Nanotechnology in Life Science: Its Application and Risk

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Abstract

From the increasing number of patent registrations, the European Commission (EC) concludes that nanotechnology ranks within the six most promising key technologies. Most successful at inventing nanomaterials—measuring one billionth of a meter—is nature, which provides blueprints of self-organizing physical-chemical nanoparticles (NPs) properties and opens new dimensions for researchers in exploiting nature's NPs and developing new products for increasing the agricultural and industrial productivity.

After summarizing product processing effects, advantages and risks for agriculture, food, nutrition, and medicine, this book chapter discusses reasons why NPs use should occur balanced and carefully controlled by health and landscape policy. Only then a successful and profitable use for the overall benefit at lowest environmental pollution is achieved.

Keywords

Absorber • Biocidal nanoparticles • Encapsulated systems • Novel food • Nanopharmaceuticals • Sensor elements • Lab on a chip analytic • Toxicity • Risk assessment

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2.1 Introduction

Nanotechnology is one of the six “key technologies” that the European Commission (EC) is considering as adequate to initiate sustainable competitiveness and growth among industries and countries. In the advancement of nanotechnology supporting obligation, an increasing number of nanotechnology-related publications and patents in the field of agriculture, foods, nutrition, and medicine encourage the EC, although industry experts stress that agricultural nanotechnology does not demonstrate a sufficient economic return to counterbalance the high initial production investments (Benckiser 2012; Parisi et al. 2015; Prasad et al. 2017b). However, the research engagement beyond the increasing number of nanotechnology-related publications and patents and the rapid progress of nanotechnology key industries are convincing arguments for the EC to support nanoresearch engagement and to explore possibilities of how the bulk of publications and patents could be transferred into marketable and profitable agricultural products over time.

The most inventive at producing nanomaterials, measuring one billionth of a meter, is nature, and its blueprints of self-organizing, physical-chemical nanoparticles (NPs) properties open new dimensions to researchers as the bulk of publications and patents substantiate. Researchers have started wrapping nanoactive substances into additives, nano inside, and develop marketable products, fabricated by medicine, food, nutrition, and agriculture-related industries. Nitrification inhibitor-containing N-fertilizers, oil-applied pesticides, formulated drugs, and bags with which these products are transported to the consumers, nano outside, are examples (Ravichandran 2010; Chen et al. 2012; Horstkotte and Odoerfer 2012; Shen et al. 2012; Benckiser et al. 2013, 2016; Prasad 2014, 2016; Aristov et al. 2016; Leung et al. 2016; Scandorieiro et al. 2016).

Through 2012, more than 68 million patents were registered within the International Patent Documentation Centre (INPADOC), the World Intellectual Property Organization (WIPO), the Patent Cooperation Treaty (PCT), and the patent offices, mostly of America, Europe, Germany, and Japan and a keyword search within this wealth of patents under the headings: nanotechnology, super absorber, agriculture, nutrition, and food technology generated 28,149 positive matches (Benckiser 2012). A closer look on the first 500 patents of the 28,149 positive matches unveiled that approximately 320 of the 500 patents or 64% belong to machine-integrated NPs parts or control devices (Connor and Jacobs, 1999; Schmitt et al. 2010; Kuhlmeier et al. 2012; Banitz et al. 2013; De Lorenzo 2014). Approximately 36% of the NPs represent metal oxides, fertilizers, pesticides, and drugs, which find use in agriculture, food technology, nutrition, and medicine (Allen et al. 2011; Benckiser 2012; Benckiser et al. 2013; Prasad et al. 2014, 2016; Heo and Hwang 2016; Palomo and Filice 2016; Shamaila et al. 2016).

The slowly useable made NPs motivated the international science and technology community and administrators to invest more engagement into converting NPs into marketable products with a broad range of applications (Fig. 2.1; Buentello et al. 2005; Tzuzuki 2009; Kong and Ziegler 2012). Yet, in this context NPs side effects of already marketed NPs products in agriculture, food technology, nutrition,

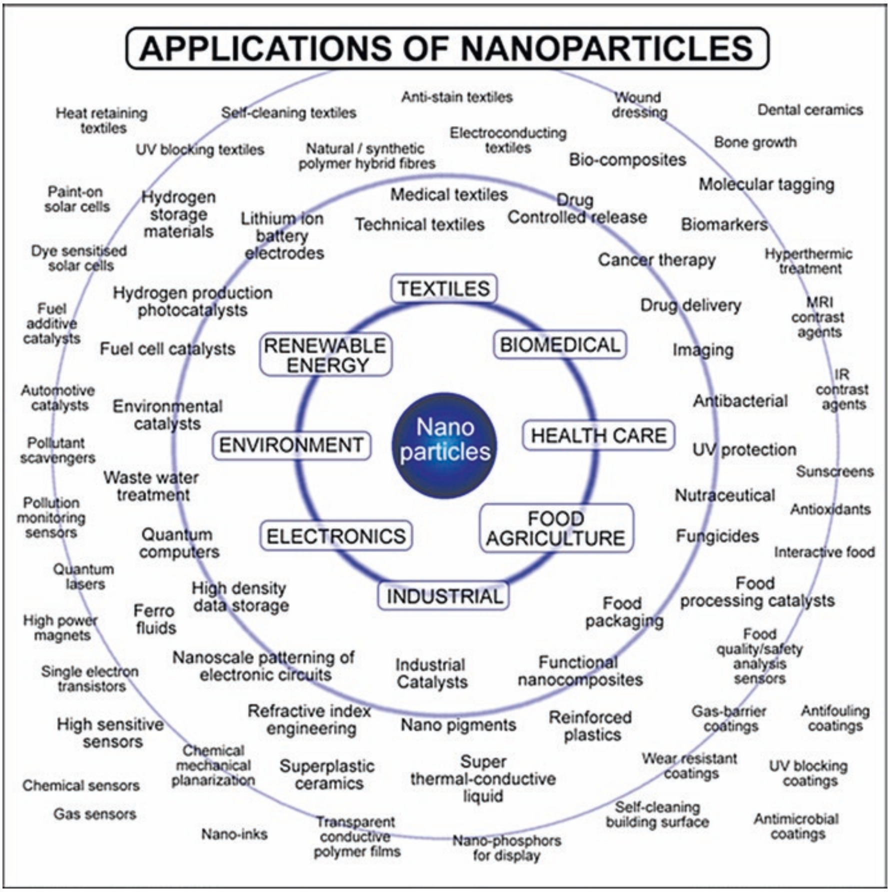

Fig. 2.1 Nanoparticle application areas (Reprint with permission of Prof Tzuzuki)

medicine are observed, because target-orientated applied NPs diffuse in nontarget environments, exhibit there unwished reactions, cause uncertainties, open debates concerning consumer perception of nanotech products, and force EC and the EU parliament on basis of little understood NPs behaviors, fates, and side effects in nontarget environments to legislate nanofood regulations (Cobb and Macoubrie 2004; Parisi et al. 2015). Continuing national and international regulations specifying debates are regularly conducted to achieve a better consumer perception of nanotech products (e.g., European Environment Agency Technical report No 4/2011; International Cooperation on Cosmetic Regulation, ICCR, Canada; the EU Biocidal Product Regulation (BPR); the provision of food information to consumers (labeling) by the European Parliament; Cobb and Macoubrie, 2004; Grobe and Rissanen 2012; Reidy et al. 2013).

NP-related inventions in agriculture, food, nutrition, and medicine marketed and applied mostly in combination with inorganic or organic super-absorbing, polymeric structured compounds, challenge not only competition and collaboration between companies and nations but also landscape policy, which has to handle NPs side effects (Grobe and Rissanen 2012; Benckiser et al. 2013; Afzal et al. 2016; Heo and Hwang 2016; Yu et al. 2016).

This book chapter discusses after summarizing NPs exploitation, product processing effects, and advantages and risks for agriculture, food, nutrition, and medicine the balancing reasons for beneficial and profitable NPs use and a successful health and landscape policy.

2.2 Nanoparticle Exploitation and Developing Products

NPs in agriculture, food, textile, packing industries, health care, medicine, and the modern electronic and renewable energy sector increase in importance, and nanostructured alumina products, controlling effectively *Sarocladium oryzae* (L.) and *Rhyzopertha dominica* (F.)—a major insect pest in stored food supplies—and the oriental fruit fly *Bactrocera dorsalis* (Hendel)—a very destructive pest of fruit effectively controlled by nanogel immobilized semiochemical pheromones are examples of NPs products with relevance in agriculture (Bhagat et al. 2013; Prasad 2014; Prasad et al. 2014; Sadeghi and Ebadollahi 2015). Encapsulated NPs products offer easy handling, transportation without refrigeration, sustained release, and stability at open ambient conditions, reducing recharging frequency and indicate ecogeniality. Pharmaceuticals and nanodrug delivery systems are in use, and for the raw material suppliers, agriculture, forestry, and the food and packing industry nano application perspectives are predicted toward the 21st century (Figs. 2.1 and 2.2; Hilder and Boulter 1999; Sticklen 2009; Ravichandran 2010; Duncan 2011; Neethirajan and Jayas 2011; Dickinson 2012; Grobe and Rissanen 2012; Horstkotte and Odoerfer 2012; Kong and Ziegler 2012; Kuhlmeier et al. 2012; Benckiser et al. 2013; Voytas and Gao 2014; Sehkon 2014; Cherukula et al. 2016; Jivani et al. 2016). The newly developed methods, DNA microarrays, nanosensing, microelectromechanical systems, and microfluidics are prerequisites for achieving NPs and encapsulated NPs products, with which protein bioseparation, biological and chemical contaminant sampling, nanosolubilization, nutrient delivery, food coloring, nutra- and pharmaceutical efficacy, food quality, the conversion of CO_2 into fuels and other chemicals, water splitting into H_2 and oxidized organic compounds, the designing of self-cleaning surfaces, water disinfection and purification, or the TiO_2 or Ni@g--PC3N4 nanophotocatalyst conversion of benzyl alcohol into benzaldehyde are improved (Fig. 2.2; Kuhlmeier et al. 2012; Deng et al. 2015; Horst et al. 2015; Liu and Lal 2015; Smith et al. 2015; Sunkara et al. 2015; Yang et al. 2015; Kumar et al. 2016; Ouyang et al. 2016; Palomo and Filice 2016). Benzaldehyde, a widely applied organic compound of economic importance in food, pharmaceutical, perfumery, and other chemical industries and anti-inflammatory, antioxidative, immunomodulating, antimicrobial properties exhibiting metal-based NPs are income promotional and broaden with products consisting of chlorohexidine and *Scutellaria baicalensis* bacteria, encapsulated mesoporous silica nanoparticles, or encapsulated baicalin—a flavonoid-based NP isolated from *Scutellaria baicalensis*—or baicalein, a traditional Chinese medicine component, offer agrifood and health safety perspectives (Fig. 2.2; Ikemoto et al. 2000; Ravichandran 2010; Jang et al. 2014; Sekhon 2014; Seneviratne et al. 2014; Cherukula et al. 2016; Leung et al. 2016; Raza et al. 2016; Shamaila et al. 2016).

2.3 Nanotechnology Advantages in Agriculture, Food, and Medicine

Self-organizing nanoprocesses, leading to novel NPs that differ in their properties from those of bulk materials, can have miniaturized devices (Kuhlmeier et al. 2012), micro-electro-mechanical systems (Jivani et al. 2016), or devices inserted in gene manipulated bacteria and archaea (de Lorenzo 2014). Such miniaturized devices broaden the diagnostic boundaries and enable researchers to develop advanced analytics and methods and to design and realize marketable NPs products, bringing innovation and benefits in societal areas, such as agriculture, food, nutrition, medicine, and related industries (Figs. 2.1 and 2.2; Horstkoote and Odoerfer 2012; Kong and Ziegler 2012). The numerous nanotechnology exploiting inventions, inter alia exemplified by the self-organized growth arrays of graphene nanoribbons on structured silicon carbide substrates, documents the continually progressing NPs success (Rogers 2010; Benckiser 2012). The wealth of ideas not only lead to nanolevel fabricated carbon nanomaterial electronics but also application possibilities in agriculture, food, nutrition, medicine, and related industries for years to come.

Miniaturized systems, integrated in technical and laboratory equipment, are such advanced that a sensitive and accurate detection cannot only be helpful to develop a broad range of technological applications but also to detect more precisely NPs, diffusing from the target site into nontarget environments and trigger unwished impacts (Afzal et al. 2016; Cherukula et al. 2016; Heo and Hwang 2016; Kumar et al. 2016; Leung et al. 2016; Palomo and Filice 2016; Ouyang et al. 2016; Raza et al. 2016; Shamaila et al. 2016; Yu et al. 2016). Nanopharmaceuticals, nanotechnology-based drugs bring a significant benefit for the patient. They have a better solubility, dissolution rate, more enhanced oral bioavailability as conventionally formulated drugs, and a pinpoint application but may concomitantly show unwished NPs side effects, nudging the need for public safety regulations (Fig. 2.2; Grobe and Rissanen 2012; Schmitt et al. 2010; Horstkotte and Odoerfer 2012; Prasad et al. 2017a; Scandorieiro et al. 2016). Nitrification inhibitors, encapsulated in nitrogen fertilizers (NIENF), control not only solubility, nanodissolution, and plant N bioavailability but concomitantly reduce N losses, NO_3^- groundwater pollution, and N_2O climate impacts (Zerulla et al. 2001; Benckiser et al. 2013, 2016; Yang et al. 2016). Decreased particle size ranges of NPs, nutra-, and nanopharmaceuticals offer the possibility of sterile filtration before application, improve dose proportionality, and reduce food effects. Continually advancing NPs detectability provides suitability in following diffusion routes that reduce administrative risk assessments.

Agriculture	Food, Nutrition, Food packing	Cosmetic, Medicine
Encapsulated nanosensors on chip basis to detect substrate-microbe-animal-plant-pathogen interactions, to monitor soil and crop growth conditions (De Lorenzo, 2014; Heo and Hwang, 2016; Aristov et al, 2016) ***Encapsulated flavor enhancers*** (nutraceuticals; Sehkon, 2014). ***Nanocapsules*** a more efficient delivering of growth hormones, vaccines, genetic engineered DNA and agrichemicals (pesticides, fertilizers targeting (Hilder, Boulter, 1999; Sticklen, 2009; Benckiser et, al., 2013; Voytas, Gao, 2014) ***Fiber crops*** for advanced textile production (Kong, Ziegler, 2012.)	***Nanostructured organics*** vitamins, antioxidants; colorants, flavouring agents ***inorganic nano-sized* nutrients, supplementing *additives*** alkaline earth metals, iron, silver, titanium dioxide, silica, non-metals calcium, magnesium, selenium for enhancing food and animal feed production, for improving absorption, taste, beverage texture bioavailability, food, or emulsions as mayonnaise by adding water nanodroplets. ***Nanosensors, biopolymer-based carriers (liposomes, nanomicelles), nanocoatings, nanofiltration*** to mask taste ingredients, protect from degradation, improve food safety by increasing contact surfaces, self cleaning properties, antimicrobial effects and achieve an otical better appearance (Duncan, 2011; Nethirajan, Javas, 2011; Dickinson, 2012).	***Analytical tools and nanoimaging*** to facilitate microfabrication of polymeric substrates, novel drug delivery, micro-electro-mechanical system devices for a controlled application, reached for a better electric light control e.g. in graphen, quantum devices by plasmon polaritons-coupled photon excitations. ***Nanomaterials based sensors, nanodevices, clinical, regulatory and toxicological issues*** for detecting and controlling pathogens and toxicants easier. ***Nanopharmaceuticals and delivery systems*** improve phiarmacological efficacy by modified physico-chemical properties and targeted body distribution (Schmitt et al., 2010; Chen et al. 2012; Horstkotte, Odoerfer, 2012; Shen et al., 2013; De Lorenzo, 2014; Jivani et al, 2016)

Fig. 2.2 Nanotechnology applications in agriculture, food, nutrition, food packing, cosmetic, and medicine

The nonprofit Frost and Sullivan Institute (FSI), dedicated to leveraging innovation to address global challenges, estimated in 2012 an annual BioMEMS growth rate of more than 15% for China. Such predicted growth rates of controlled applications by MEMS demonstrate that novel products on micron, nanometer scale basis and related industrial productivities are going to be revolutionized. The study of biological systems enters into an improved treatment of diseases with new polymer-based anticancer agent delivery systems, a development of specialized tools for minimally invasive surgery, novel cell-sorting systems allowing high-throughput data collection, and precision measurement techniques for microfabricating devices (Darshana D. BioMEMS Impact on Healthcare, Report Frost & Sullivan, Mountain View, March 30, 2012, cited by Kuhlmeier et al. 2012; Horstkotte and Odoerfer 2012; Kong and Ziegler 2012; Senior et al. 2012; Prasad et al. 2016). In the nearest future, an increase of related patents is expected (Benckiser 2012: Frost and Sullivan 2016).

Micro devices, applicable for medical and food analysis and under current development, belong to three principal branches: nanoparticles, nano fluidics, and nano sensors, and consumer-oriented developed miniaturized system products find use as automotive coatings, smart textiles, sunscreens, or easy-to-clean surfaces for bathrooms (Horstkotte and Odoerfer 2012; Kuhlmeier et al. 2012; Kong and Ziegler 2012). Such products demonstrate in their breadth of possible and expected applications private and public advantage and are perceived positively by a majority of consumers. However, the progress of nanotechnology analytics visualizes NPs side effects and spread uncertainties (Cobb and Macoubrie, 2004; Grobe and Rissanen 2012; Zimmer et al. 2012; Coppola and Verneau 2014; Gupta et al. 2015). Organizations as the European Union (EU) started communication patterns concerning definition and recommendation of nanomaterials, which resemble those of the genetically modified organism (GMO) debate. The discussion will increase the more nanotechnology-based products are marketed and with increasing detected NPs side effect industries of concern silence communication. Yet, stakeholders, risk management, mistrusting consumer organizations, and policy makers should not careen in debating NPs' benefits and risk regulations for achieving improved public safety by enhancing NPs risk assessments.

2.4 Risk Assessment of Nanomaterials in Agriculture, Food, and Medicine

During processing, separation, consolidation, and deformation of materials, natural events or human activities occur atom or single molecule changes, which may lead to risky incident events, ending in an averaged descending, undesirable adverse effects (Taniguchi 1974; Renn 2008). Risk events more broadly defined are probabilities, the likelihood of event estimates, hazard multiplied by exposure, viewed as physical harm to humans, cultural artifacts, or ecosystems (Senjen 2012). Risky can be NPs side effects, caused by uncontrolled NPs diffusion from the place of requirement into surrounding landscapes, which are increasingly observed, for example, the U.S. Food and Drug Administration (FDA) drafted and published in 2012 a risk guidance document. Defined in the risk guidance document are nanotechnology factors, which particularly NP-containing foods processing manufacturers should consider, because NPs observably cause significant changes, such as:

- Affect the identity of the food substance
- Affect the safety of the use of the food substance
- Affect the regulatory status of the use of the food substance
- Warrant a regulatory submission to FDA (Grobe and Rissanen 2012).

In this context, the scientific community—the Scientific FDA Committee—identified deficiencies in characterizing, detecting, and measuring (engineered) nanomaterials in food, feed, and biological matrices and asserted after evaluation that the availability of data for oral exposure and for any consequent toxicity is extremely limited. The majority of information concerning toxicokinetics and toxicology comes from in vitro or in vivo studies having only a confined transferability to human risks. The Scientific FDA Committee reminded the lack of methods for a satisfying testing of (engineered) nanomaterials and that due to our limited current knowledge concerning environmental NPs, impacts particularly in the food area research endeavors are required to answer open questions.

Our limited knowledge concerning side effects through nanotechnology application and the not easy to be answered questions concerning NPs in health care must be debated increasingly because of detected possible connections between nanomaterials in food or feed and gut diseases (Stracke et al. 2006; Grobe and Rissanen 2012; Böhmert et al. 2015; Xiao et al. 2016). Novel (nano) foods and feeds, consumed by humans and animals, and agrochemicals, used in plant protection or cosmetics and medicines and applied in health care, are sources from which NPs are diffusing into nontarget surrounding environments. The relative newness of NPs application and health interaction and the limited transferability of NPs animal tests to human scientific key issues complicate risk assessment dialogues between academia, industries, stakeholders, regulators, and nongovernmental organizations (NGOs). Such discussions are urgently needed to guarantee an almost safe nanotechnology application in agriculture, nutrition, and medicine and that unwanted NPs side effects, requiring practical risk assessment recommendations, can be widely prevented.

Little commented information has spread by the increasing wealth of NPS-related literature and innovations in the agrifood sector since only recently and has fueled uncertainties and made consumers wary (Brown 2009; Benckiser 2012). For public safety and risk assessment, debate-engaged NGOs claimed to expand the narrow EU Cosmetics Directive risk definition that limits the scope by predominantly focusing on insoluble or bio-persistent materials (Raj et al. 2012; Senjen 2012). NGOs call for a debate, which not only pertains to insoluble or bio-persistent materials but also includes human health and environment aspects, ownership of technology and accountability, privacy, security, surveillance and human enhancement, equity of access, and impact on national economies and industries (Senjen and Hansen 2011). In such a debate of concern should be public involvement in technology development and convergence of nanotechnology, nanobiology, and nanocomputer technology, and such a debate should not end in the emergence of a global nanodivide into a nanotechnology reinforcing toward global inequalities (Schroeder et al. 2016). The gap between rich and poor countries should not increase, and also this aspect should play a weighty role in the nanotechnology risk assessment discussion. In assessing risk-related regulations, governance regimes will act reality adaptive and avoid being archaic in the discussion of concern. They mostly will start simply by focusing on already marketed, relatively low-tech nanoproducts. Learning from the process of governing relatively simple existing products, governance regimes will reflexively speed up as more complex, later-stage novel nanoproducts emerge in structuring the adaptation process (Brown 2009).

In Europe, the European Parliament and the EU Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) have begun to take an interest in nanotechnology and have started with increased safety testing, a specific risk-assessment procedure in cosmetic and novel (nano) food industries that nanomaterials containing products can be labeled (Raj et al. 2012). NGOs suspect that the European Parliament and SCENIHR NPS concerning initiative is not only limited in scope but that the necessity of a constructive and in risk-assessment results ending dialogue will not come into effect for a long time.

2.5 Conclusions

Agriculture, food, textile, packing industries, and medicine penetrating NPs play an increasing role in health care, the sector of modern electronic and renewable energy. Public debate on NPs' benefits and risks is occurring between industries, stakeholders, process regulators, risk managing administrators, mistrusting consumer organizations, and policy makers. The described knowledge about NPs use in agriculture, food technology, nutrition, and medicine and the behavioral similarities of encapsulated NPs in marketed products in the field of applications under consideration have these in common:

(a) Enhanced NPs solubility, dissolution rate oral or plant bioavailability, and the possibility of a target-orientated application.
(b) Decreased particle size range offers sterile filtration before application.
(c) Improved dose proportionality.
(d) Concerning nanoagrifood products, a reduced food damage and N loss, NO_3^- groundwater pollution, N_2O climate impact reduction.
(e) Suitability of NP-based very sensible sensor devices enhances the detectability, and NPs diffusion routes in nontarget environments administrations can follow more easily.
(f) More satisfying reach of public safety concerning NPs side effects, risk assessments after more profound nanotechnology key-risk discussions enabled through advanced analysis, and better informed policy makers.

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