Nanomaterials in Food and Food Contact Substances – Hazards, Risks and Regulation

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ABSTRACT

The increasing number and variety of engineered nanomaterials (ENMs) used in food and food contact materials raise concerns regarding potential hazards and risks to human health. ENMs are used for a wide variety of applications from enhancing the strength and reducing the weight of food packaging materials, to helping eliminate foodborne pathogens. The unique physical-chemical properties that provide their desirable functionality may also impart unique bioactivity that could potentially lead to human health hazards and risks. Tools for evaluating risks across the life cycle of nano-enabled products are emerging though major data gaps still exist, especially regarding characterization of consumer level exposures. Furthermore, most animal and cellular toxicity studies to date focus on freshly generated nanoscale materials that are not necessarily representative of consumer-level exposures. ENM properties relevant for biointeractions can vary greatly between the raw material, the nano-enhanced food or food contact substance, and any releases that may occur across the life cycle of the nano-enhanced product. Regulatory agencies in the U.S. (EPA, FDA) are currently trying to understand and manage potential risks to human health and the environment. Meanwhile, nano product registries and mandatory reporting practices are emerging in Canada, France, Belgium, and other EU nation states, intending to facilitate monitoring and prevent potential hazards. In light of the ubiquitous nature of nano exposures from food, there is continued need for methods to integrate nano-risk assessments across the life cycle of nano-containing products.

Keywords: nanomaterials, food, food contact substances, nanotoxicology, nano regulation, consumer exposures

1 NANOMATERIALS IN FOOD

Many foods and food contact substances contain nanoscale particles. In some cases, nanoparticles are naturally occurring, such as the case with casein micelles found in milk products. Materials engineered at the nanoscale are also intentionally added for a specific function. TiO_2 nanoparticles are often used as a whitener in powdered sugar products, and SiO_2 nanoparticles are often added to clarify beers and wines and to thicken pastes. There is also widespread use of nanoscale materials in food packaging for a variety of applications, and the use of these materials is expected to increase. Nanotechnology in our Food, an open-access "living" inventory of consumer products that contain nanomaterials, consists of over 300 entries covering more than 40 types on nanomaterials an products currently available for sale in the U.S., including beer bottles, aluminum foil, plastic wrap and sandwich bags[1]. Also, a recent study by Persistent Market Research estimated the global market for nano-enabled food and beverage packaging materials to be $6.5 billion in 2013 and predicted that it will continue to grow rapidly over the next decade[2].

The advantages that nanotechnology offers in food packaging are substantial and stem from the unique physical and chemical properties of materials engineered at the nanoscale. For example, nanotechnology can reduce the weight of food packaging materials while also maintaining barrier functionality. Incorporating nanoclays such as mont-morillonite into plastic food packaging materials improves the gas barrier and mechanical properties of the packaging beyond what can be achieved with conventional materials. Nanocomposites reduce the migration of gases, flavor compounds and water vapor across packaging material while offering superior performance under the stresses imposed during thermal food processing (e.g., heating to eliminate potential foodborne pathogens), transportation and storage[3].

Human health and environmental concerns about using petroleum-based packaging materials (i.e., plastics) have led to increased interest in sustainable alternatives, some of which take advantage of nanotechnology. For example, biopolymer nanocomposites consisting of plant-derived materials as well as animal and microbial products are currently used as natural adhesives in food packaging. This application of nanocomposites may provide a safer alternative and superior performance compared with conventional chemicals, such as polyvinyl acetate, used for this purpose.

In addition to potential health and environmental concerns, poor mechanical and barrier properties make conventional-scale biopolymers ill suited for industrial applications. To address this problem, engineered composite materials, such as biopolymers layered with nanosilica particles, have been developed that exhibit improved gas-barrier properties, tensile strength and thermal stability compared with standard biopolymers. These nanocomposite packaging materials provide effective barriers against water, gases and

grease while also promoting the use of sustainable source materials[3].

Nanoscale materials are also desirable for their antimicrobial properties. Nanoscale zinc oxide and titanium oxide particles exhibit photocatalytic properties and, when incorporated into food packaging materials, help degrade harmful volatile organic compounds and kill microorganisms. Silver nanoparticles are also used in food packaging for their antimicrobial properties. Studies suggest that nanosilver can kill 650 disease-causing pathogens in food, whereas most antimicrobials kill only 5–6 such pathogens[4]. Moreover, preliminary evidence suggests that silver may be less susceptible than traditional antimicrobials to the development of bacterial resistance[5]. Nanosilver is also readily incorporated into various materials, such as textiles and plastics. In light of these reported benefits, several food-storage products currently available on the market claim that the nanosilver particles they contain help extend the shelf life of fruits, vegetables, breads, meats and other food items[5].

2 RISKS TO HUMAN HEALTH

While there is significant interest in the food packaging sector regarding the benefits of nano-enabled materials, potential risks to human health and the environment have yet to be resolved. The properties that make nanoscale materials desirable for food packaging applications (e.g., increased surface reactivity and dispersibility) can also lead to unique interactions with biological systems that often differ considerably from those demonstrated by conventional-scale forms of the same substance. This disparity is further compounded by the sheer number and variety of different nanoscale materials that require evaluation, and by a lack of standardized laboratory methods for characterizing and testing these unique materials.

To date, hazard assessment of nanoscale materials used in food packaging has focused almost entirely on the raw materials, whereby freshly generated, pure nanoscale materials are administered to animals or cells. However, consumer exposure depends entirely on whether free nanoscale particles are released into the packaged food product and, if so, in what amount. Such releases would likely be associated with transformation of various nanoscale material characteristics, including particle size, agglomeration state and surface reactivity. For this reason, academic and governmental research groups have investigated the migration of nanoparticles from food packaging materials into foodstuffs to better understand the risk of human exposure. Several studies report evidence of various nanoparticles (nanosilver, nanocellulose, nanoclay) migrating out of packaging materials at low levels and indicate that the total amounts increase with time and temperature and depend on the acidity of the food sample[4]. While these factors also influence the migration of conventional-scale substances used in food packaging, the impact of temperature and pH on transformations of nanoscale materials released from FCSs has yet to be fully explored. Furthermore, several methodological limitations make it difficult to extrapolate the results of studies showing migration of nanoscale particles into foodstuffs to real-world exposures. Often, chemical solutions representing extreme environmental conditions (e.g., very high or low pH) that are not characteristic of actual foodstuffs are used to model and measure migration. Considering that nanoscale particle migration is likely related to the compatibility between the particle, its embedded food packaging matrix and the foodstuff it contacts, these extreme conditions make estimating actual human exposure associated with off-the-shelf products difficult. These worst-case testing conditions are also a factor in the migration of conventional-scale substances used in food packaging.

Tools for evaluating risks across the life cycle of nano-enabled product are emerging[6], though significant knowledge gaps remain. Namely, there is currently limited data available characterizing the kinds and concentrations of nanoparticles at which consumers are likely exposed. There are limited *in vivo* biokinetic and toxicological studies on food grade nanomaterials. The available data mainly focus on inhalation and dermal exposure. There is limited to no data on susceptible populations (*e.g.* ulcerative colitis), and there are limited data on impacts to the gut microbiome. Lastly, there is limited knowledge regarding the possibility of food matrix effects, specifically with regards to impacts on particle properties, reactivity, agglomeration, absorption, accumulation, biodistribution, and eventually on toxicity.

3 REGULATORY STATUS IN THE U.S.

The toxicological hazards associated with engineered nanoscale materials are not well understood, and characterization of potential risks posed to humans and the environment is an active area of ongoing research. In light of the current state of knowledge, FDA released guidance documents in June 2014 to outline its general approach to nanotechnology and to provide specific guidance for using nanotechnology in the food industry[7]. The general guidance document reflects FDA's current thinking that 1) nanoscale materials are an emerging technology of major importance, with the potential for novel applications across the entire spectrum of FDA-regulated products, and 2) although these materials may not be inherently safe or harmful, FDA will continue to consider the specific characteristics of individual products. FDA encourages manufacturers to consult with the agency early in the product-development process to clarify specific scientific and regulatory questions related to the safety, effectiveness and public-health effects of nanotechnology products. Notably, FDA did not establish regulatory definitions for

"nanotechnology," "nanomaterial" or "nanoscale" and instead emphasizes that new technologies will be evaluated case by case. The guidance document for the food industry describes factors to consider when determining whether a change in the manufacturing process for an FCS affects its identity and safety. Such changes may impact an FCS's regulatory status, thereby warranting a regulatory submission to FDA. Thus, the guidance suggests that for a specific case, depending on the data generated by the manufacturer, FDA may conclude that replacing a conventional-scale substance with a nanoscale substance does not warrant a new regulatory submission, and that FDA's general FCN process is applicable. Similar to the FDA, the European Food Safety Authority (EFSA) addresses nanoscale substances in food on a case-by-case basis[8]. Testing the nanospecific form of a previously characterized conventionally scaled material is only required if there is evidence that the nano-form persists in the gastrointestinal tract. Otherwise, testing the conventionally scaled material is deemed sufficient.

4 SUMMARY AND CONCLUSIONS

Nanoscale materials are increasingly being used in food and food contact substances for a variety of applications, and such uses are expected to increase. The advantages that nanotechnology offers in food packaging are substantial and include properties such as reduced package weight, improved gas barrier and superior performance under the stresses imposed on packaged food. Although there is significant interest in the food packaging sector regarding the benefits of nano-enabled food packaging materials, potential risks to human health and the environment have yet to be resolved. The science of hazard assessment for nanoscale materials and laboratory studies to estimate the amount of nanoparticles that may migrate into food are still being developed and are fraught with substantial uncertainties. In light of data uncertainty, nano-regulation is slowly evolving in the U.S. and abroad.

REFERENCES

[1] Center for Food Safety. 2016. "Nanotechnology in our Food." Accessed on March 24, 2017 at http://salsa3.salsalabs.com/o/1881/p/salsa/web/common/public/content?content_item_KEY=14112.

[2] www.persistencemarketresearch.com/media-arelease/nano-enabled-packaging-market.asp.

[3] Arora, A and GW Padua. 2010. Review: Nanocomposites in food packaging. *J Food Sci* 75(1):R43–R49. doi:10.1111/j.1750-3841.2009.01456.x.

[4] Bumbudsanpharoke, N and S Ko. 2015. Nano-food packaging: An overview of market, migration research, and safety regulations. *J Food Sci.* doi:10.1111/1750-3841.12861.

[5] Duncan, TV. 2011. Applications of nanotechnology in food packaging and food safety: Barrier materials, antimicrobials and sensors. *J Colloid Interface Sci* 363(1):1–24. doi:10.1016/j.jcis.2011.07.017.

[6] Organisation for Economic Co-operation and Development (OECD). 2015. "Guidance Manual Towards the Integration of Risk Assessment into Life Cycle Assessment of Nano-enabled Applications." ENV/JM/MONO(2015)30; Series on the Safety of Manufactured Nanomaterials No. 57. 78p., July 7. Accessed on March 24, 2017 at http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono%282015%2930&doclanguage=en.

[7]www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm300661.htm Accessed on March 24, 2017.

[8] European Food Safety Authority (EFSA). 2011. "Scientific Opinion on guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain." EFSA J. 9(5):2140. doi: 10.2903/j.efsa.2011.2140. 36p.