

NANOTECHNOLOGY AND ITS APPLICATIONS IN FOOD AND ANIMAL SCIENCE

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ABSTRACT

Nanotechnology has the potential to manipulate matter at the nanometre scale, creating and assembling substances at a molecular level with new and interesting properties. This has offered opportunities for applications in different sectors. Recently, nanotechnology has received particular attention due to its promising applications in animal nutrition, drugs and nutrients delivery, animal reproduction, disease diagnosis and treatment. In the food sector, nanotechnology is applied to the improvement of food packaging, processing, monitoring and the development of food with new functional properties that can respond to the needs of consumers. This review will focus on the advances of nanotechnology in food sector and animal science with particular attention to animal nutrition. The implications for safety and regulation will be also discussed.

- Keywords: nanotechnology, animal science, nanofood, nanoparticles, animal health, safety -

1. INTRODUCTION

1.1 Nanotechnology background and definition

Nanotechnology is a new emerging multidisciplinary field, which is expected to revolutionize both science and society, and provides several long term benefits. In the last years nanoscience was applied to create new tools for molecular biology, new materials in optics, new delivery systems of drugs, new sensors for disease detection. More recently, nanotechnology has received particular attention due to its promising agricultural and food applications. According to the National Science Foundation and National Nanotechnology Initiative (NNI), nanotechnology is the ability to understand, control, and manipulate matter at the level of individual atoms and molecules, as well as at the "supramolecular" level, involving clusters of molecules (in the range of about 0.1 to 100 nm), in order to create materials, devices, and systems with new properties and functions because of their small structure (TANIGUCHI, 1974; DOWLING *et al.*, 2004). These particular features were used from the ancient time. Indeed, nanotechnology have been unknowingly applied from the 4th century BC, when gold nanoparticles (NPs) were used in the manufacture of porcelain in China and Egypt (DANIEL and ASTRUC, 2004) and for medical purposes (such as the treatment of arthritis or the elixir of youth) (READ, 1961). An example of the application of their optical properties was (GONELLA and MAZZOLDI, 2000; PADOVANI *et al.*, 2003) the *Lycurgus* cups, which were made during the Roman empire by using colored glasses containing silver and gold NPs (HARDEN and TOYNBEE, 1959). The cup is characterized by a dichroic effect: the glass is green if

the cup reflects light and red if it transmits it. In 1959, the physicist Richard Feynman proposed to study the matter at a molecular scale, stimulating the interest of many people. The famous talk called "there's plenty of room at the bottom" was given by Feynman at the annual meeting of the American Physical Society and is a cornerstone in the short history of the nanotechnologies (FEYNMAN, 1960).

From the beginning of this century, there has been a great increase in scientific publications regarding applications of nanotechnologies (Fig. 1).

The interest in this discipline is due to the unique biological, physical and chemical properties of the nanomaterials which can be applied to new and useful products (SARGENT and JOHN, 2010). For example, in the second half of the eighties new nanomaterials such as fullerenes (C60) and carbon nanotubes (CNTs) were developed and widely applied. In particular, the interest in CNTs is due to their property to interact with macromolecules and nanostructures of biological interest having similar size such as viruses, nucleotides and DNA, aminoacids, proteins, membranes, including also the water molecules (HAMAD *et al.*, 2002; O'CONNELL *et al.*, 2002; WANG *et al.*, 2002; PAUNESKU *et al.*, 2003; ZHANG *et al.*, 2009). Today nanotechnology has different industrial applications and is more developed in areas such as pharmaceutical sciences, microelectronics, chemistry, material and aerospace sciences (WEISS *et al.*, 2006) (Fig. 2). More recently, nanotechnology has also received considerable attention for its promising agricultural and food applications. In the food sector, nanotechnology has been applied to the improvement of food packaging, processing, monitoring and the development of foods with new functional properties that can respond to the needs

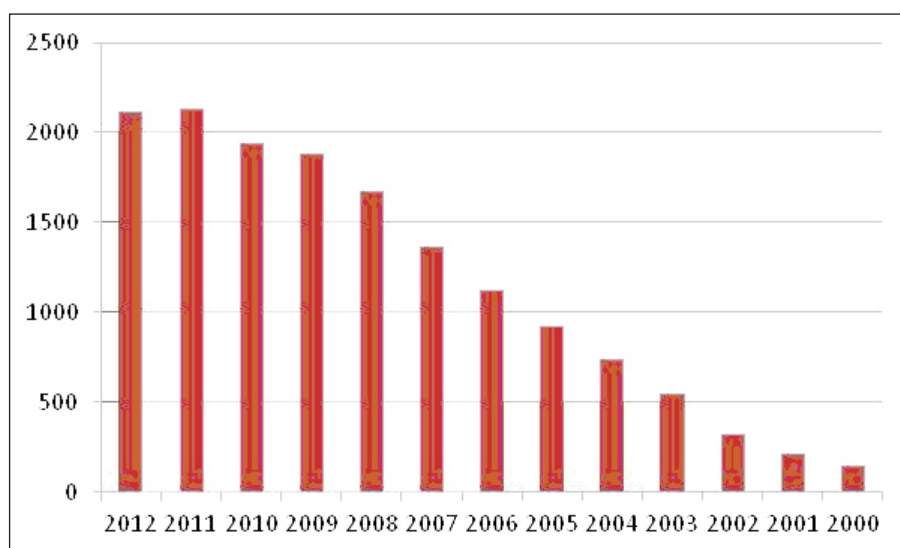


Fig. 1 - Web of Science (search keyword: nanotechnology): Number of publication in the last 10 years.

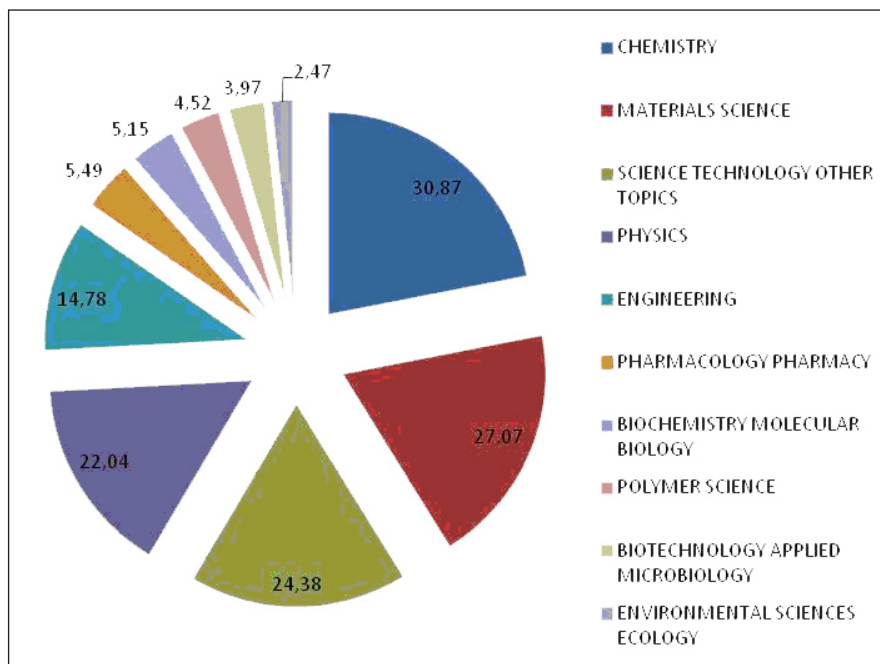


Fig. 2 - Web of Science (search keyword: nanotechnology): % of publication in the last 10 years/research topic

of consumers. The continuous development of this new discipline has led to an increased production and release in the environment of carbon nanotubes (CNTs) and nanoparticles (NPs) by different industries. In this way the population was exposed to high levels of these products that caused severe problems to human health. Therefore, different studies evaluated the toxicity of these compounds at molecular level, although the results were often conflicting (LIU *et al.*, 2012; SHVEDOVA *et al.*, 2012; SAYES *et al.*, 2011). In the next sections, advances of nanotechnology in food sector and animal science will be presented. Their implications for safety and regulations will be also discussed.

2. APPLICATION OF NANOTECHNOLOGY IN ANIMAL HEALTH AND PRODUCTION

For a long period, nanotechnology studies were focused on the medical field and in particular on the evaluation of new drugs *in vivo* (OTILIA *et al.*, 2005). More recently, the research has focused on animals of zootechnical interest. Although there are not many studies on this topic, many advantages can be obtained by applying this technology to animal production (SCOTT, 2005). Several types of nanostructures and NPs have been developed and have revolutionized the approach to animal sciences. Examples of NPs applied to animal sciences are reported in Table 1. In particular, nanotechnologies were applied to the development of novel drug delivery systems and nanosensors for the diagnosis and treatment of diseases. Thus, the effective cure

of infections, metabolic diseases, and nutritional disorders was achieved by acting at the nanometer level. Through the control of the matter at the nanometer scale, excellent results in animal health and production were also achieved.

2.1 Administration of medications and vaccines to animals

The health of animals is very important and several efforts have been aimed to afford a high level of protection from pathogens and also avoid infections in humans. Animals are vaccinated by using antigens and adjuvants that stimulate the immune response against a specific virus. However, some adjuvants can produce negative side effects. Nanotechnology represents a promising approach that can allow to reduce such adverse reactions. A new formulation with NPs constituted by calcium phosphate as adjuvant was successfully tested in a murine model for its capacity to induce antiviral immunity (HE *et al.*, 2000). There are also several ongoing studies regarding the encapsulation of vaccines with novel nanocarriers, such as spore based nanovaccines, NPs bound to antigens and synthetic virus-like particles. These formulations allow to transport a drug in the specific site of action with low parental invasion, thus decreasing of the stress of the animal (KALKANIDIS *et al.*, 2006). In this way, the efficacy of the vaccine is increased and the inflammatory response is avoided (SINGH *et al.*, 2007; CAPUTO *et al.*, 2009). At the moment, one of the most important issues of vaccine distribution is the need to maintain the cold chain, which an extension of the good

Table 1 - Overview of NPs and their application in animal science. Revisited by DE JONG and BORM, 2008.

Particle class	Materials	Application	References
Natural materials or derivatives	Chitosan Dextrane Gelatin Alginates Liposomes Starch Vicillin	Drug/Gene delivery	Damascelli <i>et al.</i> , 2003 Dyer <i>et al.</i> , 2002 Huang <i>et al.</i> , 2004 Mura <i>et al.</i> , 2011 Murata <i>et al.</i> , 1998 Roy <i>et al.</i> , 1997
Dendrimers	Branched polymers	Drug delivery	Meredith <i>et al.</i> , 2011
Fullerenes	Carbon based carriers	Photodynamics Drug delivery	Yamakoshi <i>et al.</i> , 2003
Polymer carriers	Poly(lactic acid) Poly(cyano)acrylates Polyethylenimine Block copolymers Polycaprolactone	Drug/gene delivery	Du <i>et al.</i> , 1998 Xu <i>et al.</i> , 2009
Ferrofluids	SPIONS USPIONS	Imaging (MRI)	Bernardi <i>et al.</i> , 2008 Stern <i>et al.</i> , 2007
Quantum dots	Cd/Zn-selenides	Imaging <i>In vitro</i> diagnostics	Cho <i>et al.</i> , 2007 Liu <i>et al.</i> , 2011
Various Gold nanoparticles Gold nanorods Gold nanoshells Gold nanocages	Silica-nanoparticles Mixtures of above Solid lipid formulations	Gene delivery	Kawano <i>et al.</i> , 2006 Li <i>et al.</i> , 2010 Liu <i>et al.</i> , 2007 Amarnath <i>et al.</i> , 2010 Ankamwar <i>et al.</i> , 2005 Salem <i>et al.</i> , 2003 Stem <i>et al.</i> , 2007

manufacture practice of the pharmaceutical industry (GMP). In order to bypass this requirement, vaccines were formulated in tablets instead of using liquid formulations stored in refrigerator. Moreover, other routes of administration are under evaluation. Nanotechnology represents a promising new approach that allows to improve the vaccine distribution by increasing their shelf-life (PEEK *et al.*, 2008).

2.2 New drug delivery systems

Normally drugs and probiotics are delivered to animals by injection or through the diet. The administration of drugs is realized when the first symptoms appear or in advance, as prophylaxes. Nanodevices can afford a controlled release of drugs, thus avoiding the problem of drug resistance, which arises following the extensive exposure to the drug. Antibiotics administered to animals can reach the consumer. For this reason, there is the need of a technology that could decrease the dose maintaining the same efficacy (HUH and KWON, 2011). In order to achieve this aim, the use of nanoparticles bound to antibiotics was evaluated. According to Huh and Kwon's studies, Ampicilline bound to NPs was as

effective as the unbound Ampicilline in reducing the growth of *Salmonella typhimurium* at a 40 times lower concentration of antibiotic. Such a decrease of dose was due to the NPs, which allowed a better and more specific distribution of the drug in the tissue. Controlled delivery systems were also created to deliver and monitor the delivery of vaccines or pharmaceuticals and nutrients in animals (CHEN *et al.*, 2005; MOZAFARI *et al.*, 2006; DE JONG and BORM, 2008). These formulations can be used to deliver drugs in a specific site. Other applications regards the use of NPs for gene therapy (MARSAN *et al.*, 2009; SHARMA *et al.*, 2011), tumor inhibition, as gene delivery vectors or as new engineered nanomaterials for the coating of implants (AJMONE *et al.*, 2007; KATRAGADDA *et al.*, 2010; KUZMA, 2010).

2.3 Nanosensors for diagnosis and treatment of diseases

Nanoparticles can also be used to improve the detection of microbial and chemical contaminants in animals. Examples of this application are the detection of *E. coli* by using a mannose targeting nanobiomolecule that links the pathogen (ZUCCHERI and ASPROULIS, 2012), detec-

tion of *Listeria monocytogenes* in spiked milk (DE LA TORRE *et al.*, 2005; YANG *et al.*, 2007) or *Campylobacter* (LATOUR *et al.*, 2003; FRANKLIN *et al.*, 2003) frequently found in poultry as contaminant, or polymeric NPs that are able to bind the pathogens in the gut of livestock and then are eliminated in the animal waste through the intestine (KEENER *et al.*, 2006). For the eradication of nematodes such as *Trichinella spiralis*, a frequent contaminant of pork meat, NPs composed of adjuvants, which stimulate the immune response in mice, were used and a decrease of the larvae concentration in the muscle tissue was obtained (DEVILLE *et al.*, 2005). Furthermore, nanosized sensors composed of carbon nanotubes were successfully used to detect toxic compounds and to monitor health and physiological conditions of animals (DRABU *et al.*, 2010). Nanomaterials can be used to create new kits for an early detection of contaminants with high precision. WEI *et al.* (2010) reported a specific application for the rapid detection of melamine in whole milk mediated by unmodified gold nanoparticles.

In biomedical science, one of the current challenges in disease diagnosis is the *in vivo* application of ultrasensitive image analysis of biological targets under noninvasive conditions in order to precisely detect early-stage diseases and monitor the responses to drug therapies. Nanoparticles are now emerging as novel and promising candidates for high-performance molecular imaging agents. Nanostructures, such as shells, quantum dots, NPs, dendrimers and fullerenes, were used to improve potential application in cancer imaging by magnetic resonance imaging (MRI), in order to improve cancer diagnosis and treat target tumors *in vivo* (ZHANG *et al.*, 2008; ROSENBERG *et al.*, 2010).

2.4 Nanotechnology for reproduction

At the moment, there is particular interest in the sustainable production of animals and new solutions are required to obtain an improvement in this field. Nowadays, the use of assisted reproductive technique still presents shortcomings and new technologies, which could improve it, are required (VERMA *et al.*, 2012). In particular, nanotechnologies are used for the monitoring of the fertile period, which is the major problem in farm animals. Nanotubes were applied to the detection of estrus in real time by implanting them under the animal skin. Variations of estradiol levels in the blood of animals were monitored in real time (LIU and WONG, 2007). Nanostructured immunosensors were created in order to detect progesterone in cow milk and evaluate its release during the ovulation period (CARRALERO *et al.*, 2007). The biosensor should allow to detect changes of the physiological level of the progesterone concentration with fertility tests. Silver nanoparticles were evaluated for their an-

tibacterial properties (GARDEA *et al.*, 2003) on chicken embryos. Unfortunately, the treatment was not effective and toxic effects affecting number and size of embryo lymph nodes were found (GRODZIK and SAWOSZ, 2006). Microfluidic devices were developed with the aim of physically mixing sperm and eggs, thus obtaining a cheap, reliable and quick embryos production (STUDNICKA *et al.*, 2009; PATIL *et al.*, 2009). The future plan is the *in vivo* implant of nanocapsules containing the male semen, which should be released in a controlled manner during the ovulation period in order to fertilize an egg.

2.5 Animal nutrition

Emerging evidences indicate that nanotechnology may represent a promising approach to develop new and specific products for animal nutrition. In particular nanotubes linked to nutrients can be administered to animals and released in specific sites, thus allowing the maintenance of high levels for a long time. This approach should avoid the degradation of nutrients and increase their availability (ROSS *et al.*, 2004). Sodium selenite NPs coated with metacrylate copolymers, sensitive to variations of pH, were orally administrated to ruminants and the improvement of selenium absorption was evaluated (ROMEO-PEREZ *et al.*, 2010). Silver NPs and Cu-montmorillonite NPs were used as feed additives to increase the average daily weight gain of pigs (TONG *et al.*, 2007; FONDEVILA *et al.*, 2009). Iron or selenium NPs were successfully tested as feed additives in aquaculture and improvement in animal growth performance was reported (ZHOU *et al.*, 2009). The administration of copper and zinc (HAN and BAKER, 1993; SMITH *et al.*, 1997) as growth promoters in pigs were restricted to the only improvement of animal health status. The use of nanotechnology permits a specific administration of microminerals avoiding their excessive use, which could lead to toxic effects for animals, consumers and environment (FONDEVILA *et al.* 2009 a,b). Minerals, supplements and vitamins are important in animal nutrition; for example iron is essential in animal diet during particular periods of life, such as parasite infestations, gestation and in the early stage of life (ZIMMERMAN, 1980; O'NEILL *et al.*, 2010). However, the administration of ferrous sulfate in food produces a metallic taste due to the increase of rancidity of cereals caused by acceleration of fat oxidation, thus inducing the refuse of food by animals (HURRELL, 2002). Ferric phosphate is an alternative to ferrous sulfate but its instability and low availability limit the use as iron source. However, nanoparticles of this compound overcome the stability issue, thus increasing the nutritional value of this source and allowing the administration to animals (FIDLER, 2008; ROHNER *et al.*, 2007). Moreover, nanosized vitamins are used in

poultry and livestock feed. Nanotechnology can also provide applications for medication, nutrients and veterinary care that target specific cases, such as aged animals.

3. APPLICATION OF NANOTECHNOLOGY IN FOOD PRODUCTION

The application of nanotechnology in food systems can lead to several advantages. The food safety has been improved by using sensors for pathogen detection, remote controls of food, smart systems for product tracking, encapsulation of functional food ingredients containing medicines and supplements, which are released in a specific site (WEISS *et al.*, 2006). By mean of nanotechnology, the inclusion of nano supplements or nutrients in food can improve the nutritional value of food or change its taste, color and texture. According to GARBER (2007) and SCRINIS (2007), nanofood can be defined as the manipulation of seeds, feed, pesticides and packaging at the nanometer scale or when nanotechnologies are used during cultivation, production and processing of the food. Due to the possibility to create new useful and interesting products, the food industry has applied this technology to the encapsulation and emulsion of nutrients, probiotics, supplements and to sensor development (FSAI, 2008). In addition to the needs of the industry, the interest of the consumers is to follow the path of the animal and its products throughout all the production and distribution chain giving particular attention to their safety. New compounds for agriculture were also produced by using nanofertilizers composed of hydrogels or zeolites, which improve water catchment in the soil and absorb toxic compounds at the same time (GONZALES-MELENDI *et al.*, 2008). All these possible applications can lead to an improvement of food production linked to a cost effectiveness.

3.1 Application to the food industry

The food industry is the largest manufacturing sector in the world and new technologies are necessary for its innovation. The application of nanotechnology to the food industry involves several benefits, such as products with new properties (less sugars and fats, new textures, colors, nutrients, flavors and tastes), improved food security, processing and traceability, new packaging and products having extended shelf life and improved microbial food safety (AVELLA *et al.*, 2005; CHAUDHRY *et al.*, 2008; GARBER, 2007; RHIM, 2007). It has been estimated that the market of nanotechnology will reach 1 trillion USD by 2015. In particular, packaging is considered the main commercial application of nanotech in food sector. As estimated by Richardson and PIEHOWSKI (2008), nanotechnology

will be used in 25% of food packaging within the next decade. Due to the large economic interest, large industries, such as Kraft foods, founded a nanotech consortium (15 University and Research labs) with the aim of obtaining food products that fit the tastes and needs of consumers (SANGUASNSRI and AUGUSTIN, 2006).

3.2 Food safety and decontamination

In term of food safety, one of the main issues is the contamination of cereals with mycotoxins due to its relevance for human/animal health and the economic impact on the global trade of cereal. The FAO has estimated a contamination of 25% of worldwide cereals stockpile by mycotoxins each year with an enormous economic effect (JELINEK *et al.*, 1989; LINDEMANN *et al.*, 1993). Regarding this topic, nanoabsorbents composed of magnesium oxide and embedded by silica nanoparticles has been used as effective adsorbent agents as a way to remove aflatoxins from wheat flour (LUO *et al.*, 2004; MASOERO *et al.*, 2007; MOGHADDAM *et al.*, 2010). SHI *et al.* (2009) reported the use of a modified montmorillonite to decrease the toxicity in feeds of chicks. The development of nanodevices for food safety and preservation and for the detection of biological contaminants of food, such as bacteria, fertilizers or pesticides, is very important (DINGMAN, 2008). Indeed, food pathogens can be detected with nanosensors placed in packaging materials as a sort of electronic noses or tongues, which are able to detect spoilage and contamination of food. These systems allow to detect even just one bacterium located in food in real time with a quick, simple and sensitive procedure (DAS *et al.*, 2009; LILLIE and CANTINI, 2011). The advantages of these systems consists in placing thousands of nanostructures in a nanosensor, which is able to detect the presence of any number of pathogens because it can be introduced in tiny places where pathogens hide. Different systems were applied also to drinking water. Recent studies suggest that many of the issues involving water quality could be resolved or greatly improved by using nanoparticles, nanofiltration or other products resulting from the application of nanotechnology. Innovations in the development of novel technologies to desalinate water are among the most exciting and promising targets (SAVAGE and DIALLO, 2005).

3.3 Food processing and monitoring

Food traceability is important in order to follow all steps of the production and distribution of animal products and guarantee their quality. Some procedures are illustrated in SHEFER and SHEFER (2003 a,b) and CHAKRAVARTHI and BALAJI (2010). The application of nanotechnology in

food processing includes the use of nano-ingredients that change texture and taste of food. The dispersibility of additives in food is improved by their encapsulation in nanostructures, such as micelles or liposomes, that can mask the taste of some additives or protect them from degradation (CHAUDHRY and CASTLE, 2011). In this way, the bioavailability of nutrients is increased too, thus reducing the use of additives and preservatives and obtaining a better food storage. Liposomes in particular can be used to encapsulate hydrophobic or hydrophilic ingredients. By adjusting their internal pH, the stability of the substances incorporated is increased. Different materials and shapes can be obtained, such as multiple vesicles with an onion-shaped structure. As illustrated by WEISS (2006), liposomes were successfully used to encapsulate antibacterials, thus obtaining improvement in the inhibition of bacteria growth when compared to the standard methods. This effect may be related to the delivery properties of nano-encapsulated drugs, which are released for a prolonged period of time due to a controlled release (CHEN *et al.*, 2005). Future perspectives of nanotechnology application in food processing are the production of functional food providing health benefit or products tailored to satisfy specific nutritional needs or problems, such as allergies. Recently, omega-3 microcapsules, like many other nano-ingredients, have been added to several food products (MOZAFARI *et al.*, 2006). At the moment, more than 100 nanofoods and others products containing nano-ingredients are sold in the market (Table 2) (FOE, 2008). In these products, nanotechnology has found application in primary production, stock, monitoring and retail level.

3.4 Food packaging

Food packaging represents an important category of nanotechnology application in the food sector. Several nanomaterials have been used in the food packaging for different purposes, such as antibacterial activity (nano-zinc and nano-silver oxide), control of spoilage in orange juice (EMAMIFAR *et al.*, 2011), UV protection (nano-titanium dioxide), gas barrier (plastic polymers with nanoclay), improvement of the mechanical strength (nano-titanium nitride), hydrophobic surface coating (nano-silica), etc. (CUSHEN and CUMMINS, 2012). Thus, the shelf life of the food was increased by improving the mechanical, thermal and gas properties of packaging and using environmental friendly materials (PERCH, 2007; SOZER and KOKINI, 2009). 'Intelligent' food packaging incorporating nanosensors or indicators that monitor the condition of the food have been previously described. These products give an added value to animal products, thus obtaining an overall benefit for the production and distribution chain of food products.

Table 2 - Examples of foods, food packaging and agriculture products that contain nanomaterials (modified by FOE, 2008).

Type of product	Product name manufacturer	Nano content	Purpose
Functional beverage	Oat Chocolate and Oat Vanilla Nutritional Drink Mixes Toddler Health	300 nm particles of iron (SunActive Fe) Solid hydrophobic nanospheres composed of a blend of food-approved hydrophobic materials encapsulated in moisture-sensitive or pH-sensitive bioadhesive microspheres to enable controlled release of active ingredients.	Fortified flavoured waters and milk with vitamin, mineral and other functional ingredients using nanoemulsion technology for incorporation and controlled release of bioactives. Food that can adjust its colour, flavour or nutrient content to accommodate a person's taste or health condition. Nano-sized iron particles have increased reactivity and bioavailability (Fidler <i>et al.</i> , 2004.)
Food additive	Aquasol preservative; AquaNova	Nanoscale micelle (capsule) of lipophilic or water insoluble Substances	Nano-encapsulation increases absorption of nutritional additives, increases effectiveness of preservatives and food processing aids. Used in wide range of foods and beverages. http://www.aquanova.de
Food additive	Bioral™ Omega-3 nanocochleates; BioDelivery Sciences International	Nano-cochleates as small as 50 nm	Effective means for the addition of highly bioavailable Omega-3 fatty acids to cakes, muffins, pasta, soups, cookies, cereals, chips and confectionery. http://www.nanobiotech.org/
Food additive	Synthetic lycopene; BASF	Lycovit 10% (<200 nm synthetic lycopene)	Bright red colour and potent antioxidant. Sold for use in health supplements, soft drinks, juices, margarine, breakfast cereals, instant soups, salad dressings, yoghurt, crackers etc. http://www.basf-chemtrade.de

Continued.

Type of product	Product name manufacturer	Nano content	Purpose
Food contact material	Nano silver cutting board; A-Do Global	Nanoparticles of silver	The surfaces of these cutting boards are coated with nano-silver. Pure silver particles only a tiny fraction of a millimeter in size, combat bacteria and kill 99.9 % of all germs. This safely protects your sliced food against microbes, and odorous substances won't gain a foothold. http://www.nanotechproject.org
Food contact material	Antibacterial kitchenware; Nano Care Technology/NCT	Nanoparticles of silver	Ladles, egg flippers, serving spoons etc have increased antibacterial properties. Nano-coatings are exceedingly water-resistant on outdoor materials; keeping them drier longer. Oil, coffee and other frequent stains belong to the past, if the material is treated with our protective products. http://www.nanocare-ag.com
Food packaging	Food packaging Durethan® KU 2-2601 plastic wrapping; Bayer	Nanoparticles of silica in a polymer-based nanocomposite	Nanoparticles of silica in the plastic prevent the penetration of oxygen and gas of the wrapping, extending the product's shelf life. To wrap meat, cheese, long-life juice etc www.marmarapollimer.com
Food packaging	Imperm (from Nanocor Inc.)	It is used in multi-layer PET bottles and sheets for food and beverage packaging	Used to minimise the loss of CO ₂ from the drink and the ingress of O ₂ into the bottle, thus keeping beverages fresher and extending shelf-life. www.nanocor.com
Food packaging	Aegis OXCE (Honeywell)	Polymerized nanocomposite film. The resins are a blend of active and passive nylon using O ₂ scavengers and passive nanocomposite clay particles to enhance the barrier properties for retaining CO ₂ and keeping O ₂ out.	It is an oxygen-scavenging barrier resin formulated for use in co-injection PET bottle applications e.g. beer, fruit juice and soft drinks. http://www51.honeywell.com/sm/aegis/products-n2/aegis-ox.html
Plant growth	PrimoMaxx, Syngenta	100 nm particle size emulsion	Very small particle size means mixes completely with water and does not settle out in a spray tankurf treated results in grass which is healthier, has a more durable blade with a higher tolerance to weather extremes. http://www.syngenta.com
Smart filters	DOW™FILMTEC™ reverse osmosis and nanofiltration elements	The filter consists of a polycarbonate membrane etched with tiny, evenly-sized pores less than 10 nanometers. The thiols spontaneously arrange themselves into a membrane one molecule deep, with all the thiol molecules pointing the same way.	Selective nanofilters that can distinguish molecules based on shape as well as size enabling the removal of toxins or adjustment of flavour. http://www.dowwaterandprocess.com
Water sanitation systems	Nevada-based Altair	It uses 40 nm particles of a lanthanum-based compound which absorbs phosphates from the water and prevents growth of algae	Nanotechnologies makes a water-cleaning product for swimming pools and fishponds called NanoCheck. Besides, nanoscale delivery of weedicides and soil-wetting agents may be very useful for aquatic weed control in large water bodies, and mitigation of stress due to climate change and aquatic pollution. http://www.azonano.com/article.aspx?ArticleID=663
Smart sensors	RFID technology, Sygenta sensors University Innovation center	Track real time stresses of perishable goods from farm gate to retailer's shelf	Packaging with nanosensors that indicate when a product is compromised and not safe for consumption. http://www.foodproductiondaily.com
Sanitizer Packaging	Nano ZnO Plastic Wrap		Nanoemulsion of vegetable oil, surfactant surrounded by trace amounts of alcohol suspended in water with properties to kill bacteria. Packaging with nanosensors that indicate when a product is compromised and not safe for consumption. Nanoemulsion of vegetable oil, surfactant surrounded by trace amounts of alcohol suspended in water with properties to kill bacteria. http://www.google.com/patents/EP1411913A4?cl=en

4. RISK ASSESSMENT

Besides the advantages of nanotechnology applications, the possible health hazard linked to increasing exposure to nanotechnology products and the consumption of food produced with this technology must be considered. With the increased production of NPs by many industries, the population may be exposed to high levels of these products, which may have hazardous effects on animals, humans and environment. Nanotechnology may guarantee improvement of hygienic conditions in food processing, good food quality, safety and decrease of foodborne illnesses (CHAUDHRY and CASTLE, 2011 b, BHATTACHARYA *et al.*, 2007). However, the different pathway that nanomaterials can undertake in eukaryotic cells must be evaluated in order to have a better understanding of the correlation between the health hazard of these products and their dimensions (MCKNIGHT *et al.*, 2003). For example, studies reported in the literatures proved that silver NPs, which are commercially used in packaging materials, transfer from the packaging to the food and a certain level of toxicity was demonstrated (ASHARANI *et al.*, 2008; HUANG *et al.*, 2011). The pathway of nanoparticles in the organism is not well known but some studies have demonstrated that NPs can enter in the gastrointestinal tract through trans membrane segments and can cross the placenta (BHATTACHARYA *et al.*, 2011; ELSAESSER and HOWARD, 2012). By interaction with living systems, nanomaterials may be accountable for unexpected toxicity and for this reason their use in food or food packaging may be a reason of health hazard (DAS *et al.* 2009; CHEFTEL, 2011). Other studies (BARCELO and FARRÈ, 2012; IJABADENIYI, 2012) claim that people have been exposed to NPs in the diet for long time and that food ingredients are reduced to the nanometer scale by the digestive processes in order to obtain energy and maintain physiological processes. According to this opinion, the hazard is not due to the dimensions but to the nature of the materials, which can be harmful to human and animals. The toxicity of nanomaterials at molecular level is the topic of more recent studies and the results are often conflicting (LIU *et al.*, 2012; SHVEDOVA *et al.*, 2012; SAYES *et al.*, 2011). At the moment, there is not enough information about the risks for human, animal and environment (DOWLING *et al.*, 2004; WILLIAMS *et al.*, 2005; CASABONA *et al.*, 2010). Several researchers state that regulators do not respond to this issue to safeguard the big companies that are investing on this new technology (BOSSO, 2010). A major concern is related to the consumption of foods containing nano-additives that are indigestible, insoluble and potentially bio-persistent, therefore not beneficial for consumer health. Moreover, the exposure to nanomaterials may constitute a risk for consumer because they may contain organic moieties that can carry foreign substances in the blood (MUKUL *et al.*, 2001) and can enter in the gastrointestinal tissue.

The exposure to these components of nanomaterials could produce abnormal concentrations of reactive oxygen species and activate an inflammatory response (POWELL *et al.*, 2010). Considering all these risks, an extensive study that correlate the application of nanotechnology in the food packaging with the health hazard must be carried out. At the moment, only few studies have been carried out (DAS *et al.*, 2009), but there is the need to evaluate these nanomaterials by using different assays in order to establish the risk related to their uptake. Furthermore, governments should regulate the commercialization of these products and label them, thus making the consumers aware of the presence of nanofoods in the products (SOZER and KOKINI, 2009). Following these considerations, nanomaterials should be used only after rigorous tests that establish their safety for the environment and the health of humans, fishes and animals (DOWLING, 2004; MEDINA *et al.*, 2007; BLASER *et al.*, 2008; ELSAESSER and HOWARD, 2012).

CONCLUSIONS

Nanotechnology has the potential to revolutionize the field of animal science and food production in terms of diagnostics, discovery of new drugs, drug delivery, vaccine development. The application in food production and packaging can potentially improve the nutritive value, quality and shelf life of several feed and food products with different advantages for the safety of consumers. At the moment, many of these products are either under development or at the experimental stages. At the same time, nanotechnology applications may be accountable for harmful effects for animals, humans and environment. Therefore, one of the main concerns regarding this new technology is the fear of the unknown. For this reason, further investigations are necessary in order to reassure the consumer, fill the knowledge gap about nano-toxicity and, at the same time, improve the risk assessment and evaluate their economic advantages.

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ABBREVIATIONS

Carbon nanotubes (CNTs), Good manufacture practice (GMP), International Standard Organization (ISO), Nanoparticles (NPs), National Nanotechnology Initiative (NNI).

REFERENCES

- Aguilera J.M. 2002. Materials and structures of foods. In: C.A. Brebbia, L. Sucharov and P. Pascolo (Eds.). Design and Nature: Comparing Design in Nature with Science and Engineering. 391-400. WIT Press, SouthHampton.
- Ajmone Marsan P., Tramontana S. and Mazza R. 2007. Nanotechnologies applied to the analysis of the animal genome. Vet. Res. Comm. 31: 153.
- Amarnath, K., Devarajan S. and Rathakrishnan A. 2010. Green synthesis and characterization of palladium nanoparticles and its conjugates from *solanum trilobatum* leaf extract. Nano-Micro Lett. 2: 169.
- Ankamwar B., Chinmay D., Absar A. and Murali S. 2005. Biosynthesis of gold and silver nanoparticles using emblica officinalis fruit extract, their phase transfer and transmetallation in an organic solution. J. Nanosci. Nanotechnol. 10: 1665.
- Asharani P.V., Lian W.Y., Gong Z. and Valiyaveetil S. 2008. Toxicity of silver nanoparticles in zebrafish models. Nanotechnology. 19: 1.
- Avella M., De Vlieger J.J., Errico M.E., Fischer S., Vacca P. and Volpe M.J. 2005. Biodegradable starch/clay nanocomposite films for food packaging applications. Food Chem. 93: 467.
- Barcelo D. and Farrè M. 2012. Analysis and risk of nanomaterials in environmental and food samples. Elsevier, Vol. 59.
- Benardi R.J., Lowery A.R. and Thompson P.A. 2008. Immunoshells for targeted photothermal ablation in medulloblastoma and glioma: an in vitro evaluation using human cell lines. J Neuro Oncol. 86: 165.
- Bhattacharya S., Jang J., Yang L., Akin D. and Bashir R. 2007. Biomems and nanotechnology-based approaches for rapid detection of biological entities. J. Rapid Methods Autom. Microbiol. 15: 1.
- Bhattacharyya A., Datta P.S., Chandhmi P. and Barik B.R. 2011. Nanotechnology. A new frontier for food security in socio economic development. http://disasterresearch.net/drvc2011/paper/fullpaper_22.pdf. Accessed June 15, 2011.
- Blaser S.A., Scheringer M., Macleod M. and Hungerbuhler K. 2008. Estimation of cumulative aquatic exposure and risk due to silver: contribution of nano-functionalized plastics and textiles. Sci. Total Environ. 390: 396.
- Bosso C. 2010. Nanotechnology and environmental governance: the problem(s) of uncertainty. http://eprints.internano.org/505/1/Bosso_NNN_2010.pdf.
- Caputo A., Castaldello A., Brocca-Cofano E., Voltan R., Bortolazzi F., Altavilla G., Sparnacci K., Laus M., Tondelli L., Gavioli R. and Ensoli B. 2009. Induction of humoral and enhanced cellular immune responses by novel core-shell nanosphere and microsphere-based vaccine formulations following systemic and mucosal administration. Vaccine. 27: 3605.
- Carralero V., González-Cortés A., Yáñez-Sedeño P. and Pingarrón J.M. 2007. Development of a progesterone immunosensor based on a colloidal gold-graphite-TEFLON composite electrode electroanalysis. Nanobiomaterial application in electrochemical analysis. 19: 853.
- Casabona R., Escajedo C.M., Epifanjo S., Emaldi L. and Cirion A. 2010. Safe and socially robust development of nanofood through ISO standards. Conference paper (EurSafe 2010, Bilbao, Spain, 16-81 September 2010) - Global food security: Ethical and legal challenges. 521.
- Chakravarthi V.P. and Balaji N. Applications of nanotechnology in veterinary medicine. Vet. World. 2010. 3: 477.
- Chaudhry Q. and Castle L. 2011a. Food applications of nanotechnologies: an overview of opportunities and challenges for developing countries. Trends Food Sci. Technol. 22: 595.
- Chaudhry Q. and Castle L. 2011b. Food applications of nanotechnologies: an overview of opportunities and challenges for developing countries. Trends Food Sci. Technol. 10: 1.
- Chaudhry Q., Scotter M., Blackburn J., Ross B., Boxall A., Castle L., Aitken R. and Watkins R. 2008. Applications and implications of nanotechnologies for the food sector. Food Addit. Contam. 25: 241.
- Cheftel C.J. 2011. Emerging risks related to food technology. Advances in Food Protection. NATO Science for peace. <http://www.springerlink.com/content/p585630701412061/>. Accessed June 17 2011.
- Chen Y. and Lin X. 2005. Studies on the drug release properties of nano-encapsulated indomethacin microparticles. J. Microencapsul. 22: 47.
- Cho S.J., Maysinger D. and Jain M. 2007. Long term exposure to CdTe quantum dots causes functional impairment in living cells. Langmuir. 23: 1974.
- Cushen M. and Cummins E. 2012. Migration and exposure assessment of engineered silver nanoparticles from a PVC nanocomposite food packaging. Conference Proceedings ICFSQN, UK. p. 78.
- Damascelli B., Patelli G.L., Lanocita R., Di Tolla G., Frigerio L.F., Marchianò A., Garbagnati F., Spreafico C., Tichà V., Gladin C.R., Palazzi M., Crippa F., Oldini C., Calò S., Bonaccorsi A., Mattavelli F., Costa L., Mariani L. and Cantù G. 2003. A novel intraarterial chemotherapy using paclitaxel in albumin nanoparticles to treat advanced squamous cell carcinoma of the tongue: preliminary findings. AJR Am. J. Roentgenol. 181: 253.
- Daniel M.C. and Astruc D. 2004. Gold nanoparticles: assembly, supramolecular chemistry, catalysis, and nanotechnology. Chem. Rev. 104: 293.
- Das M., Saxena N. and Dwivedi P.D. 2009. Emerging trends of nanoparticles application in food technology: Safety paradigms. Nanotoxicology 3: 10.
- De Jong W.H. and Borm P.J.A. Drug delivery and nanoparticles: applications and hazards. Int. J. Nanomedicine. 3: 133.
- De La Torre P.M., Torrado G. and Torrado S. 2005. Poly (acrylic acid) chitosan interpolymer complexes for stomach controlled antibiotic delivery. J. Biomed. Mater. Res. B 72: 191.
- Deville S., De Pooter A., Aucouturier J., Lainé-Prade V., Cote M., Boireau P. and Vallée I. 2005. Influence of adjuvant on the induced protection of mice immunized with total soluble antigen of *Trichinella spiralis*. Veterinary Parasitology. 132: 75.
- Dingman J. 2008. Nanotechnology: It's Impact on food safety. J. Environ. Health 70: 47.
- Dowling A., Clift R., Grobert N., Hutton D.R. and Oliver R. 2004. Nanoscience and nanotechnologies: opportunities and uncertainties. The Royal Society, The Royal Academy of Engineering, UK.
- Dowling A.P. 2004. Development of nanotechnologies. Mater. Today. 7: 30.
- Drabu S., Khatri S., Babu S. and Sahu R.K. 2010. Carbon nanotubes in pharmaceutical nanotechnology: an introduction to future drug delivery system. Journal of Chemical and Pharmaceutical Research. 2: 444.
- Du C., Cui F.Z. and Feng Q.L. Tissue response to nano-hydroxyapatite/collagen composite implants in marrow cavity. J. Biomed. Mater. Res. 42: 540.
- Dyer A.M., Hinchcliffe M., Watts P., Castile J., Jabbal-Gill I., Nankervis R., Smith A. and Illum L. 2002. Nasal delivery of insulin using novel chitosan based formulations: a comparative study in two animal models between simple chitosan formulations and chitosan nanoparticles. Pharm. Res. 19: 98.
- Elsaesser A. and Howard C.V. 2012. Toxicology of nanoparticles. Adv. Drug Deliv. Rev. 64:129.
- Emamifard A., Kadivar M., Shahedi M. and Zad-Soleimani S. 2011. Effect of nanocomposite packaging containing Ag and ZnO on inactivation of *Lactobacillus plantarum* in orange juice. Food Control. 22: 408.
- Feynman R.P. 1960. There's plenty of room at the bottom. Caltech Engineering and Science. 23: 22.
- Fidler M.C., Walczyk T., Davidsson L., Zeder C., Sakaguchi N., Juneja L.R. and Hurrell R.F. 2004. A micronised, dispersible ferric pyrophosphate with high relative bioavailability in man. British J. Nutr. 91: 107.
- FOE (Friends of the Earth) 2008. A summary of: out of the laboratory and on to our plates; Nanotechnology in Food & Agriculture.
- Fondevila M., Herrero R. and Casallas M.C. 2009. Silver nanoparticles as a potential antimicrobial additive for weaned pigs. Anim. Feed. Sci. Tech. 150:259.
- Franklin J.L., Sheldon B.W., Grimes J.L. and Wineland M.J. 2003. Use of biofunctionalized nanoparticles to bind *Campylobacter jejuni* in poultry. Poult. Sci. 82: 131.

- FSAI. 2008. The Relevance for food safety of applications of nanotechnology in the food and feed industries. Edited by Food Safety Authority of Ireland Abbey Court, Dublin p. 82.
- Garber C. 2007. Nanotechnology food coming to a fridge near you. <http://www.nanowerk.com/spotlight/spotid=1360.php>. Accessed June 11, 2011.
- Gardea-Torresdey J.L., Gomez E., Peralta-Videa J.R., Parsons J.G., Troiani H. and Jose-Yacaman M. 2003. Alfalfa Sprouts: A Natural Source for the Synthesis of Silver Nanoparticles. *Langmuir* 19: 1357.
- Gonella F. and Mazzoldi, P. 2000. Metal nanocluster composite glasses, in handbook of nanostructured materials and nanotechnology. Ed. H.S. Nalwa, Academic Press, San Diego, CA. Vol. 4, p. 81.
- González-Melendi P., Fernández-Pacheco R., Coronado M.J., Corredor E., Testillano P.S., Risueño M.C., Marquina C., Ibarra M.R., Rubiales D. and Pérez-de-Luque A. 2008. Nanoparticles as smart treatment delivery systems in plants: assessment of different techniques of microscopy for their visualization in plant tissue. *Annals of Botany*. 101: 187.
- Grodzik M. and Sawosz E. 2006. The influence of silver nanoparticles on chicken embryo development and bursa of *Fabricius* morphology. *Journal of Animal and Feed Sciences*. 15: 111.
- Hahn J.D. and Baker D.H. 1993. Growth and plasma zinc responses of young pigs fed pharmacologic levels of zinc. *J. Anim. Sci.* 71: 3020.
- Hamad-Schifferli K., Schwartz J.J. and Santos A.T. 2002. Remote electronic control of DNA hybridization through inductive coupling to an attached metal nanocrystal antenna. *Nature*. 415: 152.
- Harden D.B. and Toyne J.M.C. 1959. The Rothschild *Lycurgus* Cup. *Archaeologia*, Vol. 97, p. 179.
- He P., Wang Z., Zhang L. and Yang W. 2009. Development of a label-free electrochemical immunosensor based on carbon nanotube for rapid determination of clenbuterol. *Food Chemistry*, 112: 707.
- He Q., Mitchell A.R., Johnson S.L., Wagner-Bartak C., Morcol T. and Bell S.J. 2000. Calcium phosphate nanoparticle adjuvant. *Clin. Diagn. Lab. Immunol.* 7: 899.
- Huang M., Khor, E. and Lim, L.Y. 2004. Uptake and cytotoxicity of chitosan molecules and nanoparticles: effects of molecular weight and degree of deacetylation. *Pharm. Res.* 21: 344.
- Huang Y., Chen S., Bing X., Gao C., Wang T. and Yuan B. 2011. Nanosilver migrated into food-simulating solutions from commercially available food fresh containers. *Packag. Technol. Sci.* 24: 291.
- Huh A.J. and Kwon Y.J. 2011. Nanoantibiotics, a new paradigm for treating infectious diseases using nanomaterials in the antibiotics resistant era. *Journal of Controlled Release*. 156: 128.
- Hurrell R. 2002. Fortification: overcoming technical and practical barriers. *Journal of Nutrition*. 132: 806.
- Ijabadeniyi O.A. 2012. Safety of nanofood: a review. *African Journal of Biotechnology*. 11: 15258.
- ISO TC 229 (2008). Draft standard on Nanotechnologies. Terminology and definitions for nanoparticles. http://www.iso.org/iso/iso_catalogue/catalogue_tc/catalogue_detail.htm?csnumber=44278. Accessed June 17, 2011.
- Jelinek C.F., Pohland A.E. and Wood G.E. 1989. Worldwide occurrence of mycotoxins in foods and feeds, an update. *J. Assoc. Anal. Chem.* 72: 223.
- Kalkanidis M., Pietersz G.A., Xiang S.D., Mottram P.L., Crieen-Irwin B., Ardipradja K. and Plebanski M. 2006. Methods for nano-particle based vaccine formulation and evaluation of their immunogenicity. *Methods*. 40: 20.
- Katragadda C.S., Choudhury P.K. and Murthy P.N. 2010. Nanoparticles as non-viral gene delivery vectors. *Indian J. Pharm. Educ. Res.* 44: 109.
- Keener K.M., Bashor M.P. and Curtis P.A. 2006. Comprehensive review of *Campylobacter* and poultry processing. *Compr. Rev. Food Sci. F.* 3: 105.
- Khanna V., Bakshi B.R. and Lee L.J. 2008. Carbon nanofiber production: life cycle energy consumption and environmental impact. *Journal of Industrial Ecology*. 12: 394.
- Kuzma J. Nanotechnology in animal production. 2010. Upstream assessment of applications. *Livest Sci.* 130: 14.
- Latour R.A., Stutzenberger F.J. and Sun Y. 2003. Adhesion-specific nanoparticles for removal of *Campylobacter jejuni* from poultry. Available from: <http://www.reeis.usda.gov/web/>
- Li L., Baoxin L., Di C. and Lihui M. 2010. Visual detection of melamine in raw milk using gold nanoparticles as colorimetric probe. *Food Chem.* 122: 895.
- Lilie M. and Cantini A.A. 2001. Nanotechnology in agriculture and food processing. Conference proceedings, University of Pittsburgh, Eleventh Annual Freshman Conference, April 9. p. 1.
- Lindemann M.D., Blodgett D.J., Kornegay E.T. and Schurig G.G. 1993. Potential ameliorators of aflatoxicosis in weanling/growing swine. *J. Anim. Sci.* 71: 171.
- Liu W., Zhang S., Wang L., Qu C. and Zhang C. 2011. CdSe quantum dot (QD)-induced morphological and functional impairments to liver in mice. *PLoS ONE* 6: 9.
- Liu X. and Wong D.K. 2007. Electrocatalytic detection of estradiol at a carbon nanotube Ni(Cyclam) composite electrode fabricated based on a two-factorial design. *Anal. Chim. Acta.* 594: 184.
- Liu Y., Zhao Y., Sun B. and Chen C. 2012. Understanding the toxicity of carbon nanotubes. *Acc. Chem. Res. (E. Pub.)*.
- Luo D., Han E., Belcheva N. and Saltzman W.M. 2004. A self-assembled, modular DNA delivery system mediated by silica nanoparticles. *J. Control Release.* 95: 33.
- Masoero F., Gallo A., Moschini M., Piva G. and Diaz D. 2007. Carryover of aflatoxin from feed to milk in dairy cows with low or high somatic cell counts. *Animal* 1: 1344.
- McKnight T.E., Melechko A.V. and Griffin G.D. 2003. Intracellular integration of synthetic nanostructures with viable cells for controlled biochemical manipulation. *Nanotechnology*. 14: 551.
- Medina C., Santos-Martinez M.J. and Radomski A. 2007. Nanoparticles: pharmacological and toxicological significance. *Br. J. Pharmacol.* 150: 552.
- Meredith A. Mintzer M. and Grinstaff W. 2011. Biomedical applications of dendrimers: A tutorial. *Chem. Soc. Rev.* 40: 173.
- Moghaddam S.H.H., Jebali A. and Daliri K. 2010. The use of MgO-SiO₂ nanocomposite for adsorption of aflatoxin in wheat flour samples. Available from: <http://www.nanocon.cz/data/nanocon2010>
- Mozafari M., Flanagan J., Matia L., Merino M., Awati A., Omri A., Suntres Z. and Singh H. 2006. Recent trends in the lipid-based nanoencapsulation of antioxidants and their role in foods. *J. Sci. Food.* 86: 2038.
- Mukul D., Ansari K.M., Anurag T. and Dwivedi P.D. 2001. Need for safety of nanoparticles used in food industry. *J. Biomed. Nanotechnol.* 7: 13.
- Mura S., Greppi G.F., Corrias F., Innocenzi P., Marongiu D., Stara G., Piccinini M. and Secchi N. 2011. Biodegradable and antibacterial nanofilms composed of chitosan, methylcellulose and nanoparticles. *Journal of Food Science.* 76: 54.
- Murata J., Ohya Y. and Ouchi T. 1998. Design of quaternary chitosan conjugate having antennary galactose residues as a gene delivery tool. *Carbohydr. Polym.* 32: 105.
- O'Connell M.J., Bachilo S.M. and Huffman C.B. 2002. Band gap fluorescence from individual single walled carbon nanotubes. *Science.* 297: 593.
- O'Neill C.J., Swain D.L. and Kadamdeen H.N. 2010. Evolutionary process of *Bos taurus* cattle in favourable versus unfavourable environments and its implications for genetic selection. *Evol. Appl.* 3: 422.
- Otilia M.K. Israel R. and Hayat O. 2005. Role of nanotechnology in targeted drug delivery and imaging: A concise review. *Nanomedicine: Nanotechnology, Biology and Medicine* 1(3): 193.
- Padovani S.C., Sada P., Mazzoldi B., Brunetti I., Borgia A., Giulivi A., Sgamellotti F., Acapito D. and Battaglin G. 2003. Copper in glazes of renaissance luster pottery: nanoparticles, ions and local environment. *J. Appl. Phys.* 93: 158.
- Patil S.S., Kore K.B. and Kumar P. 2009. Nano-technology and its applications in veterinary and animal science. *Vet. World.* 2: 475.
- Paunesku T., Rajh T. and Wiederrrecht G. 2003. Biology of TiO₂-oligonucleotide nanocomposites. *Nature Mater.* 2: 343.
- Peek L.J., Middaugh C.R. and Berkland C. 2008. Nanotech-

- nology in vaccine delivery. *Adv. Drug Deliv. Rev.* 60: 915.
- Perch H. 2007. How is Nanotechnology being used in Food Science? <http://www.understandingnano.com/food.html>. Accessed June 11, 2011
- Powell J.J., Faria N., Thomas-McKay E. and Pele C.L. 2010. Origin and fate of dietary nanoparticles and microparticles in the gastrointestinal tract. *J. Autoimmun.* 34: 226.
- Read J. 1961. Through alchemy to chemistry. London: Bell and Sons Ed.
- Rhim J. Ng PKW. 2007. Natural biopolymer-based nanocomposite films for packaging applications. *Crit. Rev. Food Sci. Nutr.* 47: 411.
- Richardson N.S.M. and Piehowski K.E. 2008. Nanotechnology in nutritional sciences. *Minerva Biotechnol.* 20: 117.
- Rohner F., Ernst F., Arnold M., Hilbe M., Biebinger R., Ehrensperger F., Pratsinis S., Langhans W., Hurrell R. and Zimmermann M. 2007. Synthesis, characterization, and biodisponibility in rats of ferric phosphate nanoparticles. *Journal of Nutrition.* 137: 614.
- Romero-Pérez A., García-García E., Zavaleta-Mancera A., Ramírez-Bribiesca J.E., Revilla-Vázquez A., Hernández-Calva L.M., López-Arellano R. and Cruz-Monterrosa R.G. 2010. Designing and evaluation of sodium selenite nanoparticles in vitro to improve selenium absorption in ruminants. *Veterinary Research Communication.* 34: 71.
- Rosenberg J.T., Kogot J.M., Lovingood D.D., Strouse G.F. and Grant S.C. 2010. Intracellular bimodal nanoparticles based on quantum dots for high-field MRI at 21.1 T. *Magn. Reson. Med.* 64: 871.
- Ross S.A., Srinivas P.R., Clifford A.J., Lee S.C., Philbert M.A. and Hettich R.L. 2004. New technologies for nutrition research. *Journal of Nutrition.* 134: 681.
- Roy K., Mao H.Q. and Leong K.W. 1997. DNA-chitosan nanospheres: Transfection efficiency and cellular uptake. *Proc. Int. Sym. Control Rel. Bioact. Mater.* 24: 673.
- Salem A.K., Searson P.C. and Leong K.W. 2003. Multifunctional nanorods for gene delivery. *Nature Mater.* 2: 668.
- Sanguansri P. and Augustin M.A. 2006. Nanoscale materials development - a food industry perspective. *Trends Food Sci. Technol.* 17: 547.
- Sargent Jr. and J.F. 2010. The national nanotechnology initiative: overview, reauthorization and appropriations issues. <http://oai.dtic.mil/oai/oaiverb=getRecord&metadataPrefix>
- Savage N. and Diallo M. 2005. Nanomaterials and water purification: Opportunities and challenges. *Journal of Nanoparticle Research* 7: 331.
- Sayes C.M., Reed K.L. and Warheit D.B. 2011. Nanoparticle toxicology: measurements of pulmonary hazard effects following exposures to nanoparticles. *Methods Mol. Biol.* 726: 313.
- Scott N.R. 2005. Nanotechnology and animal health. *Revue Scientifique et Technique (International Office of Epizootics).* 24: 425.
- Scrinis G. 2010. Nanotechnology: Transforming Food and the Environment. <http://www.foodfirst.org/>
- Scrinis G. and Lyons C. 2007. The emerging nano-corporate paradigm: nanotechnology and the transformation of nature, food and agri-food systems. *International journal of sociology of food and agriculture.* 15: 21.
- Sharma B., Ma W., Morris I., Panyam J., Dimitrijevic S. and Labhassetwar, V. 2011. Nanoparticle mediated p53 gene therapy for tumor inhibition. *Drug Deliv. Transl. Res.* 1: 43.
- Shefer A. and Shefer S. 2003a. Multi component biodegradable bioadhesive controlled release system for food products. U.S. patent. 6589562B1.
- Shefer A. and Shefer S. 2003b. Biodegradable bioadhesive controlled release system of nano-particles for food products. U.S. Patent. 6565873B1.
- Shi Y.H., Xu Z.R., Feng J.L. and Wang C.Z. 2006. Efficacy of modified montmorillonite nanocomposite to reduce the toxicity of aflatoxin in broiler chicks. *Anim. Feed Sci. Technol.* 129: 138.
- Shvedova A.A., Tkach A.V., Kisin E.R., Khaliullin T., Stanley S., Gutkin D.W., Star A., Chen Y., Shurin G.V., Kagan V.E. and Shurin M.R. 2012. Carbon nanotubes enhance metastatic growth of lung carcinoma via up-regulation of myeloid-derived suppressor cells. *Small.* (E-print).
- Singh M., Chakrapani A. and O'Hagan D. 2007. Nanoparticles and microparticles as vaccine-delivery systems. *Expert Rev. Vaccines.* 6: 797.
- Smith J.W., Tokach M.D., Goodband R.D., Nelssen J.L. and Richert B.T. 1997. Effects of the interrelationship between zinc oxide and copper sulfate on growth performance of early-weaned pigs. *J. Anim. Sci.* 75: 1861.
- Sozer N. and Kokini J.L. 2009. Nanotechnology and its applications in the food sector. *Trends Biotechnol.* 27: 82.
- Stern J.M., Stanfield J. and Lotan Y. 2007. Efficacy of laser-activated gold nanoshells in ablating prostate cancer cells *in vitro*. *J. Endourol.* 21: 939.
- Studnicka A., Sawos E., Grodzik M., Balcerak A. and Chwalibo M. 2009. Influence of nanoparticles of silver/palladium alloy on chicken embryos development. *Ann. Warsaw Agricult. Univ. SGGW. Anim. Sci.* 46: 237.
- Taniguchi N. 1974. On the basic concept of 'Nano-technology'. *Proc. Intl. Conf. Prod. Eng. Tokyo, Part II, Japan Society of Precision Engineering.*
- Tong G., Yu-long M.A. and Zi-rong X.U. 2007. Effects of Cu(II)-exchanged montmorillonite nanoparticles on growth performance, digestive function and mucosal disaccharase activities of weaned pigs. *Chinese J. Anim. Sci.* 21: 22.
- Verma O.P., Kumar R., Kumar A. and Chand S. 2012. Assisted Reproductive Techniques in Farm Animal. From Artificial Insemination to Nanobiotechnology. *Vet. World.* 5: 301.
- Wang X., Li Y., Wei J. and De Groot K. 2002. Development of biomimetic nanohydroxyapatite/ poly (Hexamethylene Adipamide) Composites. *Biomaterials.* 23: 4787.
- Wei F., Lam R., Cheng S., Lu S., Ho D. and Li Na. 2010. Rapid detection of melamine in whole milk mediated by unmodified gold nanoparticles. *Appl. Phys. Lett.* 96: 133702.
- Weiss J., Takhistoy P. and McClements D.J. 2006. Functional Materials in Food Nanotechnology. *J. Food Sci.* 71: 107.
- Williams D., Amman M., Autrup H., Bridges J. and Cassee F. 2005. The appropriateness of existing methodologies to assess the potential risks associated with engineered and adventitious products of nanotechnologies. *European Commission Health and Consumer Protection Directorate General,* p. 1.
- Xu P., Gullotti, E. Tong, L., Highley C.B., Errabelli D.R., Hasan T., Cheng J.X., Kohane D.S. and Yeo Y. 2009. Intracellular drug delivery by poly(lactic-co-glycolic acid) nanoparticles, revisited. *Mol. Pharm.* 6: 190.
- Yamakoshi Y., Umezawa N., Ryu A., Arakane K., Miyata N., Goda Y., Masumizu T. and Nagano T. 2003. Active oxygen species generated from photoexcited fullerene (C60) as potential medicines: O2-^{*} versus 1O2. *J. Am. Chem. Soc.* 125: 12803.
- Yang H., Qu L. and Wimbrow A.N. 2007. Rapid detection of *Listeria monocytogenes* by nanoparticle-based immunomagnetic separation and real-time PCR. *Int. J. Food Microbiol.* 118: 132.
- Zhang D., Carr D.J. and Alocilja E.C. 2009. Fluorescent bio-barcode DNA assay for the detection of *Salmonella enterica* serovar Enteritidis. *Biosens. Bioelectron.* 24: 1377.
- Zhang H., Yee D. and Wang C. 2008. Quantum dots for cancer diagnosis and therapy: biological and clinical perspectives. *Nanomedicine,* 3: 83.
- Zhou X., Wang Y., Gu, Q. and Li W. 2009. Effects of different dietary selenium sources (selenium nanoparticle and selenomethionine) on growth performance, muscle composition and glutathione peroxidase enzyme activity of crucian carp (*Carassius auratus gibelio*). *Aquaculture.* 291: 78.
- Zimmerman D.R. 1980. Iron in swine nutrition. In: "National ironed ingredient association: literature review on iron in animal and poultry nutrition". West Des Moines, IA: National Ironed Ingredient Association.
- Zuccheri G. and Asproulis N. 2012. Detection of Pathogens in Water Using Micro and Nano-Technology. IWA publishing.