

ADVANCES IN NANOTECHNOLOGY FOR IMPROVED NUTRACEUTICALS- AN OVERVIEW

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Abstract

Nanotechnology is one of the revolutionizing fields which can provide long-lasting solutions to many areas of human health including food, nutrition and medicine. With the increase in population, there is a great demand for more value-added food and nutraceuticals. Therefore researchers have turned to nanotechnology to provide better solutions to these fields. Some of these techniques include the study of characterization of nanomaterials, engineered nanomaterial-based delivery systems bioavailability of the nutritional compounds in food substances, etc. Very few nanotechnology-based nutraceuticals and dietary products are available in the market. However, extensive study needs to be carried out on the use of nanotechnology for improved nutraceuticals by commercializing to satisfy consumers. Nutraceuticals have gained considerable interest due to their safety and therapeutic effects. In recent years, nanoformulations have been rising interest in nutraceuticals. Therefore in the present review article, we have focused on the applications of nanotechnology toward improved nutraceuticals. The article gives a comprehensive outline of the various techniques employed for enhancing the nutrition quality, bioavailability and stability of nutraceuticals.

Keywords: Nanotechnology, Nutraceuticals, Nanomaterials.

Introduction

'Nutraceuticals' term was for the first time proposed by Stephen L. DeFelice in 1989. It comprises the words nutrition and pharmaceutical. The term is usually used to refer to any kind of feed or its components that is going to provide benefits to health and also help in preventing or treating diseases. Because of both features, there is a great demand for nutraceuticals in the present era. But in spite of all these features in nutraceuticals still there is barrier in complete utilization after consumption to the body because of its poor bioavailability. Therefore this requires urgent attention to overcome the problem through the use of nanotechnology. Nanoscience comes to the scene as a solution to this problem. Since nanoparticles possess unique properties with a size of less than 100 nanometres enhance the ratio of surface area to volume and high reactivity with biological specimens. This leads to a higher uptake in the human body. Nanoscience makes use of nanotechnology where nanoparticles are used to significantly alter the structure, texture and quality of food and health products. Studies have shown various nanoparticle approaches and their impact in various fields such as health, food and medicine. Most of the nanomaterials used in nutraceutical formulations are either organic or inorganic. Before selecting the nanomaterials care should be taken with regard to its safety since its meant for human consumption. For safety purpose European Food Safety Authority (EFSA) and European Centre for the Sustainable Impact of Nanotechnology (ECSIN) has set guidelines before use of nanoparticles in food. In the present report, an attempt has been made to look into an overview of nanomaterials especially in the area of nutraceuticals.

Nanotechnology in nutraceuticals

Nutraceuticals that include feed and dietary supplements has health-promoting properties. Even though there is a great demand for the nutraceutical market by consumers but the drawback is its poor bioavailability. Therefore there is an urgent need for developing new nutraceutical compounds that have improved features such as enhanced solubility, stability, bioavailability and efficacy. This has been achieved by the encapsulation of nutraceuticals by nanoparticles. This technique helps in modifying their pharmacokinetics (PK) and biodistribution (BD). One of the most effective methods involves the use of plant polysaccharides (pectin, starch, gum), microbial polysaccharides (Xanthan gum, dextran) food proteins (soy proteins, casein, gelatin) and emulsifiers (lecithin, sugar esters, monoglycerides). These are considered to be safe nanoparticles. The choice of the nanoparticle is very crucial since direct contact of the ingredients happens with the target site of action in the body. Some of the nutraceuticals include phytochemicals plant polyphenols (curcumin, resveratrol) carotenoids (lycopene, β carotene, lutein) etc. These are mainly considered by researchers because of their important role in the regulation of blood pressure, reducing malignant diseases, improving digestion, enhancing immunity, controlling glucose and cholesterol levels and also reducing stress by acting as antioxidants.

Characterization of nanomaterials used for nutraceutical purposes

Many physio-chemical properties such as the composition, state of dispersion, aggregation, size distribution, surface area, porosity etc are considered for the characterization of nanomaterials. These physio-chemical properties of nanomaterials can be altered by synthetic methods or by natural methods. Synthetic method involves processing in complex matrices for nutraceutical applications and the natural method involves altering during the digestive process in the physiological system. Some of the alterations in the physio-chemical properties include alteration in surface charge, Protein adsorption, Enzymatic degradation, Structure destabilization, Surface passivation etc. Characterization of nanomaterials may be done either by primary characterization which includes characterization based on their pure state or by secondary characterization which mainly includes functional properties in complex matrices. The latter includes a study for analysis of food, biological tissues and fluids, thus helps in study of efficacy and safety of the physiological system. The steps involved in the analysis of nanoparticles used in the food industry are followed as per EFSA guidelines. Since a single technique can't be employed in the characterization, many techniques have been employed. It includes certain traditional methods like atomic absorption spectrometry (AAS), plasma mass spectrometry (ICPMS) etc and also advanced methods like single particle (SP-ICP-MS) are used in complex matrices. Even combination of techniques like HPLC and ultraviolet-visible (UV-Vis) spectroscopy is also used in the study. The study of the physical parameters of nanomaterials is also carried out by scanning and transmission electron microscopy (SEM and TEM), Light scattering techniques e.g., Dynamic light scattering (DLS). The stability of the nanoparticles can be studied by laser Doppler micro-electrophoresis method. All these methods facilitate the complete study of the characterization of nanomaterials to understand its destiny over the entire life-cycle, i.e., right from the synthesis, its physiological action in the body and excretion.

Engineered nanomaterial-based delivery systems in nutraceuticals

Different nutraceutical compounds have varied molecular and physiochemical requirements like size, stability and surface properties. Therefore each of them needs correspondingly different methods of delivery systems to address these. Nanoparticulate delivery systems used for improving nutraceuticals include Nanoliposomes, nano-emulsions, lipid nanocarriers, micelles and Biopolymeric nanoparticles.

Micelles- These are sphere-shaped particles having a diameter of about 5-100nm. They are formed upon the dissolution of surfactants in water at concentrations that exceed a critical level, known as the "critical micelle

concentration" (CMC). The ability to encapsulate nonpolar molecules such as lipids, flavorants, antimicrobials, antioxidants, and vitamins is one of the important property of micelles. Microemulsions that contain solubilized materials are also used for encapsulation of limonene, lycopene, lutein, and omega-3 fatty acids.

Liposomes- They are lipid vesicles with sizes between 20 nm and a few hundred micrometers. formed of polar lipids. They are capable of incorporating different number of functional components in their interior. Uni- or multi-lamellar liposomes are designed to encapsulate proteins. One of the study has revealed liposomes to increase shelf life of dairy products by encapsulating lactoferrin. Another study has shown that Liposome-encapsulated vitamin C retained about 50% activity even after 50 days of refrigerated storage, whereas free ascorbic acid lost its activity after just 19 days.

Nanoemulsions- They contain small droplets and are simply made of very fine oil-in-water (o/w) emulsions. They have a diameter of 50–200 nm. It consists of a mixture of two completely or partially immiscible liquids, such as oil and water, with one liquid being dispersed in the other in the form of droplets. Examples of emulsified food products include mayonnaise, milk, sauces, and salad dressings. Nanoemulsions and macro-emulsions are used mainly in nutraceuticals. They have shown to exhibit some interesting textural properties that differ from those of an emulsion containing larger droplets.

Biopolymeric nanoparticles- They are known to contain a matrix of biopolymers that are linked via intermolecular attractive forces or through chemical covalent bonds to form solid particles.

There are a wide variety of natural and synthetic polymers that are used to encapsulate and deliver compounds. Nanoparticles usually contain single biopolymer. The first polymer was developed in 1932 which contained Polylactic acid as a key component. One of the natural antimicrobial and antioxidative polymers known as chitosan is obtained from crustacean shells.

Examples of the synthetic polymers L-, D-, and D, L-poly(lactic acid) (PLA), polyglycolic acid (PGA), and polycaprolactone (PCL). Combinations of the monomers like lactide, galactide, and apolactone are used in developing copolymers.

Cubosomes- they are made up of two cubic plates. They are placed as two separate, continuous, but nonintersecting hydrophilic regions divided by a lipid layer. It is contorted into a periodic minimal surface with zero average curvature. They exhibit a nanometer structure. When compared to liposomes, cubosomes have shown to exhibit much higher bilayer area-to-particle volume ratios. Due to this nanoparticle structure they help in the controlled release of solubilized bioactives in food matrices. The cubic phase shows strong bioadhesive properties so that it can find applications in flavor release via its mucosal deposition and delivery of effective compounds.

Conclusion

In the recent past, many efforts have been done for the development of improved nutraceutical products. One such effort includes the application of nanotechnology. This imparts special properties to food and nutraceutical products, thus making food, dietary products and nutraceuticals healthier and improvement in generating new food products, improved methods of food packaging and storage. Engineered nanoparticles-based delivery systems have opened new avenues in the field of nutraceuticals by providing an enhancement in bioaccessibility, solubility, absorption, and stability in the gastrointestinal tract after human consumption by increasing health benefits. However, many challenges are still there for the researchers to come up with new

ideas for its application for various products. Moreover, before designing any nanotechnological application, care should be taken towards the safety issues for human health as guided by EFSA.

The application of nanotechnology has tremendously advanced and revolutionized the medical field including therapeutics and diagnostics. Many nanomaterials designed by researchers also include medicinal products which are approved by FDA are already in the market for use. One such product is liposomes-based drugs, which is used in the improved treatment of chronic diseases like cancer. This has led to promising better human life. Curcumin is another such nutraceutical with anticancer potential which has been proved by various animal and cell culture models, by formulation of different nanoformulations like nanoparticles, micelles, and liposomes.

Efforts need to be made for the commercialization of nanotechnological products in many countries other than the US, Japan and China. The use of nanotechnology in food, food technology and nutraceuticals needs to be concentrated by upcoming new and advanced technology for the betterment of human health. Even though scientists have improved the bioavailability and therapeutic potential of various phytochemicals *in vitro* by formulating them as nanoformulations, extensive *in vivo* studies still need to be done to prove their efficacy.

References

1. Andlauer W and Fürst P. "Nutraceuticals: a piece of history, present status and outlook". Food Research International 35 (2002): 171-176.
2. Bonifácio BV., et al. "Nanotechnology-based drug delivery systems and herbal medicines: a review". International Journal of Nanomedicine 9.1 (2014)
3. Buzea C., et al. "Nanomaterials and nanoparticles: sources and toxicity". Biointerphases 2 (2007): 17-71.
4. Chaturvedi S., et al. "Role of Nutraceuticals in health promotion". Health 4 (2011): 5.
5. Chaudhry Q., et al. "Applications and implications of nanotechnologies for the food sector". Food Additives and Contaminants 25.3 (2008): 241-258.
6. Chen H., et al. "Nanotechnology in nutraceuticals and functional foods". Food Technology 603 (2006): 6-30.
7. Cho Y., et al. "Some cases in applications of nanotechnology to food and agricultural systems". BioChip Journal 2.3 (2008): 183-185.
8. Davis ME., et al. "Nanoparticle therapeutics: an emerging treatment modality for cancer". Nature Reviews Drug Discovery 7 (2008): 771-782.
9. Davis ME., et al. "Nanoparticle therapeutics: an emerging treatment modality for cancer". Nature Reviews Drug Discovery 7 (2008): 771-782.
10. El Sohaimy S. "Functional foods and nutraceuticals-modern approach to food science". World Applied Sciences Journal 20 (2012): 691-708.
11. Gonçalves RFS., et al. "Advances in nutraceutical delivery systems: From formulation design for bioavailability enhancement to efficacy and safety evaluation". Trends in Food Science and Technology 78 (2018): 270-291.
12. Jahangirian H., et al. "A review of drug delivery systems based on nanotechnology and green chemistry: green nanomedicine". International Journal of Nanomedicine 12 (2017): 29-57.
13. Kalra E K. "Nutraceutical-definition and introduction". American Association of Pharmaceutical Scientists 5 (2003): 27-28.
14. Martinho N., et al. "Recent advances in drug delivery systems". Journal of Biomaterials and Nanobiotechnology 2 (2011): 5-10.
15. More S., et al. "Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles". EFSA Journal Guidance Document (2021).
16. Nair HB., et al. "Delivery of anti-inflammatory nutraceuticals by nanoparticles for the prevention and treatment of cancer". Biochemical Pharmacology 80.12 (2010): 1833-1843.

17. Roco MC and Bainbridge WS. "Societal Implications of Nanoscience Nanotechnology". Kluwer Academic Publishers Boston (2001): 3-4.
18. Shaikh J., et al. "Nanoparticle encapsulation improves oral bioavailability of curcumin by at least 9-fold when compared to curcumin administered with piperine as absorption enhancer". *European Journal of Pharmaceutical Sciences* 37 (2009): 223-230.
19. Shi J., et al. "Nanotechnology in Drug Delivery and Tissue Engineering: From Discovery to Applications". *Nano Letters* 10.9 (2010): 3223-3230.
20. Soares S., et al. "Nanomedicine: Principles, Properties, and Regulatory Issues". *Frontiers in Chemistry* 6 (2018): 360.
21. Thakor AS and Gambhir SS. "Nanooncology: the future of cancer diagnosis and therapy". *CA: A Cancer Journal for Clinicians* 63.6 (2013): 395-418.
22. Verleysen E., et al. "Physicochemical characterization of nanoparticles in food additives in the context of risk identification". *EFSA External Scientific Report* (2021).
23. Watkins R., et al. "Natural product-based nano-medicine: recent advances and issues". *International Journal of Nanomedicine* 10 (2015): 55-60.
24. Yada RY., et al. "Engineered nanoscale food ingredients: Evaluation of current knowledge on material characteristics relevant to uptake from the gastrointestinal tract". *Comprehensive Reviews in Food Science and Food Safety* 13.4 (2014): 730-744.