NANOTECHNOLOGIES IN FOOD AND NUTRITION

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Abstract

Nanotechnology applications are widespread. In the food sector, they are expected to bring several benefits, from farm to table, including modification of sensory properties, nutritional improvement, and “active” and “intelligent” packaging materials. As more products appear in the market, the need for accurate analytical procedures, risk-assessment studies and regulatory framework is being addressed. This review looks at recent advances in all those applications and challenges concerning the use of nanomaterials in food and nutrition.

Key words: *Nanotechnology, Food, Nutrition, Packaging, Toxicity, Regulation*

Resumo

As aplicações da nanotecnologia podem ser encontradas em diversas áreas. Espera-se que aportem diversos benefícios ao sector da alimentação, em todos os seus aspectos, incluindo a modificação de características sensoriais e melhoria nutricional dos alimentos e a inclusão em embalagens denominadas “activas” e “inteligentes”. À medida que novos produtos surgem no mercado, torna-se mais evidente a necessidade de desenvolvimento de métodos analíticos e de avaliação de riscos, bem como de legislação eficaz. Este artigo passa em revista os mais recentes avanços e desafios relacionados com a aplicação de nanomateriais no campo da alimentação.

Palavras-chave: *Nanotecnologia, Alimentação, Nutrição, Embalagem, Toxicidade, Legislação*

Introduction

The nanosciences comprise diverse areas of knowledge, and most of the scientific and technological fields are nowadays taking advantage of nanotechnology. Especially, within the areas connected to health and well-being, there exists an expectation that the use of nanotechnologies might bring large benefits, both in diagnostics and treatments. When specifically regarding the food and nutrition sector, it is believed that nanotechnologies can provide new instruments for the insertion of innovative features in foods and the control of its properties. The involvement of nanotechnologies can be found along all the food chain, from production to processing of food, including its safety, packaging, transportation, storage and delivery (Rossi et al., 2014).

Although nanomaterials can be traced back to the 4th century, the modern concept of nanotechnology dates only from the 20th century, with the first companies beginning to operate during the early 1990s (National Nanotechnology Initiative, n.d). The first feature publication concerning food nanotechnology dates from 2003 (Moraru et al., 2003), but the growing interest in the field can be substantiated through a search on a database like Web of Science™, which produced 152 results concerning publications with both words “food” and “nanotechnology” in their titles, from 2003 to the present.

This growth is also noticeable in the evolution of the global market for nano-

enabled food products and food packaging nanomaterials, which is expected to attain US$ 7 billion in 2015 and grow to around US$ 20 in 2020. More than 1200 companies are at present involved in research and development of these products (Helmut Kaiser, 2006).

As is common with the introduction of new technologies or materials in products of current human consumption, along with the development of nanomaterials applications to food products, concerns have arisen in relation to ethical matters and the risk posed to humans from their exposure.

1. Definitions of nanomaterials

The definitions concerning nanomaterials are constantly evolving and are not consistent through the different regions. The most recent definition used within the European Union (EU) is a “natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1-100 nm” (European Commission, 2011). However, some authors claim also properties ascribed to nanomaterials for materials with particle sizes in the range 100 to 300 nm (Busolo et al., 2010; Huang, 2011). The Food and Agriculture Organization and the World Health Organization, in a joint technical paper, have also adopted working definitions for various terms related to food nanotechnologies, but those are not yet considered as final (Takeuchi et al., 2014).

Nanomaterials are usually classified according to their dimensions as: i) 0-dimensional, when all three dimensions are below 100 nm; ii) 1-dimensional, with two dimensions below 100 nm; iii) 2-dimensional, when only one of the dimensions is below 100 nm; iv) 3-dimensional, for not nanometre sized materials, constituted by the assembly of nanometre elementary structures. Nanoparticles and quantum dots are examples of 0-dimensional materials; nanotubes, nanowires and nanorods are instances of 1-dimensional substances; 2-dimensional nanomaterials include ultrathin films; and nanocomposites are examples of 3-dimensional nanomaterials (Roesler et al., 2007).

Due to the novelty of the area, new engineered nanoparticles (ENPs) are constantly being developed, frequently gaining their names from similar “macro” objects, by adding the “nano” prefix: nanobubbles, nanoclusters, nanoplatelets, nanocrystals, nanofibres, nanowhiskers, nanocubes, nanomultifacets, nanowires, nanorods, nanospheres, nanoplates, nanotriangles, quantum dots, liposomes, carbon nanotubes, dendrimers, functionalized nanoparticles, and fullerenes (Hannon et al., 2015). Although the names are similar, these ENPs can exhibit markedly different chemical and physical properties relative to those of the corresponding bulk materials (Roduner, 2006).

2. Synthesis and analysis of nanomaterials

Two approaches are commonly used for the synthesis of ENPs: the “top down” method involves the reduction of larger particles by physical or chemical mechanisms; the “bottom up” method is more complex and involves the assembly of molecules and ions into nanoparticles (Hannon et al., 2015; Cushen et al., 2012). Several examples of both approaches are constantly being published, usually with a focus on environment-friendly methods (Cheviron et al., 2014).

Nanomaterials usually occur as uncomplexed metals, inorganic metals and carbon based compounds. The more commonly used are carbon and metal based materials, dendrimers and composite materials (Sonkaria et al., 2012). Other materials, such as clays, proteins and polymers can also be used to form ENPs (Rossi et al., 2014; Food Safety Authority of Ireland, 2008). Among the first nanocomposites used were polymers incorporating clay nanoparticles, in particular montmorillonite. The

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polymers used include polyamides, nylons, polyolefins, polystyrene, ethylene-vinylacetate, polyurethane and polyethylene terephthalate (Rossi et al., 2014).

The occurrence of nanomaterials in consumer products implies the need to use analytical techniques with lower sensitivity limits, able to identify and quantify substances in the nanoscale. Nanoparticles (NPs) already existed in nature before analytical techniques for their detection were developed. For example, food grade titanium dioxide (E171) contains between 17-35 % nanosized particles (Yang et al., 2014), and silicon dioxide (E551) contains aggregates with particles < 100 nm (Bouwmeester et al., 2014). Albeit a considerable number of recent publications addressed this issue, the development of adequate analytical techniques is still lagging behind the evolution of NPs (Gmoshinski et al., 2013).

3. Nanomaterials in the food industry

Nanotechnology is present in every aspect of the food industry and has the potential to be more so. At the farm level, it can be used to produce more specific pesticides, to release, in a more controlled way, compounds to increase crop yield and improve animal health, while minimising greenhouse gases emission.

During food processing, nanoproducts may be applied in transport systems and hygiene procedures, preventing equipment clogging and reducing cleaning necessity (Tepper & Kaledin, 2005); nanomaterials are used to create non-fouling surfaces, used as nano-sieves for filtration purposes (Eriksson, 1988) and as sensors for food processing; NPs can be directly added as food supplements or materials for encapsulation and food ingredients processed into nanostructures.

In food packages, ENPs can be used in surface coatings or included within the polymers used for packaging, by formation of particles *in situ* or by attachment of particles to the polymer (Yang, 2003). Nanomaterials used in food packaging can provide antimicrobial properties, allowing fresh products to maintain quality during longer periods. Materials such as silver (Ag), gold (Au), zinc oxide (ZnO), titanium nitride (TiN), alumina (Al_2O_3), and titanium dioxide (TiO_2) are used. However, given the superior antimicrobial properties of engineered silver nanoparticles, those have received more attention regarding their incorporation in food packaging (Hannon et al., 2015). TiO_2 and TiN are used in packaging, respectively for UV protection and mechanical strength (Chaudhry & Castle, 2011). In the manufacture of the so-called “active” and “intelligent” packages, package labels with nanosensors could inform the consumer about temperature abuse or microbial contamination. For this purpose, and as an example, an array of thousands of nanoparticles was developed to fluoresce at different wavelengths when in contact with food pathogens (Srinivas et al., 2010). Another application allows that, after use of a food product, its packaging may be designed for composting and thus degrade into environment-friendly compounds (Hannon et al., 2015; Chaudhry et al., 2008). Also in the field of food packaging, a recent development was the introduction of nanocomposites, polymers containing up to 5 % w/w NPs. These materials have increased mechanical and thermal performances and reduced permeability to gases (Llorens, 2012).

The integration of nanotechnology with other knowledge areas such as biotechnology and information technology has led to the development of new products. Examples are nano-biosensors for the detection of contaminants in food, delivery systems such as nano-micelle based carriers for nutritional supplements and nutraceuticals (Rossi et al., 2014) and other nanostructures for encapsulation of food ingredients and additives, in order to protect them and mask their flavour, as well as providing a controlled release, and better dispersability for water-insoluble substances (Cushen et al., 2012).

4. Nanomaterials and human nutrition

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One of the most interesting areas of application for nanotechnologies is in the acquisition of nutritional information, namely the location of a particular nutrient or bioactive compound in a tissue, cell, or cellular component. The use of these new technologies has rendered possible the detection of nutrients and metabolites and the understanding of their interactions with specific tissues, leading to measures of their bioavailability. Nanotechnologies can assist in gaining a deeper knowledge of the molecular targets of nutrient activity, allowing the concept of a more "personalized" nutrition (Srinivas et al., 2010). Applications of nanotechnology to nutrition include the modification of sensory properties of foods, the enhancement of nutritional quality, the improved delivery of nutrients and the use as a tool to better understand metabolic pathways and the physiology of nutrients (Moraru et al., 2003; Ross et al., 2004; Nickols-Richardson, 2007).

Several phytochemicals have been studied *in vitro* due to their potential as preventive and therapeutic agents for some diseases. Food probiotics are also considered beneficial for human health. However, phytochemicals have poor solubility, stability, bioavailability and target specificity in the human body, which prevents their effective use and probiotics can only be beneficial if not affected by processing methods and reach the target location in the body intact. Nanotechnology can enhance the delivery of those products through encapsulation, namely solid lipid nanoparticles (Chung et al., 2010).

Nanoliposomes can provide better bioavailability of encapsulated compounds due to their small size and large interfacial area with biological tissues (Wang et al., 2014). When steric stabilisation is needed, this can be achieved by coating the nanoliposomes with inert polymers (Momekova et al., 2007).

Nanostructured lipid carriers are a new generation of stable, biocompatible and biodegradable nanocarriers, which have a high loading capacity and are particularly suited to deliver poorly soluble compounds, such as phytochemicals (Puri et al., 2009; Gokce et al., 2012; Aditya et al., 2013). Lipid based nanoparticles can be administered through a diversity of routes, but the oral way seems to be the most preferable (Iqbal et al., 2012). However, there is scarce knowledge about the absorption and metabolism of NPs in the gastrointestinal tract (Srinivas et al., 2010). Nanoparticle technology has been successfully tested as a possible solution for the delivery of compounds such as (-)-epigallocatechin gallate, resveratrol, curcumin and quercetin (Wang et al., 2014).

5. Possible risks associated with the exposure to nanoparticles

NPs are naturally present in some foods, likely produced due to the processes used in the food manufacture. In some other cases, as the casein micelles in dairy milk, which have a 100 nm diameter, they are already present in the raw food before processing (Trejo et al., 2011). But the processing of food ingredients and additives, to reduce their size to nanoparticles, should give rise to a higher internal exposure, enhancing their absorption and bioavailability in the human body. Thus, some health problems may be associated with the consumption of NPs, ranging from different profiles of nutrient absorption to the introduction of toxic substances or microorganisms adsorbed on nanomaterials, or even diverse toxic effects at cellular level, such as oxidative damage due to production of radicals (Rossi et al., 2014). Several components found in NPs (nucleic acids, antibody fragments and proteins) may act as antigens, leading to an increase in immunotoxicity (Desai, 2012). On the other hand, it was suggested that the process of digestion takes place in the nanoscale, implicating an existing ability of the human body to process nanomaterials (Chaudhry et al., 2008).

There are three main routes of human exposure to ENPs: dermal contact, inhalation and ingestion. Other less common routes are through rectal administration, the female genital tract and direct injection into the blood. It should also be taken into account the existence of other possible sources of oral exposure to nanoparticles, namely from drugs, sunscreens, lipsticks, skin creams, and toothpastes (Rossi et al.,

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2014). However, human exposure assessment to nanoparticles is still in its infancy. Clinical trials can be used to assess short-term toxicity of NPs, but long-term toxicity due to chronic exposure needs a more careful control. The relatively few studies concerning human exposure to ENPs are related to the ingestion route. Only four human exposure models are found in the literature to quantify the risk associated with oral ingestion of ENPs from food packages (Hannon et al., 2015; Cushen et al., 2013; Cushen et al., 2014; Goetz et al., 2013; Bachler et al., 2013). Nonetheless, at present, no known *in vivo* studies were performed to evaluate the toxicity of ENPs via ingestion (Hannon et al., 2015).

The presence of NPs in food packages is one potential source of toxicity. Several studies have shown that the use of combinations of ENPs in packaging materials seems to affect the migration of substances (Fortunati et al., 2013; Kumar et al., 2005; Martínez-Abad et al., 2013). The exposure through ingestion of NPs from food packaging can be determined either by way of migration studies or *in vivo* toxicity studies. When these studies indicate an acceptable level of risk, the authorities are responsible to allow or not the use of such a product. In Europe, the European Food Safety Authority is the responsible body (EFSA Scientific Committee, 2012). In general, the few experimental studies reported suggest a very low probability of nanoparticle migration from polymer packaging materials to food (Avella et al., 2005; EFSA Panel on Food Contact Materials, 2008).

Particles naturally existing or manufactured from food compatible sources are considered food grade nanoparticles and are viewed as a solution to the inherent toxicity associated with metal ENPs (Coles & Frewer, 2013). Several food compounds can be loaded into biocompatible and biodegradable nanoparticles, in order to improve their absorption and bioavailability (Wang et al., 2014). Some examples are alcoholic lecithin and sodium caseinate added to chitosan for use as nanocapsules (Sato et al., 2011) and a paprika oleoresin used to improve the marinating process and sensory properties of poultry meat (Yusop et al., 2012).

6. Legal framework

There is a disparity between engineered nanoparticles which are intentionally manufactured to possess enhanced properties and naturally occurring nanoparticles which are unintentional.

For regulatory purposes, the distinction between ENPs and natural (or accidental) nanomaterials with the same chemical composition in food, needs to be addressed in order to selectively determine the former. Analytical methods used for this purpose can be complex and imply the use of combinations of imaging and analytical techniques. Despite the fact that labelling for ENPs in food is mandatory in the European Union since 2014, there are only a handful of available methods for determination of nanomaterials in a few food matrices (Rossi et al., 2014).

There are no specific regulations on ENPs used as food contact materials (FCMs), but some regions, including the EU, have made amendments on general legislation concerning FCMs to provide guidance for nanomaterials (Hannon et al., 2015). In the EU, the first regulation concerning new “active” and “intelligent” food packaging materials dates from 1994 (Regulation (EC), 2004). No specific mention of ENPs were however present. Only in 2011, Regulation No. 10/2011 specifically mentioned that substances migrating from food packages to foods must not exceed the limit of 10 mg dm^{-2} of the food contact material, including nanomaterials among the list of substances for use in FCMs (Regulation (EC), 2011). This regulation establishes the mandatory indication of engineered nanomaterials in food labels after December 2014. In the United States, the Food and Drug Administration issued a guidance stating that the manufacturer of a new FCM has to provide a safety assessment including safety studies in animals and humans, in order to commercialise the product (United States Food and Drug Administration, 2014). This guidance recommends that safety

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evaluation should not use data extrapolated from conventional substances, accepting only studies specifically performed on the nanomaterial.

Conclusions

The use of nanoparticles in the agri-food sector are still at development stage, with a few products having already reached the market. Most of the applications of NPs and nanotechnology are found in food packaging and nutrient supplementation, due to their unique properties, consequence of their small sizes and large surface to mass ratio. Analytical methods capable to detect NPs in food and biological samples can be categorized as imaging, separation and spectroscopic techniques, however they still require development as does the existing toxicological effects assessment assays. Finally, the ethical, safety and environmental issues raised by the introduction of nanotechnologies brought forward the need to implement and harmonize regulatory measures in relation to risk-benefit evaluation and labelling.

Referências Bibliográficas

ADITYA, N. P., Shim, M., Lee, I., Lee, Y., Im, M.-H., & Ko, S. (2013). “Curcumin and genistein coloaded nanostructured lipid carriers in vitro digestion and antiprostate cancer activity”. Journal of Agricultural and Food Chemistry, 61, 1878-1883.

AVELLA, M., De Vlieger, J. J., Errico, M. E., Fischer, S., Vacca, P., & Volpe, M. G. (2005). “Biodegradable starch/clay nanocomposite films for food packaging applications”. Food Chemistry, 93, 467-474.

BACHLER, G., Goetz, N. v., & Hungerbühler, K. (2013). “A physiologically based pharmacokinetic model for ionic silver and silver nanoparticles”. International Journal of Nanomedicine, 8, 3365-3382.

BOUWMEESTER, H., Brandhoff, P., Marvin, H. J. P., Weigel, S., & Peters, R. J. B. (2014). “State of the safety assessment and current use of nanomaterials in food and food production”. Trends in Food Science & Technology, 40, 200-210.

BUSOLO, M. A., Fernandez, P., Ocio, M. J., & Lagaron, J. M. (2010). “Novel silver-based nanoclay as an antimicrobial in polylactic acid food packaging coatings”. Food Additives & Contaminants: Part A, 27, 1617-1626.

CHAUDHRY, Q., Scotter, M., Blackburn, J., Ross, B., Boxall, A., Castle, L., Aitken, R., & Watkins, R. (2008). “Applications and implications of nanotechnologies for the food sector”. Food Additives and Contaminants, 25, 241-258.

CHAUDHRY, Q., & Castle, L. (2011). “Food applications of nanotechnologies: An overview of opportunities and challenges for developing countries”. Trends in Food Science & Technology, 22, 595-603.

CHEVIRON, P., Gouanvé, F., & Espuche, E. (2014). “Green synthesis of colloid silver nanoparticles and resulting biodegradable starch/silver nanocomposites”. Carbohydrate Polymers, 108, 291-298.

CHUNG, M. J., Kim, D. M., Kim, J. E., & Lee, G. S. (2010). *U.S. Patent No. 20100278975*. Washington, DC: U.S. Patent and Trademark Office.

*Doutor. Professor Auxiliar, Dept. Ciências da Nutrição, Universidade Atlântica. Email: pfigueiredo@uatlantica.pt

COLES, D., & Frewer, L. J. (2013). “Nanotechnology applied to European food production – A review of ethical and regulatory issues”. Trends in Food Science & Technology, 34, 32-43.

CUSHEN, M., Kerry, J., Morris, M., Cruz-Romero, M., & Cummins, E. (2012). “Nanotechnologies in the food industry – Recent developments, risks and regulation”. Trends in Food Science and Technology, 24, 30-46.

CUSHEN, M., Kerry, J., Morris, M., Cruz-Romero, M., & Cummins, E. (2013). “Migration and exposure assessment of silver from a PVC nanocomposite”. Food Chemistry, 139, 389-397.

CUSHEN, M., Kerry, J., Morris, M., Cruz-Romero, M., & Cummins, E. (2014). “Evaluation and simulation of silver and copper nanoparticle migration from polyethylene nanocomposites to food and an associated exposure assessment”. Journal of Agricultural and Food Chemistry, 62, 1403-1411.

DESAI, N. (2012). “Challenges in development of nanoparticle-based therapeutics”. The AAPS Journal, 14, 282-295.

EFSA PANEL ON FOOD CONTACT MATERIALS (2008). “21st list of substances for food contact materials”. The EFSA Journal, 888-890, 1-14.

EFSA SCIENTIFIC COMMITTEE (2012). “Scientific opinion on the safety evaluation of the substance, titanium nitride, nanoparticles, for use in food contact materials”. The EFSA Journal, 10, 2641-2648.

ERIKSSON, P. (1988). “Nanofiltration extends the range of membrane filtration”. Environmental Progress, 7, 58-62.

EUROPEAN COMMISSION (2011). “Commission recommendation of 18th October 2011 on the definition of nanomaterials (2011/696/EU)”. Official Journal of the European Union, No. L 275/38.

FOOD SAFETY AUTHORITY of IRELAND (2008). *The relevance for food safety of applications of nanotechnology in the food and feed industries*. Dublin, FSAI.

FORTUNATI, E., Peltzer, M., Armentano, I., Jiménez, A., & Kenny, J. M. (2013). “Combined effects of cellulose nanocrystals and silver nanoparticles on the barrier and migration properties of PLA nano-biocomposites”. Journal of Food Engineering, 118, 117-124.

GMOSHINSKI, I. V., Khotimchenko, S. A., Popov, V. O., Dzantiev, B. B., Zherdev, A. V., Demin, V. F., & Buzulukov, Y. P. (2013). “Nanomaterials and nanotechnologies: Methods of analysis and control”. Russian Chemical Reviews, 82, 48-76.

GOETZ, N. v., Fabricius, L., Glaus, R., Weitbrecht, V., Günther, D., & Hungerbühler, K. (2013). “Migration of silver from commercial plastic food containers and implications for consumer exposure assessment”. Food Additives & Contaminants. Part A, Chemistry, Analysis, Control, Exposure & Risk Assessment, 30, 612-620.

GOKCE, E. H., Korkmaz, E., Dellera, E., Sandri, G., Bonferoni, M. C., & Ozer, O. (2012). “Resveratrol-loaded solid lipid nanoparticles versus nanostructured lipid carriers: Evaluation of antioxidant potential for dermal applications”. International Journal of Nanomedicine, 7, 1841-1850.

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HANNON, J. C., Cummins, E., Kerry, J., Cruz-Romero, M., & Morris, M. (2015). "Advances and challenges for the use of engineered nanoparticles in food contact materials". Trends in Food Science & Technology, 43, 43-62.

HELMUT KAISER (2006). *Study: Nanotechnology in food and food processing Worldwide 2003-2006-2010-2015*. Retrieved March 2015 from http://www.hkc22.com/Nanofood.html.

HUANG, Y., Chen, S., Bing, X., Gao, C., Wang, T., & Yuan, B. (2011). "Nanosilver migrated into food-simulating solutions from commercially available food fresh containers". Packaging Technology and Science, 24, 291-297.

IQBAL, M. A., Md, S., Sahni, J. K., Baboota, S., Dang, S., & Ali, J. (2012). "Nanostructured lipid carriers system: Recent advances in drug delivery". Journal of Drug Targeting, 20, 813-830.

KUMAR, R., Howdle, S., & Münstedt, H. (2005). "Polyamide/silver antimicrobials: Effect of filler types on the silver ion release". Journal of Biomedical Materials Research – Part B Applied Biomaterials, 75, 311-319.

LLORENS, A., Lloret, E., Picouet, P. A., Trbojevich, R., & Fernandez, A. (2012). "Metallic-based micro and nanocomposites in food contact materials and active food packaging". Trends in Food Science & technology, 24, 19-29.

MARTÍNEZ-ABAD, A., Ocio, M. J., Lagarón, J. M., & Sánchez, G. (2013). "Evaluation of silver-infused polylactide films for inactivation of Salmonella and feline calcivirus in vitro and on fresh-cut vegetables". International Journal of Food Microbiology, 162, 89-94.

MOMEKOVA, D., Rangelov, S., Yanev, S., Nikolova, E., Konstantinov, S., Romberg, B., Storm, G., Lambov, N. (2007). "Long-circulating, pH-sensitive liposomes sterically stabilized by copolymers bearing short blocks of lipid-mimetic units". European Journal of Pharmaceutical Sciences, 32, 308-317.

MORARU, C. I., Panchapakesan, C. P., Huang, Q., Takhistov, P., Liu, S., & Kokini, J. L. (2003). "Nanotechnology: A new frontier in food science". Food Technology, 57, 24-29.

NATIONAL NANOTECHNOLOGY INITIATIVE (retrieved 2015, March). *Nanotechnology timeline*. in http://www.nano.gov/timeline.

NICKOLS-RICHARDSON, S. M. (2007). "Nanotechnology: Implications for food and nutrition professionals". Journal of the American Dietetic Association, 107, 1494-1497.

PURI, A., Loomis, K., Smith, B., Lee, J.-H., Yavlovich, A., Heldman, E., & Blumenthal, R. (2009). "Lipid-based nanoparticles as pharmaceutical drug carriers: From concepts to clinic". Clinical Reviews in Therapeutic Drug Carrier Systems, 26, 523-580.

REGULATION (EC) No. 1935/2004 (2004) *of the European parliament and of the Council of 27 October 2004 on materials and articles intended to come into contact with food and repealing Directives 80/590/EEC and 89/109/EEC*. Official Journal of the European Union, L 338, 4-17.

*Doutor. Professor Auxiliar, Dept. Ciências da Nutrição, Universidade Atlântica. Email: pfigueiredo@uatlantica.pt

REGULATION (EC) No. 10/2011 (2011) *on plastic materials and articles intended to come into contact with food*. Official Journal of the European Union, L 12m 1-89.

RODUNER, E. (2006). "Size matters: Why nanomaterials are different". Chemical Society Reviews, 35, 583-592.

ROESLER, J., Harders, H., & Baeker, M. (2007). *Mechanical behaviour of Engineering Materials*. Berlin, Heidelberg, Springer.

ROSS, S. A., Srinivas, P. R., Clifford, A. J., Lee, S. C., Philbert, M. A., & Hettich, R. L. (2004). "New technologies for nutrition research". The Journal of Nutrition, 134, 681-685.

ROSSI, M., Cubadda, F., Dini, L., Terranova, M. L., Aureli, F., Sorbo, A., & Passeri, D. (2014). "Scientific basis of nanotechnology, implications for the food sector and future trends". Trends in Food Science & Technology, 40, 127-148.

SATO, A. C. K., Quintas, M. A. C., Vicente, A. A., & Cunha, R. L. (2011). "Food grade nanoparticles obtained from natural source ingredients". 11th International Congress on Engineering and Food, Athens, Greece.

SONKARIA, S., Ahn, S.-H., & Khare, V. (2012). "Nanotechnology and its Impact on Food and Nutrition: A review". Recent patents on Food, Nutrition & Agriculture, 4, 8-18.

SRINIVAS, P. R., Philbert, M., Vu, T. Q., Huang, Q., Kokini, J. L., Saos, E., Chen, H., Peterson, C. M., Friedl, K. E-, McDade-Ngutter, C., Hubbard, V., Starke-Reed, P., Miller, N., Betz, J. M., Dwyer, J., Milner, J., & Ross, S. A. (2010). "Nanotechnology research: Applications in nutritional sciences". The Journal of Nutrition, 140, 119-124.

TAKEUCHI, M. T., Kojima, M., & Luetzow, M. (2014). "State of the art on the initiatives and activities relevant to risk assessment and risk management of nanotechnologies in the food and agriculture sectors". Food Research International, 64, 976-981.

TEPPER, F., & Kaledin, L. (2005). *U.S. Patent No. 6838005*. Washington, DC: U.S. Patent and Trademark Office.

TREJO, R., Dokland, T., Jurat-Fuentes, J., & Harte, F. (2011). "Cryo-transmission electron tomography of native casein micelles from bovine milk". Journal of Dairy Science, 94, 5770-5775.

UNITED STATES FOOD AND DRUG ADMINISTRATION (2014). *Guidance for industry: Assessing the effect of significant manufacturing process changes, including emerging technologies, on the safety and regulatory status of food ingredients and food contact substances, including food ingredients that are color additives*. FDA, Maryland.

WANG, S., Su, R., Nie, S., Sun, M., Zhang, J., Wu, D., & Moustaid-Moussa; N. (2014). "Application of nanotechnology in improving bioavailability and bioactivity of diet-derived phytochemicals". Journal of Nutritional Biochemistry, 25, 363-376.

YANG, P. (Ed.) (2003). *The chemistry of nanostructured materials*. Singapore, World Scientific.

YANG, Y., Doudrick, K., Bi, X., Hristovski, K., Herckes, P., Westerhoff, P., & Kaegi, R. (2014). "Characterization of food-grade titanium dioxide: The presence of nanosized particles". Environmental Science and Technology, 48, 6391-6400.

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YUSOP, S. M., O'Sullivan, M. G., Preuβ, M., Weber, H., Kerry, J. F., & Kerry, J. P. (2012). "Assessment of nanoparticle paprika oleoresin on marinating performance and sensory acceptance of poultry meat". LWT – Food Science and Technology, 46, 349-355.

*Doutor. Professor Auxiliar, Dept. Ciências da Nutrição, Universidade Atlântica. Email: pfigueiredo@uatlantica.pt