encompasses the size range from approximately 1 nm to 100 nm, a range which has been adopted in a number of other definitions as well [1]. It is noteworthy that the van der Waals diameter of a C_{60} molecule is approximately 1.1 nm. The nucleus to nucleus diameter of a C_{60} molecule is approximately 0.71 nm. Most nanoparticles (NPs) used for drug delivery are in range 200–400 nm.

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The ENMs offer great promise in many industrial and biomedical applications. However, their production processes may potentially result in human exposure by inhalation, dermal, or ingestion routes [2]. Aside from unintentional exposure during manufacture, ENMs might also be delivered to the public in our foods and medicines. Among a number of studies devoted to such issues, the work of Weir and coworkers [3] who investigated the titanium content of some common foods should be mentioned. The titanium content of the products was as high as 100 mg/serving for powdered donuts, and many products with the highest titanium contents could be characterized as sweets or candies. In addition, tremendous progress has been achieved in applying ENMs for drug delivery and tissue engineering, which also may impose risks to the patient, and even surpass their benefits [4]. Inevitably, the discharge of those anthropogenic nanomaterials along with the ones used for environmental remediation may enter water supply sources [5,6]. The quantity and form of the nanomaterials released into aquatic environments should be determined to assess the environmental risks of nanotechnology.

Clearly, the impact of these novel materials warrants strenuous and ongoing toxicological research. The fact that the physicochemical properties of the ENMs *per se*, as well as their interactions with immediate surrounding environments, determine their potential hazards, acute or chronic, direct or indirect, is extremely important [7–11]. Lack of knowledge about the transport, fate, and behavior of ENMs in the aquatic environment largely constrains our ability to assess their potential risks in a quantitative and predictable way. Furthermore, their adverse impacts on biota also vary depending on the tested species and their trophic levels. Thus, it is essential to elucidate their hazards under conditions that resemble natural environments in which they would be encountered. Consequently, two critical issues arise—first, the need to establish a reliable and standard system to clarify the real-time states of targeted ENMs in natural aquatic environments; second, the need for a nanotoxicological study with a holistic approach. This approach will provide a database on vulnerable species in multiple trophic or structural levels in an aquatic ecosystem for assessing the potential hazard of ENMs in a comprehensive way. This database may also afford an opportunity to compare results with other studies to support the formulation of more reliable conclusions.

Much of the existing research on nanotoxicity has concentrated on empirical evaluation of the toxicity of various ENMs with less attention being given to the relationship between nanomaterial physicochemical properties (including chemical composition, shape, size and size distribution, dispersion, aggregation state, surface area, surface chemistry, surface charge, and porosity) and toxicity [12]. This approach gives limited information and should not be considered adequate for predicting the toxicity of seemingly similar ENMs. Instead, if condition permits, we should adopt a systematic approach for studying the toxicity of ENMs by focusing on a group of test nanomaterials of similar physicochemical properties with variation in one particular parameter [13]. It is also noteworthy that characterization of supplied nanomaterial may not actually represent physicochemical properties of the material during or following administration. Therefore, wherever possible, independent characterization of test nanomaterials should be conducted prior to and after administration [12].

In this report, we reviewed the progress of research from many scientific entities from the standpoint of the nature and behavior of the nanomaterials themselves, to the response of organisms in aquatic ecosystems when exposed to them, and also the different approaches to nanotoxicological assessment. It is the purpose of this review to use existing databases on ENMs based on our proposed holistic approach and bridge the gap between ENMs and aquatic ecosystems.

2. Fundamental knowledge needed to understand nanotoxicology

In 1985, Harold Kroto and colleagues [14] discovered C_{60}, and shortly thereafter came to discover the fullerenes. This discovery led to much research into the behavior of these unique particles and eventually to the advent of engineered or anthropogenically produced nanomaterials, or materials on the nanoscale. Today, there are numerous ENMs that are providing the impetus to significant advances in science, engineering, industry, and commercial enterprise. The manufacture, processing, and application of nanomaterials provide opportunity for them to come into contact with humans and other organisms and plants that make up the planet's ecosystems. Along with the technology is the need for nanotoxicology, because the extent of any risk posed by these products is not known completely. Nanotoxicology can be defined as a safety evaluation of engineered nanostructures and nanodevices. Collectively, some emerging concepts of nanotoxicology can be identified from the results of studies already completed.

The ways and means of nanotoxicology discussed in this review are a summarization of the progress in discovering the mechanisms of toxicity of these nanomaterials. It is prudent to investigate not only the response from organisms exposed to them but also the fate of the ENMs themselves as they enter the natural environments. This necessitates a careful examination of the physicochemical characteristics of the nanomaterials and the use of surrogate models ranging from microorganisms, to invertebrates, to vertebrates, particularly, those of aquatic species. Building the experimental database of the relationships between the physicochemical properties of ENMs and their biological end-point response is required for the development of predictive toxicology. Relative to experimental evaluation of the safety of ENMs, computational methods are less expensive and time saving. They may also be efficient alternatives for predicting the potential toxicity and environmental impact of new nanomaterials prior to when they are mass produced. Therefore, the quantitative structure–activity relationship (QSAR) study commonly used to predict the physicochemical properties of chemical compounds is quickly emerging in pharmaceutical and nanotoxicological research.

Among many physicochemical characteristics, crystal structure of NPs is critical in determining their toxicity. The specific spatial arrangement of atoms is closely relevant to their potential oxidative reactivity. NPs demonstrate different