OPINION

The unseen impact of nanoparticles: more or less?

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The nano-revolution[1] has created a market for nano-based products and is expected to change industrial production and economics over the decades to come[2]. As this new field is breaking the barriers between fundamental disciplines such as chemistry, physics and biology, the application field is also getting broad such as health (medical products such as heart valves, drug-delivery systems and imaging techniques), sports (sports equipment), food production (pesticide delivery, nutrient delivery, etc.), environmental remediation (remediation of pesticides), cosmetics, etc.[2–7]. However, majority of the nanoparticles are being introduced into the market on the basis of claimed benefits[2] and the eco-toxicological profile of many of these products is unknown to the scientific community. The rising number of works on the toxic (geno-toxicological) effects of nanoparticles clearly warrants that apart from the benefits, nanotechnologies also produce uncertainties and risks[2]. Although nanoparticles are widely used for analytical and in imaging field, many researchers consider it as an emerging contaminant and have started developing sensitive analytical methods for their detection from environmental samples[8]. Therefore, the present article discusses the potential environmental risks and uncertainties associated with the use of nanoparticles and highlights few factual cases from the literature to ascribe the toxic and bioaccumulative potential of such particles. While our deliberations are not intended to overlook the past and ongoing remarkable contributions of various researchers in this booming field, we urge the scientific community to have a detailed geno-toxicological and eco-toxicological approach to ensure the safety and risks before the field utilization of such particles, products or any formulations.

Recently, studies demonstrated that silica (70 nm) and titanium dioxide (35 nm) nanoparticles can cross the placenta barrier in pregnant mice and cause neurotoxicity in their offspring[9], and cobalt–chromium nanoparticles (29.5 ± 6.3 nm in diameter) can damage human fibroblast cells[10]. Similarly, it has been proposed that inhaled multiwalled carbon nanotube can reach the subpleural tissues in mice and may cause pleural fibrosis and/or mesothelioma[11]. Hu and Gao[12] studied the neurotoxicity of nanoparticles and proposed their possibility of crossing blood brain barrier (BBB). Similarly, engineered nanoparticles are being considered as an emerging class of pollutants with eco-toxicological impacts on marine ecosystems because the particles can end up in waterways and reach the sea[13]. Kim *et al.*[14] assessed the influence of citrate-capping silver nanoparticles (cAgNPs) on *Caenorhabditis elegans* and found that it could induce dermal effects that cause burst scars on the epidermis and make it vulnerable to secondary infections by bacteria. The impacts of metallic nanoparticles on agricultural crops are well documented. Lee *et al.*[15] reported that AgNPs significantly reduce the seedling growth of *Phaseolus radiatus* and *Sorghum bicolor*. Additionally, the brown tips and necrosis detected in the exposed roots of both plants were an indication of the phytotoxicity of nanoparticles[15]. Similarly, Lin and Xing[16] reported that ZnO nanoparticles were able to concentrate in the rhizosphere of *Lolium perenne*, enter the root cells and inhibit the seedling growth of ryegrass. In another case, the inhibitory effect of water-soluble fullerenes on *Arabidopsis thaliana* at the cellular level was observed and it was found that fullerene retarded roots with shortened length and resulted in the loss of root gravitropism[17].

Contrary to the above findings, some workers reported that CeO_2 and ZnO nanoparticles have increased the root and shoot growth in edible plants such as soybean, wheat, corn and alfalfa[18–20]. Moreover, it has been reported that nano TiO_2 improved the germination, seedling growth and photosynthetic rate in wheat and spinach in comparison to the untreated control plants[21]. However, it is widely accepted that the uptake, bioaccumulation, biotransformation and risks of nanoparticles for food crops are still not well understood and few nanoparticles and plant species have been studied so far and very few references are available on the biotransformation of nanoparticles within the food plants[22]. Furthermore, the detailed biomagnification of nanoparticles in food chain is also not known[22] (Figure 1). However, previous studies have reported that nanoparticles can accumulate in living organisms and can be transferred from prey to predator (trophic transfer)[23–27] and even these materials can be biomagnified. Ferry *et al.*[28] proved that gold nanorods can readily pass from the water column to the marine food web in three laboratory constructed estuarine mesocosms containing sea water, sediment, sea grass, microbes, biofilms, snails, clams, shrimp and fish. Similarly, in an experimental microbial food chain, Werlin *et al.*[29] demonstrated that CdSe quantum dots were accumulated in bacteria *Pseudomonas aeruginosa* and were transferred and biomagnified in a protozoa *Tetrahymena thermophila* that preyed on the bacteria. Interestingly, the quantum dots concentration in the protozoa predator was approximately five times higher than the bacterial prey[29].

Although there is an increasing concern regarding the unknown toxicity of nanoparticles, lack of proper experimental methods for the validation of toxicological assays is a major impediment in nanotoxicology itself. A recent editorial in *Nature Nanotechnology* clearly pointed out the various challenges faced by this relatively new field. It raised an important question to the scientific world regarding the growing uncertainty and toxicity of nanoparticles as 'twenty years of research has confirmed that nanoscale materials can display unexpected and unusual toxicity, but just how much have we learnt about the interactions between engineered nanomaterials and humans, animals and the environment?'[30]. Most importantly, the editorial mentioned some worrying aspects of nanotoxicology such as: (i) materials that are not harmful in bulk form may well be toxic on the nanoscale[30]; (ii) nanoparticles are also more likely to react with cells and various biological components such as proteins, and to travel through organisms[30,31]; (iii) traditional toxicological assays to find out the dose–response relationship are not workable in the case of nanoparticles because unlike the soluble chemicals tested for dose–response studies, nanoparticles have shapes and surface areas, and they can diffuse, aggregate/agglomerate and sediment according to their size, density, and physical and chemical properties in solution[30]; (iv) many toxicity studies of nanoparticles have been done at much higher doses than is realistic, so that the resultant toxicity profile is not sufficient to interpret or extrapolate the realistic toxicity of these materials[30]. The editorial also concluded with a pragmatic comment that 'the big challenges in the coming years are to understand how physical and chemical properties of nanomaterials govern their interactions and responses, and to inform the public on the benefits and risks associated with the use of nanomaterials'[30].

The above assertions clearly indicate that the field of nanotoxicology is still in its infancy and much of the assayed toxicity of nanoparticles may be less or higher than the actual toxicity. So we have to design new ways and means to calculate the real toxicity of nanoparticles. Even the standard phytotoxicity tests such as germination and root elongation may not be sensitive enough or appropriate when evaluating nanoparticle toxicity to plant species[32]. Therefore, as mentioned by Saez *et al.*[1], the successful integration of various disciplines underpinning the fundamentals of nanoparticles such as physics, chemistry, biology, materials science and engineering and the applied disciplines such as molecular, toxicological and eco-toxicological approaches together with societal and regulatory contexts are essential for outlining the broad implications of nanoparticles on human health and the environment. Furthermore, detailed life-cycle assessment of every nanoparticle/material either in bulk form or in nano form is essential for ensuring the safety of the material. Without this exercises, we cannot promote the use of nanoparticles or nano-based products.

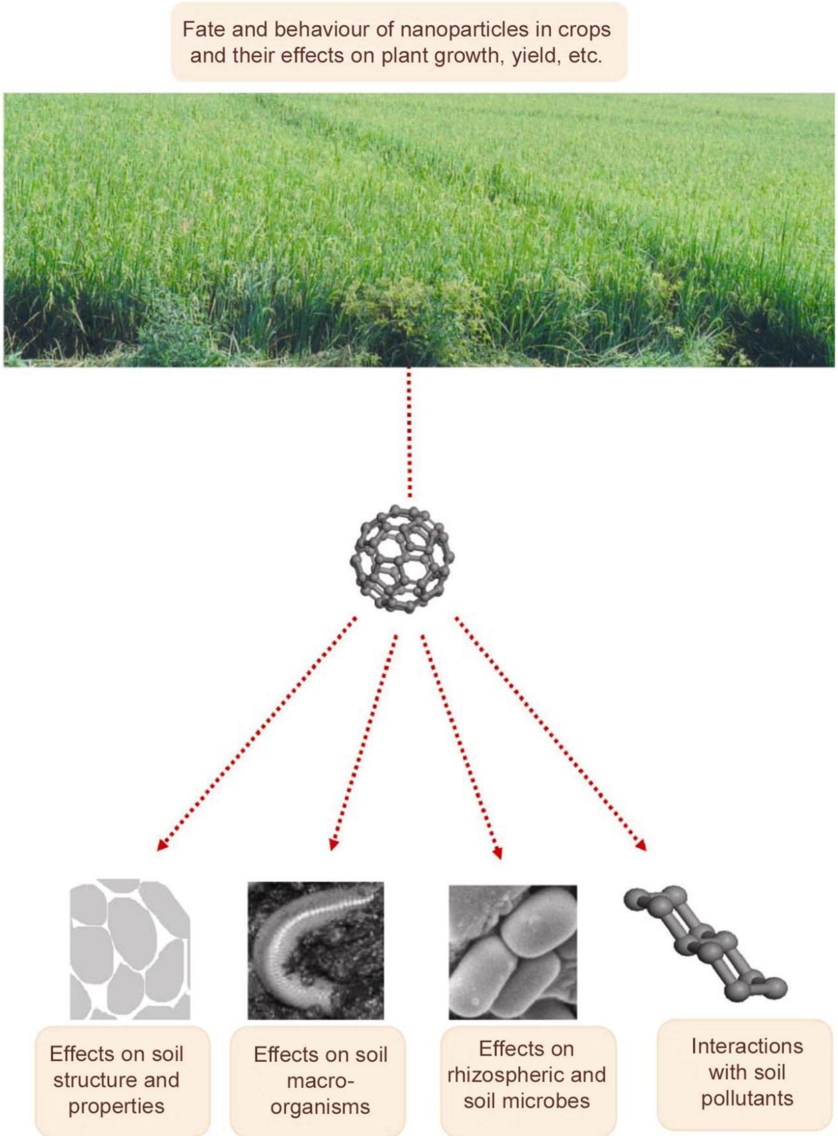

Figure 1. The possible interaction of nanoparticles in soil system. The unseen impacts of nanoparticles may be less or worse than known. However, proper evaluation based on realistic experimental and real-time models is essential to ensure the safety and efficacy of nanoparticles on humans, plants, non-targeted organisms and the ecosystem as a whole.

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