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Risk Ranking of ENPs of Human Health Concern

Yingzhu Li, Enda Cummins
School of Biosystems and Food Engineering, University College Dublin
Belfield, Dublin 4, Ireland
li.yingzhu@ucdconnect.ie

Abstract **-** Nanotechnology has numerous applications with increasing usage in industry, the corresponding risks need to be assessed, particularly in relation to concern for consumer health while also recognising nanoparticles as a novel class of pollutants. However, due to current knowledge gaps regarding toxicity, and the wide ranging market applications of engineered nanoparticles (ENPs), traditional risk assessment, based on material flow of pollutants, may not be feasible. In this context, a proactive specialised risk ranking for ENPs, which matches current data availability, was developed. In accordance with the standard risk assessment methodology, market information, exposure scenarios, and toxicity studies were introduced to develop a risk scoring system. Exposure and hazard potential (dermal, inhalation and oral routes) were characterized for the most used ENPs within Europe. A risk prioritisation was provided by this model. Nano-TiO_2 was ranked as the most critical ENP, which is due to the large quantities used and the many exposure pathways through the consumer market. The second highest ranked ENP was found to be AgNP, which is mainly due to the many environmental sinks, especially through water sources. Key information gaps were also highlighted for upgrading the quantification level of the ENP risk assessment. This model can pave the way for the full quantification of ENP risk potential, and previse the potential ENP risks throughout their life cycle and corresponding consequences for human health.

Keywords**:** Engineered nanoparticles, risk ranking, health and safety, Europe.

1. Introduction

With the rapid development of nanotechnology, engineered nanoparticles (ENPs) are ubiquitous in people's daily life. Their growing utilisation inevitably leads to increased human and environmental exposure to ENPs, which generates corresponding potential risks to human health. The release of hazards could occur along the whole life cycles of ENPs, including during manufacturing, utilisation, and disposal processes. The corresponding exposure scenarios are different for people followed by different intake likelihoods. The potential hazard severity of ENPs could also be differentiated according to their various forms in consumer products and transformations in exposure scenarios. Therefore, risk assessment of ENPs should consider both the exposure and hazard. It coincides with the chemical risk assessment approach which has been suggested by REACH for ENP risk assessment [5].

Even though ENPs have been shown to have unique physicochemical and toxicity properties in in-vivo animal tests, the conventional risk assessment methodology for traditional chemicals can be applied to ENPs [1]. Chemical risk assessment (CRA) has been successfully used by the World Health Organisation (WHO) and the Organisation for Economic Co-operation and Development (OECD) to guide chemical regulations [2]. It consists of four connected steps, incorporating both hazard and exposure assessments to form a comprehensive risk characterisation for pollutants.

Therefore, hazard and exposure assessments were regarded as two critical elements to construct the risk assessment framework. As they are equally valued according to REACH, they are equally weighted in this model. Scenario analysis of ENPs have been intensively conducted in the last number of years. Among them, material flow analysis (MFA) has been the most emphasized methodology. However, analytical measurements of concentrations in the environment is currently not reliable [3]. Additionally, among different types of ENPs, mismatches exist on physicochemical knowledge and flow information in the market and environment, which means very limited ENPs can be quantified by the predicted environmental concentrations (PEC). Even so, their flows in the environment are still assessed with a certain amount of uncertainty. Caballero-Guzman and Nowack [4] report the limited coverage of exposure scenarios in MFAs with 20% in the industry and 36% in products. Therefore, in this study, a ranking methodology was developed with suitable accuracy for assessing ENP risks under the current analytical techniques. The objective of this paper is to develop a risk ranking methodology to prioritize ENPs used in Europe and potentially representing a novel threat to human health and providing a feasible risk assessment strategy for ENPs by organizing available qualitative and quantitative data.

2. Methods

2.1. Model structure, boundary, and parameters

The framework of the ENP risk assessment is based on the guidance on information requirements and chemical safety assessment as used by REACH [5]. To conduct a general strategy for assessing risks that can be used for different types of ENPs, a risk ranking model was selected. A risk scoring system was established to provide ordinal scales for risks instead of numeric estimates. Exposure and hazard were assessed by both quantitative and qualitative data to form a semi-quantitative risk ranking for ENPs.

According to MFAs and environmental fate models (EFM) for ENPs, there are three exposure sources to ENPs for humans, including three environmental compartments (water, air, and soil) and consumer products. Consumer exposure results from utilisation scenarios and possible environmental contact. As generally interpreted, nanomaterials in products could be present in the environment after the use phase. However, as toxicity performance of ENPs has revealed, the mechanism for ENPs to induce in-vivo effects begins with the intake of nanoparticles. It means that the part of ENP quantities that was taken in by humans in the use phase was extinct and would not be released into the environment. The concept also fits into the environmental exposure scenarios. Whereas, in the two exposure scenarios through the environment and products, both current market information and knowledge of ENP environmental fate highly limit the reliable prediction of intake amount of ENPs by humans [4], even with the aid of statistical analysis. In the light of this issue, the mass flows of ENPs and intake probabilities were separated in this model. All the ENP quantities in different compartments were seen as having the potential to result in human exposure and used as quantitative data to scale a quantity score (Q). The introduction of a coefficient namely the exposure coefficient (E) was designed specifically for evaluating exposure likelihoods according to different exposure scenarios. As shown in the figure of the model input and output (Fig 1), the exposure coefficients could be determined by various parameters which depended on the current understanding of ENP behaviour in different scenarios, which also serving as a flexible part for further arrangement with the increasing knowledge of ENP fate.

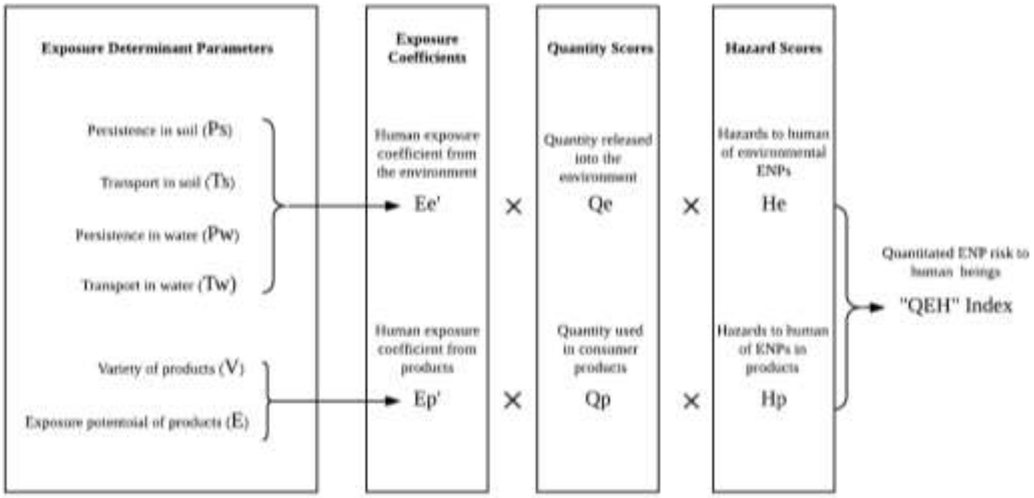

Fig. 1: Inputs and outputs of the risk ranking model.

Currently, ENP behaviour in the environment are characterised in relation to persistence and transport ability [6]. Chemical properties and the environmental conditions determine the persistence of nano-scale particles. Transport ability describes the physicochemical stability during spatial transportation. Since there is currently no standardized scale to quantify ENP physicochemical properties or behaviour in the environment, comparative data for all types of ENPs in the ranking scope were derived from ENP behavioural studies. ENPs are scored using qualitative data to calculate the exposure likelihood in the environment (E_e'). In the same manner, qualitative data from an open dataset [7] of ENP containing consumer products were scored to form the exposure coefficient for consumers in their daily life (E_p').

The hazard potential is assessed in parallel with the exposure potential for ENPs. Therefore, a hazard score was designed correspondingly. As one of the most unique properties of novel pollutants, the hazard performance of nanoparticles greatly depends on variations of sophisticated characteristics. The open dataset of ENP containing consumer products in the European market provides individual hazard potential levels, which incorporate potential exposure pathways for different types of consumer products [8]. Toxicity information for dose-response relationships was collected from toxicity studies for three potential exposure pathways (dermal, inhalation, and oral routes). Values were scored to represent hazard potential through the environmental exposure (H_e) and assigned according to the respective potential exposure pathways from three environmental compartments. For example, the potential exposure of ENPs from water could be through dermal contact or drinking, the H_e was thus picked from scores of dermal and oral toxicity.

2.2. Ranking process

Q and H scores were rescaled from 1 to 5, E_p is the coefficient with the range from 0 to 1. As there are four compartments of risk sources, the combination of three parameters namely the QEH index has the range from 0 to 100 for each type of ENPs. QEH index equally weighed exposure and hazard potentials of ENPs for people, which is calculated by the equation below.

$$\text{QEH Index} = Q_p \cdot {E_p}' \cdot H_p + \sum_{e}^{3} Q_e \cdot {E_e}' \cdot H_e \qquad (1)$$

Where “p” represents product; “e” represents the compartment soil, water, or air.

3. Results and discussion

The prioritisation of potential risks of the most commonly used ENPs according to potential health risk to humans and corresponding sources of potential risk in Europe are demonstrated through the QEH index by the funnel chart (Fig 2). The top four ENPs with highest potential risks generally have exposure scenarios involving contact through consumer products, except AgNP, which has greater concern from the environmental exposure scenario through the aquatic system. Nanoclays are the only exception in the ranking without potential risk from products.

Nano-TiO_2 was found with the highest risk index of 7.919, and nano-CeO_2 with the lowest risk index of 0.625, out of the maximum value in the range of the QEH index which is 100. However, the inflow of ENPs into the European market is estimated to increase by more than 5 fold from 2014 to 2020, even based on a pessimistic estimation [9].

The transition from semi-quantitative to quantitative risk assessment is the future pathway for regulating ENPs. Possible uncertainties that hinder this process come from data gaps and deficiencies. For example, lack of systematic market monitoring and regulation jeopardizes the enhancement of product labelling. Similarly, lack of physicochemical knowledge of ENPs leads to difficulty in estimating intake potential in different exposure scenarios. The main cause being the scarcity of behavioural knowledge of ENPs.

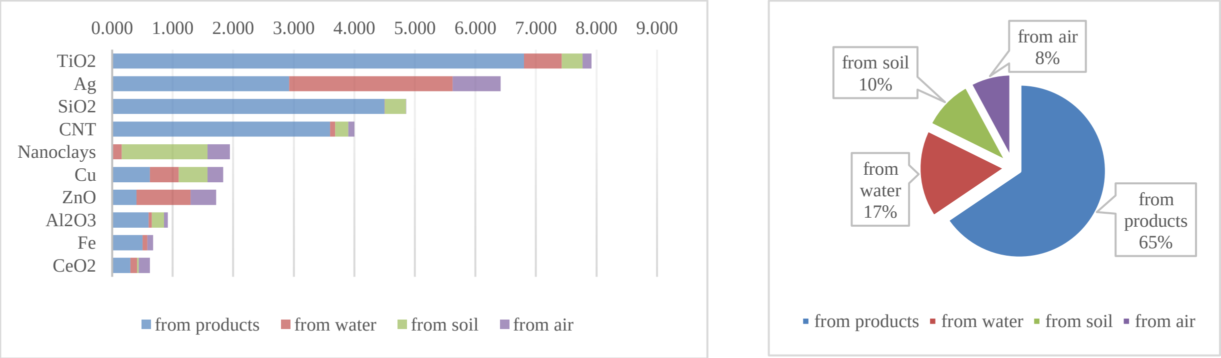

Fig. 2: Prioritisation for 10 most used ENPs and Compartmentalisation of risk sources in Europe.

4. Conclusion

A semi-quantitative risk ranking model was developed and applied to the European ENP market. The risk during the life cycle of ENPs was assessed holistically and sectionally according to the exposure scenarios. The model provides the prioritisation of the most used ENPs in Europe as novel pollutants with potential concern for human health. Nano-TiO_2 is the most concerning type which should be highlighted in the use phase, followed by nano-SiO_2 and carbon nanotube (CNT). As the second critical type of ENPs, AgNP has a higher risk ratio from the environmental exposure for humans compared to the exposure through products. Overall, ENPs currently applied in Europe are at a low risk level but increasing rapidly with the expansion of nanotechnology. Prospectively, behaviour in environmental compartments, especially in aquatic systems, should be prioritised with regards to risk evaluation and human health concern.

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