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Review

Trends of Nanoencapsulation Strategy for Natural Compounds in the Food Industry

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Abstract: Nanotechnology is an emerging field in the food industry that will be important for future industrial production to address rising customer concerns and expectations for natural, nutritious, and healthful food items. People are increasingly motivated to purchase unprocessed food or even high-quality processed foods with minimum chemical additives, highlighting the need to investigate natural alternatives for commercial purposes. Natural compounds are becoming more popular among consumers since they are safer than synthetic chemical additions; however, their most functional compounds are sensitive to the adverse conditions of processing and the digestive tract, impairing their use in food matrices, and industrial-scale applications. Nowadays, nanoencapsulation of natural products can be the most suitable nanotechnology to improve stability, solubility, and bioavailability. The nanostructure can be incorporated into food during production, processing, packaging, and security. Despite the many studies on nanoencapsulation, there is still some misunderstanding about nanoencapsulation systems and preparation techniques. This review aims to categorize different nanoencapsulation techniques (chemical, physicochemical, and physicomechanical), highlight eco-friendly methods, and classify the nanoencapsulation systems as groups (polymer, lipidic and metallic). The current review summarizes recent data on the nanoencapsulation of natural compounds in the food industry that has been published since 2015 until now. Finally, this review presents the challenges and future perspectives on the nanoencapsulation of bioactive compounds in food science.

Keywords: nanotechnology; nanoencapsulation systems; bioactive compounds; technique; food manufacturing; food safety

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1. Introduction

Current consumers demand healthier food and are motivated to purchase unprocessed or even high-quality processed foods with minimum chemical additives [1]. The importance of conserving food quality and health benefits without disturbing nutritional value in industrial processes has been a challenge [2]. This high awareness of society to adopt preventive health measures has driven the research to develop a natural compound with bioactive properties that could replace synthetic compounds [3].

Natural products are a broad group of chemical compounds created spontaneously by living organisms such as bacteria, fungi, plants, and aquatic species, each with its own set of biological functions that have various applications, mainly in human and veterinary medicine, food, and agriculture [4,5]. Food-derived bioactive compounds are a varied range of molecules that include lipid-soluble and water-soluble molecules, as well as micro/macromolecules. Among the principal bioactive compounds, we can find vitamins, minerals, flavonoids, phenolic acids, alkaloids, carotenoids, peptides, and fatty acids [6]. The physical and chemical stability of bioactive compounds is dramatically affected by harsh environmental influences during processing and storage, and is altered by physiological conditions within the body during digestion and absorption [7]. Indeed, encapsulation seems to be one of the most promising strategies for protecting fragile materials from adverse conditions or deterioration caused by oxidative conditions [8].

The nanoencapsulation process includes putting solid, liquid, or gaseous components in small receptacles known as capsules. They can be manufactured in nano sizes (<100 nm) employing a variety of materials for the capsule's membrane creation, with the usage of bio-based components, such as polysaccharides, gums, proteins, lipids, and blends of these, standing out [9–11].

Nanoencapsulation in food products offers several benefits, namely, enhancing bioactive compounds' stability and solubility, preventing deterioration during manufacturing, transport, and storage, masking nasty tastes, obtaining higher activity levels of the nanoencapsulated ingredients, and controlling release [12–21]. Nanocapsules may be included in food during production, processing, packaging, and security [14]. Recent reviews have highlighted the potential use of nanoencapsulation of natural compounds in specific areas, such as improving food shelf-life [22], as food additives [23], as antimicrobials [24], or as antioxidants [12,19].

Numerous technologies are available for preparing nanoencapsulation systems. Emulsification, coacervation, inclusion complexation, solvent evaporation, nanoprecipitation, and extraction are the most typical procedures to create nanoencapsulation systems [17–21]. However, no studies have focused on classifying the different nanoencapsulation methods for food components. Furthermore, in studies, there is still misunderstanding between the nanoencapsulation systems and the techniques; for example, in Vasisht's (2023) study, nanoemulsion was referred to as a system when it is actually a preparation technique [25]. Nevertheless, the literature review revealed no previous studies on eco-friendly nanoencapsulation techniques.

Based on the presented background, this review aims to categorize the various nanoencapsulation techniques (chemical, physicochemical, and physicomechanical) by highlighting eco-friendly techniques and classifying nanoencapsulation systems (polymer, lipidic, and metallic). Additionally, it summarizes recent data on the nanoencapsulation of bioactive compounds in the food industry and food safety, published from 2015 until now. Finally, the review will address the challenges and future perspectives of nanoencapsulation in food science.

During the bibliographic search, the main keywords used were as follows: nanoencapsulation, bioactive compounds, preparation technique, and food industry. The cloud in Figure 1 was obtained by VOSviewer software (version 1.6.19, www.vosviewer.com accessed on 5 May 2023) using the Scopus online database. The size of the circles indicates the frequency of occurrence of each of the keywords, and the curved lines express their links, i.e., co-occurrence. The figure shows that the most frequent keywords were nanotechnology, nanoencapsulation, and bioactive compounds, which follow the main objective of the review.

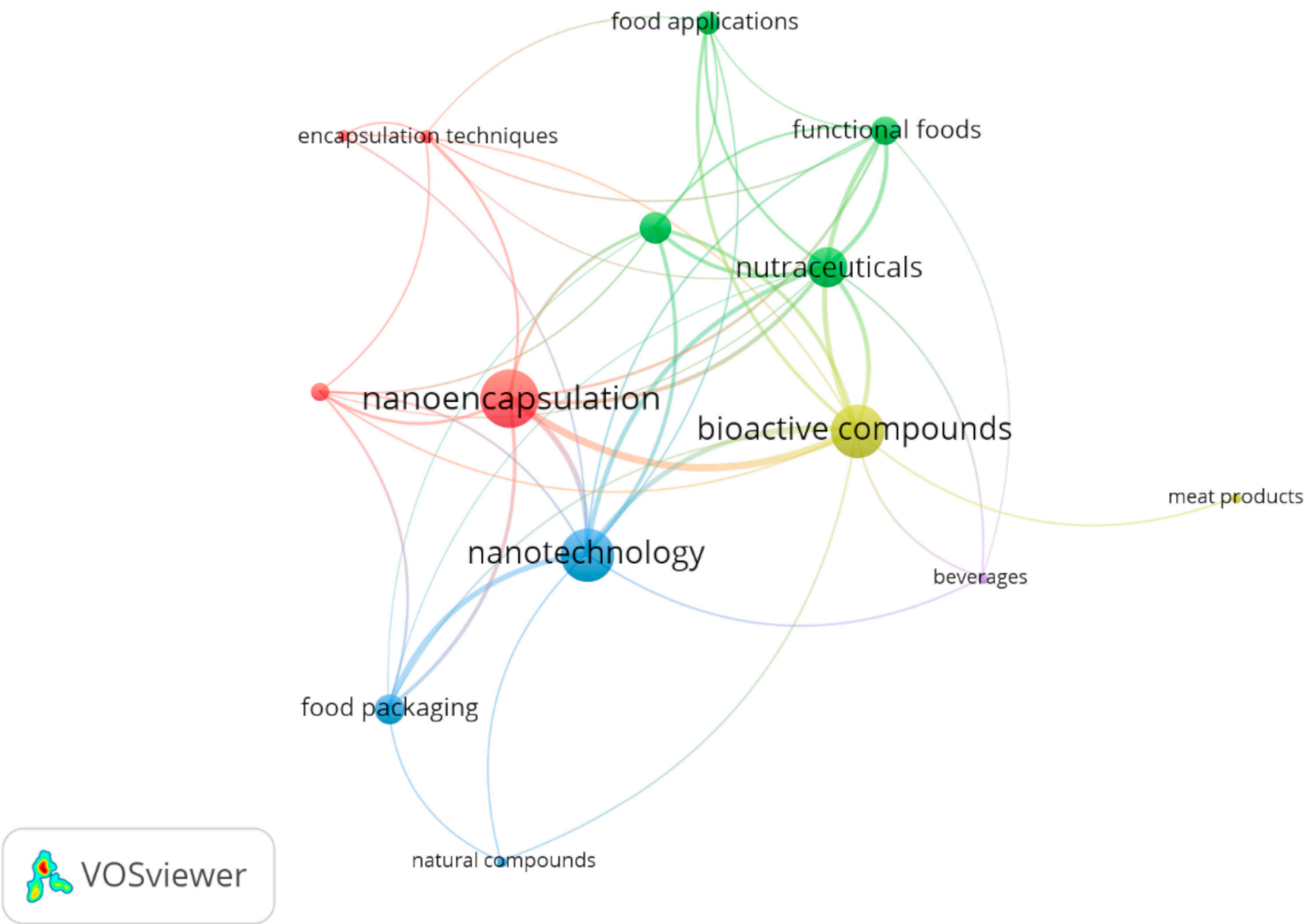

Figure 1. Keywords co-occurrence mapping of nanoencapsulation, bioactive compounds, preparation technique, and food industry. (Bibliometric data were extracted from the Scopus online database and elaborated by VOSviewer software (version 1.6.19, www.vosviewer.com accessed on 5 May 2023)).

2. Nano Encapsulations System

The encapsulation of compounds is accomplished by absorption, incorporation, chemical interaction, or dispersion [10,11]. Nowadays, several materials are used as shells of natural compounds, allowing various nanocapsule types [9]. Based on this context, we will classify the nanoencapsulation family's system and list the materials that are commonly employed in each family.

2.1. Lipids Systems

2.1.1. Liposome

A liposome (Figure 2) is a colloidal unit of phospholipid bilayer vesicles discovered by Bangham et al. in the 1960s [26]. Liposomes are produced from naturally occurring phospholipids with a variety of lipid chains. Phospholipids' polar regions are found on the surface of liposomes, while their fatty acid chain regions are kept separate from the water by a bilayer hydrophobic nucleus. Nanoliposomes are smaller liposomes having hydrophilic and lipophilic areas that can entrap compounds in lipid bilayers with various lipotropic properties. Nanoliposomes can encapsulate unstable substances such as drugs, vitamins, antioxidants, and antibacterial agents. Based on the number of bilayers in the structure and their size, liposomes may be structurally classified into several categories [27–29].

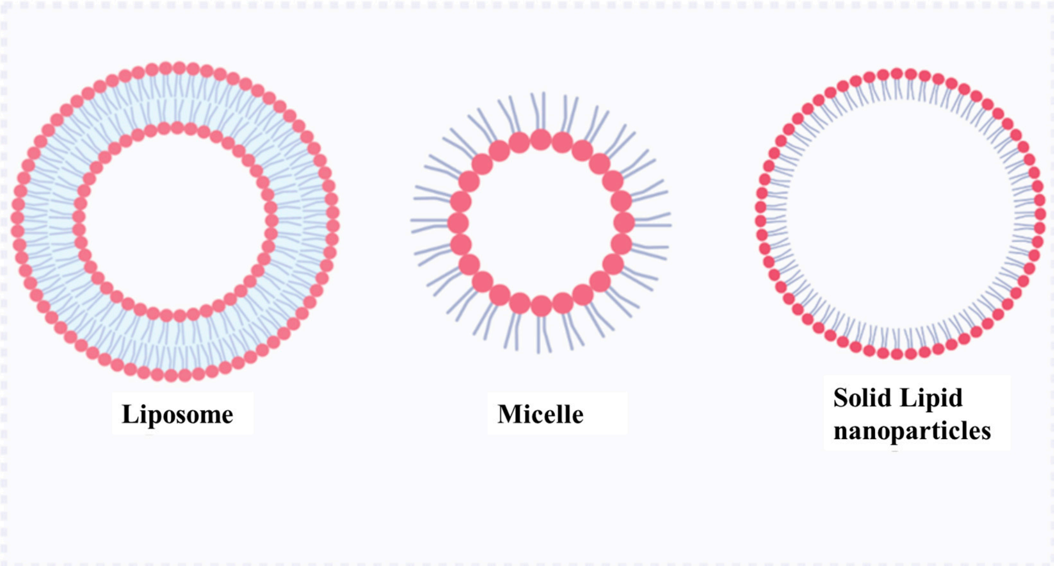

Figure 2. Lipids systems.

2.1.2. Micelle

Micelles are lipid-containing molecules that condense into spheres in aqueous liquids (colloidal dispersions). Since fatty acids are amphiphilic and feature polar head groups and hydrophobic chains, they can form micelles. A micelle's nonpolar hydrophobic tail group is found inside and away from water, while its polar head group generates a surface. Roundness and reduced steric hindrance are characteristics of fatty acids that form micelles. The two hydrophobic chains of the fatty acids in glycolipids and phospholipids are too heavy for micelles, which prefer "lipid bilayers". Micelles form on their own as a result of hydrophobic interactions between molecules [30–32].

2.1.3. Solid Lipid Nanoparticles

Colloidal dispersions of solid lipid nanoparticles (SLNs) are made up of particles having a lipid core that has hardened and is covered in an emulsifier molecule layer. Therefore, they are structurally comparable to traditional emulsions, with the exception that the droplets in SLNs are entirely crystalline rather than liquid. Typically, SLNs are made by homogenizing an oil phase and a water phase containing a hydrophilic emulsifier at a temperature over the melting point of the lipids. After that, to solidify the created nanoemulsion, it is cooled below the temperature at which the lipid phase crystallizes. At the intended temperature of operation, edible lipids used to manufacture SLNs should be crystalline, but they also need to be able to be melted to integrate the bioactive component. Glyceryl palmitostearate, glyceryl monostearate, glyceryl behenate, palmitic acid, tripalmitin, steric acid, tristearin, and waxes are examples of edible lipids that are used to make SLNs [33–35].

2.2. Polymer Systems

2.2.1. Alginate

Alginate is a naturally occurring polymer that may be found predominantly as a structural element in marine brown seaweed (*Laminaria hyperborea* and *Macrocystis pyrifera*) and as capsular polysaccharides in several soil bacteria, including *Pseudomonas* and *Azotobacter* [36]. Alginate is a linear polysaccharide copolymer made up of two (1-4)-linked mannuronic acid and guluronic acid monomers, and two C5 epimer repeating units (Figure 3). The alginate source affects the quantity and distribution of each unit, and these building blocks control the characteristics and behavior of the polymer. By joining with the monovalent ions, the carboxylic groups in alginate can create salts, such as sodium alginate [37]. Alginate can be synthesized in neutral or charged form, making a wide range of compounds compatible. Alginate may create two different forms of gel, an acid or an ionotropic gel, depending on the pH of the surrounding medium. These gels provide several physicochemical features. A crucial characteristic of alginate and its derivatives is that they gel when exposed to divalent cations, such as calcium, due to an ionic interaction between cations and the carboxyl groups on the polymer's backbone [38].

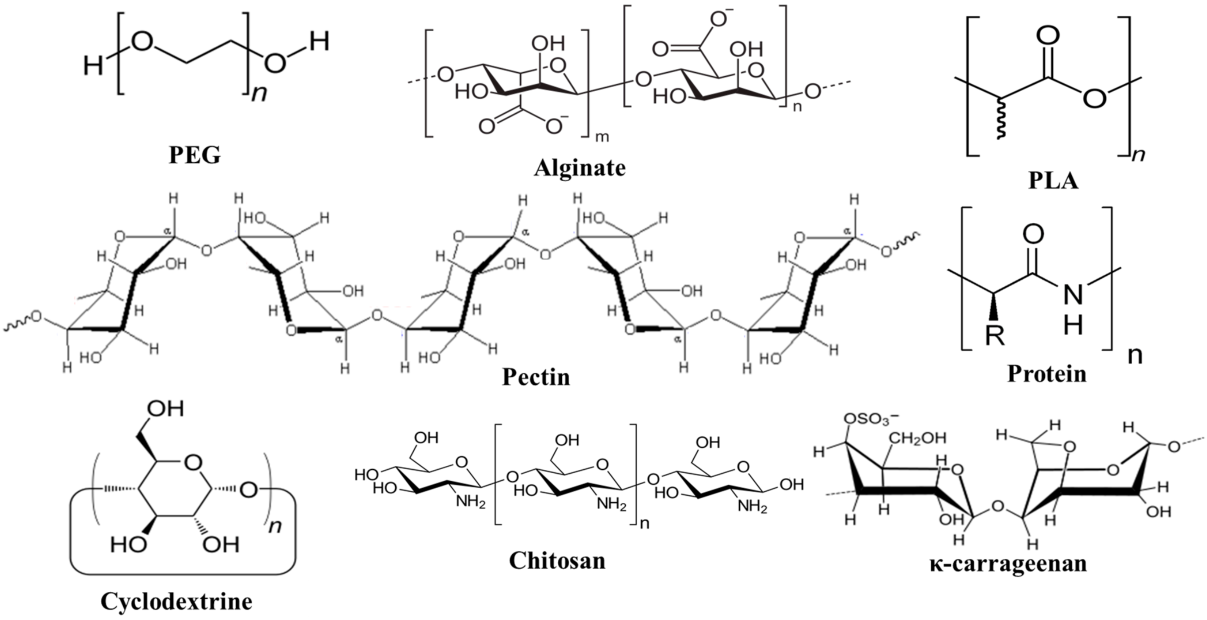

Figure 3. Structure of polymer systems.

2.2.2. Carrageenan

A sulfated polyglactin that includes ester sulfate at a concentration of between 15 and 40% is known as carrageenan. It is composed of units of 3,6-anhydrous-galactose and D-galactose (Figure 3) that alternate and are connected by glycosidic linkages of 1,4 and 1,3. Red seaweed is used to extract carrageenan, which can have positive benefits due to the heterogeneity in its structure and characteristics [39]. Carrageenan molecules' positions and numbers of sulfate ester groups, together with the amount of 3,6-anhydrous-galactose present, can all affect the biopolymer's characteristics [40]. Based on their structural differences, carrageenan has been produced in six different types (κ-, ι-, λ-, μ-, ν-, and θ-carrageenan). The most manufactured polymer is κ-carrageenan, which has a high gelling capacity. The massive amount of -OH helps the helix shape develop by creating many hydrogen bonds [41,42].

2.2.3. Chitosan

A naturally occurring polycationic linear polysaccharide produced from chitin, chitosan is ((1 4)-linked 2-amino-2-deoxy-D-glucose) (Figure 3). Chitin is a plentiful, renewable polymer, and its deacetylated derivative, chitosan, is a popular biopolymer [43]. The shells of shrimp, crabs, and other crustaceans contain chitin (-(1 4-N-acetyl-D-glucosamine), which may react with alkaline sodium hydroxide to produce an N-deacetylation product also known as chitosan [44]. The reaction between the amino groups of chitosan and its protonation, which produces NH^{3+}, together with its linear chains, results in the development of electrostatic contacts with molecules containing negatively charged groups. Furthermore, chitosan chains' inclusion of this functional group and a hydroxyl enables chemical alterations [45].

2.2.4. Cyclodextrin

The enzymatic breakdown of starch by cyclodextrin glucosyltransferase produces cyclodextrins (CDs), torus-shaped oligosaccharides with α-(1,4) connected glucose units

(Figure 3). The most prevalent cyclodextrin type is the natural α, β, and γ CDs. CDs have an interior cavity into which molecules can fit. When a molecule enters, it forms an "inclusion complex," a non-covalent contact involving both the host and the guest molecule. According to reports, the volumes of α-, β-, and γ-CD is 0.174, 0.262, or 0.427 nm^3, respectively [46,47].

2.2.5. Pectin

Pectin (Figure 3) is a complex blend of polysaccharides that is acquired from the cell walls of plants; it is polymolecular and polydisperse. Additionally, its composition might change based on the source and the issues experienced in isolation [48]. The main component of pectin, D-galacturonic acid units, is connected in chains by -(1-4) glycosidic linkage. It also has branch areas made of mono-sugars such as D-xylose, D-glucose, L-rhamnose, L-arabinose, or D-galactose. Some of the uronic acid carboxyl groups contained in pectin chains are found naturally as methyl esters, while others are chemically produced by treating other uronic acid carboxyl groups with ammonia [49].

2.2.6. Polyethylene Glycol (PEG)

Repeated ethylene glycol units [-$(CH_2CH_2O)_n$] (Figure 3) make up the hydrophilic polymer known as polyethylene glycol (PEG). Anionic polymerization of ethylene oxide and a hydroxyl group can be used to create it (from water, ethylene glycol, or any diols). PEG can be made through epoxyethane ring-opening polymerization. Different levels of polymerization and activated functional groups can be found in commercially available PEGs [50,51].

2.2.7. Polylactic Acid

The hydrophobic polymer polylactic acid is also known as poly-hydroxy acids, polyesters, or aliphatic polyesters [-$(C_3H_4O_2)_n$] (Figure 3). Lactic acid (LA; 2-hydroxypropanoic acid), a water-soluble monomer that is available in two enantiomeric forms, L-(+)-LA and D-(-)-LA, serves as the basis for its synthesis. When poly-L-lactic acid (PLLA) and poly-D-lactic acid (PDLA) homopolymers are created from pure L- and D-lactic isomers, respectively, PLA can be generated. On the other hand, poly-D, L-lactic acid (PDLLA) copolymer is generated with a racemic mixture of L- and D-monomers [52–54].

2.2.8. Protein

Proteins are polymers made up of amide bonds connecting the 20 natural amino acids. Some amino acids are not generated from ribosomes, such as L-3,4-dihydroxyphenylalanine (DOPA), hydroxyproline (Hyp), dityrosine, and selenomethionine, and these substances are created by posttranslational modifications (Figure 3). These non-ribosomal peptides and amino acids are frequently involved in the structure and function of proteins [55]. Hydrogen bonding, electrostatic contacts, hydrophobic interactions, van der Waals interactions, and metal coordination are noncovalent and weak interactions that help proteins molecularly self-assemble in the range of nanoarchitectures. Although the amplitude of these interactions individually may be negligibly small, when taken together, the overall interactions are considerable and can control the structural conformation of the assembled nanostructures [56].

2.3. Metallic Systems

Metallic nanoparticles (MNPs) have attracted a lot of attention because they may be used to create antimicrobial treatments that have the potential to extend food's shelf life by preventing bacteria development [57]. These qualities are crucial in applications involving food technology. In this context, MNP-based films, hydrogels, and sensors are gaining popularity as tools in the field of food science. The use of MNPs in food, an intelligent system for food preservation, has been demonstrated in several studies. Additionally, MNP-based sensors are employed to identify food pollutants, namely, microorganisms [58]. Different MNPs, which serve as a vehicle not only for one type of particle, but also as a hybrid system that permits the coupling of natural chemicals with MNPs, may be easily mixed with biopolymers and polymers. Silver nanoparticles (AgNPs), copper nanoparticles (CuNPs), gold nanoparticles (AuNPs), zinc oxide nanoparticles (ZnO NPs), and titanium dioxide nanoparticles (TiO_2 NPs) are among the metals utilized in metallic nanoencapsulation. Several physical, chemical, and biological methods have been developed for MNPs fabrication and or synthesis [59].

3. Preparation Methods

Several technologies are available for preparing nanoencapsulation systems. The most common techniques used to produce nanoencapsulation systems include emulsification, coacervation, inclusion complexation, emulsification solvent evaporation, extraction, nanoprecipitation, electro-spraying (spray drying), and electro-spinning [60–80]. These techniques can be categorized into chemical, physicochemical, and physical-mechanical methods, depending on the approach used to form the nanoencapsulation systems.

3.1. Chemical Techniques

Basic chemical processes include emulsions, suspensions, precipitations, sol-gels, and polymerizations. These chemical processes have the benefits of producing nanocapsules with high purity, high uniformity, tiny particle size, narrow size distribution, dispersibility, superior chemical homogeneity, and increased reactivity [60]. In most cases, "emulsification" techniques include first producing an emulsion of a liquid core in a continuous phase by shaking, stirring, homogenizing, or spraying procedures [61]. A shell is created in a second stage by organic polymerization; the emulsion is homogenized using microfluidizers, or the suspension is atomized to allow the solvent to evaporate. The continuous phase begins with a low molecular weight polymer, and as the polymerization progresses, the polymer steadily expands and concurrently entraps the core substance to create the completed nanocapsules. The capsule shell is created at/on the droplet surface by polymerization of the reactive monomers in the "interfacial polymerization" approach [62]. The emulsion is created by dispersing the core material into the continuous phase, where the monomer is dissolved. The mixture is given a co-reactant, which causes the polymerization at the core interface and produces the capsule shell [63]. The "sol-gel" method is a technique that involves making a solution or sol, and gel, then solidifying and heating the organic and inorganic molecules. By creating a colloidal suspension (sol) and then gelating the sol to form a network in a continuous liquid phase, "sol-gel" encapsulation creates inorganic networks (gel) [64]. The "suspension cross-linking" can be used to achieve nanoencapsulation in addition to the chemical methods discussed above. The creation of nanocapsules can also be accomplished using "hydro-thermal methods," in which chemical reactions occur in water at high temperatures and high pressures, and "oxidation processes," which directly oxidize and deoxidize raw materials while they are in the liquid phase or quasi-liquid phase [65]. The different chemical methods are summarized in Figure 4.

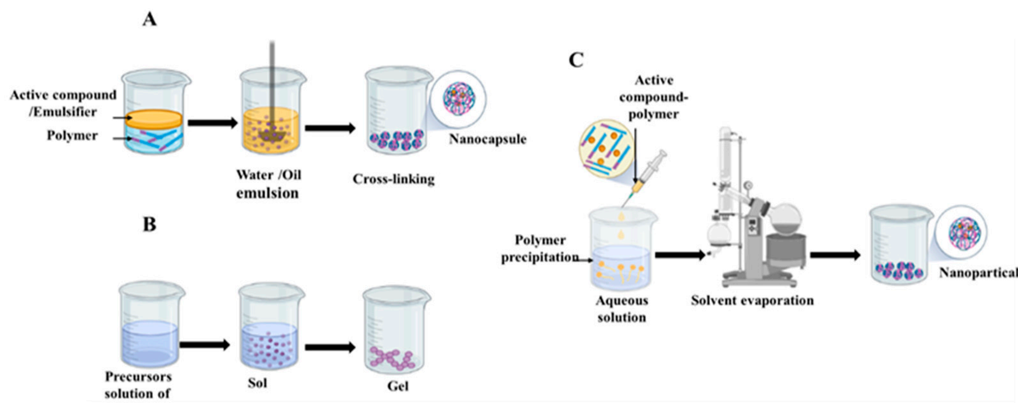

Figure 4. Principe of the chemical preparation methods: emulsion polymerizations (**A**), sol-gels (**B**), and precipitations (**C**).

3.2. Physicochemical Technique

Physical-chemical procedures are those used in nanoencapsulation that integrate chemical and physical techniques. For instance, "phase inversion nanoencapsulation" (PIN) is a technique for biodegradable polymer nanospheres that is particularly effective in encapsulating pharmaceuticals, proteins, or plasmid DNA, without denaturing in capsules: This technique results in the formation of nano- and microspheres by the addition of the active ingredient to a diluted polymer solution, often in methylene chloride, which is then quickly placed into a non-solvent (petroleum) bath without stirring [66]. Simple and complicated coacervation methods are used in phase separation. Except for how the phase separation is achieved, the mechanism of capsule creation is the same in both techniques. A desolvation agent, such as gelatin or ethyl cellulose, is added to the aqueous or organic media in a simple coacervation to facilitate phase separation; in contrast, a complicated coacervation includes complexation between two oppositely charged polymers that are both soluble in an aqueous medium. When forming an aqueous polymer solution (1–10%) at 40–50 °C, where the hydrophobic core material is also dispersed/dissolved, nanoencapsulation by coacervation is accomplished (Figure 5) [67]. Generally, "inclusion complexes" (Figure 5) refer to the supramolecular interaction (Van der Waals forces, hydrogen bonds, or the entropy-driven hydrophobic effect) of the material that has been enclosed into a cavity-bearing complex or shell [68]. Supercritical fluids (Figure 5) constitute the foundation of other physicochemical methods for nanoencapsulation. These procedures include solubilization of the main constituent in a supercritical fluid to disperse it in a matrix material (usually carbon dioxide). The core is enclosed by the matrix material once the carbon dioxide has been removed [69]. In contrast to the nanoencapsulation methods previously mentioned, other physicochemical processes include "controlled precipitation" [70], and "layer-by-layer deposition" [71].

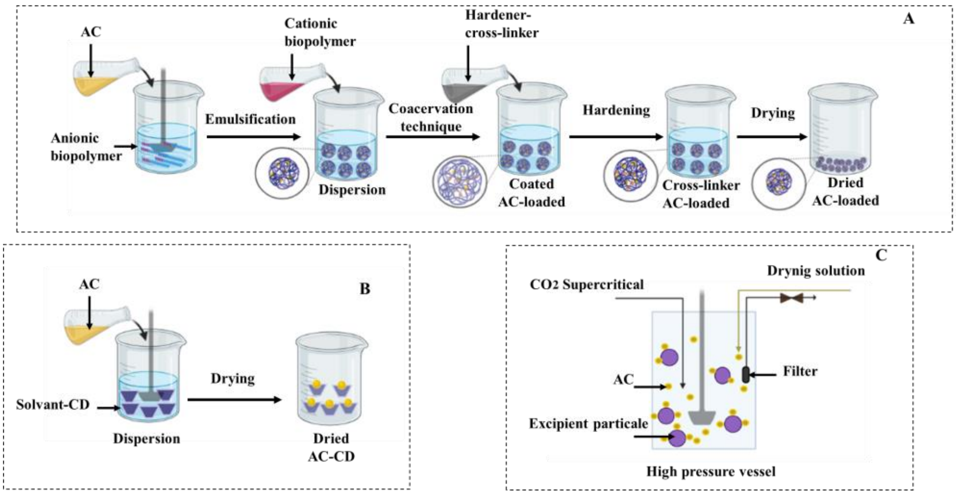

Figure 5. Coacervation and phase separation (**A**), inclusion complexes (**B**), and supercritical fluids (**C**).

3.3. Physical-Mechanical Technique

Spray drying, solvent evaporation/solvent extraction, and electroencapsulation-based procedures are the three most common physicomechanical strategies for encapsulating desired species at the nanoscale scale [72]. Figure 6A shows the "spray drying" method is extensively used to encapsulate flavors, oils, and perfumes. Core particles are atomized into a heated chamber and disseminated in a polymer solution of wall material in a "spray drying process." The shell material hardens onto the core particles as the solvent evaporates, resulting in polypore or matrix-type capsules. The spray drying process limits particle size to 100 nm using a one-droplet-to-one-particle mechanism [73]." Solvent evaporation/solvent extraction" (Figure 6C) is a process that involves dissolving a polymer together with the core substance in an organic solvent that is water-immiscible. The tiny polymer droplets containing the encapsulated substance are added dropwise to an aqueous solution. Simple solvent evaporation (heat or decreased pressure) or solvent extraction with a third liquid precipitant for the polymer and miscible with both water and the solvent can be used to eliminate the solvent [74]. The "solvent evaporation/solvent extraction" technique is used with the "freeze-drying" procedure [75]. A simple bottom-up technique for creating capsules with submicrometer sizes is "electrospraying" (Figure 6B). It is a technique for atomizing liquids using electrical forces. The capillary nozzle is kept at a high electric potential during "electrospraying," electrical shear stress is applied to the flow out of the nozzle, causing tiny droplets. With this technique, the size of droplets varies from hundreds of micrometers to tens of nanometers and can be managed electrically by varying the flow velocity and voltage delivered to the nozzle [76]. For instance, "impacting of two oppositely charged droplets" is a technique where both droplets' streams are released from two independent capillary nozzles maintained at opposite potentials, one of the capillaries at the positive and the other at the negative. This technique is known as "electrospraying/evaporation of colloidal suspension," which involves electrospraying a suspension first, followed by solvent evaporation solidifying the shell. A suspension of the core material is electrosprayed into a bath that contains a gelatinizing or polymerizing chemical similar to the "electrospraying/gelatinization of colloidal suspension" technique. On the core material, this agent creates a tough envelope [77].

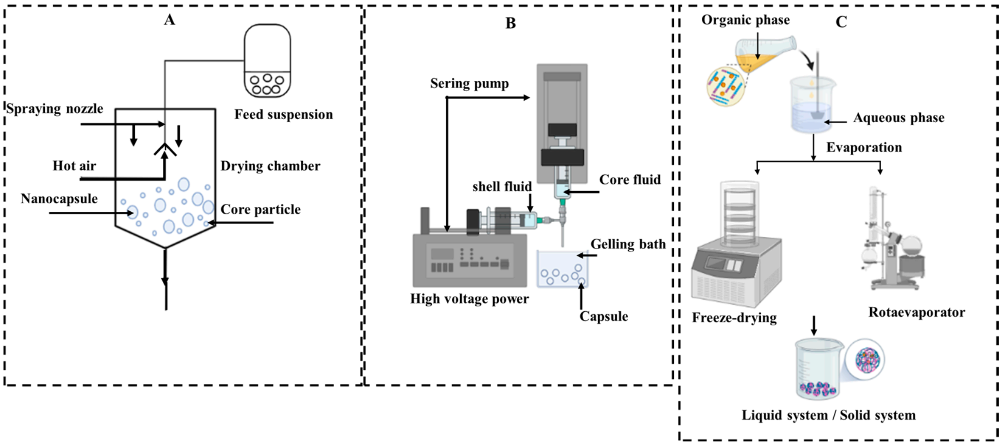

Figure 6. Significant physicomechanical strategies for nanoencapsulation: spray drying (**A**), electrospraying (**B**), and solvent evaporation/solvent extraction (**C**).

The potential is maintained by using two coaxial capillaries; the "electrocoextrusion" procedure sprays two liquids simultaneously into the electronanoencapsulation cavity. In this technique, an annular nozzle between the capillaries allows the envelope liquid to pass, while the core liquid emanates from the central capillary. It is essential to remember that this technology cannot be employed unless the core liquid has a high resistivity and the envelope has a suitably high conductivity [78]. It is possible to encapsulate materials into nanofibers and spherical nanocapsules using electronanoencapsulation techniques. The process of "electrospinning" creates nanofibers by supplying a suspension of the core material in a polymer solution from a spinneret, which forms a droplet at the spinneret outlet. This approach involves immersing an electrode in the suspension to create an electric field, positioning the counter-electrode away from the spinneret, and starting the jetting process [79]. The procedures of "melt-solidification" [80], "vibrating and coaxial nozzle" [78], and "pan coating" [81], in addition to the already mentioned, can be employed to encapsulate desirable species at the nanoscale. These preparation techniques can also be considered as green technology and eco-friendly, as most of them do not use organic solvents [82,83].

4. Nanoencapsulation Systems Advantages in the Food Industry

Foods and food products can deteriorate due to microbiological, enzymatic, physical, and chemical changes, which can deteriorate their quality, nutritional content, and safety, while also causing unwanted changes in shelf life, physicochemical, and sensory quality [84]. The use of synthetic additives in food was increasingly frequent [85]. However, producing safe foods with little or no artificial preservatives is one of the most pressing challenges for food manufacturing industries because synthetic agents and chemical food additives can have side effects on human health (Table 1) and an adverse environmental effect [86]. As a result, users' preference for natural sources has lately risen, and increased consumer demand for safe food items has compelled the food industry to adopt natural herbal and plant-origin preservatives rather than synthetic preservatives in safe food manufacturing [87]. Natural chemicals found in herb and spice extracts, essential oils, and other secondary metabolites from plants, microbes, and enzymes are gaining popularity but are still underutilized. Because they are considerably safer and pose no health hazards to consumers, their application as bio preservatives and additives may open up new possibilities in food safety and quality preservation [88].

Table 1. Synthetic preservative side effects on human health.

Synthetic Preservative	Side Effects	Reference
Nitrates and nitrites	Methemoglobin, loss of consciousness and death, especially in infants.	[89]
	Carcinogenic.	[90]
	Alzheimer's, Parkinson's, and type 2 diabetes fatalities.	[91]
	Headache, sweating, redness of skin, nausea and weakness.	
Formaldehyde	Potent irritants (skin, eye and lung).	[91]
	Sperm DNA damage	
Sulfites	Severe allergic reactions and asthma.	[92]
Parabens	Neurological damage (in rats), potent irritants, and allergens.	[93]
	Pregnant women's exposure of certain toxic chemicals may have an adverse effect on embryonic brain development.	

Recently, nanoencapsulation has attracted more and more attention from the food and healthcare sectors due to the numerous benefits it offers [94]. The minimal particle size and significant surface area give nanostructured materials exceptional properties and capabilities for their application in the food industry. Nanoencapsulation associated with natural compounds improves the efficiency of food processing and food safety [95]. The main improvements focus on changing the texture of food products, encapsulating edible substances or additives, developing original flavors, and improving the bioaccessibility/bioavailability of food components [6,20]. Figure 7 summarizes the main areas of the food sector covered by nanoencapsulation and its benefits.

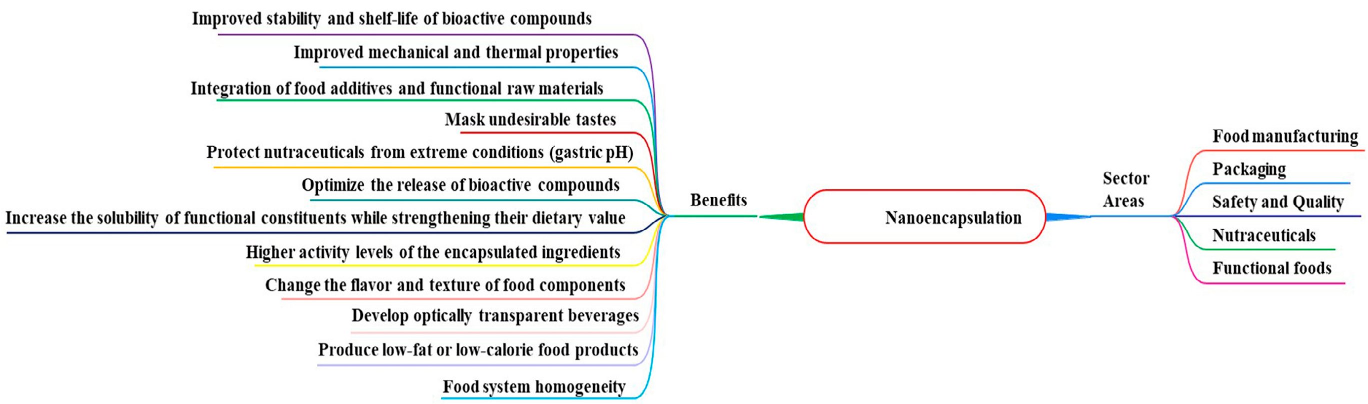

Figure 7. The five general areas covered by nanoencapsulation in the food sector and their benefits.

5. Case Studies of the Application of Natural Compound Nanoencapsulation in the Food Industry

5.1. Incorporation into Food Matrices

5.1.1. Dairy Products and Beverages

Dairy products have been associated with better bone health, as well as a decreased risk of stroke, metabolic syndrome, and some malignancies. Additionally, because of their high protein content, they are a tasty and nutritious alternative for inclusion in a healthy diet throughout the day [96]. Widely recognized for their biological potential, studies indicate that the incorporation of polyphenols into dairy matrices is not feasible given the occurrence of interactions with food constituents, specifically between dairy proteins [97]. Nanoencapsulation has been proposed as one technique for avoiding these interactions, as a physical barrier between phenolic chemicals and the matrix [98]. An example of this is the difficulty of incorporating compounds with relatively low solubility in water, such as polyphenolic compounds and essential oils, a limitation in which their incorporation into CDs and PE-based nanoparticles has proven to be effective in overcoming [99,100]. From an organoleptic point of view, the encapsulation of bioactive compounds can help improve the product's characteristics and reduce its volatility, prolonging its aromatic properties [100,101]. Nanoencapsulation improves nutritional properties and protects the environment of bioactive compounds in milk and milk products [99,102–104] (Table 2). Olive leaf extract is entrapped within nanoliposomes with a good encapsulation efficiency for application in food products, improving, for example, the antioxidant activity in yogurt [101]. Nanoencapsulated vitamin D3 shows the benefits of nanotechnology in dairy product fortification, and its effects on participants' physical and mental health have been assessed [105–107].

For the same advantage cited previously, the nanoencapsulation of bioactive compounds has been applied in beverages. Curcumin was incorporated in orange juice, maintaining satisfactory pH, °Brix, and color stability, during three days of storage (8 °C) [108]. The bioactive compounds extracted from Egyptian prickly pear peel were encapsulated in sodium alginate and chitosan, and their antioxidant activity and application in guava juice were evaluated [109]. An overview of the nanoencapsulation of natural compounds applied in juice is listed in Table 2.

Table 2. Example of nanoencapsulation application in dairy products and beverages.

Agent	Nanoencapsulation Systems	Preparation Technique	Biological Activity	Food Application	Reference
VitD3	Liposome	Thin-film dispersion	Improve the usage of spray-dried whey powder as a functional ingredient.	Spray-dried whey powder	[19]
Clove Essential Oil (CEO)	Polyethylen glycol	Nanoemulsions	Conservation/ antioxidant potential.	Industrial fresh double cream cheese	[99]
Chlorogenic acids	Beta-cyclodextrin	Lyophilization	Polyphenols effect/the profile of volatile aroma compounds.	Caramel cottage cheese	[100]
Olive leaf extract	Liposomes	Ethanol injection	Examined considering syneresis, antioxidant activity, pH, acidity, color, and sensorial properties.	Yogurt	[101]
Phenolic extract of jaboticaba	Lipid	Nanoemulsions	Evaluated the total phenolic content/cow milk antioxidant activity.	Cow milk	[103]
skipjack tuna eyeballs oil (STEO-NL)	Liposomes	Ethanol injection	Fortification	Cow milk	[104]
VitD	Lipid	/	Evaluate the effect of 1500 IU nanoencapsulated vitamin D used for fortifying.	Milk and yogurt	[105]

Table 2. *Cont.*

Agent	Nanoencapsulation Systems	Preparation Technique	Biological Activity	Food Application	Reference
VitD	Precirol (Solid lipid)	Homogenization ultrasound	Fortifying dairy Products.	Milk/yogurt	[106]
VitD	Lipid	Homogenization with ultrasound	Fortified effect/anti-oxidant balance in adults.	Yogurt	[107]
Curcumin	Polyvinylpyrrolidone (PVP)	Solvent	Evaluated the fight against microbial contamination.	Orange juice	[108]
Bioactive Compounds Extracted from Egyptian Prickly Pears Peel Fruit	Sodium alginate and chitosan	Solvent evaporation	Protect and improve their stability and bioavailability and evaluate their activity comparing to synthetic ones.	Guava juice	[109]
Wheat germ oil (WGO)	Casein micelles	pH changes and ultra-sonication	Fortification of dairy Product.	Labneh	[110]
Fish oil	Gum Arabic	Freeze drying	Protecting against environmental conditions.	Fermented milk	[111]
Phenolics extract of grape and apple pomace	Chitosan and soy protein	Nanoemulsions	Enhancement of the native antioxidant activity of commercial apple and pineapple juices.	Apple and pineapple juices	[112]

5.1.2. Meat and Meat Products

Meat is an excellent source of proteins, fats, vitamins, and minerals with a high biological value (vitamin B12, zinc, selenium, phosphorus, and iron). However, they are subject to bacterial growth and lipid oxidation, which are the main factors in the degradation and loss of physical, chemical, and sensory qualities [113,114]. The meat quality and shelf life were improved by bioactive molecule nanoencapsulation, directly to the meats or indirectly by adding to animal feed, to overcome the digestive system problems and physicochemical properties (hydrophobic and volatile) limits [115,116].

The impact of nutritional supplementation with encapsulated bioactive compounds can improve meat quality, such as broilers' meat cholesterol reduction [115,117]. Curcumin nanoparticles on broiler chicks' humoral immunity, blood metabolites, and growth performance were assessed by Badran et al. (2020) [118]. The investigation by Amiri et al. (2021) shows the positive effects of essential oils (nanoencapsulated garlic essential oil) on broiler chicken performance and intestinal healthin vivo as well as in vitro (antibacterial and antioxidant characteristics) [119].

Furthermore, the nanoparticle impacts the expression of the mucin2 gene and the *Lactobacilli* population in the ileocaecal digest. Other studies have focused on broiler growth performance and immune function [120–123] (Table 3). Antibacterial and antioxidant compounds are used in meat and meat product preservation as meat surface coatings [124–126]. The effect of Trachyspermum Ammi essential oil as an antibacterial agent on turkey fillet storage was investigated by Kazemeini et al. (2021) [127]. The findings support that the previous nanoemulsion essential oil-loaded alginate exhibited an important antibacterial ability against *Listeria monocytogenes*. Their growth was inhibited even after twelve days of refrigeration. To avoid lamb meat spoilage and extend its shelf life, Pabast et al. (2018) have used Satureja khuzestanica essential oils with an edible chitosan nanoparticle coating. The microbiological outcomes after twenty days of storage were still satisfactory with nanoliposome coating treatments [128].

Meat enrichment has attracted the interest of researchers. Nanoencapsulation and ultrasound were used to enhance the lipid profile of pork meat. The pork meat was submerged in a nanovesicle fish oil solution and treated with ultrasound. The omega-6/omega-3 ratio in pork meat was beneficially modified, indicating that pork meat has a superior fatty acid profile [129]. Using a combined FTIR-PCA approach, Hădărugă et al.

(2022) investigated the similarities/dissimilarities of raw and processed chicken breast and thigh lipids complexed by CDs [130]. The lipid nanoencapsulation using a food-grade natural CD was performed using kneading. Nanoencapsulation using CDs improved the thermal and oxidative status of the chicken lipid.

Along the same lines, Elbarbary et al. (2015) used chitosan vitamin C nanoparticles in meat lipids oxidative protection research. That complex shows an important antioxidant power, with lipids peroxidation down 75% [131].

Table 3. Summary of selected meat and meat product nanoencapsulation studies.

Agent	Nanoencapsulation System	Preparation Technique	Biological Activity		Food Application	Reference
Cumin essential oil,	Chitosan	Ionic gelation	Growth performance/ immune responses.		Broiler chickens	[115]
Melastoma malabathricum L. Fruit extract (Anthocyanin)	Chitosan	Ionic gelation	Blood lipid profile.	Feed additive	Broiler chicken	[117]
Curcumin	Solid lipid nanoparticles	Solvent -evaporation	Growth performance, immune response/ antioxidant activity.		Broilers chickens	[118]
Garlic essential oil	Chitosan	Ionic gelation	Antibacterial//antioxidant activities /growth performance.		Broiler chickens	[119]
Garlic extract	Metal nanoparticles (Calcium)	/	Antioxidant status, lipids profile, immune response.		Broiler chickens	[120]
Mint (*Mentha piperita*), thyme (*Thymus vulgaris*), and cinnamon (*Cinnamomum Verum*) essential oils	Chitosan	Ionic gelation	Growth performance, immune, and intestinal bacteria.		Broiler chickens	[122]
Phaleria macrocarpa fruits extract	Chitosan	Ionic gelation	Antioxidant and antimicrobial activities, and growth performance.		Chickens	[123]
Peppermint (*Mentha piperita*) Extract	Alginate	Emulsion	Growth performance, blood parameters/immune response.		Broiler chickens	[132]
Silymarin Seeds (*Silybum marianum*)	Alginate	Emulsion	Antioxidant/hepatoprotective activities.		Broiler chickens	[133]
Flaxseed oil: omega-3 fatty acids	Protein-sodium alginate	Nanoemulsions	Targeted delivery/bioavailability/growth performance/blood lipid profile.		Enrich broiler meat	[134]
Red onion (*Alyssum homolocarpum*) and seed gum (*Lepidium sativum*) extract	Biopolymeric	Nanoemulsion	Antioxidant and antimicrobial activities.		Beef fillet	[135]

Table 3. *Cont.*

Agent	Nanoencapsulation System	Preparation Technique	Biological Activity		Food Application	Reference
Pomegranate (*Punica granatum* L.) peel extract	Alginate nanospheres	Nanoemulsion	Antimicrobial activity.	Conservation	Chicken meat	[136]
clove essential oil (*Eugenia Caryophyllata*)	Lipid nanoparticles	Nanoemulsion	Antibacterial and antioxidant activities.		Chicken fillets	[124]
Lemon Essential Oil	Chitosan	Nanoemulsion	Antioxidant activity.		Fish burger	[125]
Allium sativum L. essential oil (garlic)	Liposomes	/	Antimicrobial activity.		Beef meat-based hamburger	[126]
Trachyspermum Ammi essential oil	Alginate	Nanoemulsion	Antibacterial activity (against *Listeria monocyte genes).*		Turkey fillets	[127]
Satureja khuzestanica essential oil	Liposomes	/	Antibacterial and antioxidant activities.		Lamb meat	[128]
Fish oil: omega-3 fatty acids	Liposome	Solvent evaporation	Meat quality and nutritional value.		Enrich pork meat	[129]
Raw and processed chicken breast lipid	β-Cyclodextrin	Nanoemulsion	Lipid protection.		Chicken	[130]
Rosmarinus officinalis essential oil	Chitosan-benzoic/acid nanogel	Solvent evaporation	Antibacterial activity.		Beef cutlet	[137]
Star anise essential oil, Polylysine, and Nisin	Protein isolate	Nanoemulsion	Antimicrobial activity.		Yao meat	[138]
Thyme essential oil (*Thymus vulgaris* L.)	Chitosan	Nanoemulsion and ionic gelation	Antimicrobial and antioxidant activities.		Beef burgers	[139]
Jujube gum andnettle oil	/	Nanoemulsion	Antimicrobial and antioxidant activities.		Beluga sturgeon fillets Seyed	[140]
Eugenol	Gelatin-chitosan	Solvent evaporation	Antibacterial and antioxidant activities.		Chilled pork	[141]
Laurus nobilis leaf extract	Liposome	Nanoemulsion	Oxidative, microbial, bacterial and sensory properties.		Minced beef	[142]

5.2. Food Packaging

Active chemicals, such as antimicrobials or antioxidants, can be added to packing material and gradually diffuse into the food for a longer-lasting effect. Unfortunately, many active agents are challenging to include directly in biopolymer-based films due to their volatile nature, difficulty dissolving in water, chemical instability, matrix incompatibility, or impacts on film properties. The resulting encapsulated active compounds can subsequently be integrated into food packaging materials to alter their functional performance [143].

Different nanoencapsulated systems associated with essential oils were used in the preparation of antibacterial packaging (Table 4), such as nanofiber film for beef packaging, containing tea tree oil (TTO) complexed in beta-cyclodextrin (β-CD) [144]. The antibacterial test of plasma-treated TTO/CD-inclusion complex poly(ethylene oxide) (PEO) nanofibers demonstrated a sustained antibacterial action on beef after seven days of storage, which is in line with the practical applications of TTO/-CD-inclusion complex PEO nanofibers [144]. The film-based Ziziphora clinopodioides-Rosmarinus officinalis essential oil encapsulated in sodium alginate (NaAlg) nanoparticles might effectively decrease bacterial growth and oxidative or sensory degradation of lamb patties during storage. Nanoparticles also successfully reduced the development of the patties' discoloration and foul odor [145]. Chrysanthemum essential oil encapsulated in chitosan successfully extended the shelf life of beef combined with its delayed release and antibacterial properties, thus having a broad prospect in food packaging [146]. The authors of [147] developed packaging containing essential oils from *Ocimum gratissimum* L. and *Ocimum basilicum* L. encapsulated in PLA nanofibers. This study evaluated the antifungal and antiocratoxigenic activities against A. *niger* of PLA nanofibers containing essential oil, and the impact of these packages on the physicochemical characteristics, freshness, and shelf life of table grapes. As a consequence, the created active packaging offers promise and may be acceptable for use in fruits.

Table 4 shows how phenolic chemicals, flavonoids, and vitamins were employed in conjunction with encapsulating structures to create food packaging. Thymol electrospun with polylactic acid (PLA) and poly(-caprolactone) (PCL) showed controlled release antioxidant and antibacterial potential as active food packaging [148]. M.H. Alvarez-Hernandez et al. (2021) evolved an antifungal energetic packaging and a C_2H_4 scavenger for cherry tomatoes, containing thymol encapsulated in chitosan. The C_2H_4-scavengers had been found to be beneficial in controlling postharvest fungal sicknesses as well as keeping fruit pleasant [149]. Many foods include lipids or proteins that are susceptible to oxidation, which can alter the nutritional content, shelf life, and quality. A film comprising solid lipid nanoparticles encapsulated in alpha-tocopherol, for example, displayed improved antioxidant capability, and controlled release of -tocopherol established its potential as active packaging for food preservation [150]. Recently, Y. Lei et al. (2023) demonstrated the possibility of creating an innovative kind of intelligent colorimetric film using pectin, sodium alginate, cellulose nanocrystals, and anthocyanins produced from red cabbage (RCA), that may be utilized for real-time shrimp freshness monitoring [151].

Table 4. Example of nanoencapsulation systems associated with bioactive compounds used in food packaging.

Agent	Nanoencapsulation System	Preparation Technique	Biological Activity	Reference
Pomegranate peel	Alginate	Emulsification	Antimicrobial	[136]
Tea tree oil	Beta-cyclodextrin (β-CD)	Co-precipitation	Antibacterial activity	[144]
Chrysanthemum essential oil	Chitosan	Electrospinning	Antibacterial	[146]
Essential oil (*Ocimum basilicum Ocimum gratissimum*)	Polylactic acid	Solution blow spinning	Antifungal activity-antiocratoxigenic activity	[147]
Thymol	Polylactic acid Poly (ε-caprolactone)	Electrospinning	Release behavior, antibacterial activity, antioxidant activity	[148]
Thymol	Chitosan	Emulsification	Antifungal	[149]
α-tocopherol	Solid lipid nanoparticles	High homogenization technique	Antioxidant	[150]
Anthocyanins	Pectin, Sodium alginate, Cellulose nanocrystals	Hydrogel film	Antioxidant activity	[151]
Garlic essential oil	Liposomal, chitosan	Thin-layer hydration-sonication	Antioxidant activity, Microbial and chemical changes	[152]
Oregano essential oil (Carvacrol)	β-cyclodextrin	Kneading	Controlled EO release, antioxidant activity	[153]
Gallic acid	Hydroxypropyl methylcellulose	Electrospinning	Antioxidant activity	[154]
Phycocyanin	Polymers (PLLA: PVA)	Electrospinning/electrospraying	Antioxidant activity	[155]
Cinnamodendron dinisii essential oil	Chitosan-zein	Precipitation/casting method	antioxidant activity and antimicrobial activity	[156]
Anthocyanins	Chitosan/Alginat/Protein	Electrospinning	Antioxidant/antibacterial	[157]
Clove essential oil	Protein (ZEIN-sodium caseinate)	Modified antisolvent precipitation	Antimicrobial, antibacterial activity	[158]

Table 4. *Cont.*

Agent	Nanoencapsulation System	Preparation Technique	Biological Activity	Reference
Eugenol	Poly (lactic acid)/nanoparticles (MgO and ZnO/Gelatin	Electrospinning	Antioxidant activity, Antibacterial activity	[159]
Mentha spicata L. essential oil	Protein (Sodium caseinate)/MgO nanoparticles	Electrospinning	Antimicrobial activity	[160]
Cuminaldehyde	Hydroxypropyl-β-cyclodextrin	Electrospinning	Antibacterial	[161]
Coconut oil and solid hydrogenated palm oil (cinnamaldehyde, eugenol, and thymol)	Solid lipid nanoparticles	Nanoemulsion	Antifungal (*Rhizopus stolonifer*, *Alternaria* spp., and *Aspergillus niger*)	[162]
Cinnamon and oregano essential oils	Chitosan/polyvinyl alcohol/b-cyclodextrin	Electrospinning	Antifungal activity	[163]

5.3. Dietary Supplements/Nutraceuticals and Functional Foods

Nanoencapsulation systems containing natural bioactive compounds and nutrients as nutraceuticals or pharmaceuticals, such as phenolic compounds, carotenoids, essential oils, essential fatty acids, vitamins, and others (minerals, enzymes, and pre/probiotics), can be used as a favorable technological approach to produce functional foods, supplements, and drugs [102]. A brief overview of nanoencapsulation studies of natural bioactive compounds and nutrients through various nanoencapsulation techniques and systems is provided in Table 5.

In the food industry, encapsulation has been studied, particularly in the creation of nanoencapsulation systems for phenolics, antioxidants, and phytochemical substances. For example, Hadavi et al. (2020) and Dehcheshmeh and Fathi (2019) discovered that nanoliposomes and tragacanth/zein nanofibers enhanced saffron's water solubility and thermal stability, respectively [164,165]. Jain et al. (2021) effectively manufactured whey protein isolate nanospheres using an electrospray technique to increase the stability and antidiabetic activity of bioactive component extracts [166]. Liu et al. (2020) and Drosou et al. (2022) constructed liposomes and pullulan/whey protein isolate based on an ethanol injection and coaxial electrospinning methods, respectively, which enhanced the storage stability and bioavailability and provided excellent protection through β-carotene against simulated gastrointestinal environments. All these reports suggested that suitable encapsulation systems could be essential to improve the bioaccessibility and thereby the in vivo efficacy of phenolics and antioxidants [138,167].

Some researchers have shown the ability of nano-formulations to load phenolic compounds and antioxidants investigated as dietary supplements/nutraceuticals or functional foods. As an example, a study by Peng et al. (2018) and Zheng et al. (2018), designed a stable and sustained-release nanoencapsulation system for curcumin through small lipid particles. It was indicated that the developed nanoemulsions gave bioaccessibilities that were similar to those of the best commercial formulation tested [168,169]. Furthermore, Bateni et al. (2022) studied the effects of nano-curcumin supplementation on oxidative stress, systemic inflammation, adiponectin, and NF-κB in patients with metabolic syndrome. They claimed that in a 12-week supplementation with 80 mg/day nano-micelle, curcumin improves mean malondialdehyde, total antioxidant capacity, and adiponectin [170]. Mauri et al. (2021) incorporated hydroxytyrosol in nanogels prepared with polyethylene glycol/polyethyleneimine. They showed that the nanogels do not induce oxidative stress, thus demonstrating their biosafety, and exhibit good therapeutic effects against hepatic steatosis, a significant decrease in the intercellular triglyceride levels, and restoring cell viability [171]. On the other hand, Li et al. (2018) and Jiang et al. (2022) revealed that the antioxidant capabilities of typical flavonoids such as quercetin and catechin can be increased by loading into nanofibers and nanoparticles. The resulting nano-formulation exhibited excellent dietary performance and good antioxidant capacity that was superior to nonencapsulated flavonoids and displayed a sustained release in an in vitro experiment [172,173].

The nanoemulsions produced using caseinate showed the highest oxidative stability, improved stability during in vitro digestion, and reduced the rate of lipolysis of fish oil emulsions. Raeisi, et al. (2019) constructed Persian gum-chitosan based on an electrostatic layer-by-layer deposition method, which enhanced the physicochemical characteristics and thermal stability of co-encapsulated fish oil/garlic essential oil [174].

Another group of nutrients applied in nano-formulations is vitamins. As an example, Zhang et al. (2022) and Xiang et al. (2020) encapsulated vitamin D3 within nanoparticles that improved storage stability and sustained release in simulated gastrointestinal digestion [175,176]. Furthermore, Baek et al. (2021) nanoencapsulated vitamin C with cellulose/chitosan nanocapsules; they claimed that these novel nanocarriers enhanced stability, antimicrobial activity, and vitamin release [177]. In another study, Parthasarathy et al. (2016) revealed that the oral bioavailability of vitamin E in nanoemulsion form was enhanced in vivo, with a 3-fold increase over the conventional emulsion [178]. Resende et al. (2020) nanoencapsulated vitamin A. The in vitro assays simulating gastrointestinal digestion suggested that the nanoparticles are not altered in the stomach. The biocompatibility of the formulations showed no toxicity in fibroblasts. With the developed nanoparticles, 80% of the added vitamin reached the intestine in the digestibility assay [179].

Table 5. Nanoencapsulation of natural bioactive compounds and vitamins as nutraceutical/pharmaceutical in functional foods and dietary supplements (Vit: vitamin).

Agent	Nanoencapsulation Systems	Preparation Technique	Biological Activity	Reference
Curcumin	Saponin micelles nanoparticles	pH-driven loading method	The curcumin nanoparticles greatly increased its in vivo bioavailability.	[168]
	Corn oil/sodium hydroxide	Nanoemulsions	The developed curcumin nanoemulsions gave bio accessibilities that were similar to those of the best commercial formulation tested.	[169]
	Nano-micelle soft gel capsules	Industrial product (Exir-Nano-Sina, IRC:1228225765)	A 12-week supplementation with 80 mg/day nano-micelle curcumin improves mean malondialdehyde, total antioxidant capacity, and adiponectin in patients with metabolic syndrome.	[170]
Keto-Curcumin	Lipid systems	Nanoemulsion	Preserving the antioxidant activity and improving their stability.	[180]
Curcumin and Vit. D3	Nanoliposomes	Continuous supercritical CO_2	Improving the stability and antioxidant activity.	[181]
Quercetin and Curcumin	Micelles/casein	Vigorous shaking	Encapsulation systems revealed high entrapment efficiency and bio-protection. The cytotoxicity of co-encapsulated bioactives was higher than that of free forms.	[182]
Vitamin D3 and Curcumin	Lipid-core nanocapsules	Interfacial deposition of preformed polymer technique	Regulating inflammation and purine metabolism in a model of arthritis.	[183]
Anthocyanins	Nanocomplexes of chitosan hydrochloride/carboxymethyl chitosan	Electrostatic interaction	Encapsulated form improved the stability.	[184]
	Chitosan nanoparticles	Ionotropic gelation	Attenuates hyperlipidemic aberrations in male Wistar rats by inhibiting lipid peroxidation, increasing antioxidant enzyme activity and suppressing development of lipogenesis.	[185]

Table 5. *Cont.*

Agent	Nanoencapsulation Systems	Preparation Technique	Biological Activity	Reference
Quercetin	Cellulose nanofibers	Nano-formulations	Nano-formulation exhibited excellent dietary performance and good antioxidant capacity that was superior to nonencapsulated and displayed a sustained release in an in vitro experiment.	[173]
	Soluble soybean polysaccharide/chitosan	pH-driven encapsulation procedure	Encapsulated quercetin exhibits better biological activity and enhanced solubility in an aqueous solution.	[186]
	Chitosan/lecithin	Electrostatic deposition	The storage stability and antioxidant activity were improved.	[187]
Catechin	Nanocyclodextrin/metal/organic	Solvothermal assisted ultrasound	Improving the storage stability and exhibiting superior bioavailability.	[172]
	Starch nanoparticles	Ultrasonication treatment and homogenization	Bioactive properties were retained at a higher level upon in vitro digestion.	[188]
Epigallocatechin gallate	Double shell material chitosan recombinant soybean seed H-2 ferritin	Electrostatic interactions	Promote stabilization and absorption.	[189]
Carotenoids	TritonX100/Tween 80	Nanoemulsions	Retention of antioxidant efficiency.	[190]
β-carotene	Pure pullulan/whey protein isolate	Coaxial electrospinning	Provided greater protection against oxidative degradation under different storage temperatures. Improved stability at low humidity environments	[167]
	Long or medium chain triglycerides	Excipient nanoemulsions	Nanoemulsions have considerable potential for improving nutraceutical bioavailability from dietary supplements.	[191]
Vit.C and β-Carotene	Liposomes (lecithin, cholesterol/ phosphate-buffer solution	Ethanol injection	Improving the storage stability and bioavailability.	[192]
Hydroxytyrosol	Polyethyleneglycol/ polyethyleneimine nanogels	Multi-step procedure (activation of PEG; PEI functionalization; formation of nanogel network)	Nanogels improved therapeutic effects against hepatic steatosis (significant decrease in the intracellular triglyceride levels, restoring cell viability).	[171]
Picrorhiza kurroa extract	Pluronic-F-68 copolymer-based biodegradable PLA nanoparticles	Nanoprecipitation	Provides nutraceutical with increased suitability for better hepato-protection by enhancing intestinal absorption and bioavailability.	[193]
Phenolic extracts	Liposomes	Nanoemulsions	Protection of phenolic compounds under stomach conditions and increase their bioaccessibility.	[194]
Bioactive compounds of *Tinospora cordifolia* leaf extract	Whey protein isolate	Electrospray	Increase of 28.12% in vitro antidiabetic activity.	[166]
Saffron extract	Tragacanth/zein nanofibers	Electrospinning	Enhancing thermal stability.	[164]
Saffron	Nanoliposomes	Heating method	Increase solubility.	[165]
Fucoxanthin	Casein/chitosan	Homogenization, and injection into the electrospray system	The nanomaterial improved water solubility and bioavailability.	[195]
Crocin, Safranal/Picrocrocin	Pectin/whey protein/water–oil	Nanoemulsions and nanodroplets	High storage stability and controlled release.	[196]
Fish oil	Caseinate/glycated caseinate	Nanoemulsions	Improved stability during in vitro digestion, increased oxidative stability, and reduced the rate of lipolysis.	[197]
Fish oil and Garlic essential oil	Persian gum/chitosan	Electrostatic layer-by-layer deposition	Improve physicochemical characteristics and thermal stability (excellent thermal stability of >250 °C).	[174]

Table 5. *Cont.*

Agent	Nanoencapsulation Systems	Preparation Technique	Biological Activity	Reference
Omega-3 fatty acids	Solid lipid nanoparticle	Emulsion	Enhancing the growth inhibitory effects of ω-3 PUFAs in human HT-29 CRC cells after encapsulation.	[198]
	Lipid	Nanoemulsion	Nanoparticles caused greater and more sustained formation of NO and enhanced their anti-aggregatory effects.	[199]
Probiotic strains	Starch/sodium alginate	Electrospinning	The viability rate of lactobacilli and bifidobacteria strains in the acidic environment and simulated gastrointestinal condition enhanced significantly.	[200]
Vit. D3	Ovalbumin-pectin nano complexes	Antisolvent precipitation	Enhanced storage stability and sustained release in simulated gastrointestinal digestion.	[175]
	Lipid	Nanoemulsion	Improvement of bioaccessibility, bioavailability, and stability.	[176]
	Lipid	Homogenization/sonication	Improved bioavailability.	[201]
	Oil (ethylene glycol, kolliphor-RH-40 in-water emulsion	Sonication	Increased gut bioavailability, and improved stability.	[202]
	Lipid	Hot high-pressure homogenization	Improved the oral bioavailability.	[203]
	Nano-niosomes (Span 60 and Tween 80/isopropyl alcohol)	Thin layer hydration and sonication	Increasing effects on encapsulation efficiency and antioxidant capacity.	[204]
Vit. C	Modified cellulose nanocrystal/chitosan nanocapsules	Ionic gelation	Improving the stability, antimicrobial activity, and vitamin release.	[177]
	Nanoliposomes	Thin-film evaporation	Control the stability.	[205]
Vit. B2	Alginate/chitosan	Ionotropic polyelectrolyte/pre-gelation	Increase vitamin stability and release.	[206]
Vit. B9 (folic acid)	Casein nanoparticles	Coacervation/dried using spray-drying	Preventing its release in an acid environment and promoting its oral bioavailability through in vitro and in vivo studies.	[207]
	Liposome	Proliposome/suspension	Prolonged release and solubility of folic acid.	[208]
Vit. A	Lipid nanoparticle	Organic solvent-free sonication	Biocompatibility of the formulations showed no toxicity in fibroblasts and assured oral bioaccessibility.	[179]

6. Nanoencapsulation Application in Food Safety Sensors

Food safety is directly tied to human health and societal stability. Food safety is a major concern for governments all around the world. Food preservation treatment and food quality inspection are the two critical lines of defense in the fight to maintain food safety [209]. As a result, research has concentrated on developing simple, efficient, and environmentally friendly quality inspection and preservation systems. The most prevalent food quality detection tools are presently sensory identification, microbiological detection and analysis, physical and chemical analysis, and instrumental analysis [210].

Conventional sensors include the target analyte, recognition element, signal transducer, and processor. These techniques are often limited by issues such as expensive costs, complicated detection processes, low accuracy, and long processing times [211,212]. Nanotechnology is employed to develop nanosensors and nano(bio)sensors for detecting food contaminants, changes in color, odor, texture, adulteration, and infections in food systems. Nanosensors of this type could be integrated into packaging materials. The method that a food sensor is affixed to packaging must satisfy the sensor's specifications for it to work. Several sensors, for example, must be placed so that their signal could be interpreted by the user while interacting with the food [213]. The inclusion of nanosensors into food packaging has resulted in several advantages over traditional sensors, including better sensitivity and specificity, faster analysis, higher sample throughput (multiplex systems), decreased assay complexity, and lower cost [214]. Gold nanostructures, aluminum nanoparticles, nanotubes, and some other active nanostructures have been or can be utilized as microbial or other food safety nanosensors in food packaging [215–217]. Lastly, Gallic acid-AuNP@Tollens' was used to quantify analytes in real samples. The plasmonic resonance of GA-AuNP@Tollens' was used to detect formaldehyde and benzaldehyde across a linear range of 10–150 nM and 0.15–0.75 M, respectively. Both optimization and detection were performed at 409 nm UV absorbance. The suggested approach yielded detection limits of formaldehyde and benzaldehyde of 20.08 nM and 0.12 M, respectively. For both analytes, the smartphone-based detection approach demonstrated high linearity, with an R-Square value of 0.95 [218]. Federico Mazur et al., (2020) designed a liposome-based approach for detecting *Listeria monocytogenes* via *Listeriolysin O* sensing (LLO). LLO generates pores in liposome membranes, releasing encapsulated cysteine, which causes gold nanoparticles to aggregate, resulting in an observable red-to-purple color shift. In PBS and human serum, the system had an LOD of 12.9 and 19.5 g/mL, respectively. Although the sensor's efficiency was not shown in food samples, its paper-based structure and quick test time of about 5 min make it appropriate for non-laboratory applications such as agricultural settings [219]. A similar membrane-based technique was also utilized to detect alpha-hemolysin, a toxin secreted by *Staphylococcus aureus*, in milk samples. The method was created to identify toxins in cow's milk to assist in the diagnosis of mastitis and the administration of antibiotics. The technique might potentially be used to detect the presence of contaminants in milk before it is consumed. The technique detects the toxin in phosphate-buffered saline (LOD = 3.62 g/mL) and milk (LOD = 6.62 g/mL) using PDA vesicles functionalized with phospholipids and cholesterol [220].

7. Challenges and Future Perspectives

Physical techniques of synthesis usually involve the use of costly instruments, high temperatures and pressures, and large amounts of energy. Chemical procedures sometimes necessitate the use of expensive metal salts as well as hazardous or toxic solvents [221]. Meanwhile, green approaches employ diverse biotechnological technologies to generate nanoparticles via biological pathways (microorganisms, plants, or viruses) or their byproducts (such as proteins and lipids) [222]. Green nanotechnology has sparked widespread attention due to its inherent characteristics of speed, simplicity, environmental friendliness, and low cost [223]. To accomplish the more efficient synthesis of nanocarriers, researchers can use novel technologies such as electrostatic spinning and electrostatic spraying with easy operations and moderate reaction conditions in the future.

Even though nanocomposites have been widely employed in functional ingredient delivery, food creation, and active food packaging preparation, the applications have centered on the nanoparticles incorporating nanocomposites [224]. In addition, other nanocarriers, such as nanoemulsions, nano-micelles, nanoliposomes, and nanogels, have fewer uses. There are also benefits over nanoparticles, such as increased loading capacities and absorption efficiencies [225]. The application ranges of various nanoencapsulation systems should be widened.

Nanomaterials are increasingly being used in industrial applications, including the food sector, to bring new benefits to customers and additional features. Although advantageous, improvements in nanotechnology are also linked with increased potential toxicity and ecotoxicity, owing primarily to the peculiar qualities of nanoparticles (shape, tiny size, chemical composition, structure, and increased surface area) [226]. Nanoparticles, despite their small size, may infiltrate and translocate through the circulatory and lymphatic systems, eventually reaching human tissues and organs [227]. Nanoparticles can cause irreversible cell damage through oxidative stress or organelle injury. As a result, future research should focus on nanocarrier toxicity to assure the production of safe and non-toxic nanocarriers. Many experiments have been conducted to improve the targeted release of nanoencapsulation systems in certain regions of the human body, such as the gastrointestinal system. However, the majority of these carriers have only partially accomplished the controlled release at the target site, and have simply lowered the release consumption of nanoencapsulation systems in other locations. As a result, how to reduce the loss of nanoencapsulation systems in other parts and improve the targeted recognition and stable release of nanoencapsulation systems by chemical modification/surface functionalization of nanocarrier raw materials, or preparing nanocarriers with different raw materials at the same time, remains an area of future research. Exact assessment of nanoparticle discharge into the environment and occupational exposure is challenging. Information is desperately needed to better understand nanoparticle-biological interactions and processes [228]. While a continual stream of in vitro studies points to potential paths, in vivo nanoparticle studies have failed to establish a coherent system. In vivo, examination is one step closer to therapeutic application and reflects the organism's adaption and damage more directly. Despite significant development in the field of nanotoxicology, there is still a gap between validation and evidence-based research [229]. Current toxicological tests must be modernized, and new technologies (such as proteomics, functional genomics, high-throughput screening, and metabolomics) must be progressively integrated into these investigations. These new methods will reduce the rate of false positives while also accelerating and validating the assessment of nanoparticle toxicity.

Safety and health, as well as regulatory rules, should be considered during the production, processing, active packaging, and consumption of nano-processed food items [230]. Regarding the regulatory implications of nanostructures in the food and medical industries, no formal law is established internationally. The majority of nations currently lack precise standards for assessing the danger of encapsulated nano-products. The prospects for the nanoencapsulation of bioactive compounds highlight the need for their worldwide regulation to facilitate their safe use and marketing. Various studies reporting the beneficial effects of nanostructured bioactive compounds support this trend and offer a promising future direction for research.

8. Conclusions

Nanoencapsulation of natural compounds is observed as one of the sector areas in which nanotechnology will play a significant part. The evolution of numerous processes and systems has resulted in applications with varying degrees of complexity and adaptability, with the physicochemical qualities of the bioactive component playing a role in the formulation approach. The nanoencapsulation of natural compounds has found usage in various food industries, such as incorporation into food matrices, packaging, dietary supplements/nutraceuticals, and functional foods. However, further research is necessary to understand the safety and toxicity of nanomaterials. It is also essential to develop global regulations that will promote the safe marketing of new nanotechnology products, which have the potential to improve health outcomes.

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