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David G. Capco
Yongsheng Chen *Editors*

Nanomaterial

Impacts on Cell Biology and Medicine

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Preface

The rapidly developing field of engineered nanomaterial has expanded in many commercial areas. More recent studies have begun to provide a foundation for understanding how nanomaterials influence cells and how they also can serve as methodological tools for studies in medicine and cell biology. At the cellular level, recent investigations have shown the effects of nanomaterials on specific subcellular structures, such as the actin-based brush border network in cells with an increasing emphasis on the barrier function of epithelial tissues, while other studies have shown involvement of nanomaterials in specific cytoplasmic signal transduction events such as the rise in intracellular free calcium, a signaling event known to regulate many changes in cell architecture and function. In parallel, nanomaterials are increasingly used in medicine for drug delivery, treatment of cancer, and an increasing number of new applications. In this regard the subject of nanomaterial crosses disciplinary boundaries between medicine, biology, and engineering, and this has resulted in some of the advances and implications being over overlooked. One of the intentions of this book is to bring this diverse area into sharper focus.

Nanomaterials are used in medicine in a variety of ways including cancer targeting and ablation. They can also target cells through modification of their surface chemistry, and because of this are used as tools for drug delivery. They have been used for tissue contrast enhancement and as wavelength-specific probes for fluorescent imaging. Nanomaterials have also been employed to track stem cells as well as to alter their state of commitment. The usage of nanomaterials has become so common that they are present in a number of consumer products. This book presents chapters, from a variety of experts, in areas relevant to cell biology and medicine in order to demonstrate the breadth of applications.

This book was written for advanced undergraduates in cell biology, engineering, and medical professionals. Most chapters have different but relevant methods sections that explain key technological manipulations. Every attempt was made to make these sections practical and understandable, but with enough information in each chapter to be of interest to researchers as well.

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1 Presence in, and Release of, Nanomaterials from Consumer Products

Yu Yang and Paul Westerhoff

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Abstract

Widespread use of engineered nanomaterials (ENMs) in consumer products has led to concerns about their potential impact on humans and the environment. In order to fully assess the impacts and release of ENMs from consumer products, this chapter provides an overview of the types of consumer products that contain nanomaterials, the potential release mechanisms of these ENMs from consumer products, and the associated human exposure. Information from two large datasets on consumer goods associated with ENMs, namely, the U.S.-based Project for Emerging Nanotechnologies from the Woodrow Wilson International Center, and the European-based National Institute for Public Health and the Environment of Netherlands, have been summarized. These databases reveal that silver, titanium, carbon-based ENMs are the major nanomaterials associated with consumer products. The presence and potential release of silver, titanium, carbon-based, and other nanomaterials from consumer goods available in published literature are also summarized, as well as the potential human exposure scenarios of inhalation, ingestion, dermal, and combination of all means. The prospecting of nanomaterial in water and biosolids provides further evidence of ENM occurrence, which could be linked to the use of nanomaterials containing consumer goods. Finally, this overview provides guidelines on toxicity studies, which calls for further efforts to analyze the

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biological effects of ENMs on human beings and their exposure pathways in consumer products.

Keywords
Engineered nanomaterials • Presence • Release • Consumer products • Nanosilver • Titanium • Carbon

1.1 Introduction

Nanomaterials are typically defined as having "internal or surface structures in one or more dimensions in the size range 1–100 nm" [1]. Metallic and carbon-based nanomaterials, in particular, are comprised of novel physicochemical properties, and because of their small size and high surface-area-to-volume ratio are viewed differently than their bulk material. Over the past two decades, the clear advantages in using nanomaterials for consumer products have led to a new stage in nanotechnology development [2]. This, in turn, has fueled a dramatic growth in the nanotechnology industry, from a $10 billion enterprise in 2012 to an anticipated up to $1 trillion by 2015 [3]. As these industries continue to create products with unique elements and geometries, the human and ecological risks stemming from engineered nanomaterials (ENMs) may increase as a result of potential hazards [4]. Evaluating these risks, therefore, necessitates development of new tools and models that are better able to assess both exposure levels and toxicity of nanomaterials. This chapter focuses on strategies to quantify the presence of major classes of ENMs in consumer products and their release into water or air after use. ENMs include nano-silver, titanium dioxide, and carbon based nanomaterials.

Nanotechnology advances that have taken place in different disciplines over the years have led to widespread ENM applications in many everyday products. Nano silver (nano Ag), for instance, has been used in pesticide, medicine, socks, fabrics, or disinfectant sprays [5–7]. Colloidal silver is known to have been employed by industry for over 100 years [6]. In fact, the earliest example of nanosilver use can be traced to the Roman Lycurgus Cup, which is a bronze and glass cup created in the fourth century AD [8]. The glass material in the cup, which is able to scatter green light and transmit red light, contains particles that are 70 nm in diameter composed of silver (70 %) and gold (30 %). Nano titanium dioxide (nano TiO_2) is used in personal care products, such as sunscreens or toothpaste, food for coloring and texture, paints, and self-cleaning industry cleansers [9, 10]. Multi-walled carbon nanotubes have been used both in the electronic industry, and the textile industry, where it appears in the form of flame retardants in plastics, polymers, and fabrics [11–13]. Clearly, nanomaterials are prevalent in many consumer products, and exposure to humans potentially exists in physical forms, such as dermal, ingestion, and inhalation.

While the release of ENMs from consumer goods is an inevitable outcome of human activity, such release is often intentional (e.g., disposal of used toothpaste down the drain, dissolution of nano Ag into sweat), which leads to not only human exposure, but also to discharge into the environment [10, 14]. Sewage has been identified as a major conveyor of ENMs from consumer products and industrial processing [15]. The occurrence of ENMs in sewage can provide us one measure of the amount of human exposure that takes place. Therefore, proper sewage treatment becomes a critical intervention strategy in order to prevent ENM release to the environment, and thus limit ecosystem/human exposure to ENMs. ENMs can enter into wastewater treatment plants (WWTPs) through washing and other recreational activities [5, 16]. Nano Ag released from silver containing plastics and textiles from daily washing enters drains and sewers and ends up in WWTPs [5, 17, 18]. Similarly, Nano TiO_2 enters water caused by washing, bathing, and swimming [19, 20]. Both macro- and nano-scale TiO_2 have been detected in WWTP effluents, with the majority of the Ti accumulated in biosolids. Nanosilver can be absorbed to biosolids and converted into nano- Ag_2S under anaerobic conditions [21–24]. Recent work has shown that many ENMs can be removed from sewage water, and concentrated into biosolids ([5, 25–27].

In the U.S., 40 % of biosolids end up in land applications [28]. Land amendment, which occurs as a result of these biosolids, leads to the transport of ENMs into soils [22, 28]. Sanitary landfill sites, which receive used textiles (clothes, socks) and other consumer products, are another repository of ENM containing solid wastes [24, 29, 30]. Life cycle analyses have suggested that over 50 % of ENMs produced globally ends up in landfills [15]. Thus, the use of ENMs in consumer products can potentially affect solid waste treatment, and once again, landfills may emerge as a location to assess retrospectively changes in use patterns of products incorporating nanotechnology.

The rapid rise in nanotechnology application in consumer products means that a more comprehensive investigation is needed into the exposure risks posed by ENMs to humans and the environment. David Warheit, who chaired the committee on health and environmental safety of nanomaterials for the European Centre for Ecotoxicology and Toxicology of Chemicals, has aptly remarked: "The number of implication studies has not caught up with the number of application studies" [31]. Therefore, the need for more studies of ENM implication continues to grow.

To understand both the implication and application aspects of ENMs, we provide here a comprehensive summary of consumer products that contain nanomaterials, potential paths for ENM release from consumer products, and the range of associated human exposure. Prospecting the presence of ENMs in water and sewer biosolids provides us with information and guidelines on toxicity tests, while addressing important questions: At what concentration levels do ENMs exist in the environment? Which chemical form of ENMs (e.g., oxidation state) should be tested for dose-response experiments?

1.2 Categorization of Consumer Products with Nanomaterials from Databases

In 2005, The Woodrow Wilson International Center for Scholars initiated the Project for Emerging Nanotechnologies (PEN), which aimed to provide an inventory of nanotechnology-based consumer products (either containing nanomaterials or production processes incorporating nanotechnology). For simplicity, all the information obtained from this project is cited as the Woodrow Wilson database in this chapter [32]. Originally, the inventory cited 54 different products in 2005; in 2011, the number of products increased to 1,317, representing a 24-fold increase during a 6-year period [32]. Of the total number of 1,317 products in 2011, 45 % (587), 28 % (367), and 20 % (261) originated in the U.S., Europe, and East Asia, respectively [32]. The number of nanotechnology-based products was projected to continue as advances in nanotechnology were further applied to consumer products. This inventory provides information such as product name, company, manufacturer or supplier, country of origin, category and subcategory, product description, and date of update [32]. Updates to this inventory were halted in 2011, as funding and priorities changed. More recently, Virginia Polytechnic Institute and State University's Center for Sustainable Nanotechnology (VT SuN) and the Woodrow Wilson International Center for Scholars have been partnering on a new effort to compile the Nano Consumer Products Inventory (NCPI), which incorporates the PEN dataset (http://www.nanotechproject.org/cpi/).

In 2010, an inventory of consumer products containing nanomaterials published by the National Institute for Public Health and the Environment (RIVM) of Netherlands was made available in the European market. The RIVM, based on advertisements of manufacturers, cited 858 products in 2010, showing a six-fold increase of 143 products that contained ENMs in 2007 [33]. Similar to the database maintained by the Woodrow Wilson center, the RIVM stated the following: "No verification of the actual presence of nanomaterials via measurements in claimed consumer products has been made" [33].

We re-categorized product information in the RIVM database to be consistent with those used in Woodrow Wilson database. Figure 1.1 provides a comparison of the Woodrow Wilson and RIVM databases. The quantity of each product depicted here is based on this re-arrangement.