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# Novel technologies for the encapsulation of bioactive food compounds

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Recent advances in nanoscience and nanotechnologies offer a revolutionary approach to the development of novel and healthier foods. Nano-technological and micro-technological carriers based on biomolecules may be tailored in order to deliver molecules, e.g., drugs, nutraceuticals and others, to any organ and tissue in the body. New micro- and nano-biocarriers based on food-grade polysaccharides, proteins, lipids and their blends, coacervates and also hybrid inorganic-biological molecules provide novel platforms to enhance the bioavailability, stability and delivery efficiency of bioactive molecules in the body.

## Addresses

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## Introduction

World trends are changing from the extensive production of goods based on the extraordinary abundance of natural resources in the planet to limited ones applying intensive green and more complex technologies to produce and distribute products for consumers everywhere. Under this framework, nano- and micro-technologies are opening new opportunities for the development of more evolved and technologically sophisticated foods during the present century. It is considered that nanotechnologies will impact on all food chains, starting from production (agriculture, livestock farming, pisciculture, etc.) and covering all intermediate steps of processing, packaging, storage, distribution, and selling to the consumer's table. In 2015, the world market for food nanotechnologies was estimated at US\$ 2.6 billion [1]. In addition, although global food

production grew significantly in the 20th century, 842 million people are still undernourished, and moreover food demand is expected to increase to 35% by 2030 [1]. Considering this landscape, nanotechnologies are becoming strong tools to be explored and developed at global scale. However, food nanotechnologies are still in infancy; more than 200 applications are in different phases of development but only few products have reached the market. The novel trends in food technology involve many nanotechnological devices, and new developments mainly comprise food areas of processing, functionalization, packaging, tracking and preservation. In this context, nanotechnology advantages could include the development of nanoobjects (nanogels, nanocapsules, etc.) for molecular encapsulation and improvement of food quality and/or digestion, control of food composition (healthy foods), specific nutraceutical delivery (e.g., vitamins, cofactor, proteins, etc.), foods for specific applications (special purpose and fortified foods), alternative noninvasive feeding (e.g., skin, mucosal), enhancement of sensorial properties (e.g., flavor, color, taste, smell, form) [2]. Techniques and methodologies, as well as some characteristics and synthesis of nanodevices for the food industry, were recently reviewed [3,4\*,5\*].

In addition, nanotechnologies will provide novel approaches for packaging by increasing safety on food production and food preservation, enhancing shelf life, avoiding microbial growth and contamination, stabilizing foods under extreme environmental conditions (e.g., high humidity or dryness, cold and hot temperatures), creating physical barriers (e.g., prevent oxidation, avoid external substance adsorptions, water resistance) [6]. The main advantages of nanostructures compared to standard devices are the high surface area/volume ratio providing increased load solubility, high dispersion of dose, enhanced bioavailability of cargo molecule, and improvement of targeting and controlled release [7].

Nanotechnological devices were defined by the National Science Foundation (NSF, USA) as any object with dimensions between 1 and 100 nm. However, this restrictive definition comes from physics without taking into account the interaction between nanoobjects and living cells and organisms that can be extended to the micro-universe. It is clear that any form of life can be considered as a 'nanotechnological object' based on the principle of molecular self-assembly [7]. Besides, since ancient times to our days, many raw materials have been combined and processed to create nanostructured foods [8].

The aim of the present work is to summarize the recent advances in molecular encapsulation in food nano- and micro-devices.

### Devices at nano- and microscales

The strategies to develop nanodevices are based on two main approaches: the top-down methodology, in which molecules are mixed, homogenized, and/or reacted, followed by some industrial processes (e.g., extrusion, grinding, filtration) to create nano- or microstructures. The other one is the bottom-up strategy, which involves chemical reactions between molecules mediated by different interactions (e.g., van der Waals, ionic and hydrophobic interactions) under controlled physicochemical environmental conditions to produce self-assembly structures [7].

In the case of foods, the molecules required to synthesize nanotechnological devices to encapsulate bioactive compounds must be GRAS (Generally Recognized As Safe, FDA, US), under and new regulations are still under discussion [9]. Among them, biopolymers such as carbohydrates and proteins are the most relevant to produce nanostructures in foods, but also other molecules such as fatty acids, natural esters, lipids, peptides are used. The main nanostructures described in the literature to be used in foods are lipidic carriers, biopolymeric particles made from proteins or polysaccharides, nanocomposites and gel structures (Figure 1). However, hybrid structures, coacervates (molecular assembly without defined chemical

composition) and tailored carriers composed of several molecules are in the phase of development.

### Lipidic carriers

Lipidic carriers can be classified as liposomes, nanoemulsions, solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs) (Figure 2) [10,11,12\*\*].

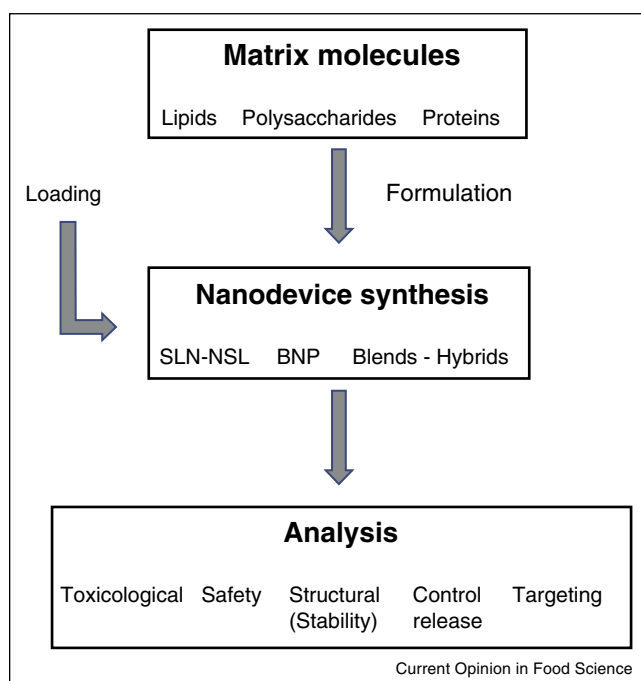
Nanoliposomes are submicron bilayer lipid vesicles composed of lipids and phospholipids resembling the lipidic bilayer of cellular membranes. The lipidic moieties contain a hydrophilic head and a hydrophobic acyl chain 'tail' and have bifunctional physicochemical properties useful for interacting with many functional groups of a high variety of molecules. Another feature of acyl chains is their length and the degree of saturation, which can cause great changes in membrane stability (temperature of phase transition). In addition, nanoliposomes may have other types of molecules such as sterols inserted inside the lipid bilayer, e.g., cholesterol, which increases the structural stability and regulates the fluidity of vesicles mostly by steric hindrance. The main characteristic of the nanoliposomes is the variability of the chemical composition providing a tailorable 'make a wish' platform required for the customers (loading, target, environment).

Nanoemulsions are physical dispersed colloidal nanodroplets prepared by mixing two immiscible liquid phases, generally defined as oil and aqueous phases. The quantitative ratio of the phases, generally in the range 5–20%, determines the characteristics of the nanoemulsions, such as oil dispersed in water (O/W), water dispersed in oil (W/O), and the biocontinuity, where oily and watery microdomains coexist in the liquid system. However, the main drawback of nanoemulsions is the requirement of surfactants and/or co-surfactants in order to stabilize the formulations and get a particle size of about 500 nm [12\*\*,13].

Solid lipid nanoparticles (SLNs) are considered as nano-scale lipid matrices in which lipids are dispersed in aqueous solutions with surfactants using a high energy method (e.g., sonication) (Figure 2A). SLNs are prepared from emulsions composed of lipids with melting points generally higher than body and/or room temperatures. The main advantages of SLNs are the encapsulation of active labile molecules that should be protected from environmental conditions such as photoprotection, moisture, and oxidation. On the other hand, the synthesis of SLNs requires highly purified lipid molecules to crystallize in a perfect lattice; nevertheless, it provides small space for the cargo, limiting loading capacity, and sometimes compatibility within the matrix [14].

Nanostructured lipid carriers (NLCs) are considered the evolution of SLNs in order to avoid problems with loading amount and also load extrusion from the matrix

Figure 1



Strategy for the development of molecular carriers.

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