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Research progress on the composition, preparation and application of nanoemulsions

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Abstract
A nanoemulsion is a homogeneous dispersant formed spontaneously from two mutually immiscible solutions in the presence of surfactants, co-surfactants, etc. It can improve some shortcomings of its lower stability, solubility, and bioavailability due to the active substances by its own structure; more and more are used in food and pharmaceutical industries to improve product stability, utilization, shelf life and functional performance. This paper reviews the main components of nanoemulsions and describes in detail the standard methods of preparing nanoemulsions and their progress in the food field, with a view to providing references for their further application and process optimization.

Keywords: *nanoemulsion; composition; preparation; progress in application*

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I. Introduction

With the enhancement of people's health awareness, people pay more and more attention to the safety, nutritional value and efficacy of food [1]. Therefore, the food industry is searching for natural alternatives by incorporating various bioactive compounds such as polyphenols, vitamins, lipids, coenzymes and bioactive peptides in the food matrix to fulfil the demand [2-3]. However, the low bioavailability and poor stability of these compounds in the free state make it difficult to maintain their benefits over a more extended period, significantly limiting their use in the food industry [4]. To meet these challenges, encapsulation methods such as nanoemulsions, microemulsions, microcapsules, and liposomes have received wide attention. Nanoemulsions are the most widely used.

Nanoemulsion, also known as microemulsion and miniemulsion[5], is a non-homogeneous colloidal particle system consisting of at least two immiscible liquids, where one of the immiscible emulsions is aqueous and the other must be oily [6]. Nanoemulsions help maintain stability, improve physicochemical properties [7], and increase bioavailability. In addition, nanoemulsions have the advantages of small droplet size, good water solubility, homogeneous and stable system, and higher embedding rate compared to ordinary emulsions [8]. Nanoemulsions have excellent properties that form the basis for their application in the food sector. This paper reviews the main components of nanoemulsions and standard preparation methods to highlight their application in food delivery. The application of nanoemulsions in the food field is discussed. Currently, nanoemulsions are mainly used in the fields of bacteriostatic and antiseptic, improvement of food quality, food ingredient substitutes, and encapsulation and delivery of bioactive substances. The above studies were conducted to provide a basis for further application and process optimization of nanoemulsions.

II. Composition of nanoemulsion

The composition of nanoemulsions is crucial for their biostability, embedding rate, and utilization, and this paper details the main components used in their formulation.

Oil phase

The oil phase of the nanoemulsion can be a simple core or an oil solution of the functional active ingredient. The addition of the oil phase, when the nanoemulsion encapsulates a higher number of functional active ingredients, can be kept low to meet consumers' need to limit their fat intake.

Selection of oil phase

The oil phase is typically a nonpolar solvent. Certain functional active ingredients, such as carotenoids, are long-chain hydrophobic molecules that need to be dissolved in oil or other matrices first when constructing nanoemulsion systems. Commonly used oil phases include medium-free fatty acids, glycerol, and flavoured and essential oils [9]. Different oil phases have different properties, such as molecular weight, polarity, water solubility, viscosity, density, and refractive index, all of which affect emulsion particle size, stability, digestive properties, and core bioavailability [10].

Properties of the oil phase

Solubility. The solubility of the functional, active ingredient in the oil phase limits the core loading of the emulsion system and can affect bioavailability [11], so the solubility of the core is the first consideration when selecting the oil phase, and the size of solubility is related to the interaction between the functional, active ingredient and fatty acid chains. Ye et al. [12] utilized coconut oil as an oil phase to improve the solubility and antioxidant capacity of curcumin and found that the nanoemulsion encapsulated with coconut oil had a higher solubility than free curcumin and its retention was higher by about 57% or so.

Water solubility. The relative water solubility of the oil phase affects the stability of the emulsion; when the solubility of the oil phase is relatively large, such as short-chain triglycerides or certain essential oils, the formation of small oil droplets diffusion rate is faster and easier to enter the aqueous phase, the occurrence of Ostwald ripening caused the destabilization of the emulsion [13]. Lim et al. [14] constructed sweet orange oil nanoemulsions using modified starch as an emulsifier and found that the addition of ester gum to the oil phase could inhibit the Ostwald ripening. The ester gum also acted as a weight gainer to inhibit the emulsion and improve the system's physical stability.

oil viscosity. Generally, the oil phase's viscosity is larger than that of the water phase. When the viscosity increases, on the one hand, it affects the migration of the emulsifier molecules at the interface. On the other hand, the deformation time of the oil droplets in the homogenization equipment increases with the viscosity of the dispersed phase, which affects the rate and effectiveness of droplet crushing. Allied et al. [15] affected the oil phase viscosity by adding mineral oils of different viscosities and found that the particle size of the nanoemulsion was proportional to the viscosity.

Aqueous phase

The aqueous phase of nanoemulsion mainly consists of emulsifiers and co-emulsifiers, and rheology modifiers, antioxidants, metal chelating agents, and antiseptics can be added to improve product quality. The emulsifier adsorbed on the oil-water interface reduces the surface tension, reduces the energy required for droplet fragmentation, increases the resistance of droplets to flocculation and merger, and maintains the stability of the emulsion system.

Selection of aqueous phase

The aqueous phase usually consists of water but may contain polar components, including carbohydrates, proteins, co-solvents, minerals, bases and acids [16]. The type and concentration of the aqueous phase determine the polarity, phase behaviour, pH, rheological behaviour, and interfacial tension of the nanoemulsion, affecting its preparation and stability.

Properties of the aqueous phase

Aqueous concentration. The general aqueous phase concentration not only affects the conformational changes in the nanosolution droplet spacing but also causes changes in the stability of the droplets. Nandy et al [17] investigated the effect of different concentrations of polyacrylic acid on the stability of nanoemulsions and found that as the concentration of polyacrylic acid increased, the nanoemulsion droplet spacing increased and became less stable.

Aqueous phase type. Different types of aqueous phases have different properties. The nature of the aqueous phase can affect the area of the nano-emulsion single-phase region in the phase diagrams. For example, some aqueous phases contain additives such as buffers, isotonic agents, antimicrobial agents, etc., making it challenging to form nano-emulsions or slow down the formation process.

twice with ion-sputtering gold spray. The fermented bean curd was analyzed by SEM method (Quanta 250 field emission ambient scanning electron microscope, Thermo Fisher Scientific, USA), and electron microscope images of the fermented bean curd were obtained.

III. Preparation method of nanoemulsions

Low-energy technologies

Nanoemulsions can be produced using low-energy methods, which are based on the spontaneous formation of small droplets when the composition or environment of the surfactant-oil-water system is controlled [18].

Spontaneous Smulsification Method

The spontaneous emulsification method involves the emulsification of oil droplets into water containing an emulsifier under continuous stirring conditions. It is based on the mixing of the organic, surfactant, and aqueous phases, where the surfactant molecules migrate from the organic phase to the aqueous phase to form an oil-in-water system, which allows for the production of fine emulsions [20]. Spontaneous emulsification is primarily a diffusion-driven process. This method is regulated by changing the temperature without changing the composition or keeping the temperature constant while changing the interface properties and composition [21]. The method does not require any special equipment and allows the preparation of nanoemulsions under ambient conditions. Sayyar [22] et al. used lecithin as a carrier oil, Tween 80 as an emulsifier, and polyethylene glycol as a co-surfactant to prepare nanoemulsions by spontaneous emulsification method, and the experiments showed that curcumin nanoemulsions have excellent physical stability in water, and at the same time, their properties such as antioxidant effect and antimicrobial activity were significantly improved. The preparation of nanoemulsions using the spontaneous emulsification method has the advantages of low cost, health and safety, simple operation, and scalability. However, the preparation conditions of the nanoemulsion system are strict [10], and it is currently only suitable for use in the laboratory for small-batch production.

Phase Inversion Temperature Method (PIT)

In the PIT method, the hydrophilicity and hydrophobicity of nonionic emulsifiers change with temperature [23]. Surfactants are predominantly hydrophilic, and at lower temperatures (below PIT), the hydrophilic head of the surfactant is highly hydrated and more inclined to dissolve in water, with positive spontaneous curvature, forming emulsions of the O/W type. At high temperatures (above PIT), the hydrophilic head of the surfactant is less hydrated and more inclined to dissolve in the oil, with negative spontaneous curvature and the formation of W/O emulsions. When the temperature is PIT, a bicontinuous or liquid crystal phase is formed in the system, and the spontaneous curvature is close to zero. The interfacial tension reaches a minimum to form fine emulsion droplets [24]. Chuesiang et al. [25] successfully prepared an antimicrobial cinnamon essential oil nanoemulsion using the phase inversion temperature method. The nanoemulsion's strong antibacterial effect significantly prolonged the shelf life of rhubarb fish.

The phase-inversion-temperature method of preparing nanoemulsions does not require expensive equipment, but it requires the use of a large number of surfactants and is only applicable to emulsifiers whose HLB values are sensitive to temperature. This method has a narrow scope of application, so it is only applicable in nanoemulsion systems with nonionic surfactants as emulsifiers.

Phase Inversion Component Method

The phase inversion component method is used to prepare nanoemulsions by changing the ratio of components in the emulsion system to induce a phase transition in the system [10]. Safaya et al. [26] prepared neem oil nanoemulsions using the phase inversion component method using surfactant Tween 80. The hydrophilic-lipophilic value of the nanoemulsion prepared by this method is 10.7, which has bacteriostatic solid properties.

The phase inversion component method does not need to change the system's temperature, and its operation is relatively simple and suitable for mass production. However, this method requires the use of more surfactants to prepare nanoemulsions, and the prepared emulsions need to be evaluated for safety experiments.

High-energy technologies

This method requires vast energy to disrupt the dispersed phase, resulting in stable nanoemulsions. The energy demand for this destruction is accomplished by mechanical devices [27]. The size of the droplets obtained by the high-energy technology depends on the intensity of the energy.

High-pressure homogenization method

High-pressure homogenization is one of the standard methods for preparing nanoemulsions. High-pressure homogenizers usually consist of a pressure valve, a positive displacement pump, and a homogenizing chamber. Conventional high-pressure homogenizers have pressures ranging from 50 to 100 MPa and up to 350 MPa [28]. After adding the coarse emulsion to the positive displacement pump, the coarse emulsion will enter the homogenizing chamber through a tiny valve under high pressure; the cavitation effect generated by high-intensity vibration and shear rate shears large droplets of coarse emulsion into nano-sized droplets, the most petite droplet sizes are even up to 1 nm, resulting in nanoemulsions with higher kinetic stability [29]. Liu et al. [30] investigated the effect of using high-pressure homogenization on cinnamon oil nanoemulsions. They found that as the pressure increases, the particle size expands as the destructive force increases, and then the particle size loses its emulsifier function due to the high temperatures generated by the high pressure.

The high-pressure homogenization method has the advantages of simple operation, low price, large processing capacity, and not quickly destroying the emulsion layer. This method is widely used in biopharmaceutical processes.

Ultrasonic method

The ultrasonic method utilizes ultrasonic instruments that can form bubbles inside the liquid. The increase in the bubbles causes the liquid to break up sharply, forming turbulence and shear, which in turn breaks up the large droplets into smaller ones [31]. The efficiency of ultrasound depends on the processing time, power, emulsifier concentration type, and fluid viscosity [32]. Mehmood et al. [33] investigated an ultrasound-assisted homogenization process for the preparation of β-carotene nanoemulsions. They found that the ultrasonic treatment could effectively improve the embedding rate of β-carotene within a certain range of ultrasonic power.

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High-speed shear method

The high-speed shear method uses a high-speed shear emulsifier through the high-speed rotation of the rotor and stator in the relative motion between the powerful shear force; the material is crushed, dispersed, and emulsified to achieve uniform mixing and emulsification of liquids. Silva et al. [34] utilized the high-speed shear method and found that the antimicrobial properties and stability of thymol nanoemulsions prepared by this method were enhanced.

High-speed shear is a relatively simple method for preparing nanoemulsions. However, it is destructive to the sample, and the emulsions prepared have a large particle size, usually used in combination with high-pressure homogenization.

IV. Application of nanoemulsion in food field

Nanoemulsions are widely used in the food industry to improve food products' safety, shelf life, flavor, quality, and nutrition.

Antibacterial and antiseptic

Microbial contamination is one of the significant causes of food spoilage and can lead to considerable economic losses, increased waste, environmental pollution, and food safety problems. Traditional bacteriostatic and preservative methods, such as low-temperature preservation, cannot provide long shelf life for fresh food, thus making it highly perishable; chemical preservation cannot guarantee absolute safety, modified atmosphere packaging requires high operational requirements, and the study of browning and softening-related gene expression in electric radiation preservation is not yet precise. Based on the above problems, more and more researchers have begun to study a bacteriostatic and preservative efficient, safe, and environmentally friendly method to reduce food spoilage rate. As a natural preservative, nanoemulsion not only has high antimicrobial and strong oxidizing properties but can also be safely used in food. Zhao et al. [35] encapsulated bioactive ingredients in food-grade nanoemulsions to investigate their effect on fish spoilage. They found that the nanoemulsions significantly reduced microbial colonization and delayed protein and fat oxidation, which significantly prolonged the freshness date of fish.

Improvement of food flavor

Food flavor is one of the determinants of food quality and the most critical factor in determining food consumer preferences. Flavor substances combine with different parts of the senses to produce different senses of smell and taste, bringing different feelings to people. Taste is a chemical sense. According to the solubility of flavor substances, they can be divided into water-soluble flavor substances and fat-soluble flavor substances. However, many flavor compositions are unstable and can alter their organoleptic properties due to heat, oxygen, chemical interactions, or volatilization.

Nanoemulsions can improve the flavor and aroma of food products, making them more appealing. Therefore, the flavor substances are embedded using a suitable delivery system for their protection, delivery, and slow release. Constructing a reasonable flavor substance system to increase the solubility of certain flavor substances and reduce the loss of volatile components is crucial. Suyanto et al. [36] used nanoemulsions to encapsulate fruit flavors to prepare emulsion flavor systems. It was found that the encapsulated flavors reduced the volatilization of fruit flavors.

As a fat substitute

Nanoemulsions can be used in bakery products to replace some of the fats and reduce the fat content in baked goods, showing great potential in developing low-fat baked goods. Ekin et al. [37] studied low-fat cookies prepared by oil-carrying nanoemulsions with particle sizes ranging from 169.8 to 363.4 nm in place of shortening and the effect on their quality. The results showed that the ductility of low-fat cookies increased significantly from 5.17 to 7.84 in the control group, the hardness decreased by 18.40% to 40.27%, the saturated fatty acid content decreased from 63.35% to 36.64%, and the unsaturated fatty acid content increased from 35.59% to 57.39%, and that the substitution of shortening by nanoemulsions did not decrease the sensory qualities of the cookies. The overall low-fat cookie quality, greasiness, and flavor of low-fat biscuits had higher sensory scores. Even if fat is reduced in cookie formulations, quality defects caused by fat deficiency can be eliminated with nanoemulsions, which may be attributed to the fact that the smaller particle size of nanoemulsions increases the specific surface area of the oils, providing a potential fat substitute for the development of low-fat baked goods

Embedding and delivery of bioactive substances

Studies have reported that the bioavailability of bioactive substances encapsulated in droplets increases with decreasing droplet size [38]. Therefore, nanoemulsions are commonly used in the food industry to encapsulate functional substances such as polyphenols, vitamins, and amino acids. These substances are usually mixed with the oil phase prior to the formation of the nanoemulsion. Once the emulsion is formed and delivered to the body, the large surface area of the tiny droplets allows for rapid digestion by digestive enzymes, which promotes the release and absorption of the active substances [39]. Inapurapu et al. [40] evaluated nanoemulsions with emulsion sizes ranging from 100 to 200 nm as carriers for the encapsulation of ω 3 fatty acids, and the nanoemulsions significantly increased the bioavailability of ω 3 fatty acids (53%) compared to those loaded with only the oil phase (34.7%). Therefore, the larger surface area in nanoemulsions is considered one of the main reasons for improved bioavailability.

V. Conclusions and outlook

Over the years, nanoemulsions have received significant attention due to their excellent properties, including behaviors such as large specific surface area, stability, wettability modification ability, and tunable rheology. This paper reviews the main components of nanoemulsions and standard preparation methods to highlight their application in food delivery. The applications of nanoemulsions in the food field are discussed. Currently, nanoemulsions are mainly used in the fields of bacteriostasis and preservation, improvement of food quality, food ingredient substitutes, and encapsulation and delivery of bioactive substances. In the future, the preparation process of nanoemulsions should be further optimized to establish an ideal system of solubility, functionality, and bioavailability of bioactive lipophilic compounds so that they can be more widely used in the field of food to produce safer and more nutritious food.

Author contributions

Shuangying Jia: Conceptualization; Investigation; Writing original draft, Writing – Review & Editing.

Xunyi Xun: Writing – Review & Editing.

Xinhe Zhao: Conceptualization; Investigation; Writing original draft, Writing – Review & Editing.

Declaration of Competing Interest

All authors declare they have no conflicts of interest for the work presented in this manuscript.

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