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Review

# Nanoencapsulation of Essential Oils as Natural Food Antimicrobial Agents: An Overview

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**Abstract:** The global demand for safe and healthy food with minimal synthetic preservatives is continuously increasing. Natural food antimicrobials and especially essential oils (EOs) possess strong antimicrobial activities that could play a remarkable role as a novel source of food preservatives. Despite the excellent efficacy of EOs, they have not been widely used in the food industry due to some major intrinsic barriers, such as low water solubility, bioavailability, volatility, and stability in food systems. Recent advances in nanotechnology have the potential to address these existing barriers in order to use EOs as preservatives in food systems at low doses. Thus, in this review, we explored the latest advances of using natural actives as antimicrobial agents and the different strategies for nanoencapsulation used for this purpose. The state of the art concerning the antibacterial properties of EOs will be summarized, and the main latest applications of nanoencapsulated antimicrobial agents in food systems will be presented. This review should help researchers to better choose the most suitable encapsulation techniques and materials.

**Keywords:** essential oils; antimicrobial activity; nanoencapsulation; food preservation



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## 1. Introduction

In recent decades, the global food loss caused by microbial spoilage has increased year by year [1]. Moreover, the recent outbreaks of foodborne diseases associated with *Escherichia coli* O157:H7, *Salmonella Saintpaul*, *Listeria monocytogenes*, and so on, have made microbiological safety a priority, especially during food processing and storage [2].

Food antimicrobial agents are chemicals which can prevent and inhibit the growth of microorganisms, and they are usually used in conjunction with other preservation procedures to extend the shelf life of foods. Currently, the main preservatives used in the food industry are chemically synthesized ones [3]. As consumer awareness increases, there is a growing concern of the potential carcinogenic and mutagenic risks associated with chemical preservatives like nitrites and parabens. “Fresher”, “more natural”, and “minimally processed” food is being demanded. In this sense, the development of alternative natural and low-toxic antimicrobial agents to replace traditional synthetic antimicrobial substances has received a lot of attention.

Essential oils (EOs) are volatile and aromatic secondary metabolites of plants, which are mainly developed for their flavor, fragrances, and biological properties. In recent years, EOs and their biologically active compounds have been widely explored for their antibacterial and antifungal efficacy against foodborne pathogens (bacteria, molds, and related toxins) [4]. However, the use of EOs in food preservation is often limited because of

their processing costs and other disadvantages, such as their low efficacy as compared to synthetic antimicrobial agents, their intense aroma, and their instability or insolubility in water. Therefore, an effective intervention system is necessary to preserve the activity of natural food antimicrobials when using them in the food industry. Nanotechnology has proven to be a useful tool for this purpose, which could provide the protection of natural antimicrobial agents against degradation, and improve the bioavailability and the target delivery of antimicrobial agents, thereby decreasing the amount of antimicrobials required for effective food preservation [3]. Hence, the application of nanotechnology in the food industry has been one of the fastest growing fields in the past few years.

Based on what has been learned so far, the aim of this review is to summarize the up-to-date account and advances concerning the potential of EOs as food antimicrobial agents. Meanwhile, the strategy for nanoencapsulation of EOs and its application in food are also discussed.

## 2. Synthetic and Natural Food Antimicrobial Agents

Food antimicrobial agents can destroy and inhibit the growth of microorganisms and consequently improve food safety for the consumers, as well as extend the shelf life of food products. According to their sources, they can be classified in two groups: synthetic antimicrobial agents and natural antimicrobial agents.

### 2.1. Synthetic Antimicrobial Agents

Although consumers have begun to worry about the safety of synthetic antimicrobials used in food products, they are still widely used in the food industry to date. The main synthetic antimicrobials used are sorbic acid and its salts, benzoic acid and its salts, parabens, propionic acid and its salts, and sodium diacetate (Table 1). They have the advantages of having strong antimicrobial activity at low concentrations, high industrial availability, and low cost, but most of the end products of their metabolism can lead to food color change and flavor and nutrient deterioration, and even endanger human health [5].

**Table 1.** Commonly used synthetic antimicrobial agents for Food.

Chemical Compound	Application Range	Mechanism of Action or Application Effect
Benzoic acid and benzoates	Particularly used in acidic foods	Destruction of bacterial cell membrane, inhibition of cell membrane absorption of amino acid and respiratory enzymes, blocking condensation of acetyl-CoA, etc.
Sorbic acid and sorbates	Dried meats and acidic foods	Binding to biological enzymes and inhibiting enzyme activity.
Paraben (Hydroxybenzoates)	Bakery products, soft drinks, cosmetic	Destruction of cell membranes, denaturation of intracellular proteins, inhibition of the activity of respiratory enzymes and electron transport enzymes.
Propionic acid and propionates	Baked products such as pastries, bread, etc.	Binding to biological enzymes and inhibiting their biological activity. They have a good inhibitory effect on molds and Gram-negative bacteria under acidic pH, especially to prevent the production of aflatoxins.
Dimethyl dicarbonate	Beverages	Passing through the cell membrane and interacting with enzymes in the microbial cells to block intracellular metabolism.
Sulfur dioxide and sulfites	Dried fruits, wine making	Hydrogen ions generated by the decomposition of sulfite can cause damage of bacterial surface proteins and nucleic acids to kill microorganisms.

## 2.2. Natural Antimicrobial Agents

“Natural antimicrobial agent” refers to natural active substances extracted from plants, animals, or microorganisms, such as polyphenols, flavonoids, tannins, alkaloids, terpenoids, isothiocyanates, polypeptides, and oxidized derivatives thereof. Based on the safety issues and the exploration of healthier and natural products, natural antimicrobial agents are more acceptable to consumers than synthetic antimicrobials [6]. The activities of some common natural antimicrobials against bacteria and fungi are summarized in Table 2. In the past few years, many researchers have conducted a large number of experiments about active substances to study their antibacterial effects. The main antibacterial mechanisms are: (i) destruction of cell membranes; (ii) complexation of metal ions; (iii) damage of the genetic material of microorganisms; (iv) leakage of cell contents; (v) inhibition of metabolic enzymes; and (vi) consumption of cellular energy in the form of ATP [7,8]. The bacteriostatic effects of these natural active substances are influenced by many factors, such as their own chemical properties (acid dissociation constant, hydrophobic/hydrophilic ratio, solubility, and volatility), target microorganisms (species, strains, and genes), environmental factors (pH, ionic strength, water activity, temperature, and atmospheric composition) and food properties (ingredients and initial bacterial amount) [8].

**Table 2.** Commonly used natural antimicrobial agents for food preservation.

Antimicrobial Compound	Main Source	Target Microorganism			Reference
		Gram-Positive Bacteria	Gram-Negative Bacteria	Fungi	
Plant Origin					
Essential oils	Thyme	<i>Staphylococcus aureus</i> <i>Listeria monocytogenes</i>	<i>Shigella sonnei</i> <i>Shigella flexneri</i> <i>Escherichia coli</i> O157:H7 <i>E. coli</i> <i>Salmonella enteritidis</i> <i>Salmonella typhimurium</i>	<i>Botrytis cinerea</i> <i>Candida albicans</i> <i>Penicillium digitatum</i>	[9,10]
	Clove	<i>S. aureus</i> <i>Bacillus cereus</i> <i>L. monocytogenes</i>	<i>E. coli</i> <i>S. enteritidis</i>	<i>C. albicans</i> <i>Trichophyton mentagrophytes</i>	[10,11]
	Cinnamon	<i>Lactobacillus delbrueckii</i> <i>L. monocytogenes</i> <i>S. aureus</i>	<i>E. coli</i>	<i>Saccharomyces cerevisiae</i>	[12]
	Oregano	<i>L. monocytogenes</i> <i>Bacillus subtilis</i> <i>S. aureus</i>	<i>E. coli</i> <i>Pseudomonas aeruginosa</i> <i>Salmonella enterica</i> <i>S. typhimurium</i>	<i>C. albicans</i> <i>P. digitatum</i> <i>S. cerevisiae</i>	[10,13]
Plant Extracts	Grape seed	<i>L. monocytogenes</i>	<i>S. typhimurium</i> <i>E. coli</i> O157:H7	<i>Candida maltosa</i>	[14,15]
	Olive leaves extracts	<i>B. cereus</i> <i>L. monocytogenes</i>	<i>E. coli</i> <i>E. coli</i> O157:H7	<i>Candida oleophila</i>	[16]
	Rosemary	<i>B. cereus</i> <i>L. monocytogenes</i> <i>S. aureus</i>	<i>E. coli</i> <i>S. enteritidis</i> <i>S. typhimurium</i>	<i>Aspergillus</i> <i>S. cerevisiae</i> <i>C. albicans</i>	[17]
Animal origin					
Lysozyme	Chicken eggs Vegetables Insects	<i>Bacillus</i> <i>Clostridium</i> <i>L. monocytogenes</i> <i>L. spp.</i>	Weak inhibitory effects	<i>Aspergillus</i> , <i>Candida</i> , <i>Fusarium</i> , <i>Sporothrix</i> , <i>Paecilomyces</i> , <i>Penicillium</i> , <i>Saccharomyces</i> .	[18]
Lactoferrin	Milk	<i>B. cereus</i> <i>Bacillus stearothermophilus</i> <i>L. monocytogenes</i>	<i>E. coli</i> <i>S. enteritidis</i> . <i>Klebsiella spp.</i> <i>S. enteritidis</i>	No effect	[18]
Chitosan	Shellfish	<i>S. aureus</i> <i>L. monocytogenes</i> <i>B. cereus</i>	<i>S. typhimurium</i> <i>Yersinia enterocolitica</i>	<i>Aspergillus flavus</i> <i>S. cerevisiae</i> <i>Zygosaccharomyces bailii</i>	[19]

Table 2. Cont.

Antimicrobial Compound	Main Source	Target Microorganism			Reference
		Gram-Positive Bacteria	Gram-Negative Bacteria	Fungi	
Microbial origin					
Natamycin	<i>Streptomyces natalensis</i>	No effect	No effect	<i>Penicillium candidum</i> <i>Aspergillus. flavus</i> <i>S. cerevisiae</i> <i>Byssoschlamys nivea</i> <i>Hemerocallis fulva</i> <i>Zygosaccharomyces bailii</i>	[20]
Nisin	<i>Lactococcus lactis</i>	<i>C. botulinum</i> (spores) <i>L. monocytogenes</i> <i>S. aureus</i> <i>Lactobacillus. plantarum</i>	No effect	No effect	[21]
Polylysine	<i>Streptomyces.</i>	<i>S. aureus</i> <i>Lactococcus lactis</i> <i>B. subtilis</i>	<i>E. coli</i> <i>S. typhimurium</i>	<i>Aspergillus niger</i> <i>T. mentagrophytes</i>	[22]

### 3. Essential Oils as Food Preservatives: Current Status and Challenges

Essential oils (EOs) are synthesized as secondary metabolites in different plant organs to provide protection against external factors [23]. They have strong antibacterial activity and are often used as sanitary products and cosmetics, and so on [6]. EOs are naturally derived substances that can be distilled by water vapor from different tissues of plants, such as flowers, leaves, stems, roots, and fruits. EOs are volatile, usually lipophilic, with a low molecular weight and a strong odor [23]. In addition, most of the EOs have low mammalian toxicity and are ephemeral in nature, which makes them relatively safe for the health and environment [24].

#### 3.1. Advances in Research on EOs as Antimicrobial Agent

A large body of literature has shown that EOs are proven to have antimicrobial properties, allowing them to be used for the preservation of several food products [6]. Many EOs have been tested in vitro against different microorganisms, such as bacterial cells to fungi as summarized in Table 3. The chemical constituents of plant EOs are mainly divided into four types: terpenoids, aromatic compounds, aliphatic compounds, and sulfur-containing nitrogen compounds [23]. The bacteriostatic mechanism of different components is usually not a single mode of action, but a multi-point mechanism of action [25,26]. There are two main ways in which plant EOs and their main components affect microorganisms: one is to change the morphological structure and composition of microbial cells and mycelia, such as cell membrane, cell wall, and organelles [27]; the second is to reduce or inhibit the production and germination of spores, reducing or blocking the pathogens from continuing to harm the offspring [28].

**Table 3.** Summary of the main recent studies concerning the antibacterial mechanisms and effects of essential oils (MIC: Minimum Inhibitory Concentration).

Essential Oils	Bacteriostatic Mechanism	Antimicrobial Activity
Cumin	Cuminaldehyde and cuminalcohol can destroy cell membrane	Antimicrobial activity against <i>Aspergillus flavus</i> (MIC: 650 µg/mL) [29]; cumin EOs (≥30 µL/100 mL) combined with nisin (≥0.5 µg/mL) can inhibit <i>S. typhimurium</i> ; cumin EOs (≥15 µL/100 mL) in combination with nisin (≥0.5 µg/mL) inhibited <i>S. aureus</i> [30]; inhibition of <i>S. typhimurium</i> and <i>E. coli</i> (MIC: 0.125% and 0.250%, v/v) [31].
Oregano	Caused by carvacrol and thymol	2% (w/v) oregano EOs inhibited <i>S. aureus</i> , <i>E. coli</i> , and <i>Pseudomonas aeruginosa</i> (inhibition zone diameters: 342.36, 21.53, and 9.70 mm, respectively) [32]; antimicrobial activity against <i>L. monocytogenes</i> , <i>S. typhimurium</i> , <i>E. coli</i> , etc. [33].
Lemon	Limonene inhibits cellular respiration	Antimicrobial activity against <i>C. jejuni</i> C338, <i>C. coli</i> , and <i>B. cereus</i> (inhibition zone diameter: 28.3, 35.3, and 23.7 mm, respectively) [34]; inhibition of <i>S. cerevisiae</i> MB-21, fission yeast MB-89, <i>Geotrichum candidum</i> MB-102, and <i>Pichia pastoris</i> MB-196 (MIC: 0.245~0.51, 0.06~0.25, 0.5~1.0, and 0.5~0.73 µL/mL, respectively) [35].

Table 3. Cont.

Essential Oils	Bacteriostatic Mechanism	Antimicrobial Activity
Cinnamon	Cinnamaldehyde can act on enzymes and cell wall. It can alter cell membrane permeability, inhibit ATPase activity and amino acid synthesis, and deplete proton potential energy	0.1–0.3% ( <i>w/v</i> ) cinnamon EO inhibited <i>L. monocytogenes</i> (6.0 log CFU/mL) [36]; 2.0% ( <i>w/v</i> ) cinnamon EO inhibited <i>E. coli</i> O157:H7 (2.0 log CFU/mL) [37].
Marjoram	Ethanol steroids (protein denaturation and dehydration), terpin-4-opening (destruction of cell membrane results, leakage of intracellular substances) [38]	Antimicrobial activity against <i>S. cerevisiae</i> , <i>Fission yeast</i> , <i>Geotrichum candidum</i> , and <i>Pichia pastoris</i> (MIC: 0.5–1.0, 0.0625, 0.5 and 0.5 µL/mL, respectively) [35].
Peppermint	Caused by menthone, menthol, menthyl acetate, limonene and β-pinene	Gaseous peppermint EOs inhibits <i>E. coli</i> O157:H7 (MIC: 0.625 µL/mL); inhibition of <i>S. aureus</i> , <i>Bacillus cereu</i> , <i>E. coli</i> MTCC108, and <i>Yersinia colitis</i> (0.10%: 1.3–4.8 log CFU/mL, 0.20%: 1.8–5.7 log CFU/mL, 0.25%: 0.4–2.6 log CFU/mL and 0.15%: 1.1–5.2 log CFU/mL, respectively) [39].
Clove	Eugenol can destroy the structure of cells	Antimicrobial activity against <i>S. mutans</i> (MIC: 1000 µg/mL) [40], <i>L. monocytogenes</i> (1.6–4.3 log CFU/mL), <i>L. sinensis</i> (0.2–0.8 log CFU/mL) [37].
Garlic	Organic sulfur compounds destroy cell membrane and intracellular macromolecular structure	Inhibition of <i>E. coli</i> O157:H7, <i>S. aureus</i> , <i>S. enteritidis</i> , <i>L. monocytogenes</i> , and <i>L. plantarum</i> (inhibition zone diameter: 9.3–11.36, 11.36–13.45, 8.43–10.48, 9.89–11.96, and 6.13–9.21 mm, respectively) [41].
Clary sage	Ethanol steroids (protein denaturation and dehydration), linalool (destroying cell membrane structure, inhibiting Gram-negative bacteria), caryophyllene (inhibiting Gram-positive bacteria) [35]	Antimicrobial activity against <i>S. cerevisiae</i> , <i>Fission yeast</i> , <i>Geotrichum candidum</i> , and <i>Pichia pastoris</i> (MIC: 0.5–1.0, 0.375–0.875, 1.0, and 0.5–1.0 µL/mL, respectively) [35]; 20,000 µg/mL EOs prolonged the lag phase of <i>E. coli</i> (3.20–6.40 h) and inhibited <i>L. monocytogenes</i> [42].
Rosemary	Camphor and eucalyptus oil have an oxidizing effect and enhance the antibacterial activity of terpenoids	Antimicrobial activity against <i>S. aureus</i> , <i>L. monocytogenes</i> , <i>E. coli</i> , and <i>Vibrio cholerae</i> [42].

### 3.2. Challenges in the Use of EOs as Food Antimicrobials

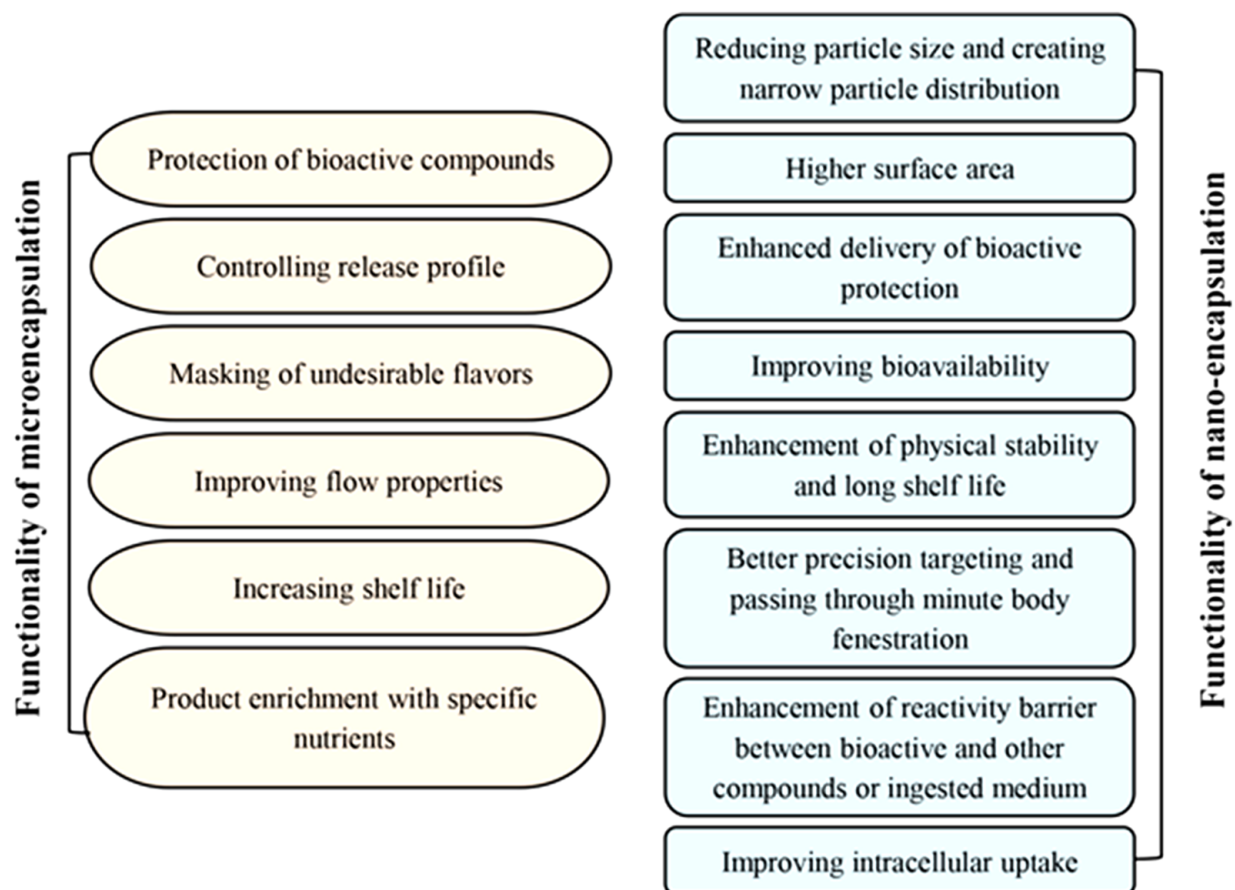
Due to their “green” nature, essential oils have received consumer attention for their use as a substitute for traditional food preservatives, which is a considerable market. However, EOs have a variety of internal and external critical challenges hindering their process as food preservatives: (i) EOs normally have low solubility in aqueous mediums and the reached concentrations are not able to exert significant biological activities; (ii) the scarcity of raw materials means that the quantity of EO obtained after extraction is generally insufficient for commercial applications; (iii) the high processing cost are also some of the major challenges; (iv) EOs are unstable due to their volatilization and oxidation, and thus are difficult to store, which may change the functional composition of active compounds (in actual production, it is necessary to rely on suitable carriers or adopt appropriate methods to achieve good antibacterial and fresh-keeping effects); (v) some EOs have a strong aroma even at low doses (in food systems, EOs can bind to lipids, proteins, and carbohydrates, so for a certain dose to achieve antibacterial effects, it may have a negative impact on food sensory qualities) [29]; and (vi) the collection and identification of plants, as well as the quality of raw materials, require a more systematic evaluation, especially safety assessment.

There is still a lack of systematic research on the effects of plant EOs and their main components on the quality of food, fruit, and vegetable flavor [43]. Until now, most of the current studies are studying EOs as a whole or selecting single components in EOs. However, there are few studies about the interactions between various components and different EOs. Most of the research is carried out in the presence of a single microorganism and constant environmental conditions [26]. There are few studies on the coexistence of various microorganisms and the mode of action in food systems, because temperature, moisture, pH, and other factors in food products have a certain influence on the bacteriostatic effect and can be a barrier factor. Therefore, it is necessary to conduct an in-depth study on the synergistic antimicrobial effect of the barrier factors [25].

The main challenges of using EOs as food-preserving agents can be overcome to some extent by using nanoencapsulation, rather than applying the EOs directly to food products as free antimicrobials. The incorporation of EOs into nanosized encapsulation systems can significantly improve their physical properties, such as dispersibility, dispersion stability, turbidity, and viscosity, and thus promote their functional activities, in comparison to free EOs [44]. Moreover, nanoencapsulation can also be used to protect EOs against oxygen, light, pH, moisture, and degradation during processing and storage; to improve the solubility of lipophilic compounds in aqueous media; to mask unpleasant taste and aroma; and to release them in the desired location at an appropriate rate through efficient design of the capsules and proper selection of wall materials [45].

#### 4. Nanoencapsulation versus Microencapsulation

In order to enhance the applicability of active compounds for food products, or to protect them against deteriorating environmental conditions, encapsulation is considered a viable alternative [46]. In general, encapsulation is defined as a carrier matrix in which a bioactive substance is entrapped, which allows one to control the rate of bioactive release [47]. A comparison of the functionality of micro- and nanoencapsulation has been reported by [48], as shown in Figure 1.



**Figure 1.** Advantages of nano- and microencapsulation [48]. Reprinted with permission from Ref. [48]. Copyright 2018 Elsevier.

Particle size has been shown to be an important factor affecting the functional characteristics of capsules [49]. Nanoencapsulation is considered to be the use of a carrier with a size of less than 1 micron (1000 nm), possessing different properties than ordinary encapsulation. According to some specific regulations, however, particularly in the pharmaceutical field, the size of carriers should be less than 100 nm for them to be considered

as nanocapsules [50]. The nanometric size of delivery systems can increase the surface area and consequently the dispersion in the food matrices. They are easier to disperse and to suspend in water to form uniform and stable colloidal suspensions and may have good sustained-release effects in comparison to microsized delivery systems. Based on their smaller size, nanocapsules have the potential to increase the passive cellular absorption mechanisms, promoting the effective release of active substances inside the target cells, and consequently increasing the efficiency of active substances and their bioavailability. Meanwhile, nanoparticles may penetrate into the tissues (such as the liver) through the capillaries, and are absorbed by the cells in the tissues; thus, the active substance can be efficiently delivered to the target cells in the body [51]. In the case of emulsions-based delivery systems, there are some interesting physical properties that can be used to distinguish nano- and microemulsions. Microemulsions generally exhibit multiple scattering of visible light, which means they have an opaque white appearance. Conversely, nanoemulsions are much smaller than visible wavelengths, and therefore, appear almost optically transparent [52]. This character can be considered as a very advantageous feature for nanoemulsions in the beverage industry.

Despite the numerous technologies for the encapsulating of biologically active compounds which have been studied, only a few techniques, namely spray-drying and freeze-drying, are widely applied in the food industry [53]. Typically, emulsification technology is the first step of encapsulation. There are two types of emulsification techniques used to produce encapsulation systems: a top-down approach and a bottom-up approach. The top-down methods involve changing large structural materials into small structures by reducing the size, and shaping the structure through external mechanical destructive forces. Top-down methods generally include high-pressure homogenization, microfluidization, and microchannel homogenizers [48]. They are commonly used for the encapsulation of hydrophilic and hydrophobic compounds, but have less control over the particle size and structure of the produced emulsion, and are only suitable for a limited type of matrix [54]. The bottom-up approach generally includes self-assembly, phase inversion, and spontaneous emulsification, which are affected by factors such as pH, temperature, concentration, and ionic strength. Meanwhile, low-energy methods are also used as preparatory steps for other nanoencapsulation methods (e.g., spray-drying, complex coacervation, extrusion, electro-spinning, and electro-spraying [55]). They allow better control of the properties of the capsules and consume less energy. However, low-energy methods require large amounts of stabilizers and are used with limited types of oils and surfactants. [56]. Various techniques for encapsulating have been proposed in the literature, but none of them can be considered as standard and suitable for the encapsulation of all biologically active compounds [55]. However, the best strategy could be selected according to the properties of the core compound and the encapsulated material, including their molecular weight, polarity, solubility, particle size distribution, and food matrix composition.

To date, for microencapsulation, a number of methods have been developed. However, for nanoencapsulation, the method is more complex than those used for microencapsulation [48]. Table 4 summarizes the commonly used encapsulation techniques to encapsulate active substances and lists some recent research reports about nano- and microencapsulation.

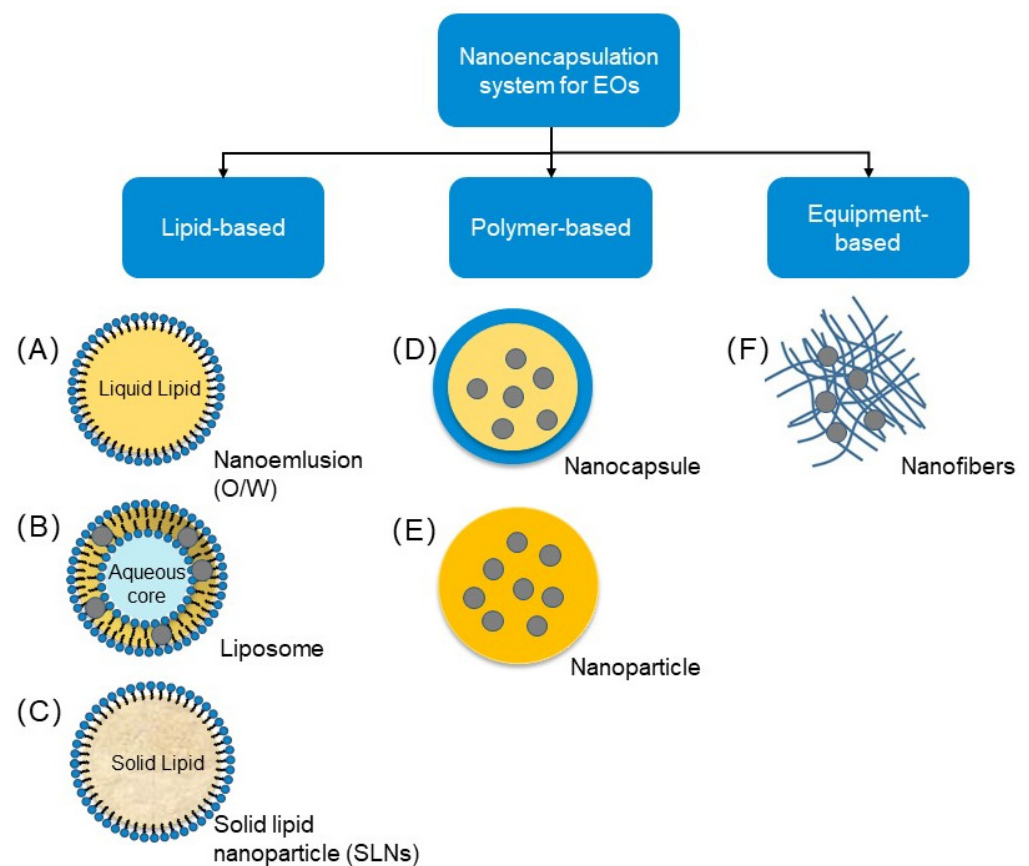


**Table 4.** Summary of recent studies on micro- and nanoencapsulation of food bioactive compounds.

Encapsulation Method	Description	Nanoencapsulation	Microencapsulation
Emulsification	Emulsification is a process of mixing two immiscible solvents, and the resulting product is referred to as an emulsion. It can be divided into top-down approaches (high-shear stirring, high pressure homogenization, microfluidization, and ultrasonication) and bottom-up (phase inversion temperature, emulsion phase inversion, and spontaneous nanoemulsification) approaches.	Vitamin E encapsulated by Tween-80 [57]; vanillin encapsulated in poly (lactic-acid) nanoparticles [58]	Curcumin encapsulated by Tween 80 and polyglycerol polyricinoleate [59]; lycopene encapsulated in plant (soy and pea) or dairy (whey and sodium caseinate) proteins [60]
Spray drying	The basic theory of spray-drying is to feed the liquid into a drying chamber in the form of tiny droplets containing biologically active compounds, supplying hot air to the drying chamber, forming microcapsules in the drying chamber, and recovering them through a cyclone.	Folic acid encapsulated by whey proteins and resistant starch [61]; curcumin encapsulated by chitosan/Tween 20 [62]	Propolis extracts bioactive compounds encapsulated by maltodextrin matrices with or without nature gums [63]; cocoa volatile compounds encapsulated by maltodextrins and modified starch [64]
Freeze drying	The basic principle of freeze-drying is to freeze water contained in a solution or suspension and then evaporate the water molecules from the solution or suspension.	Fish oil encapsulated by poly-ε-caprolactone and Pluronic F68 [65]	Blackberry by-product extract encapsulated by maltodextrins [66]; flaxseed oil encapsulated by sodium alginate, whey protein, and maltodextrin [67]
Extrusion	Extrusion technique involves the injection of a bio-based solution into another solution to promote gelation and produce a hard and dense encapsulation system.	Seed oils encapsulated by sodium alginate and high methoxyl pectin [68]	Canola oil encapsulated by alginate and high methoxyl pectin [69]; quercetin encapsulated by carnauba wax, shellac, or zein [70]
Complex coacervation	Coacervation is a well-known implemented technique to produce micro- and nanosystems. The basic mechanism is the formation of an emulsion by electrostatic attraction between oppositely charged molecules to produce the encapsulating structure.	Folic acid encapsulated by casein nanoparticles [71]; anthocyanins encapsulated by whey protein isolate and beet pectin [72]	Algal oil encapsulated by soy protein isolate and chitosan [73]; β-carotene encapsulated by casein and gum tragacanth [74]
Electro-spinning and electro-spraying	They are two modes of electrohydrodynamic processes that use a charged jet to rotate or spray a polymer solution to produce fibers or particles.	Rose hip seed oil encapsulated by zein prolamine fiber [75]; β-carotene encapsulated by zein prolamine fiber [76]	D-limonene encapsulated by seed gum and tween 20 [77]; fish oil encapsulated by a composite zein fiber [78]

## 5. Main Strategies for Nanoencapsulation of Essential Oils

Nanoencapsulation has promising applications to solve the existing problems of essential oils (EOs), since it has been shown to be an effective means to enhance the stability of EOs against degradation during storage, mask unpleasant taste, and release the antimicrobial at a controlled rate [44,79]. In this review, data surveys in the literature have found the most applied methods for essential oils and various types of nanocarriers, which are summarized in Figure 2. According to the different encapsulating materials, they are mainly divided into two categories: lipid-based nanoencapsulation systems and polymer-based nanoencapsulation systems. In addition, some nanoencapsulation of antimicrobial agents can be implemented with specially developed equipment, such as electro-spinning, electro-spraying, and nanospraying dryer.



**Figure 2.** Schematic representation of the different nanoencapsulation systems for EOs.

### 5.1. Biopolymer-Based Nanoencapsulation

Biopolymers are widely used as a wall material for the encapsulation of antimicrobial agents. Various sources serve as the origin of the biopolymer, which can be used in its native form or modified to acquire certain required properties. In general, EOs can be encapsulated in food-grade biopolymers such as proteins (whey proteins, caseins, zein, gelatin, etc.) and polysaccharides (starch, chitosan, cyclodextrin, pectin, alginate, etc.), as well as derived composite materials [2]. Biopolymer-based nanoencapsulation can produce nanocapsules (Figure 2D) or nanospheres (Figure 2E). In nanocapsules, the oily core is surrounded by polymer walls, while nanospheres are matrix systems in which the core is dispersed in the polymer matrix [80]. Several different technologies are normally used for the production of nanocapsules or nanospheres, such as complex coacervation [71], freeze-drying [81], spray-drying [61], and ionic gelation [82].

#### 5.1.1. Polysaccharide-Based Biopolymers

Polysaccharide-based biopolymers can be classified as homopolysaccharides or heteropolysaccharides depending on the number and types of monosaccharide units constituting the chain. Because of the different chemical properties of the monosaccharide units, the polysaccharides also have different degrees of polymerization (unit monosaccharide number), molecular weight, hydrophobicity/hydrophilicity, electrostatic charge, gelation properties, and viscosity, which are different from each other. Polysaccharides used for encapsulation usually have the following advantages: low toxicity and low cost, high stability in a wide pH range, and good biodegradability [81].

Cyclodextrins (CDs) are cyclic oligosaccharides with a truncated cone shape and are derived from starch, which is a traditional wall material used to prepare nanocapsules [83]. In this process, the inner side of  $\beta$ -cyclodextrin is an inner wall of a cavity formed by a combination of a hydrophobic epoxy group and a C-H bond, and the outer side of the

ring is a primary alcoholic hydroxyl group on C<sub>6</sub>, which exhibits a hydrophobic inner side and a special structure of the outer hydrophilic structure. The molecular structure can form an inclusion complex with many guest molecules, and the core material is coated in the cavity, which can slow down the reaction with the control of light and oxygen. Meanwhile, β-cyclodextrin can mask the pungent odor of some oils, compared with other wall materials. Lee et al. [84] used β-cyclodextrin as a cryoprotectant to prepare eugenol nanocapsules by the emulsion diffusion method. The morphology and structure of the nanocapsules were analyzed by scanning electron microscopy. The results showed that β-cyclodextrin can be used as a cryoprotectant to maintain the physical stability of eugenol and protect eugenol from freezing damage [85].

Chitosan (CS) is a cationic polysaccharide found in nature, which is obtained by deacetylation of chitin. CS is suitable for the preparation of nanocarrier systems because of its biodegradability, pH sensitivity, and easy chemical modification [86]. Although chitosan nanoparticles can be prepared by different methods, ionic gelation is the most widely used method. The method is simple and mild, and the activity of the encapsulated substances can be maximized. Mohammadi, Hashemi et al. [87] prepared chitosan nanoparticles (125–175 nm) by this method, and their results showed that encapsulated EO improved stability and enhanced antifungal activity against *Botrytis cinerea*. In another study, ionic gelation, applied to prepare O/W emulsion, was carried out to obtain chitosan nanoparticles enclosing thyme essential oil [88].

Starch is an interesting renewable polysaccharide and one of the main sources of glucose in the human body. Moreover, the modifications of its physical, chemical, or biochemical characteristics can impart a variety of unique properties to this biopolymer. Therefore, starch and/or its derivatives are often used for the encapsulation of active substances such as carotenoids and essential oils [89]. Chin et al. [90] obtained starch nanoparticles (300–400 nm) by dissolving sago starch in NaOH/urea, adding the obtained starch solution dropwise to absolute ethanol under magnetic stirring, and centrifuging the obtained suspension.

### 5.1.2. Protein-Based Biopolymers

Proteins are promising nanocarriers for delivery purposes due to their interesting functional properties: their molecular structures are dependent on their amino acid sequence and environmental factors such as pH, ionic strength, temperature, good emulsifying capacity, solubility, stability, and so on, as well as their ability to modify the texture, the flavor, and the color of the food matrices into which they will be incorporated [2].

Casein is an amphiphilic protein that has a strong tendency to spontaneously self-assemble into micelles in aqueous solution, and it can also interact with other proteins or organic compounds to form micellar complexes. Casein or caseinate have been found to be of valuable use as nanoencapsulating natural biopolymers due to their balanced hydrophobic and hydrophilic amino acid moieties. Zimet et al. [91] self-assembled omega-3 polyunsaturated fatty acids and casein to prepare nanomicelles with a particle size of 50–60 nm. Narayanan et al. [92] used a polylactic acid-glycolic acid copolymer to assemble with casein to prepare nanoparticles with a distinct core-shell structure. In another study, the authors used casein micelles and nano-gold particles to obtain casein-nano-gold-conjugated nanoparticles with a particle size of about 200 nm [93]. The interactions between iron oxide nanoparticles and casein micelles were also studied to prepare iron oxide/casein composite nanoparticles with an average particle diameter of 38 nm [94].

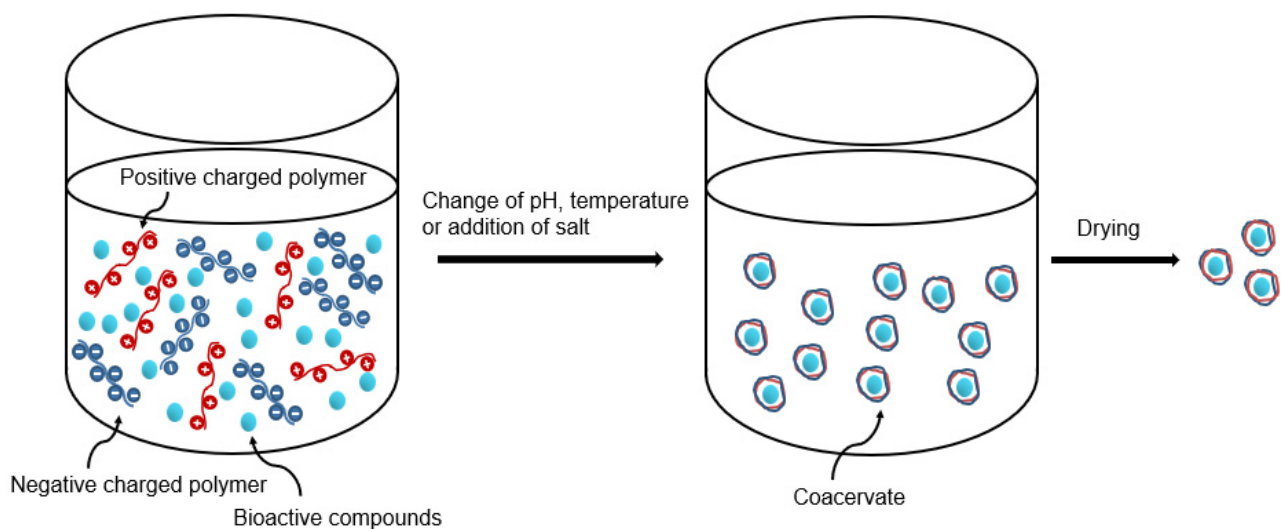
Zein is a group of prolamins that are insoluble in water. It has both hydrophilic and lipophilic properties and good biocompatibility. Its hydrophobic region can be polymerized into colloidal particles with a diameter of 50–550 nm. Using the phase separation technique, [95] encapsulated three essential oils—oregano, red thyme and cassia seed essential oils—into zein nanospheres. Whey proteins have been reported as an effective encapsulation system for different hydrophobic antimicrobial agents, and they were widely used in the design of protein-polysaccharide complex systems [96]. Polysaccharides-protein

encapsulation systems are more valuable than pure single biopolymer systems because of their higher chemical and colloidal protection. Ghasemi et al. [97] embedded orange peel oil into whey protein and pectin matrices by complex coacervation. Their results showed that the obtained nanocomposites had particle sizes of 360, 182, and 185 nm at pH 3, 6, and 9, respectively. Encapsulating materials based on complexed biopolymers are discussed in the next section.

### 5.1.3. Complexation of Biopolymers

The combined use of various biopolymers provides different functions and promising properties compared to a single biopolymer [98]. Biopolymer nanoparticles can be synthesized from food-grade biopolymers by self-association of individual biopolymers or by phase separation in biopolymer mixtures [99]. The ability to control and modify the interactions involved can help food technicians in designing new molecular structures to develop foods with more desirable structural properties.

Among the cited techniques, the most widely used to prepare nanocapsule systems is the complex coacervation method, as shown in Figure 3. Two kinds of polyelectrolytes with opposite charges are used as the wall material, and the core material is dispersed in the wall material solution. By changing the pH value, temperature, and concentration of the solution, or by adding an inorganic salt electrolyte to modify the electrostatic interactions in the system, the solubility of the wall material can be reduced to form nano/microcapsules. The commonly used polyelectrolytes are oppositely charged proteins and polysaccharides, such as gelatin, gum Arabic, carboxymethyl cellulose, alginate, chitosan, and polylysine. To obtain stable complexes, it is important to control the environmental conditions to form oppositely charged polymers with sufficient intensity of ionic interactions. The process of the complex coacervation method is relatively mild. Esfahani et al. [100] successfully prepared nano-sized fish oil capsules (26–114 nm) with high encapsulation efficiency using gum Arabic and gelatin.



**Figure 3.** General process scheme for capsule preparation by complex coacervation.

### 5.2. Lipid-Based Nanoencapsulation

Although biopolymer-based nanoencapsulation methods have different advantages, they do not have the potential for mass production due to the need to apply different complicated chemical or thermal processes for monitoring. Lipid-based nanocarriers have the potential for industrial production with the advantages of high encapsulation efficiency and low toxicity [101]. Lipid-based nanoencapsulation, such as nanoemulsions, liposomes, and solid lipid nanoparticles, are formed from lipid components, which are

generally biodegradable and are believed to be available in the pharmaceutical and food industries [101].

### 5.2.1. Nanoemulsions

Nanoemulsions (Figure 2A) are nanoscale droplets of a multiphase colloidal dispersion formed by dispersing one liquid in another immiscible liquid by mechanical agitation [102]. Depending on the hydrophobic or hydrophilic nature of the antimicrobial agent, an O/W or W/O emulsion system can be used to stabilize the oil-soluble or water-soluble agent, respectively. Emulsions containing nanodroplets with a size range less than 100 nm have properties different from those of conventional emulsions, especially the viscosity, color, and dispersion [52]. The emulsion stability is also different. In fact, while microemulsions are thermodynamically stable and form spontaneously, nanoemulsions are kinetically stable [103]. On the other hand, nanoemulsions are generally prepared by both top-down (high-energy) and bottom-up (low-energy) approaches, while microemulsions are produced by low-energy approaches only [104]. Top-down approaches use mechanical energy to form nanodroplets; however, low-energy methods are based on changes in process parameters, such as temperature and phase composition, to achieve nanoemulsions with less energy input [105].

For high-energy methods, the most generally used methods are high-shear mixing, high-pressure homogenization, microfluidization, and microchannel homogenization [2]. The emulsification process is divided into two stages: (i) breaking down the coarse droplets into smaller droplets, and (ii) absorbing the emulsifier onto the newly formed interface to prevent re-coalescing [106]. Nanoemulsions obtained by high-energy methods are thermodynamically unstable colloidal systems dispersed in the second phase in the form of 50–1000 nm droplets. Since the droplets of the nanoemulsions are small, they have kinetic stability under certain conditions, and phase separation, flocculation, coalescence, or precipitation in the system will not occur for a long time. Hashtjin and Abbasi [107] used ultrasonic as the external energy source, and used the response surface method to optimize the nano-emulsification of orange peel EOs. The results showed that when the ultrasonic power was 94%, the ultrasonic time was 138 s, and when the ultrasonic treatment temperature was 37 °C, the prepared orange peel EOs nanoemulsion can reach a particle size of 12.68 nm. Nirmal, Mereddy et al. [108] successfully incorporated lemon myrtle EOs (LMEO) into a water system by using ultrasonication to form a nanoemulsion. The minimum average droplet size achieved for LMEO was  $16.07 \pm 0.13$  nm, and LMEO nanoemulsions showed higher antibacterial activity than LMEO alone. For low-energy methods, the most commonly used techniques are phase inversion temperature, emulsion phase inversion, and spontaneous nanoemulsification. Nanoemulsions obtained by low energy are thermodynamically stable systems formed by the action of oil phase, water phase, and a large amount of emulsifier or surfactant. Meanwhile, the compatibility is better, and the droplets are uniform and small in size [109]. A limitation of this approach is that a large amount of organic solvent surfactant is required to prepare the emulsion, so the application of the low energy method is limited in the food field. Jun et al. [110] used Span-80 and Tween-80 as surfactants and glycerin as a co-surfactant to prepare grapefruit EOs oil-in-water type nanoemulsions. The particle size was about 21 nm, and the stability was good. Xue et al. [111] used casein and soy lecithin to finely emulsify thyme oil by nanoemulsification and obtained a thyme oil nanoemulsion with better antibacterial activity than free oil. In another study, the authors successfully prepared a thyme EOs nanoemulsion with a particle size of 150–250 nm using triglyceride as an additive [112].

### 5.2.2. Nanoliposomes

Nanoliposomes (Figure 2B) (also known as lipid vesicles) are lipid-based encapsulation carriers commonly used in foods and drugs [113]. Their structure is a phospholipid bilayer. Liposomes have many excellent properties, such as the ability to bring drugs into cells (cell targeting), biological affinity, and low drug toxicity, as well as increasing drug stability

and tolerance [114]. Compared to common liposomes, nanoliposomes can simultaneously embed two active substances with different solubilities [115]. Another important advantage of nanoliposomes is targeting, delivering and releasing their load at target sites in vivo and in vitro [116]. In order to encapsulate lipophilic antimicrobials and essential oils into liposomes, these compounds should be pre-dissolved together with the phospholipids. This procedure needs to input energy, allowing the phospholipids to aggregate to form a double-layered capsule and to obtain a thermodynamic equilibrium in the aqueous phase to attain the nanoscale size [117]. Various nanoliposome preparation techniques have been employed, including lyophilization, freezing, spray-drying, and supercritical fluid (SCF) technology [101]. Nieto et al. [118] used a membrane dispersion ultrasonic method to prepare liposome-embedded EOs, and found that the liposomes played a better role in the protection of foods, especially meat. Bai et al. [119] used ethanol injection combined with spray-drying technology to prepare liposome-encapsulated coix seed oil, thus overcoming the shortcomings of coix seed oil instability and its poor water solubility, and enhancing its absorption in the intestine. Detoni et al. [120] developed a liposome-based carrier agent for the *Zanthoxylum tinguassuiba* EO in multi- and unilamellar vesicle, and they observed that the carrier system successfully enhanced the thermal stability and bioactivity of EO. The liposome-encapsulated nisin fully inhibited the growth of *E.coli* O157:H7 at concentrations lower than that reportedly required for unencapsulated nisin.

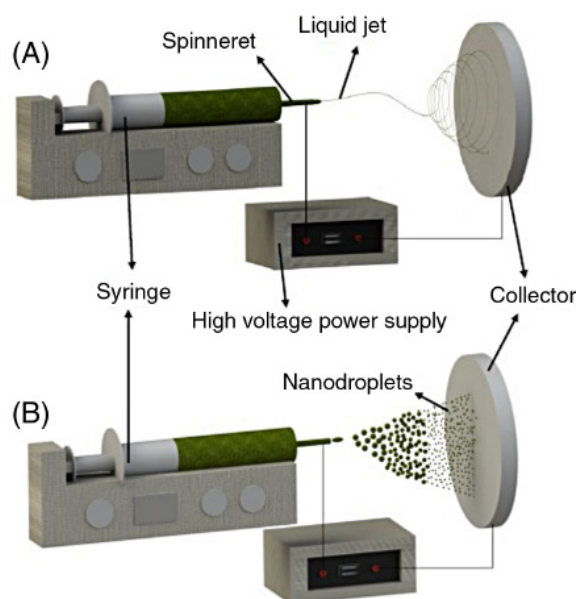
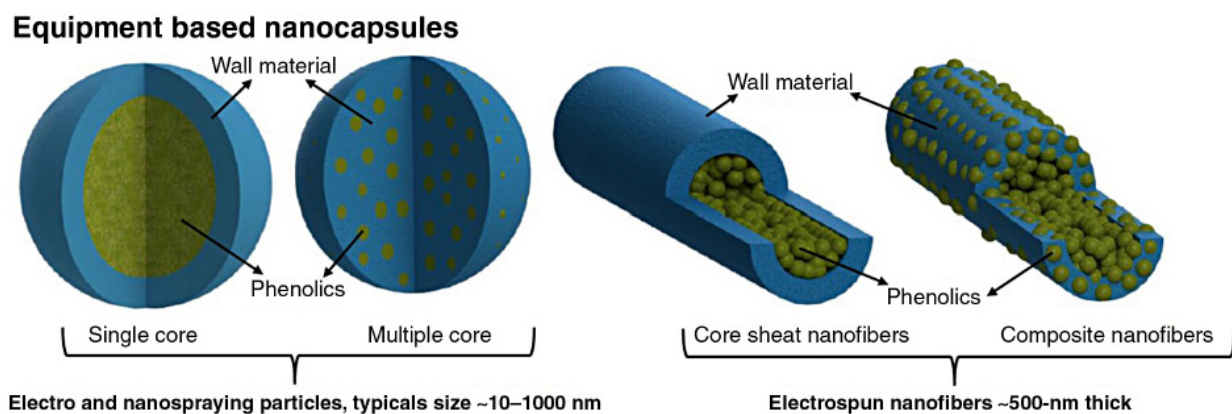
### 5.2.3. Solid Lipid Nanoparticles

Solid lipid nanoparticles (SLNs), also known as nanostructured lipid carriers, are suspensions of nano-sized solid lipid particles dispersed in an aqueous medium. SLNs (Figure 2C) are mainly prepared from solid lipids, such as fatty acids (e.g., palmitic acid), triglycerides (e.g., trilaurin), steroids (e.g., cholesterol), and partial glycerides (e.g., glyceryl monostearate) [114]. From a formulation point of view, SLNs are very similar to emulsions, but they are obtained using a lipid that is solid at room temperature to form a lipid phase, which results in solid dispersed particles rather than oil droplets. Due to the solid nature of SLNs, they have higher stability and longer storage time than aqueous liposomes [121]. The volatility and instability of EOs could be significantly reduced by SLNs systems [122,123]. Nevertheless, there are only two basic production techniques for large-scale production of SLNs in food processing: thermal homogenization and cold homogenization [124]. Nasser et al. [123] prepared *Z. multiflora* essential oil-loaded SLNs as delivery agents of eugenol using glyceryl monostearate (lipid phase), Tween 80, and Poloxamer (surfactant). Their results showed that solid lipid nanoparticles exhibited stronger antifungal activity at low doses than free oil. Prisa et al. [125] prepared cholesterol-loaded curcumin SLNs using the high-pressure homogenization method. The prepared SLNs showed a particle size range of 112–163 nm, and the drug embedding rate was up to 71%. The results have shown that cholesterol lipid structure leads to enhanced permeability of bacteria, and this can improve the antibacterial ability of curcumin.

### 5.3. Equipment-Based Nanoencapsulation

In order to encapsulate bioactive compounds, it is usually necessary to use some general equipment, including homogenizers, grinders, mixing equipment, and so on. However, certain specific requirements, such as nanofibers and nanofibrous scaffolds, can be implemented only by specialized developed equipment such as electrospinning and electrospray (Figure 4) [126]. Electrospinning and electrospray are two types of electrohydrodynamic procedures that use charged jets to rotate or spray a polymer solution to produce fibers or particles. The prospect of using both technologies in food preservation is promising due to the following advantages: amendable size with large surface area, ability to carry heat-sensitive compounds, and possibility of mass production. Electrospinning technology has been used to prepare antimicrobial nanofibers (Figure 2F) to encapsulate bacteriocin in probiotics for sustained release during food processing and storage [127]. Ghayem-pour and Mortazavi [128] successfully encapsulated peppermint essential oil into alginate

biopolymer using the electro-spraying method. Their results showed that the peppermint EOs did not degrade during the encapsulation process and showed a high encapsulation efficiency (96.4%).



**Figure 4.** Examples of equipment-based nanoencapsulation: (A) electrospinning and (B) electro-spraying [129]. Reprinted with permission from Ref. [129]. Copyright 2017 Elsevier.

## 6. Effect of Nanoencapsulation on the Antimicrobial Activity of Essential Oils

As mentioned above, the direct application of essential oils as food antibacterial agents in the food industry faces challenges such as water insolubility, physical and chemical degradation, and effects on the sensory properties of foods. In the past few decades, nanotechnology has gradually become one of the most important technologies in the food industry, especially to improve the anti-corrosion potential of EOs, which may solve these shortcomings in their application [79]. Table 5 reports the latest studies on the efficacy of encapsulated EOs and their bioactive compounds against foodborne pathogens.

Aguitar et al. [130] and Pesavento et al. [131] reported studies about the antibacterial effects of clove basil, left-handed aroma, oregano, rosemary, and thyme EOs against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Listeria*. They found the low water solubility and oxidizability of EOs reduce the antibacterial activity of EOs. It has been reported that the EOs are encapsulated by a suitable wall material to prepare nano-

sized particles, which can improve the low water solubility of the EOs and improve the stability of its biological activity, thereby improving the antibacterial properties of EOs [132]. Salvia et al. [133] found that emulsified citronella oil and clove EOs with nanoemulsification had a stronger antibacterial effect on *Escherichia coli*. Li et al. [134] studied the effect of surfactant and oil phase composition on the antibacterial activity of eugenol cyanophenol nanoemulsion. It was found that the antibacterial activity could be strengthened after nanoemulsification. In the process of nanoemulsification of eugenol, when adding the ionic surfactant (Tween-80), the antibacterial activity of the nanoemulsion is higher than that of the added non-ionic surfactant (dodecyl sulfate) during the ripening process. Moreover, the lower the amount of soybean oil added to the clove oil, the stronger the bacteriostatic action against *Escherichia coli*. Esmaeili et al. [135] used chitosan to encapsulate sesame oil into nano-sized granules to explore its sustained-release effect and biological activity. As a result, the antioxidant activity of unencapsulated celery oil was stronger than that of chitosan-embedded EOs nanoparticles, but the encapsulated EOs showed stronger antibacterial ability against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Cactus rod*, *Escherichia coli*, *Salmonella typhimurium*, and *Bacillus subtilis* than unencapsulated EOs. The same situation was observed when studying the antibacterial activity of D-limonene and oregano EOs after emulsification [136].

Compared with the free EOs, encapsulation can improve the water solubility of EOs, and when the size of EO droplets reaches the nanometer level, this helps to reduce the mass transfer resistance of the nano-scale transport system and enhances the ability of somatic cells to passively adsorb droplets of EOs, thereby reinforcing the antibacterial activity of EOs [137]. Acevedo et al. [138] found that the emulsified thyme EOs after nano-emulsification had a significant enhancement effect on the bacteriostasis of *E. coli*. Moghimi et al. [139] prepared EO nanocapsules from *thymus daenensis* by sonication. They then compared the antibacterial effect of nanocapsules on food spoilage bacteria with that of unencapsulated EO. The results showed that the minimum inhibitory concentration of EOs nanoemulsions was 0.4 mg/mL, and its antibacterial activity was 10 times that of unencapsulated EOs. Studies have found that different sizes of limonene and cinnamic acid nanoemulsions have no significant difference in the inhibitory effect on spoilage yeast or *Escherichia coli*, which was closely related to the composition of the emulsion system [12].

In addition, compared to a conventional emulsion, nanoencapsulated lipophilic antimicrobial agents are generally believed to penetrate more easily through the microbial membrane, resulting in an improved bactericidal activity. This is because the dispersion of the lipophilic antimicrobial agent in the nanoemulsion will result in an increase of the interactions with the binding sites on the targeting bacteria. It can be assumed that antimicrobial agents may more fully contact the cells and promote efficient release of the active substance in the cell, thereby providing an opportunity to increase its bioavailability and consequently enhancing the bacteriostatic effect. However, there have been results reported by Salvia-Trujillo [133] and Buranasuksombat et al. [140] which showed that the antibacterial activity of encapsulated EOs was not affected by the droplet size. These clearly controversial results suggest that a decrease in droplet size does not necessarily mean the enhancement of the function of the essential oil nanoemulsions.

**Table 5.** Efficacy of nanoencapsulated essential oils and other bioactive compounds as food preservatives.

Delivery System	Bioactive Compounds	Encapsulating Material	Techniques	Size	Major Findings	References
Nanoemulsion (prepared by low-energy methods)	Thymol	Zein-Sodium caseinate	Emulsion polymerization	65.8–87.6 nm	Compared with the control, the encapsulated thymol was more effective in lowering <i>S. aureus</i> counts during a period of 13 days	[141]
	Vitamin E	Edible mustard oil with Tween-80	Emulsion diffusion	~86 nm	High encapsulation efficiency close to 100%; the antioxidant and antimicrobial activity of nanoemulsions was improved	[57]
	Cuminum cyminum oil	Chitosan-caffeic acid	Ionic gelation	<100 nm	When tested under unsealed condition, nanogel-containing oils showed better antimicrobial activity than the free oils against <i>Aspergillus flavus</i>	[29]



Table 5. Cont.

Delivery System	Bioactive Compounds	Encapsulating Material	Techniques	Size	Major Findings	References
Nanoemulsion (prepared by high-energy methods)	Peppermint oil	Medium-chain triacylglycerol	High pressure homogenization	<200 nm	Nanoemulsions containing EO showed improved antimicrobial activity against <i>Listeria monocytogenes</i> and <i>Staphylococcus aureus</i>	[112]
	Eucalyptus oil	Tween 80	Ultrasonication	17.1 nm	Nanoemulsions containing eucalyptus showed to inactivate <i>B. cereus</i> at 0 min, <i>S. aureus</i> at 15 min, and <i>E. coli</i> at 1 h	[142]
	Essential oils (Lemongrass, clove, tea tree, thyme, geranium, marjoram, palmarosa, rosewood, sage or mint)	Sodium alginate and tween 80	Microfluidization	<20 nm	The antibacterial activity depends on the type of essential oil used in the formulation, not their droplet size	[133]
	<i>Thymus capitatus</i> oil	Soybean oil and SDS (sodium dodecylsulfate)	High pressure micro-fluidizer	~110 nm	Nanoencapsulated EO exhibited higher antibacterial inhibition diameters against <i>Staphylococcus aureus</i> compared to those formed by free EO	[143]
SLNs	Nisin	Cetylpalmitate, Softisan 378, Softisan 154, Imwitor 900 and Witpsol E85	High pressure homogenization	119 nm	The antibacterial activity of nisin-loaded SLNs against <i>L. monocytogenes</i> and <i>L. plantarum</i> was up to 20 and 15 days, respectively, while the free nisin was only 1 day and 3 days, respectively.	[144]
	<i>Zataria multiflora</i> oil	Glyceryl monostearat and Precirol®	High-shear homogenization and ultrasound	255.5 nm	<i>Z. multiflora</i> essential-oil-loaded SLNs exhibited strong antifungal activity compared to free oil against <i>Aspergillus ochraceus</i> , <i>Aspergillus niger</i>	[123]
Nanoliposome	Nisin	Soy and marine lecithin	Microfluidization	151~181 nm	Lecithin-encapsulated nisin exhibited higher stability for 6 weeks and showed better antibacterial activity compared to free nisin	[145]
	Rose essential oil	Phosphatidylcholine and cholesterol	Supercritical fluid technology	<100 nm	The liposomes formed by the supercritical process have high encapsulation efficiency and small particle size with a unimodal distribution	[146]
Polysaccharide-based	Cardamom oil	Chitosan nano-particles	Ionic gelation	50~100 nm	The encapsulation efficiency of chitosan nano-composites was more than 90%; it exhibited excellent anti-microbial potential against <i>Escherichia coli</i> and <i>Staphylococcus aureus</i> .	[147]
	Lemon ironbark oil	Cashew gum	Spray dryer	27.7~432.6 nm	Nanoencapsulated oil showed improved activity against Salmonella Enteritidis.	[148]
	Lime oil	Chitosan	Phase inversion emulsification	100~300 nm	Nanoencapsulated lime EO exhibited enhanced antibacterial activity against <i>Staphylococcus aureus</i> , <i>Listeria monocytogenes</i> , <i>Shigella dysenteriae</i> , and <i>Escherichia coli</i>	[149]
Protein-based	Thymol/carvacral	Zein	Emulsion diffusion	263 nm / 275 nm	The encapsulated EOs in zein nanoparticles can increase their solubility by up to 14 times without affecting their ability to scavenge free radicals or to control <i>E. coli</i> growth	[150]
	Thymol	Sodium Caseinate	High shear homogenization	~130 nm	Compared with thymol crystals, the encapsulated thymol exhibited significantly improved anti- <i>Listeria</i> activity in milk with different fat levels	[82]
Biopolymer-based	Eugenol oil	Whey protein and maltodextrin	High-speed homogenizer	100~300 nm	The nanoencapsulated eugenol showed improved antimicrobial activity against <i>E. coli</i> and <i>L. monocytogenes</i> than the free oil	[151]
	Terpenes mixture and D-limonene	Starch and soy lecithin	High Pressure Homogenization	100~400 nm	The addition of low dose of the nanoencapsulated terpenes can delay the microbial growth (1.0 g/L terpenes) or completely inactivate microorganisms such as <i>Lactobacillus delbrueckii</i> , <i>Saccharomyces</i>	[117]
Equipment-based	Peppermint oil	Alginate biopolymer	Electrospinning and electro spraying	~80 nm	The nanoencapsulated peppermint oil exhibited a high antimicrobial activity against <i>E. coli</i> and <i>S. aureus</i> bacteria	[128]

## 7. Applications of Nanoencapsulated Natural Antimicrobial Agents

The use of nanoencapsulated natural antimicrobial agents in food is a crucial challenge. A large number of spoilage and pathogenic microorganisms that contaminate food systems require extensive activity of the antibacterial systems [152]. The purposes of using the nanoencapsulation system in food industries include the following four: (1) stabilizing the volatile antimicrobial agents, such as essential oils, to prevent evaporation during processing; (2) reducing the interaction of antimicrobials with food substrates; (3) controlling the release rate of antimicrobial agents in food matrices to extend the exposure of microorganisms to antimicrobial agents; (4) improving the solubility of antibiotics in unhealthy foods to expand the range of applications of antibacterial drugs. It is reported that more than 400 companies have used nanoscience to manufacture food and packaging materials [153].

### 7.1. Aqueous Food Systems

The two most common beverage systems are divided into carbohydrate-based products and dairy-based products. Carbohydrate-based products, such as juices and soft drinks, normally contain a certain amount of carbohydrates, but no or only a small amount of protein and lipids. A problem with the application of antimicrobial agents to carbohydrate-based products is the incorporation of hydrophobic compounds into the food system. Dairy-based products such as milk generally contain large amounts of proteins and fats, so the interactions between antimicrobial agents and these complex food compounds and their stability during pasteurization can be a serious challenge for the food industry. Nanoencapsulation technology can be used to solve these problems. In this context, zein-encapsulated nisin and thymol oil showed better bacteriostatic effects than free antimicrobial agents after 4 h [154]. The use of nanoencapsulated thymol essential oil resulted in a prolonged effect on *Listeria monocytogenes* within seven days of shelf life at 32 °C, making the number of bacteria lower than the detectable limit in skim milk [82]. In juices, both tea tree oil and cinnamaldehyde nanoemulsions showed concentration-dependent inhibition of microbial load on inoculation [117]. Juices containing minimal concentration of nanoencapsulated terpene showed retarding microbial growth (1.0 g/L of terpene) or complete inactivation of microbes (5.0 g/L of terpene), while minimizing sensory properties [117].

### 7.2. Solid Food Systems

Nanoencapsulation technologies are also used in solid food matrices to improve uniform mixing and extend shelf life. Gökmen et al. [155] used spray-drying method to encapsulate omega-3 unsaturated fatty acid with high-linear corn starch, and added it to dough in different amounts to study its effect on bread quality. The results show that nano-capsules can effectively reduce the oxidation of unsaturated fatty acids during the bread baking process, thereby greatly improving the quality of bread products, and reducing the oxidation of harmful fatty acids and the production of harmful substances during the baking process [155]. Degnan and Luchansky [156] investigated the activity of liposome-encapsulated pediocin AcH in beef slurries. Their results showed that encapsulating pediocin AcH in liposomes can increase the recovery of pediocin activity in heated beef muscle and beef tallow pulp by an average of 27.5% and 28.9%, respectively, compared with similar beef pulp with free pediocin.

### 7.3. Active Food Packaging

In order to improve food packaging and extend the quality and freshness of perishable products, the food industry has established a new packaging system named “active packaging”. It is intended to deliberately incorporate functional ingredients that release or absorb substances from the food or food matrices [157]. In this regard, the usage of essential oils in active packaging has become a good alternative to improve the shelf life of food products [158]. Chitosan in the form of films and nanoparticles has been reported

to be used in food packaging to prevent microbial infections [159]. Chitosan nanoparticles (110 nm) have been developed and can be used as a coating by spraying directly onto the surface of apple slices to produce a discontinuous coating [160]. Compared to uncoated samples, the chitosan nanoparticle coating showed more effective antimicrobial activity against yeast and mold, as well as thermophilic and mesophilic bacteria [160]. Chitosan/pentasodium tripolyphosphate nanoparticles containing carvacrol have been shown to have antibacterial activity, with the minimum inhibitory concentration being determined to be 0.257 mg/mL [161]. This suggests that the encapsulated carvacrol in chitosan nanoparticles improved its antibacterial activity. Edible coatings based on chitosan-containing lemon oil have been successfully used to inhibit the endogenous flora present on sesame leaves, and their shelf life was extended by seven days compared to untreated samples [162].

## 8. Legislative Aspects Concerning the Use of Nanoparticles in Food Products

As shown in the previous section, food nanotechnology is applied into many aspects of the food field, such as food packaging, additives, and food preservation. Many conventional molecules used as food additives or in packaging materials can be found at nanometer scale in food products. For example, food-grade TiO<sub>2</sub> nanoparticles have been found up to approximately 40% in the nanometer range [163,164]. Although nanomaterials like TiO<sub>2</sub> nanoparticles are generally recognized as low in toxicity at conventional conditions, long-term exposure to such nanomaterials may cause adverse damages. The United States Food and Drug Administration (FDA or USFDA) and the European Commission (EC) are the main sources for legislation and regulation on food nanotechnology. A recent literature review summarized the risk assessment of the conventional particle size of substances in food products [165]. However, the development of nanotechnology in the food industry should not be blamed. Before applying nanomaterials to the food field, appropriate risk assessments can be made on the physical and chemical properties of nanomaterials and their absorption, biodistribution, metabolism, and body excretion, to alleviate the effects of nanotoxicity.

## 9. Conclusions

Consumer demand for safe natural products has driven the search for mild food preservatives in recent years. In this case, natural antibacterial agents, such as essential oils, have the potential to provide quality and safety benefits and have a reduced impact on human health, but they still have some drawbacks. The advancements in nanotechnology can protect active compounds from degradation, improve their solubility, and control their release compared to adding the antimicrobial compound directly to the food products. However, most of them are only produced on a laboratory scale because there is still a lack of systematic research. Before these natural bacteriostatic agents are widely used in the research and development of food, the following challenges need to be properly addressed: (i) a better understanding of the mechanisms of encapsulated natural bacteriostats is necessary to provide a solid foundation for engineering new antimicrobial systems and strategies; (ii) costs should be carefully evaluated, because the use of some natural antimicrobial agents is still expensive, as well as the production of nanocapsules; and (iii) future research must address the synthesis of new synergistic formulations based on EOs and their nanoencapsulation, to reduce their adverse effects on sensory properties and improve their antimicrobial efficacy in food matrices.

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