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# Sustainable Functional Nanofoods: Formulation Opportunities and Application Challenges

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**Abstract:** Nanotechnologies are an emerging scientific field that refers to the science of nanosized materials and structures. They can provide numerous innovative opportunities within the food industry, with applications in areas such as food production, processing, packaging, preservation, agriculture, water treatment, etc. In the food industry, organic or mineral nanoparticles measuring between 1 and 100 nanometers demonstrate significantly improved properties —often enhanced by a factor of ten— compared to conventional materials. Nevertheless, the use of materials at the nanoscale can also present challenges related to potential impacts on human health, the environment and regulatory challenges, akin to those faced by other emerging technologies. The integration of nanofoods requires careful evaluation of the risks associated with new products. Nonetheless, the benefits of food nanotechnology are gaining momentum. Regulations must become more stringent regarding the use of nanomaterials or nanofoods, particularly concerning safety protocols. The modernization of food production still has to face some drawbacks of the new approaches to be implemented for routine production. Scientific research must provide the expected solutions to these limitations for making functional nanofoods more sustainable.

**Keywords:** Nanotechnology, Nutraceutical, Food, Bioactive compound, Nanomaterial, Toxicity, Sustainability

## 1. Introduction

Nanotechnology refers to the science of nanosized materials and structures. By reducing their size to the nanoscale, their properties can be modified and their performances are improved. This technology has been widely applied to pharmaceutical and cosmetic sectors[1]. Currently, it is an emerging technology used in passive and active nanotechnology. Passive nanotechnology exploits the inherent properties of nanoparticles, such as size and shape, to improve the delivery of food ingredients or additives by utilizing physiological conditions that enhance their stability, bioavailability, and targeted accumulation in food matrices. In contrast, active nanotechnology involves modifying nanoparticles with specific functional groups or ligands that interact with food components, enabling more precise delivery of nutrients, preservatives, or flavor enhancers to desired locations within the food system. Research is underway to develop effective nanostructures useful to the food industry as nanoingredients, nanocarriers, etc[2–4].

Nanotechnologies play a valuable role in the food industry; it may offer society and consumers several benefits. It covers almost every aspect of the food industry, from food agriculture, processing, storage, and transportation[5]. Furthermore, nanofood technologies are being applied in a variety of food contexts, primarily as additives[6] and supplements[7].

Nanofood ingredients can be utilized to modify or improve the appearance, color, flavor, sweetness or sourness, aroma, and texture of food. Additionally, these ingredients can help enhance or reduce absorption and serve as preservatives[8].

In order to produce and process healthy, safe, and high-quality foods, a diverse range of nanomaterials is available for use in food nanotechnology, spanning from inorganic nanoparticles (silicon dioxide, zinc oxide, iron oxide, titanium dioxide, silver, and gold), to organic (mostly natural products: carbohydrates, lipids, and proteins) and combined nanomaterials[9].

Nanostructures such as particles, fibers, vesicles, and tubes are of at least one dimension smaller than 100 nanometers. These entities are the basis of nanostructured materials in surface or in volume and serve to encapsulate different components. In food processing, the development and research on nanotechnology are of great importance. It is applied in the design of packaging and also to improve the organoleptic properties of food or contributes to food safety (inhibition of bacterial growth), etc. (Figure 1)[2,4].

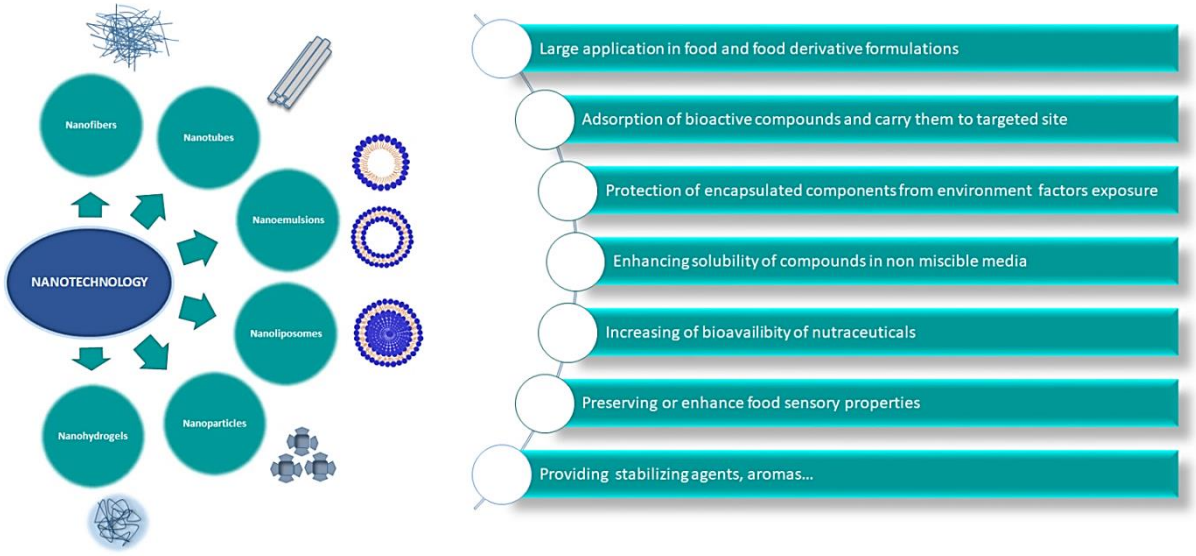


**Figure 1.** Types of nanostructured materials and their main purposes.

Two approaches are adopted when designing nanofoods. The first approach, called the Top-down approach, is based on the use of physical processes. The second approach, known as the bottom-up approach, can be regulated by governing different non-covalent forces and self-assembly[10,11].

The use of nanotechnology has been behind the development of many structures with broad industrial applications. Bioactive molecules are incorporated, adsorbed, or dispersed in these nanostructures[3,12,13]. Nanoencapsulation employs natural or synthetic polymers

assembled in nanostructures to encapsulate a single or several compounds. Nanoencapsulates applied in foods are often composed of eco-friendly materials to overcome some constraints like toxicity, biodegradability, and bioavailability[14].

Ultimately, nanotechnologies can introduce innovative approaches to creating functional foods, enabling the integration of bioactive compounds while preserving the sensory experience for consumers and enhancing the absorption of specific components[5,15,16]. However, the knowledge of nanotechnology's impact on human health remains very limited. Nevertheless, research carried out on animal models indicates worrying risks, suggesting that nanoparticles may pose significant health risks, including oxidative stress and decreased cell viability. These potential adverse effects raise concerns about the long-term safety of nanotechnology in functional foods. More research might provide solutions for making sustainable nanofoods. Indeed, understanding the nanotoxicity mechanisms is crucial to developing personalized healthcare and redesigning nanoparticles with reduced ecotoxicity.

## 2. Nanotechnologies opportunities: approaches for food applications

By reducing their size to the nanoscale, nanomaterials' performances could be improved. Encapsulation of bioactive molecules (biocompounactives), aromas, stabilizing agents, and other compounds occurs within different types of nanostructures. The most encountered methods include nanoliposomes, and nanoemulsions. Other methods, such as nanoparticles and nanotubes, are less frequently used and are applied for specific purposes. Below, we will deal with the different nanostructures developed recently, their applications, and the novelties of the design of new nanostructures for food application.

### *2.1. Nanofood Materials*

#### *2.1.1. Nanoliposomes*

Nanoliposomes are nanostructures made of unilamellar or multilamellar vesicles in a spherical form of amphiphilic lipid molecules forming vesicles that delimit two compartments (Figure 2). The use of nanoliposomes allows for the encapsulation of both hydrophilic (bilayer spheres) and hydrophobic (between two lipid layers of a bilayer sphere or a single-layer sphere) bioactive compounds, enhances their bioavailability and stability and ensures non-toxicity by using natural emulsifiers.

The process of liposome formation in general and nanoliposomes in particular is not spontaneous. It is a complex process that requires specific energy inputs to overcome the inherent stability of lipid bilayers. Applied treatments, such as sonication, hydrostatic

pressure, and incorporation of cholesterol are essential as they provide the necessary energy to manipulate lipid structures, enabling the controlled formation of liposomes and nanoliposomes for various applications, including drug delivery systems. The spatial arrangement resulting from the bending of the molecules depends on the nature of the lipids, the presence of structure-stabilizing agents such as sterols, and the energy applied[17–19].

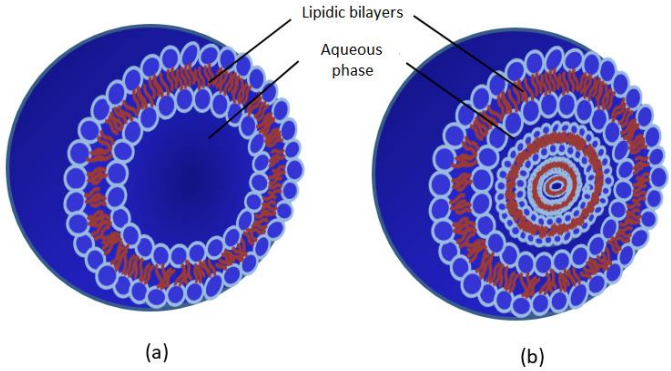


**Figure 2.** Monolamellar (**a**) and multilamellar (**b**) nanoliposomes.

Since their discovery in the early 1960s[18,20], liposomes have attracted great interest in pharmacology as nanovectors of many active ingredients. Today, the industrial application of liposomes has expanded to food where they are used for the encapsulation of many components (Table 1).

Nanoliposomes form colloidal structures, acting as nanocarriers to enhance the bioavailability of bioactive molecules. Numerous lipid nanovesicles have been developed for food application due to their nanosized structure and natural properties (biodegradable and non-toxic). The use of nanoliposomes is constantly increasing and constitutes a unique vector for many molecules in food technology. Indeed, nutrients, nutraceuticals, enzymes, food additives, and food antimicrobials were encapsulated in these lipid-based nanovesicles[17,21].

The use of phospholipids for vesicle formation has been widely reported in the literature. Lipid vesicles formed in aqueous media are bilayer with amphiphilic inner and outer surfaces forming colloidal nanostructures. Natural extracted phospholipids (egg, soy, or milk) are used for nanoliposomes elaboration resulting in safe nanostructures applicable in the food industry. They form a membrane-like structure that contributes to the protection of the encapsulated material from environmental factors such as biochemical and chemical changes due to enzymatic, pH, temperature, and ionic strength variations and consequently enhancing cellular uptake. In addition, nanoliposomes trap strong odors and flavors from certain encapsulated bioactive compounds[21–23].

Recently, the stability of the many products retained in nanoliposomes has been studied. Pigments, peptides, polyphenols, vitamins, and essential oils have been encapsulated in nanoliposomes and undergone a set of tests to verify the performance of the nanoliposomes. The results of these investigations showed high stability, effective retention, and good bioavailability of bioactive compounds in nanoliposomes. These studies support a great interest in liposomal nanoencapsulation in food formulation[21,24,25].

Anthocyanins (ACNs) are natural pigments widely used as food colorants. They are known for their antioxidant, anticancer, and anti-inflammatory properties. Encapsulated anthocyanins demonstrated significant potential for use in the development of nutraceuticals and functional foods[12,26,27]. Anthocyanin-loaded nanoliposomes elaborated by combining ethanol injection methods with ultrasonication improved their *in vitro* stability, bioavailability, and antioxidant activities. Recent studies highlight the importance of biopolymers coating in the stability of nanoliposomes. Some have used two types of biopolymers chitin and pectin to stabilize nanoliposomes based on a layer-by-layer approach[28,29].

Similarly, Neohesperidin and Pelargonidin-3-O-glucoside (P3G) were encapsulated in Pectin-Chitin conjugated nanoliposomes (P-CH-NL). Biopolymer coating acts as a physical barrier ensuring protection and controlling the release of bioactive compounds. P-CH-NL exhibits greater physical stability to salt and pH under oxidative, thermal, and UV conditions[30,31].

In order to develop more stable nanoliposomes, innovative systems based on the use of new phospholipids have been recently developed. Marine phospholipids were tested for vitamin C nanomelusion formulation. The encapsulation efficiency was attempted at 52% and nanoliposomes showed better stability at 4°C for 49 days[32]. This means that out of the total amount of vitamin C that was intended to be encapsulated in the formulation, approximately 52% was successfully incorporated into the nanoliposomes. Moreover, this metric is crucial as it indicates how effectively the nanoliposomes can trap and stabilize vitamin C, which is known to be sensitive to degradation under various conditions.

Varying amounts of marine phospholipids were tested during the formulation process. The study indicated that increasing the phospholipid concentration correlated with enhanced antioxidant activity but did not show a direct relationship with the encapsulation efficiency of vitamin C[32]. Thus, optimizing the phospholipidic rate is essential for balancing both stability and antioxidant properties in the final product.

In another work, nanoliposomes of shrimp oil were created using ultrasonication and microfluidization techniques. The ultrasonication method produced smaller-sized nanoliposomes with higher encapsulation efficiency (93.64%) and enhanced stability. N-3 fatty acids were retained more effectively in nanoliposomes than in unencapsulated oil. The encapsulation in nanoliposomes also concealed the unpleasant fishy smell of shrimp oil. Indeed, ultrasonicated nanoliposomes offered oil stability compared to unencapsulated oil[33,34].

**Table 1.** Recent nanofood materials.

| Nanostructure | Encapsulated component | Main material used | Applied technique | Main performances | References |
|---|---|---|---|---|---|
| **Nanoliposome** | Anthocyanins (ACNs) | Soy lecithin and cholesterol | Ethanol injection + ultrasonication | Encapsulation efficiency over 90%<br>Mean particle size 53.8 nm<br>Nanoliposomal encapsulation enhances stability, antioxidant effect and cellular uptake of ACNs | [28] |
| | Vitamin C | Marine phospholipids | Thin film evaporation method | Encapsulation effciciency up to 52%<br>Antioxidant activity increases with increasing phospholipids rate<br>Vitamin C stable at 4°C for 49 days | [32] |
| | Thymol and carvacrol | Soybean phosphatidylcholine | Thin film hydration | Size 230–270 nm,<br>Acceptable polydispersity (0.24-0.31),<br>Elevated encapsulation efficiencies (~99%)<br>Stable at 4–22 °C, over the duration of 28 days.<br>Antimicrobial activity against Salmonella already adhered to glass. | [35,36] |

| Nanostructure | Encapsulated component | Main material used | Applied technique | Main performances | References |
|---|---|---|---|---|---|
| | Rosemary essential oil<br>Greek Sage essential oil | Phospholipon® 90G (P90G) and cholesterol | Thin film hydration | 65% and 57 % of Rosemary and Greek Sage EOs encapsulation efficiencies, respectively<br>40% of released EO in 1 h and 100% in 3 h<br>Stability for one month at 4 °C<br>High anti-lipid peroxidation activity (80%–100%)<br>A significant inhibition zone for *Klebsiella pneumoniae* comparable to neomycin. | [37,38] |
| | Neohesperidin (NH) | Soybean lecithin and cholesterol | Thin-film hydration method combined with the electrostatic interaction technique | Nanoliposome Surface decorated by pectin and chitosan.<br>NL size < 398 nm with negative zeta potentials<br>Approximately stable at 4°C for 30 days<br>Increasing retention of Neohesperidin to 95.66%<br>No particle charge disturbance in low ionic solution. Slight decrease in a high ionic solution<br>P-CH-NH-NL exhibited a retention rate close to 100% (UV and antioxidant stability)<br>P-CH-NH-NL and CH-NH-NL were comparatively more stable in preserving NH than NH-NL | [29,39] |

| Nanostructure | Encapsulated component | Main material used | Applied technique | Main performances | References |
|---|---|---|---|---|---|
| | Pelargonidin-3-O-glucoside (P3G) | Soybean lecithin and cholesterol | Dried thin film and sonication<br>Nanoliposome coating with chitin and pectin | Stable, small and homogeneous P-CH-NL (0.5 wt% of P)<br>No visible aggregation within a week.<br>Encapsulation efficiency up to 56.7 %<br>P-CH-P3G-NL stable at low pH<br>P3G retention over 97% under UV, oxidative and thermal stress | [31] |
| | Shrimp oil | Lecithin | Ultrasonication and microfluidization methods. | Stable and small size of US nanoliposomes.<br>High efficiency of US nanoliposomes (93.64%)<br>n-3 fatty acids were retained more effectively in nanoliposomes than in unencapsulated oil.<br>Undesirable fishy odor of shrimp oil masked | [34] |
| **Nanoemulsion** | β carotene | Chitosan (CS)-gallic acid (GA) conjugates f β-carotene (BC) nanoemulsion (NE) | Layer-by-layer technique. | Highest antioxidant activity obtained by high molecular weight of chitosan (HCS)-GA conjugate nanoemulsions. | [40] |
| | | Oil in water nanoemulsion based polysaccharide conjugates isolated from Chin brick tea | Ultrasonication | Stable nanoemulsions (d<140nm)<br>Resistance to pH, salt, and heating<br>Enhancing stability and bioavailability of β carotene. | [41] |

| Nanostructure | Encapsulated component | Main material used | Applied technique | Main performances | References |
|---|---|---|---|---|---|
| | | | | Tea polysaccharides reduce the extent of lipid digestion. | |
| | | Peppermint oil nanoemulsions | Stabilized by a combination of casein (CN) and PGFE emulsifiers. | Fine stability of nanoemulsion when ratio PGFE/ CN is <0.5.<br>Relative stability 7 days of storage at 55 °C. | [42,43] |
| | | Nanoemulsion of oil-in-water (O/W) tea polyphenols-β-carotene (TP-BC) | Ultrasonication + high-pressure homogenization | TP-BC nanoemulsion exhibited greater stability and a higher retention rate of BC compared to the BC nanoemulsion. | [44] |
| | Vitamin D3 | Caprylic/capric triglyceride (CCTG), Kolliphor®HS15 | W/O inversion phase | Excellent encapsulation efficiency<br>NE-20 nanoemulsion, created using 30% (v/v) Kolliphor, 20% (v/v) CCTG, and 50% (v/v) water, achieved a higher zeta potential, smaller particle size, and enhanced emulsion stability and release. | [45] |
| | Cinnamon essential oil (CEO) | Medium chain triglycerides (MCT) and Octenyl succinic anhydride (OSA)-modified starch as emulsifier | High pressure homogenization | Incorporation of MCT significantly enhace nanoemulsion stability.<br>Various bacterial strains growth is inhibited by CEO nanoemulsions (Gram-bacteria were more sensitive). | [46] |
| | Clove, cinnamon and lavender EOs | Soybean oil (25%) and EO (75%) (individuals or mixture) | High pressure homogenization | Stability of nanoemulsion enhanced by reducing emulsion size.<br>Inhibition of *E. coli* growth up to 98% . | [47] |

| Nanostructure | Encapsulated component | Main material used | Applied technique | Main performances | References |
|---|---|---|---|---|---|
| | Curcumin based nanoemulsion | MCT and Quillaja saponin/ whey protein isolate | Microfluidization | Nanoemulsions mixed with commercialized salad dressing.<br>Nanoemulsions stability is pH depending.<br>Droplet size is stable after 7 days storage. | [48] |
| | Thyme oil | Thyme oil -based nanoemulsion stabilized by polyvinylpyrrolidone (PVP) coated with chitosan. | Sonication technique | Nanoemulsion with diameter in the range of 13 to 28 nm and Zeta potential of -48 mV.<br>Gamma irradiation stabilized Thyme oil-PVP-chitosan nanoemulsion (18 months).<br>PVP induced fine droplets formation.<br>Inhibition of *C. Albicans* and *S. aureus* enhanced by gamma irradtion treated nanoemulsion. | [49] |
| **Nanoparticles/ nanocomplexes** | Curcumin (CUR) | Lysozyme/κ-carrageenan (Lys-CRG) complex nanoparticles | Freeze drying of CUR-LYS-CRG complexe formed | Encapsulation efficiency over 96%<br>Curcumin-loaded nanoparticles are stable with high antioxidant activities.<br>The LYS-CRG complex protects curcumin from digestion process. | [50,51] |
| | Vitamin D3 | Ovalbumin-pectin nanocomplexes | Freeze drying of OVA-PEC-VD3 complexe formed | Encapsulation efficiency of 96.37%<br>OVA-PEC-VD3 complexe of 250 nm<br>Storage stability improved.<br>Vitamin D3 release closer to Fick release. | [52,53] |

| Nanostructure | Encapsulated component | Main material used | Applied technique | Main performances | References |
|---|---|---|---|---|---|
| | Curcumin | Core-shell biopolymer (sodium caseinate/sodium alginate modified zein nanoparticles) | Freeze drying of complex formed | Increasing encapsulation efficiency up to 92% with increasing ratio Alginate/NaCas (A-C).<br>Smaller size, thermal and pH stability exhibited by the nanocomplex A-C5:5.<br>Alginate prolonged curcumin release.<br>Improved stability and bioavailability compared to free polyphenols. | [54,55] |
| **Nanohydrogels** | Lactoferrin | Glycomacropeptide based nanohydrogel | Thermal gelation and freez drying/nanospray dryng | Freeze-dried nanohydrogel samples demonstrated greater resistance to thermal degradation and were completely rehydrated without any agglomerates, in contrast to spray-dried nanohydrogels. | [56,57] |
| | Atrazine | Chitincl-<br>poly (acrylamide-co-itaconic acid) nanohydrogel | Microwave method | Maximum adsorption equal to 204.08 mg/g.<br>pH 14 favorable for maximum (42 %) atrazine adsorption. | [58] |
| | Thiophanate methyl | Guar gum-cross linked-Soya lecithin nanohydrogel sheets (NHS) | Microwave method | Spontaneous adsorpyion process<br>Maximum NHS fungicide capacity of 59.205 mg/g.<br>pH 6.8 generalizes the positive surface of the absorbent.<br>73% remained adsoprtion during the sixth cycle. | [59,60] |
| | Pimaricin | poly(N-isopropylacrylamide) | Nanohydrogel powder swelled<br>in distilled water and mixed with | Antifungal protective effects of the pimaricin-loaded nanohydrogel coating in Arzúa-Ulloa DOP cheeses. | [61,62] |

| Nanostructure | Encapsulated component | Main material used | Applied technique | Main performances | References |
|---|---|---|---|---|---|
| | | nanohydrogels copolymerized with acrylic acid (PNIPA-20AA(5)) | an aqueous solution of commercial pimaricin overnight at 25°C. | Nanohydrogels prevent cheese weight loss after long storage yellow surface coloration changes. | |
| **Others** | β-carotene | Whey protein isolate fibrils (WPIF) | Self-assembled at low pH and different heating times at 85°C.<br>Freeze drying | Encapsulation efficiency ranged from 76.55% to 92.11%.<br>β-carotene addition gave highly ordered WPIF secondary structure.<br>WPIF had better colloidal stability. | [63,64] |
| | Natamycin (Nata) | Gelatin-based nancomposite film functionalized with zein/casein nanoparticles (Z/C NPs) | Nata-Z/C NPs synthesized using pH co-precipitation method.<br>Film formed by mixing gelatin and NPs prepared, then oven dried. | Nata-Z/C NPs evenly distributed throughout the gelatin film.<br>Strong antifungal activity of nanocomposite film against *A. niger*, *B. cinerea* and *P. citrinum*. | [65] |

### *2.1.2. Nanoemulsions*

Nanoemulsion process is based on the principle of emulsification in a nanosized scaling. This change of scale would be behind the expansion of its application including the pharmaceutical, cosmetic, food and chemical industries. This process is characterized by the fineness of the droplets formed. The diameter is a few tens or hundreds of nanometers in diameter (50 to 500 nm). These nanostructures can greatly improve the performance of these formulations. It is also possible to carry molecules that are not soluble in water, by incorporating them into nanoemulsions[66].

With nanoemulsions, the reduction of the droplet size increases the efficiency of the treatment by a better diffusion and dispersion of the compounds. Moreover, this size reduction improves the stability — in the kinetic sense of the term — of the emulsion, thus

limiting the use of stabilizing agents. So, the formation of nanoemulsions must be controlled to take advantage of their assets. Several emulsification techniques have been studied to optimize the performance of nanoemulsions[67].

The production of submicron emulsions of oil-in-water can be obtained spontaneously or ensured by different processes including high pressure homogenization, ultrasonication or microfluidization. In the process of spontaneous emulsification, the organic phase, which is mixed with water, transitions into a stable emulsion within the aqueous phase. This means that the components of the organic phase become dispersed throughout the water, resulting in the formation of an emulsion[67,68].

In High-Pressure Homogenization, oil and aqueous phase mixture is subjected to intense turbulence and hydraulic shear by passing under high pressure (500 to 5000 psi) through a small inlet port producing extremely fine emulsion particles. This process produces very low particle-size nanoemulsions (up to 1nm). Several parameters affect the emulsion size, including the homogenization pressures, oil/water ratio, and product content. While in microfluidization the product passes through the microchannels of a microfluidizer, under high pressure (500 to 20000 psi), producing very fine particles of the submicron range[69].

Ultrasonication produces extremely small droplets by utilizing an ultrasonic probe, which generates high-frequency sound waves. These sound waves create intense shear forces that break down larger oil droplets into much finer sizes, resulting in a stable nanoemulsion[70]. Nanoemulsions occupy a prominent place in food applications. It's a common colloidal system used for encapsulation of biocompounactives[3,71].

β-Carotene serves multiple functions, acting as both a food coloring agent and a bioactive ingredient in foods. However, its sensitivity to temperature, UV, and pH causes the loss of its biological activity. Therefore, it is necessary to develop a new delivery system[72], ensuring stable encapsulation of β-carotene[13,73]. Recently biopolymers were used for nanoemulsion stabilization. The highest antioxidant activity was observed when β-carotene was encapsulated in nanoemulsions stabilized by high molecular weight chitosan (HCS) conjugated with glutaraldehyde (GA)[40].

In the same context, β-carotene was encapsulated in nanoemulsion stabilized by polysaccharide conjugates isolated from Chin brick tea. Nanoemulsions obtained were resistant to pH, salt, and heating. In addition, natural polysaccharides enhance the stability and bioavailability of β-carotene. Tea polysaccharides coating limits considerably lipid digestion compared to whey protein isolate coating[41].

Hujun Xie and co-workers (2021) have been able to also encapsulate β carotene using peppermint oil nanoemulsions. Nanostructures were stabilized by casein. The nanoemulsions exhibited a relative stability of seven days during storage at 35°C[43]. It has been recently shown that tea polyphenols, when used in the aqueous phase for preparing nanoemulsions, contribute to the improved oral bioavailability of β-carotene. The antioxidant properties of polyphenols protect β-carotene from decomposition caused by chemical and light oxidation. According to Zeta potential measurements, tea polyphenol-β-carotene nanoemulsions are more stable than β-carotene nanoemulsions alone[44].

Nutrient stability poses a significant challenge for the food industry, particularly during the fortification of foods and beverages with Vitamin D. One example of addressing this issue is by developing vitamin D3 water-in-oil (W/O) nanoemulsions using varying proportions of caprylic/capric triglyceride (CCTG), Kolliphor® HS15, and water. Vitamin D3 (cholecalciferol) nanoemulsions were tested under various storage conditions. The formulation containing 30% (v/v) Kolliphor, 20% (v/v) CCTG, and 50% (v/v) water demonstrated high encapsulation efficiency and enhanced stability. The effectiveness of these nanoemulsions was demonstrated through sensory evaluations in fortified buttermilk, indicating that this method effectively protects nutrients, particularly vitamin D3[45].

Other studies have explored nanoemulsions containing essential oils, which protect biocompounactives during digestion. Cinnamon essential oil nanoemulsions were produced using high-pressure homogenization, with stability enhanced by the incorporation of medium-chain triglycerides. The size of these nanoemulsions is influenced by homogenization pressure, oil phase ratio, and the amount of modified starch used. Additionally, the antimicrobial effects of cinnamon essential oil were amplified by increasing its water solubility, thereby enhancing interactions with microbial cell membranes[70].

The instability of anthocyanins presents a challenge in the food industry. This issue is addressed by encapsulating fruit concentrate from the underutilized plant *Carissa spinarum* (CS) with polyphenols in nanoemulsions (CSNE) using ultrasonication. The CSNE demonstrated significant anti-quorum sensing (QS) activity against *Chromobacterium violaceum* (73.7%) and inhibited biofilm formation by 70.1% in *Pseudomonas aeruginosa* and 64.4% in *Yersinia enterocolitica*[74,75].

Not long ago, food industries have expressed significant interest in developing various types of nanoemulsions. Essential oil-based nanoemulsions have been created to reduce virulence and biofilm formation, which pose considerable economic and health challenges[46,47]. These innovations represent a promising advancement in applications within the food industry.

A natural antioxidant emulsifier, tea polysaccharide conjugate (TPC), was extracted from Chin brick tea and utilized to create β-carotene nanoemulsions. TPC demonstrated strong antioxidant properties, enabling the formation of stable nanoemulsions with a particle size of less than 140 nm. The β-carotene maintains its chemical stability more effectively in nanoemulsions that utilize TPC as an ingredient compared to those formulated with Tween 80 or Whey Protein Isolate (WPI). This increased stability is attributed to the high antioxidant activity of TPC. Antioxidants help protect β-carotene from degradation caused by factors such as light, heat, and oxygen. In contrast, Tween 80 and WPI do not provide the same level of antioxidant protection, which can lead to a greater loss of β-carotene stability in their formulations. Thus, TPC derived from Chin brick tea can function as a dual-purpose ingredient in emulsified foods, providing both antioxidant protection for β-carotene and enhancing the overall nutritional profile of the product[44].

*2.1.3. Nanohydrogels*

Hydrogels are networking structures characterized by their ability to absorb water (more than 90% of their weight). This property is defined as a three-dimensional macromolecular network with high hydrophilicity ensured by hydrophilic functional groups such as OH, COOH, and $CONH_2$. The behavior of the hydrogel is influenced by environmental factors, including temperature, pH, and ionic strength[76]. Thus, hydrogels can swell or deflate according to the variations of the surrounding environment.

Producing nanohydrogels shows a real potential for application in food. Proteins and polysaccharides and their derivatives are the main materials used for these purposes[77]. These natural polymers are able to form gel network with two opposite structures; well-ordered filamentous or randomly branched aggregates[78,79].

Food industry faces many problems related to food safety. Microbial contamination is a serious problem for fresh and non-thermally treated foods like cheeses. Industrials used food preservatives to limit microbial growth. Thus, pimaricin is a fungicide widely used in the cheese industry. Its low solubility and stability loss under acidic conditions limit its application in cheese coating. Ficinos team proposed a pimaricin-loaded PNIPA- 20AA(5) nanohydrogels as a smart and active cheese coating. Artificially fungal contaminated cheeses were coated with pimaricin-loaded PNIPA-20AA(5) nanohydrogel. The contamination rate was lower compared to other treatments. The smart nanohydrogel coating enables the controlled release of pimaricin into the cheese while preserving the natural ripening process of the cheeses[61,62].

Developing new nanohydrogel-based coatings encounters many problems because of their sensitivity to environmental conditions. In this perspective, Bourbon *et al*. (2020),

evaluated the effect of drying methods on nanohydrogels stability. Samples were submitted for spray drying and freeze drying. This research highlights the influence of drying process in physical chemical properties of protein networking abilities. Compared to spray-dried nanohydrogels, freeze-dried nanohydrogels were more resistant to thermal degradation and fully rehydrated with no agglomerates observed during rehydration. These findings will guide the choice for future industrial applications[57].

Other nanohydrogels were developed for other purposes including water and food pollutants retention. Chitin-cl-poly(acrylamide-co-itaconic acid) nanohydrogel was synthesized using a microwave technique and evaluated for its effectiveness in removing atrazine, a commonly used herbicide. Additionally, guar gum-crosslinked soya lecithin nanohydrogel sheets were employed to effectively eliminate the fungicide thiophanate methyl from aqueous solutions. Both studies utilized natural materials recognized for their non-toxic properties, bioavailability, and physicochemical stability, attributed to their functional groups, which contributed to their high efficiency in removing pollutants such as fungicides and pesticides[58–60,80].

*2.1.4. Nanoparticles, nanocomposites and others*

Recent studies highlight the importance of nanoparticles, nanocomposites and nanofibrils as nanocarriers for nutraceuticals[81]. Lysozyme/κ-carrageenan complex nanoparticles were performed and used to encapsulate curcumin[50]. The protective role of LYS-CRG-NPs on CUR is confirmed through the assessment of CUR's antioxidant activity and thermal stability. The CUR-LYS-CRG complex nanoparticles exhibited a rapid release of CUR, achieving 62.56% within the first 1.5 hours. Following this initial phase, CUR release remained consistent from 1.5 and 3 hours, ultimately reaching a total release rate of 67.23% after digestion[82,83].

Utilizing complexes created from protein-polysaccharide combinations to regulate the release and safeguard active compounds has emerged as a viable approach in the food industry [54]. For example, ovalbumin-pectin nanocomplex was successfully used for vitamin D3 encapsulation. It showed a good sustained-release effect[53].

A blend of alginate and caseinate was employed to alter the structure of zein nanoparticles. By encapsulating curcumin within these biopolymer nanoparticles, its antioxidant activity was enhanced, and its release was prolonged under conditions simulating the gastrointestinal tract[54,84].

As heating time increased, whey protein isolate (WPI) underwent hydrolysis into polypeptides, which then self-assembled into fibrils. Chao Zhang and colleagues (2021)

explored the use of WPI fibrils for the stable encapsulation of β-carotene (BC). The binding of WPI to BC resulted in an increase in α-helix and β-sheet content, indicating a highly ordered structure. The WPI fibrils, characterized by a high aspect ratio and random orientation, effectively facilitated the encapsulation of BC[63,64].

Other protein models combined with nanomaterials were developed in order to improve their physicochemical and antifungal properties. In fact, Natamycin-loaded zein/casein nanoparticles were effectively integrated into gelatin films. The zein/casein colloidal nanoparticles demonstrated stability and enhanced the dispersibility of natamycin. Additionally, the gelatin films containing these natamycin-loaded Z/C nanoparticles exhibited improved in vitro antifungal activity against three common fungi: *Aspergillus niger*, *Botrytis cinerea*, and *Penicillium citrinum*. Consequently, these gelatin-based nanocomposite films show great promise for use as antifungal edible films in food packaging applications[65,85].

### *2.2. Nanotechnologies for Functional Foods*

Nanotechnology has emerged as a highly promising technology poised to transform the food industry. The application of nanotechnology in processing and packaging has demonstrated its effectiveness within food systems[86,87]. There are two types of applications depending on whether these substances are in or in contact with processed foods.

#### *2.2.1. Food nanomaterials as additives*

Intentional additions to food products are substances deliberately included to enhance qualities such as texture, appearance, and nutritional value. Examples include texturing agents like anti-caking additives, which improve the flow of food powders such as freeze-dried soups and powdered sugar; pigments that enhance the visual appeal of food; and innovative additives designed to enrich products with bioactive substances that offer additional health benefits[88]. The purpose of those applications is to incorporate lipophilic or hydrophobic substances directly into food products (liquid or solid), without any additional step in the production chain and, in the current state of knowledge, without consequences on the organoleptic qualities and nutritional value of the finished product.

They involve, for example, the encapsulation in nanomicelles of phospholipids of preservatives (antioxidants such as coenzyme Q10) or substances with “health” claims such as Omega3 fatty acids, phytosterols, beta-carotene, isoflavones and vitamins. A wide range of nutrients, bioactive compounds, and phytochemicals can be encapsulated in biocompatible and biodegradable nanoparticles, enhancing their stability, aqueous solubility, bioavailability, and circulation time within the body[89–91].

As there is a growing awareness of the importance of eating nutritious foods, biomolecules such as carbohydrates, proteins, fats, vitamins and fiber are increasingly incorporated into products such as ice cream, chocolate and soft drinks. Nano-emulsions are used to create ice creams that retain the fatty texture while having a lower fat content. All this is often accompanied by additional flavors, colorings and nutrients with cost-effective components and processing[67, 92]. Certain biomolecules, like vitamins, are delivered to the human body in a more efficient form by encapsulating carotenoids in nanoparticles and mixing them with cold water[93].

The market for food supplements, functional foods (Nutraceuticals) or drugs is very greedy for these nanotechnologies. Functional foods can be classified into 5 major families[94–96]:

- Natural foods: containing naturally healthy compounds, such as fruits and vegetables.
- Modified foods: products from which a harmful substance has been eliminated, reduced, or substituted with a component that offers beneficial effects.
- Fortified Foods with additional nutrients (juices enriched with vitamins).
- Enriched product: A food to which nutrients or compounds which do not normally contain them have been added, such as margarines with added probiotics.
- Improved products refer to items in which the concentration of a particular component has been increased. This enhancement can be achieved either through an optimized feed composition — meaning that the ingredients provided to the animals or plants have been carefully selected and balanced for better nutrient absorption — or through specific breeding conditions that promote higher yields or enhanced qualities in the final product. By modifying the diet of chickens, for example, we obtain eggs enriched in omega-3.

*2.2.2. Food contact materials*

The coating with nanosilver on the walls of freezers and refrigerators also falls into the category of Multiple-criteria decision analysis (MCDA). The technological advantage lies in the use of a surface biocide that can inhibit the growth of bacteria, fungi, and viruses within these food preservation chambers[23,97].

For food packaging, the desire to ultimately ban the use of plastics of petrochemical origin has paved the way for the development of so-called "bio-based" (from renewable

sources) and biodegradable materials[98]. If the advantage is certain for reasons of respect for the environment and waste management, the current weakness of these new materials is based on the loss of "barrier properties", those aimed at protecting the food from any degradation and contamination. Nanoparticles integrated into these novel materials (nano-composites) enhance the original functions of packaging, such as protecting and preserving food, and improve its conservation[23,88,97].

Nano-composite materials enhance resistance (e.g., carbon nanotubes in light and rigid bottles), tightness (against UV, water, and gas), and tortuosity (e.g., montmorillonite nanolamellae in the material's thickness, limiting oxygen passage to food). Additionally, incorporating nanosilver or TiO2 (for photocatalysis) into packaging imparts biocidal properties, protecting packaged food from bacterial contamination (suitable for "freshness" sachets and trays)[88].

This approach is similarly applied in "smart" labeling, which involves nano-sensors in contact with food (at least in the headspace) designed to provide information about the preservation status of food items. These sensors can detect microbial contamination, spoilage, or aromas indicative of the ripeness of the packaged product. These technologies primarily utilize nanoparticles that undergo color changes due to oxidation, such as inks that detect oxygen and contain light-sensitive TiO2 nanoparticles[99,100]. Nanotechnology enables the miniaturization of these processes, allowing them to be integrated into conventional labels or applied directly to packaging.

## 3. Challenges for Sustainable Functional Nanofoods

The use of nanomaterials in the food industry and agriculture has seen significant growth, offering potential benefits to consumers. However, food nanotechnology is confronted with significant challenges related to human health, environmental concerns, and safety issues. Due to their unique physicochemical properties and high reactivity, nanoparticles can affect essential cellular processes. This interference may result in one or more toxicity outcomes, potentially disrupting these critical functions[101,102].

Nanotoxicology is a rapidly evolving field within toxicology that focuses on evaluating the toxicological characteristics of nanoparticles to determine their potential impact on environmental and consumer health[103–105].

### *3.1. Nanofoods Health Implications*

Nanoparticles provide a large number of different properties, and the risks they present will vary as a consequence. While some types of nanoparticles may pose minimal

risks to human health, others could be significantly more hazardous. Nanoparticles can have serious consequences for health when they accumulate in high concentrations in tissues, subsequently leading to tissue malfunction or damage[106,107].

The ongoing discussion regarding the safe implementation of nanotechnologies in the food industry has primarily centered on uncertainties and insufficient toxicological data[108,109]. Nanoparticles can enter the human body through various pathways, including skin exposure, inhalation, and ingestion, which allows them to migrate between organs and potentially cause internal damage[3,101,110].

The evaluation of the toxicity of chemicals is currently based on the performance of standardized tests in animals for systemic or local manifestations following acute or repeated administration of increasing doses. For food additives, tested according to these protocols, manifestations of toxicity were only detected at very high doses. These substances, like amorphous silica SiO2 (E551), are therefore considered to be generally recognized as safe (GRAS)[111].

The issue concerns "health" targets that are not yet fully studied, such as the intestinal microbiota and the immune system associated with the intestine[112–114], then in the progressive accumulation of (nano-)insoluble particles in systemic organs (liver, spleen, gonads, etc.) as well as the fetus[115–117].

The development of sequencing methods has made it possible to realize that the intestinal flora represents an essential organ for many physiological functions. Disturbances in the balance of the microbiota and its functions in the intestine (dysbiosis) are not only associated with digestive pathologies, but also respiratory, neurological, cardiovascular, or metabolic pathologies[118]. While chemicals in food, including emulsifiers and sweeteners, can disrupt the gut microbiota, the potential impact of food nanoparticles on the gut microbiota continues to be uncertain[119–122].

Studies demonstrated a potential link between elevated dietary intake of nanoparticles and the occurrence of certain diseases[123]. They demonstrated a correlation between the level of inhaled NPs and an alteration in heart rate and arterial diameter[124–127]. Another study in human volunteers with asthma who inhaled carbon nanotubes indicates increased inflammation of the pulmonary epithelium, pulmonary vasoconstriction, and the onset of bronchial hyperactivity, as well as a drop in leukocyte levels[128].

Researchers have noticed that the toxicological response was connected to "dose by mass", i.e. the higher the dose that experimental animals are exposed to, the more serious the side-effects have been reported. Nevertheless, the toxicity of nanoparticles is not only mass-

dependent but might also be dependent on their specific physicochemical properties[129]. Once the nanoparticles reach the circulation; they can interact with components of blood such as plasma proteins, cells, and homeostasis factors. Toxicological data indicates that interactions of nanoparticles with plasma proteins may decrease their toxicity[130].

Intrinsic properties of nanoparticles influence their biological interaction. So, it is important to assess these properties to determine the toxic potential of nanomaterials[131]. The size of nanoparticles, ranging from 1 to 100 nm, is comparable to that of protein globules (2–10 nm), the diameter of a DNA double helix (2 nm), and the thickness of cell membranes (approximately 10 nm). This similarity in scale enables nanoparticles to easily penetrate cells and their organelles and effectively engage with the negatively charged sugar-phosphate backbone of DNA, thereby inhibiting transcription[132–134]. For instance, metallic nickel nanoparticles may demonstrate an increased carcinogenic potential, indicating that precautionary measures should be implemented when using nickel nanoparticles or their compounds in nanomedicine[135].

Although nanoparticles are often distinguished by their unique characteristics compared to conventional particles, shape, and morphology are also critical factors to consider when evaluating their toxicity. The impact of other factors, like chemical composition and crystal structure, should not be ignored[3,136]. In comparison with conventional chemicals, the kinetics of nanoparticles might be different. However, there is a need for further investigation into nanoparticles absorption and distribution in comparison to the conventional counterparts[137].

The distribution of nanoparticles can be influenced by their unique physicochemical properties, including size, shape, aggregation state, and surface chemistry, making it challenging to predict their biological behavior. Primarily, nanoparticles are cleared from circulation by Kupffer cells in the liver and macrophages in the spleen[3,138].

Once nanoparticles enter the bloodstream, they can interact with biological components like proteins and cells, leading to their distribution across various organs and tissues. Within these locations, nanoparticles may remain unchanged or undergo modification or metabolism, particularly in the liver. The resulting metabolites are then excreted through the kidneys in urine or via the liver in bile. This cellular ability to metabolize and eliminate nanoparticles helps to mitigate their potential toxicity[139,140].

Nanoparticles can be excreted through various routes, including sweat, seminal fluids, mammary glands, saliva, and exhaled breath. However, the primary routes of elimination are via urine (kidneys) and feces (biliary duct). Due to their resistance to phagocytic uptake,

nanoparticles can persist within cells of an organ for extended periods before moving to other organs or being eliminated[130,138]. In some circumstances, when nanoparticles deposit in kidneys and cannot be filtered by the glomerulus, they often lead to serious nephrotoxicity. Likewise, nanoparticles can deposit in the liver and some cases, trigger hepatotoxicity[40,130,141,142].

Scientific research has shown that many types of nanoparticles can be toxic to cultures of human cells and tissues, causing increased oxidative stress, production of inflammatory cytokines, DNA mutations, and even cell death[3,143]. However, for obvious reasons, studies on humans are scarce. The knowledge of nanotechnology's impact on human health remains very limited. Nevertheless, research carried out on animal models indicates worrying risks.

### *3.1.1. Mechanisms of nanotoxicity*

Nanoparticles penetrate the human body mainly through ingestion (Gastrointestinal assimilation), inhalation (from the nose downwards to the respiratory bronchioles) or dermal contact (skin) and, directly in systemic circulation via intraperitoneal (i.p.) or intravenous (i.v.) injection[136] (Figure 3). Penetrated nanoparticles may trigger a variety of potentially adverse effects because of various physicochemical and physiological mechanisms, depending on their intrinsic properties, such as size, shape, surface area, surface charge, crystal structure, coating, and solubility; in addition to some environmental factors, like temperature, pH, ionic strength, salinity, and organic matter[144].

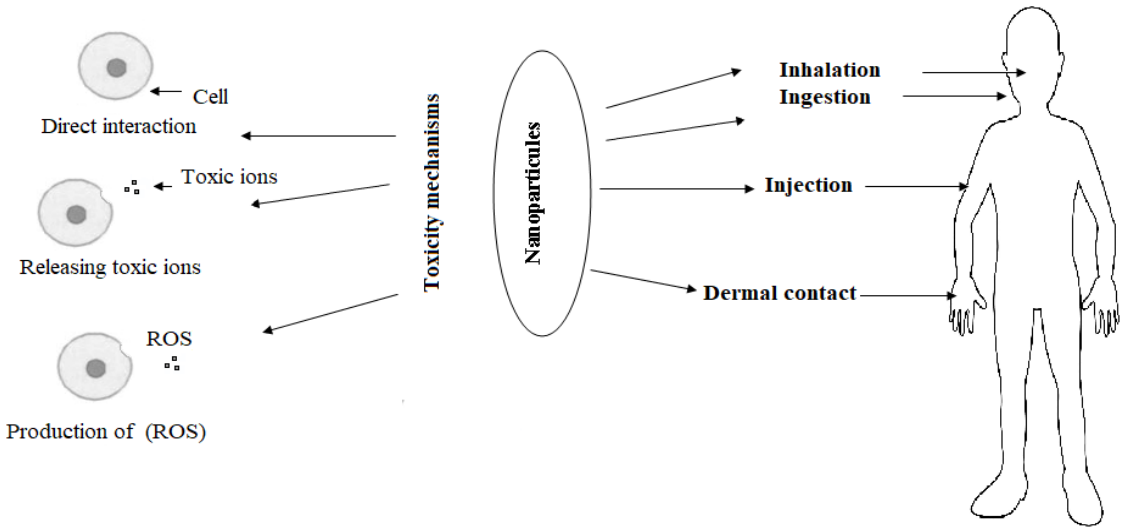


**Figure 3.** Administration routes of nanoparticles into the human body and their main mechanisms of toxicity.

Understanding the toxicity mechanisms of nanoparticles is crucial not only to avoid nanoparticle intoxication but also to develop personalized healthcare[138] and to redesign

nanoparticles with reduced ecotoxicity and environmental impact[145]. Some important toxicity mechanisms of nanoparticles involve[131,146–149]:

1) Direct interaction with cell membranes: Nanoparticles can associate directly with the cell surface, potentially damaging the membrane or triggering internal signaling pathways that lead to cellular damage and death.

2) Dissolution and release of toxic ions: Nanoparticles may dissolve, releasing toxic ions that can impair essential enzyme functions or directly interact with cellular DNA, causing further harm to the organism.

3) Generation of reactive oxygen species (ROS): Nanoparticles can produce ROS and other free radicals, leading to oxidative stress. This oxidative stress can damage cellular components, including lipids, proteins, and DNA, ultimately contributing to various health issues such as cancer, renal disease, neurodegeneration, and cardiovascular or pulmonary diseases.

### *3.1.2. Essential nanotoxicity challenges*

The small size of nanoparticles increased their ability to reach different systems of the human body by crossing capillaries and membrane barriers, including the blood-brain barrier, which normally protects the brain from toxins in the bloodstream, the skin, the lungs, the intestines, and the placental barrier. These nanomaterials interact with different macromolecules and alter their structure. As a result, nanoparticles are transported through the bloodstream and lymphatic system to various organs and tissues, particularly the brain, heart, liver, kidneys, spleen, bone marrow, and nervous system[132]. The toxicity of nanoparticles is influenced by factors such as the dose, concentration, duration of exposure, and their abundance and persistence within tissues[139,150].

#### *3.1.2.1. Neurotoxicity*

Nanoparticles can access the brain by crossing the blood-brain barrier, and several pathological conditions, such as hypertension and allergic encephalomyelitis, have been directly associated with increased permeability of the blood-brain barrier to nanoparticles in experimental studies[151–153].

As previously noted, nanoparticles have the potential to induce oxidative stress in human cells. They can penetrate cellular membranes and travel to various organs, which may result in inflammation of the gastrointestinal tract and contribute to the development of neurodegenerative diseases, including Parkinson's and Alzheimer's. Additionally, these

particles can cause DNA damage. Long-term exposure to nanoparticles has been associated with adverse effects on the kidneys, liver, and other essential organs[80,151].

The typical neurotoxic mechanisms associated with nanoparticles include the excessive generation of reactive oxygen species (ROS), which results in oxidative stress. This can trigger the release of cytokines, leading to neuroinflammation and disturbances in apoptosis that ultimately result in neuronal death. The effects of neurotoxicity may be either reversible or irreversible, impacting specific areas of the central nervous system or affecting the entire system[154,155].

*3.1.2.2. Reprotoxicity and embryotoxicity*

Nanoparticles can cross placental barriers and reach the fetus, potentially resulting in embryotoxicity. This process can trigger a cascade of events, including damage to the placental barriers, increased production of reactive oxygen species (ROS), inflammation, and altered gene expression (Figure 4), all of which may contribute to delayed or abnormal fetal development[156].

Since the fetus in the uterus lacks adequate defense mechanisms and is vulnerable to toxins, the buildup of nanoparticles can effortlessly cause fetal malformations[157–159]. Also, nanoparticles are related to various disorders in animals, including hepatotoxicity, pulmonary injury, immunotoxicity, neurotoxicity, renal toxicity, and reproductive toxicity (irreversible testis damage)[160–163].

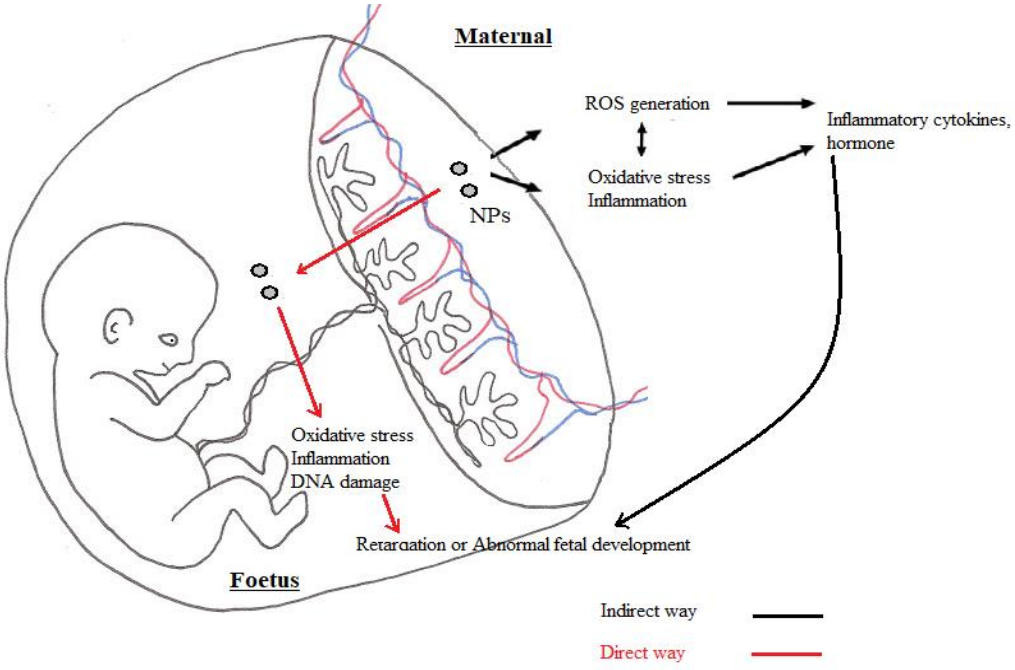


**Figure 4.** The main pathways of fetal toxicity caused by nanoparticles.

*3.1.2.3. Nanogenotoxicity and mutagenicity*

The genotoxic effects of nanoparticles are typically closely associated with oxidative damage to DNA and proteins, which stems from oxidative stress due to the overproduction of reactive oxygen species (ROS) and reactive nitrogen species (RNS). This oxidative stress, induced by nanoparticles, is considered one of the most well-established and recognized mechanisms underlying their potential toxic activity[164].

The mechanisms of ROS and RNS production mediated by nanoparticles could be grouped into three groups: intrinsic production, production by interaction with cellular targets, and production mediated by the inflammatory response. Nanogenotoxicity is classified into three groups[164–167]:

- Direct DNA Damage: This group involves nanoparticles causing direct harm to DNA structures, leading to mutations or other genetic alterations.
- Oxidative Stress-Induced Damage: Nanoparticles can induce oxidative stress, resulting in the overproduction of reactive oxygen species (ROS) that damage DNA and proteins.
- Inflammatory Responses: This category encompasses the inflammatory responses triggered by nanoparticles, which can lead to changes in gene expression and contribute to genotoxic effects.

*3.1.2.4. Immunotoxicity and allergenicity*

Nanoparticles exhibit a wide range of physicochemical properties that enable them to interact with various immune cells, including macrophages, monocytes, dendritic cells, and lymphocytes. These interactions can lead to nonspecific inflammatory responses characterized by the overproduction of reactive oxygen species (ROS) and the release of pro-inflammatory cytokines. Consequently, the engagement between nanoparticles and the immune system has the potential to trigger immunosuppression, hypersensitivity, immunogenicity, and autoimmunity, affecting both innate and adaptive immune responses[168].

Nanoparticles have the ability to penetrate various systems within the human body by crossing membrane barriers. So they can behave like foreign materials that could worsen various pathologies, such as chronic obstructive pulmonary disease (COPD) and asthma. When inhaled into the lungs, nanoparticles can trigger inflammation and the formation of granulomas[169,170].

The immunotoxicity of nanoparticles is extensive and can manifest in various ways, ranging from acute inflammation to lung, liver, and systemic damage, depending on their physicochemical properties such as composition, structure, and route of administration. When administered intravenously, nanoparticles interact with blood cells and proteins, potentially leading to adverse effects[168,171–173].

### *3.2. Impact on Environment and Ecology*

As nanotechnology continues to expand into large-scale applications within the food industry, it is anticipated that nanostructured materials and their by-products will inevitably enter the environment, posing significant risks. This situation has raised serious concerns regarding environmental safety and public health[80,174–176]. There are many environmental effects and risks associated with nanotechnology applications which can be summarized in Figure 5.

Assessing the environmental risks associated with nanomaterials is complex due to their diverse properties and behaviors. Factors such as size, shape, and charge significantly influence their kinetic (absorption, distribution, metabolism, and excretion) and toxicological characteristics. Consequently, even nanomaterials with identical chemical compositions can exhibit vastly different toxicities based on variations in size or shape. Thus, relying solely on particle size is insufficient for distinguishing between more or less hazardous materials and technologies[177–179].

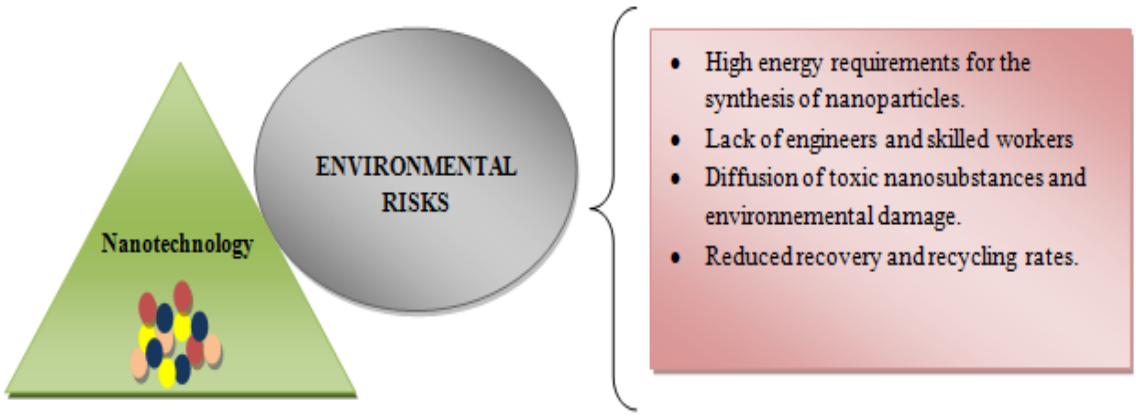


**Figure 5.** The potential environmental damage linked to nanotechnology.

Nanomaterials pose risks related to their handling and potential release into the environment, including water, air, and soil. These risks can evolve throughout the life cycle of the products containing them, necessitating careful consideration to safeguard biodiversity, public health, and the well-being of workers involved in their production or

use[180]. To mitigate the risks associated with nanomaterials, it is essential to implement comprehensive strategies that include thorough risk assessments to identify hazards and exposure routes, engineering controls such as fume hoods and local exhaust ventilation, and the use of appropriate personal protective equipment (PPE) for workers. Additionally, providing training on safe handling practices, establishing protocols for regular monitoring of exposure levels, and advocating for regulatory frameworks that address the lifecycle impacts of nanomaterials can significantly enhance safety and protect public health and the environment.

### *3.3. Regulatory Challenges of Nanofoods*

Many categories of products/ingredients are subject to a regulatory framework, requiring prior authorization subject to a risk assessment through the expertise of an industrial file. However, it is not possible to identify the marketed products relating to nanotechnologies from notifications or authorizations existing in the current state of all regulations in the food field. Indeed, the currently planned requirements do not characterize the notion of particle size (a fortiori nanoparticulate) as a sensitive and decisive criterion for authorization[181].

The scope of the regulation (EC) No258/97 relating to novel foods or food ingredients concerns inter alia “foods and food ingredients to which a production process which is not commonly used has been applied, when this process leads to significant changes in the composition or structure of foods or food ingredients in their nutritional value, their metabolism or their content of undesirable substances”. This regulation in its current formulation may cover nanotechnology developments in foods. However, no food or ingredient has so far been evaluated under the "Novel Food" approach due to production in nanotechnology[182].

Regulation (EC) No 258/97 has been replaced by Regulation (EU) 2015/2283, which streamlines the approval process for novel foods in the European Union while maintaining high safety standards. This new regulation expands the definition of novel foods to include products from new technologies and traditional foods from outside the EU, and it establishes a centralized authorization procedure managed by the European Commission and the European Food Safety Authority (EFSA). Additionally, it promotes innovation through data protection provisions and simplifies the approval process for traditional foods with a history of safe use.

- Food additives for human consumption; no product presented as derived from nanotechnologies or of nanoparticulate size has so far been evaluated as a technological additive or auxiliary. However, it should be noted that substances may have been authorized as additives or processing aids in a conventional form

and have since been developed, marketed and used in food in nanoparticulate form without the obligation of further notification, evaluation or prior authorization. Silica dioxide (SiO2) is authorized as a food additive (E551) but silicas of nanometric size have long been used in food for their rheological properties under the same additive number (precipitated silicas and pyrogenic silicas for example). The same is true for titanium dioxide (TiO2) authorized as a food additive (E171)[183].

- Food flavorings; are governed by a community regulatory system, also under review. This device provides for the evaluation of flavoring substances but does not explicitly consider the particle size or the development of a complex device of the encapsulation type.

- Food supplements or food fortification, to the previously mentioned difficulty is added the current absence of an exhaustive positive list of authorized substances[182].

- Packaging in contact with food, similar difficulties are encountered. Community regulations make it possible to regulate the authorization of the use of substances entering into materials in contact with food, however intelligent or active materials, which constitute the privileged niche of potential applications of nanotechnologies, are mentioned in a framework regulation without variation to date of specific evaluation methods[184].

The regulation 1169/2011 of the European Parliament relating to consumer information on foodstuffs (known as INCO) provides for the labeling of nanomaterials used as ingredients. Yet implementing mandatory labeling for nanoparticles is a difficult and treacherous regulatory step. The main concern is how to regulate a product or activity shrouded in scientific uncertainty[185].

### *3.4. Acceptability of Functional Foods by Consumers*

In the past, foods were known primarily for their supply of nutrients necessary for the normal functioning of the body. However, over the past two decades, consumers have shifted from the simple need to satisfy hunger to consuming food for the maintenance of well-being and the reduction of disease risks[12,186].

Eating behavior is influenced by four primary determinants: personal factors (such as individual preferences and health status), psychological factors (including emotions and attitudes towards food), social factors (like family, friends, and societal norms), and cultural

factors (which encompass traditions and beliefs). Additionally, the characteristics of the functional products themselves also play a significant role in shaping eating habits. The challenge of consumers' choice of nanofoods can be explained by the same factors, which play an important role in determining their acceptability[187].

Other factors that are positively correlated with demand are high levels of education, income, sensitivity, awareness, familiarity with these products and their knowledge, intention to purchase, and willingness to consume these foods for various reasons[188]. Note that the roles of family, friends, dietitians, and doctors as well as the presence of children at home play a positive role in the demand for functional products. Packaging, convenience, natural properties, and brand confidence in the marketing of the food are also factors that positively influence the purchasing behavior of this type of product[189–191].

Consumers often categorize foods as either "good" or "bad," with the reputation of health foods closely tied to natural and unprocessed products. As a result, many individuals perceive processed foods containing artificially introduced healthy ingredients as less desirable[10,192]. A substantial segment of the global population believes that functional foods merely serve as a remedy for unhealthy lifestyles, advocating for a holistic approach to healthy eating and living rather than reliance on individual food products[80,193]. One potential strategy for attracting these consumers to nanofoods is to highlight the enhanced sense of well-being associated with the use of functional foods[22,194].

## 4. Nanofoods and Applications in the Microbiological Laboratory

The incorporation of nanofoods into the food business signifies a substantial advancement, especially in microbiological applications. Suri *et al.*[195] assert that nanotechnology is crucial in creating effective delivery methods for antibacterial and antibiotic agents, hence enhancing therapeutic effectiveness against foodborne pathogens.

Granata *et al.*[196] assert that nanoparticles, whether organic or inorganic, may encapsulate antimicrobial agents, including antibiotics, targeting specific pathogenic microbes. This is achieved while preserving the nutritional and sensory characteristics of the meal.

Encapsulating bioactive pharmaceuticals into nanoscale structures like nanoliposomes and nanoemulsions might significantly enhance their stability and bioavailability[197]. Antibiotics serve as examples of such structures, but the emergence of bacterial resistance remains a significant challenge in food microbiology[198].

This facilitates the regulation and prolongation of antibiotic release, hence assisting in the reduction of bacterial resistance development. Nanoemulsions containing essential oils, such as cinnamon oil, exhibit improved antimicrobial effectiveness against many pathogenic species, including *Escherichia coli*, *Salmonella typhimurium*, and *Staphylococcus aureus*[199].

These nanoemulsions not only protect the active compounds during food processing but also maintain the effectiveness of the ingredients throughout the storage and distribution of food products. Furthermore, metallic nanostructures, such as titanium dioxide (TiO2) and silver nanoparticles, are often used for their antibacterial attributes[200–202]. Their biocidal properties prevent the growth of microorganisms on food packaging surfaces, hence extending the shelf life of perishable foods by limiting the proliferation of harmful bacteria.

Research by Istiqola and Syafiuddin in 2020[203], along with Azam *et al*. in 2023[204], indicates that the incorporation of silver nanoparticles into packaging materials may effectively suppress the proliferation of bacteria such as Listeria monocytogenes and Staphylococcus aureus, which are associated with numerous foodborne illnesses.

Furthermore, the utilization of nanotechnology in the food industry makes it possible to develop intelligent antibacterial films that are capable of detecting microbial contamination[205–209]. The presence of pathogens induces a response in these films, leading to the release of antimicrobial agents embedded within them onto the surface. This ensures that the food is protected continuously while it is stored.

To improve food safety, the microbiological uses of nanofoods, namely the encapsulation of antibiotics and antimicrobial agents, provide novel potential for innovation. Moreover, nanostructures facilitate the improvement of antibacterial therapies, reduce the hazards linked to antibiotic resistance, and safeguard food from microbial contamination. This also extends the safeguarding of food against microbial contamination.

## 5. Conclusion

Nanotechnology is a rapidly evolving field that presents innovative applications across various sectors, particularly in food and agroindustries. It offers significant advantages, such as enhanced delivery systems for nutraceuticals and antibacterial agents, which can improve food quality and safety. However, the unique properties of nanomaterials at the nanoscale raise important safety concerns, as these materials may interact unpredictably with biological systems and the environment. Current research has not conclusively established harmful effects of nanotechnology on human health or ecological systems, yet the potential for adverse outcomes necessitates comprehensive research and the

establishment of robust regulatory frameworks to safeguard public health and environmental integrity.

While the integration of nanotechnology into food production shows promise, challenges remain, particularly regarding the safety and toxicity of nanomaterials. The application of these materials is still in its early stages, with most undergoing *in-vitro* testing rather than *in-vivo* assessments. As the field progresses, it is essential to enhance production processes, minimize toxicity, and implement stricter safety guidelines. Continued scientific investigation is crucial for addressing existing gaps in knowledge and ensuring that the benefits of nanotechnology can be achieved without compromising health or environmental safety. By emphasizing safety and sustainability, it is possible to harness the potential of nanotechnology effectively while mitigating associated risks.

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