#### **REVIEW**



# Recent Advances in Natural Product-Based Nanoemulsions as Promising Substitutes for Hazardous Synthetic Food Additives: A New Revolution in Food Processing

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#### **Abstract**

The recent increase in chronic diseases worldwide is a major cause for concern, with processed foods containing synthetic additives being a leading contributor. These additives are commonly used in the food industry for processing, storage, and packaging, and prolonged exposure to them can pose serious health risks. To address this issue, there is a growing demand for bio-based food additives that are environmentally friendly, free of side effects and chronic diseases like cancer, and promote overall health. Nanoemulsion technology can be used to create these natural-based additives, effectively enhancing their solubility, stability, and bioavailability. As such, natural-based nanoemulsions have the potential to become the next generation of food additives and pave the way for healthier food products. This study provides an overview of the production of natural-based food additives using nanotechnology approaches, examining their effects on different food products and in vitro and exploring their mechanisms of action.

**Keywords** Food additives · Nanofood · Natural nanoemulsion · Food processing · Chronic disease · Food safety

#### Introduction

Food additives are a group of synthetic or natural substances intentionally added to food products for specific technological or sensorial objectives and contribute to food processing

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operations (Barzegar et al., 2021a; Bearth et al., 2014). Food additives such as flavorings, colorants, preservatives, nutritional additives, antioxidants, sweeteners, stabilizers, and thickeners have special functions. Thus, the application of these substances is an indispensable part of food processing (Martins et al., 2019). Evidence demonstrates that long-term exposure to synthetic food additives adversely affects human health. Figure 1 depicts some of these severe complications derived from artificial food additive consumption (Barzegar et al., 2021b; Hosseini et al., 2021; Jaye et al., 2020; Kazmi et al., 2017; Ousji & Sleno, 2020; Reza et al., 2019; Singh et al., 2020; Wang et al., 2021). Therefore, natural-based food additives could be used as promising alternatives for artificial types. Consumer awareness about the health risk of artificial food additives brings about a growing demand for substances with natural origins, whereas some technological challenges demonstrated in Fig. 1 have restricted the direct incorporation of natural additives such as essential oils into foodstuffs (da Silva Gündel et al., 2018; de Carli et al., 2018; Flores-Andrade et al., 2021; Mehmood et al., 2021; Pérez-Soto et al., 2021; Ren et al., 2018; Sonu et al., 2018). This theory came to light that nanotechnology could potentially overcome these formidable limitations and eventually facilitate the utilization of natural-based food additives in the



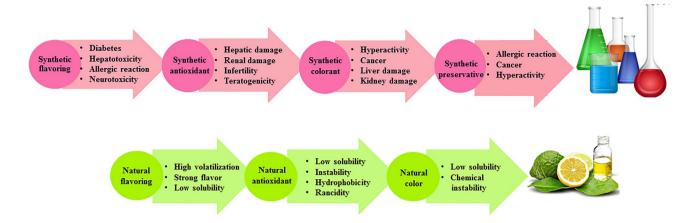


Fig. 1 Side effects caused by synthetic food additive consumption and some technological drawbacks of natural food additives

food industry. Nanotechnology also covers all of the main objectives of the food industry, such as extending the food shelf life, providing the nutrients required for human health, providing attractive colors, flavors, and texture, and focusing on the safety aspect of food products and economic growth.

Nanotechnology is an emerging technique developing in many sectors, including pharmaceutics, cosmetics, agriculture, and the food industry (Ashaolu, 2021). Indeed, nanotechnology is regarded as a new technique conducted at the nanoscale, about 1 to 100 nm. Different food characteristics such as stability, color, taste, texture, bioavailability, and flavor could be modified by nanotechnology approaches (Sahoo et al., 2021). This technique also develops new food packaging, functional food, nano-sized food components, nanonutrients, and nanoemulsions (Handford et al., 2015). Generally, the primary goals of nanotechnology are to modify and upgrade the safety, quality, nutritional value, and shelf life without cost increment (Dasgupta & Ranjan, 2018).

Nanoemulsions are suitable carriers for some target components, including drugs, flavors, fatty acids, antioxidants, color, and antimicrobial substances (Ashaolu, 2021). Nanoemulsions, one of the products of nanotechnology, can efficiently modify and improve stability, compatibility, solubility, bioavailability, and other technological limitations the food industry may face (Mandal et al., 2023; Sahoo et al., 2021). Natural-based food additives on the nanoscale could readily distribute in those parts of the food matrices, where microorganisms could grow and proliferate. This type of delivery system could enhance the bioavailability of target ingredients without a negative effect on the sensory characteristics of food and increase the shelf life (Donsì & Ferrari, 2016a). So, using green food additives becomes successfully possible in the form of nanoemulsions with a suitable formulation.

The technological limitations pointed out in Fig. 1 could impressively compensate by nanoemulsions. So this paper dealt with the nanoemulsion concept in more detail and

reviewed various studies about natural-based nanoemulsions as a green alternative for synthetic food additives and then paved the way for applying these promising options for future food and guaranteeing human health.

# Food-Grade Nanoemulsion Formulation and Fabrication Techniques

To date, different publications scrutinized the main principles of nanoemulsions, such as their formulations, physicochemical properties, and fabrication procedures (Choi & McClements, 2020; Das et al., 2020; Li et al., 2021; Siraj et al., 2021). Therefore, the primary information about nanoemulsions is summarized in this section. The application of these delivery systems as a healthy alternative for artificial food additives has been thoroughly reviewed in the next section.

# **Characteristics and Composition**

Nanoemulsion is introduced as oil-in-water (o/w) or water-in-oil (w/o) emulsion with mean droplet sizes (diameter) usually ranging from 20 to 200 nm (Das et al., 2020; Marzuki et al., 2019). Nanoemulsions are similar systems to macroemulsions but with nano-sized droplets. This delivery system is thermodynamically unstable and kinetically stable (metastable) colloidal dispersion, in which two immiscible liquids are distributed and stabilized by emulsifiers. Nanoemulsions are optically turbid or lucent and stable to temperature and pH variations (Aswathanarayan & Vittal, 2019). Several nanoemulsion applications, especially in the food industry, are depicted in Fig. 2.

This system is generally formulated with three main ingredients: oil or lipid phase, water or aqueous phase, and emulsifier (Barradas & de Holanda e Silva, 2021). Based



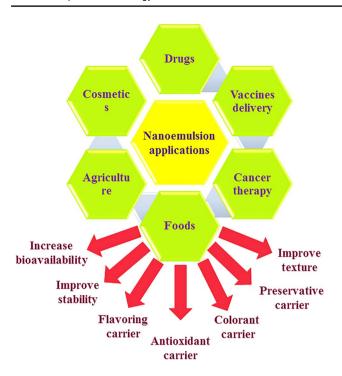


Fig. 2 Nanoemulsion applications and their specific functions in food industry

on the expected application of food nanoemulsions, such as increasing and improving stability, bioavailability, taste, and texture add, various ingredients, including preservatives, vitamins, minerals, coloring, and flavoring agents, can be applied as dispersed phase (Barradas & de Holanda e Silva, 2021). It has been confirmed that the o/w and w/o nanoemulsion comprises a core-shell structure. For instance, the amphipathic shell in an o/w nanoemulsion is composed of surface-active molecules, while the lipophilic core consists of nonpolar molecules. Different compounds involving omega-3 fatty acids, essential oils, fat-soluble vitamins, waxes, and other lipophilic ingredients can be established as lipid phases in food nanoemulsions. The polar-solventlike water is formed in the aqueous phase. It should be highlighted that stabilizers like emulsifiers are required to prevent nanoemulsion breakdown (sedimentation, coalescence, creaming, Ostwald ripening, flocculation) (Marhamati et al., 2021). Thus, food-grade emulsifiers as the third main ingredient of nanoemulsions were explained in the following (Aswathanarayan & Vittal, 2019; Barradas & de Holanda e Silva, 2021).

## **Food-Grade Emulsifiers**

Emulsifiers are identified as surface-active molecules used to stabilize two immiscible phases in food-grade nanoemulsions (Artiga-Artigas et al., 2018). In other

words, nanoemulsion fabrication requires proper absorption of an emulsifier at the oil-water interface to reduce interfacial tension and eventually facilitate nanoemulsion formation. The emulsifier could effectively coat oil droplets to inhibit aggregation and coagulation (Dasgupta et al., 2019). It is well established that emulsifier is a key factor in increasing consistency against external stresses, consequently leading to long-term stability and storage time (Marhamati et al., 2021). It should be pointed out that the balance between the hydrophilic and hydrophobic attributes of emulsifiers specifies their performance. Therefore, hydrophilic-lipophilic balance (HLB) demonstrates the strength of an emulsifier molecule's hydrophilic and lipophilic moieties. The HLB number typically ranges from 1 to 18. If the HLB number rises, the emulsifier tends to be soluble in the water phase, and this type of emulsifier is more suitable for use in o/w nanoemulsions (Marhamati et al., 2021). HLB value applies to determining the optimum performances of different emulsifiers, which is required for nanoemulsion formation with eligible characteristics (Ashaolu, 2021). Generally, emulsifiers could be categorized based on various aspects such as their performance mechanism, HLB value, chemical structure, and also molecular weight (Marhamati et al., 2021). In the current study, emulsifiers are classified into synthetic and natural groups.

#### **Synthetic Emulsifiers**

This type of emulsifier is categorized into various subsets depending on their electric charge, including cationic, anionic, nonionic, and amphoteric. Emulsifiers with cationic properties contain a positive charge on the active part of the molecule (hydrophilic head). Along with the abovementioned property, these molecules also demonstrated notable antiseptic and antibacterial attributes. Anionic emulsifiers contain a negative charge on the active part of the molecule (hydrophilic head) and may comprise sulfate, carboxylate, phosphate, and sulfonate groups. Amphoteric emulsifiers include both negative and positive charges. They may indicate anionic, cationic, or nonionic characters depending on the pH of the solution. Nonionic emulsifiers do not have an electric charge, and they constitute hydrophilic (polyols, poly oxy ethylene, or poly oxy propylene) and lipophilic (fatty alcohols or saturated/unsaturated fatty acids) moieties. Nonionic types have been extensively utilized for nanoemulsion formulations due to lower toxicity and irritability. It was also declared that these emulsifiers indicated a high capability to produce nanoemulsions with both top-down and bottom-up procedures (Arancibia et al., 2017; De et al., 2015).



#### **Natural Emulsifiers**

Due to their health-promoting effects, there is a growing demand to replace artificial emulsifiers with natural ones. The most striking attributes of natural emulsifiers are their biodegradability and biocompatibility. They also resist diverse environmental circumstances, including different temperatures, pH levels, and pressure. These emulsifiers likely exert more stability than nanoemulsions (Barradas & de Holanda e Silva, 2021). Polysaccharides, proteins, lipopolysaccharides, and phospholipids are deemed natural emulsifiers. Bioemulsifiers (sophorolipids, mannoproteins, saponins, and rhamnolipids) are also natural emulsifiers. Lipoproteins, lipopeptides, and glycolipids are bioemulsifiers separated from plants or produced by fermentation (Lam & Nickerson, 2013; Varvaresou & Iakovou, 2015). Cellulose, pea protein, chitin, zein, starch, soy protein, cocoa, and kafirin are natural colloidal substances used as emulsifiers in o/w emulsions (Marhamati et al., 2021). According to previous studies, some of the main emulsifiers are illustrated in Table 1.

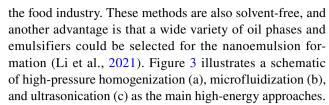
#### A Summary of Fabrication Techniques

The fabrication methods of nanoemulsions are generally based on two engineering approaches: (1) high-energy approaches (top-down) and (2) low-energy approaches (bottom-up) (Donsì & Ferrari, 2016b). It is evident that emulsifiers play a pivotal role in reducing interfacial tension and shear energy necessitated to decrease the curvature of the formed droplets (Barradas & de Holanda e Silva, 2021). To see which types of aforementioned approaches should be employed, the following factors must be considered: the oil phase and emulsifier features and the physicochemical and functional aspects necessitated for the ultimate application (McClements & Jafari, 2018). The droplet sizes, as one of the significant factors in nanoemulsion formulation, could be different due to various fabrication procedures, system compositions, and process situations (Li et al., 2021).

A growing body of literature has completely described the various nanoemulsion production techniques. This section presents a brief overview of the main fabrication approaches.

#### **High-Energy Approaches (Top-Down)**

High-energy approaches are based solely on the high value of strong energy supplied by mechanical equipment, which generates disruptive forces to break up oil and water phases and eventually forms nano-sized droplets (Ozogul et al., 2022). The high-energy approaches are the most common methods used to fabricate food-grade nanoemulsions. These techniques have been extensively applied to fabricate nanoemulsions on large industrial scales, such as in



High-Pressure Homogenization (HPH) is the usual emulsification technique employed for nanoemulsion fabrication on the factory and laboratory scale (Jasmina et al., 2017). HHP is based on compressing a coarse emulsion via a small channel under high pressure. To prepare a preexisting coarse emulsion, the oil, water, and emulsifier are mixed and then fed into the valve of HHP equipment (Saffarionpour, 2019). This method is scalable with more control for reducing droplet size. At the same time, this method requires more energy and expense (Barradas & de Holanda e Silva, 2021).

Microfluidization is one of the efficient methods, which converts a coarse emulsion into nanoemulsion by compressing the stream across the specified narrow channels with high pressure. The emulsion stream quickly bumps into each other or collides with the walls of the microfluidizer instrument. The high velocity of collisions generates turbulence, cavitation, and shear forces, which break the large droplets into tiny and fine droplets (Barradas & de Holanda e Silva, 2021). This procedure requires lower pressure than HPH (Donsì & Ferrari, 2016a).

**Ultrasonication** fabricates nanoemulsion with high-frequency waves, which provide a disruptive force for breaking up the oil and water phase. The connected device generates ultrasonic high-frequency waves to increase cavitation and bring about mechanical vibration (Barradas & de Holanda e Silva, 2021; O'Sullivan et al., 2017). The performance of this technique is related to the type of emulsifier, process time, power, fluid viscosity, emulsifier amount, and interfacial tension (Ozogul et al., 2022). This fabrication method could produce nanoemulsions for laboratory investigations with a low amount of material (Marzuki et al., 2019).

# Low-Energy Approaches (Bottom-Up)

These fabrication approaches are particularly based on physicochemical processes. The fundamental principle of bottom-up methods is that nano-sized oil droplets spontaneously produce when the composition of an oil-water-emulsifier blend or the environment changes (Aswathanarayan & Vittal, 2019). It should be declared that physicochemical attributes, including solubility, composition, pH, ionic strength, and temperature, are the most important factors for the nanoemulsion formulation by low-energy approaches (Aswathanarayan & Vittal, 2019; Donsì & Ferrari, 2016b). These methods are capable of fabricating fine droplets at low expense. Another benefit is related to the simplicity of performance and scale-up. At the same time, the yield of



**Table 1** The classification of food-grade emulsifiers

Emulsifier group	Types	Name
Synthetic	Cationic	Dodecyl trimethylammonium bromide
	Anionic	Sodium dodecyl sulfate
		Alkanol-XC
		Diacetyl tartaric acid esters of monoglycerides
		Fatty acid salts
		Stearyl lactylate salt
		Citric acid esters of mono- and diglycerides
	Nonionic	Polyethylene glycol (35) castor oil
		Acetic acid esters of mono- and diglycerides
		Polyoxyehtylene-660-12-hydroxy stearate
		Polyoxyethylene 4-lauryl ether
		Span 20
		Span 80
		Tween 20
		Tween 80
		Tween 40
		Tween 60
		Sucrose fatty acid ester (L1695)
		Brij 97
		Polyoxyethylene 6-lauryl ether
		Decaglycerol monolaurate (ML750)
		Polyglycerol esters of fatty acids (PGEs)
		Spans 20 (sorbitan monolaurate)
		Spans 40 (sorbitan monopalmitate)
		Spans 60 (sorbitan monostearate)
		Spans 80 (sorbitan monooleate)
		Tween 20 (polyoxyethylene sorbitan monolaurate)
		Tween 40 (polyoxyethylene sorbitan monopalmitate)
		Tween 60 (polyoxyethylene sorbitan monostearate)
		Tween 80 (polyoxyethylene sorbitan monooleate)
	Amphoteric	_
Natural	Polysaccharides	Modified starch
		Arabic gum
		Beet pectin
		Corn fiber gum
		Soy polysaccharide
		Cellulose
		Xanthan
		Galactomannans
	Proteins	Gelatin
		Whey protein isolate (WPI)
		Whey protein concentrate (WPC)
		Whey protein hydrolysate (WPH)
		Beta casein
		Sodium caseinate (SC)
		Calcium caseinate (CC)
		Soy
		Egg
		CC
		Plant proteins
	Saponins	Plant proteins Quillaja saponin

(Barradas & de Holanda e Silva, 2021; Marhamati et al., 2021)



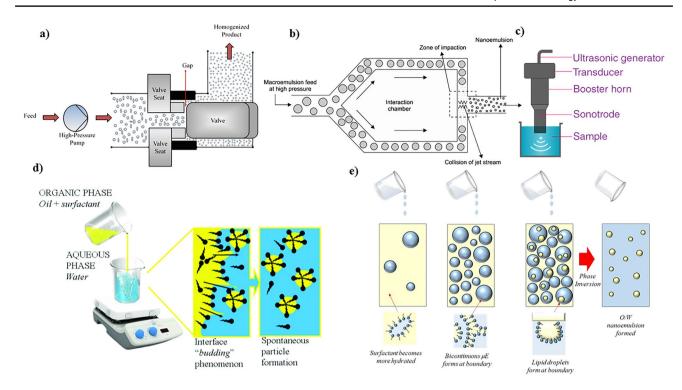


Fig. 3 High-energy approaches (high-pressure homogenization (a), microfluidization (b), and ultrasonication (c)) and low-energy approaches (spontaneous emulsification (d) and principles of phase inversion temperature, phase inversion composition, and emulsion inversion point (e))

these approaches is low and needs solvents during the process. There is also a strict limitation for applying various oils and surfactants (Dey et al., 2018; Komaiko & McClements, 2014). These approaches, which have been explained in different studies in more detail, are summarized in the following. Figure 3 exhibits spontaneous emulsification (d) and principles of phase inversion temperature, phase inversion composition, and emulsion inversion point (e), which are the same for all. The distinctive characteristics of these three methods are described in the following.

**Spontaneous Emulsification** occurs when an organic phase and an aqueous phase are blended. This organic phase comprises oil, surfactant, and a water-miscible solvent. The spontaneous reaction of this procedure arises from the initial nonequilibrium states of two phases when they diffuse to each other without external energy (Ozogul et al., 2022).

Phase Inversion Temperature (PIT) is a subset of phase inversion-based procedures. These methods are fundamentally based on the chemical energy produced from phase conversion phenomena within emulsification. These processes occur when some remarkable environmental variations happen (Helgeson, 2016). In the PIT method, solubility and optimum curvature of nonionic surfactants change by temperature. In these systems, conversion from w/o emulsion happens at high temperatures to o/w emulsion at low temperatures (Jasmina et al., 2017).

**Phase Inversion Composition (PIC)** procedure is partly similar to the PIT method. At the same time, the difference is

that in PIC, changing the composition or formulation of emulsion leads to changes in the solubility and optimum curvature of surfactants at stable temperatures (Farshbaf-Sadigh et al., 2021).

**Emulsion Inversion Point (EIP)** method is similar to spontaneous emulsification. This technique involves titrating water into an organic phase involving oil and surfactant with continuous stirring. The water droplet amount in the oil phase develops until a critical point is attained, and afterward, a phase inversion takes place from w/o to o/w emulsion (Jasmina et al., 2017).

# Natural-Based Nanoemulsions as a Promising Substitute for Synthetic Food Additives (Next Generation of Food Additives)

#### **Nanobio-Preservatives**

Foodstuffs are always subject to microbial or chemical spoilage. This challenge underlies serious problems in food industries, including food safety threats, economic losses, and waste increment. Various conventional synthetic preservatives have been introduced to prevent food spoilage (Hassoun & Emir Çoban, 2017). In comparison, there is a growing demand for natural-based preservatives for the abovementioned reasons. For instance, essential oils



as natural antimicrobials and antioxidants have recently attracted remarkable attention (Moghimi et al., 2016). The ample evidence demonstrates that these plant metabolites involve various bioactive ingredients (Donsì & Ferrari, 2016a; Ozogul et al., 2017; Yazgan et al., 2017). The high chemical instability, intrinsic hydrophobicity, high volatility, low water-solvability, and intense flavor have been known as formidable limitations which impede the direct application of essential oils in food and beverages (Jamali et al., 2021). Thus, utilizing these natural components as nanoemulsion could overcome these problems. Table 2 represents the future generation of food additives with natural origins.

#### Nanobio-Antibacterial

In one of the recent investigations, the antibacterial activity of ginger, cinnamon, and cardamom essential oils was studied against Escherichia coli and Staphylococcus aureus. The key ingredients of ginger essential oil are  $\alpha$ -curcumene,  $\alpha$ -zingiberene, trans- $\gamma$ -cadinene, and β-sesquiphellandrene. It was also pointed out that oxygenated monoterpenes, such as 1,8-cineole, and monoterpene hydrocarbons are major components of cardamom essential oil. Eugenol and cinnamaldehyde are the two main active elements of cinnamon essential oil. These chemical components attach to the microbial cell membranes, change normal penetration mechanisms, and invade the bacterial cells. Essential oils could also inhibit the synthesis of DNA, RNA, proteins, and polysaccharides that deter bacterial growth. The nanoemulsion of these essential oils was fabricated by self-emulsification method using Tween 80 (HLB 15), glycerol (HLB 4.5), and 2,2-diphenyl-1-picrylhydrazyl (DPPH). The average droplet size of the obtained nanoemulsion was achieved at less than 110 nm. This nanoemulsion indicated acceptable physical stability within 40 days at  $5 \pm 1$  °C. The combination of 68% cinnamon, 10% ginger, and 22% cardamom is the ideal oil phase and showed the smallest mean droplet sizes, highest zeta potential, and antibacterial activity due to synergistic effect (Jafarizadeh-Malmiri et al., 2022). Mayonnaise is a favorable dressing made chiefly of vegetable oils, egg yolk, vinegar, lemon juice, citric acid, etc. In this regard, there is a high risk of mayonnaise contamination with some foodborne pathogens. The amount of vinegar in mayonnaise formulation as a natural antibacterial ingredient is inadequate. Thus, the application of sodium benzoate is particularly obligatory for microbial control. The *Thymus* daenensis Celak (T. daenensis) essential oil composed of linalool, thymol, and carvacrol as effective key elements was applied as a natural replacement for sodium benzoate. An Ultra-Turrax prepared the coarse emulsion at 3000 rpm,

and then, an ultrasonic homogenizer (400 W, frequency: 20 kHz) fabricated the nanoemulsion of the abovementioned essential oil. The suitable stability and antibacterial activity against Salmonella Typhimurium, Listeria monocytogenes, and Escherichia coli were gained by optimal formulation of nanoemulsion (essential oil: Tween 80, ratio 1:1, 15 min sonication). A striking result, which emerged, is that the antimicrobial performance of this optimal nanoemulsion was similar to sodium benzoate. Meanwhile, the desirable sensorial characteristics were also obtained in this optimal nanoemulsion formulation (Mansouri et al., 2021). The existence and growth of *Clostridium sporo*genes in foodstuffs is a concerning issue in the food industry. Sodium nitrite, as a synthetic additive, uses its antibacterial effect in meat products to control Clostridium sporogenes. In addition, nitrite salts improve flavor, color, and texture and induce lipid oxidation. However, evidencebased information has demonstrated that nitrite salts produce N-nitrosamines that is carcinogenic to human. Thus, the effect of different natural-based additives such as Tahiti lemon, oregano, cinnamon, Chinese pepper, and cardamom essential oils in nanoemulsions was assessed as an alternative to high sodium nitrite concentration in mortadella-type sausages. The main active ingredients of Chinese pepper are 35.37% neral and 48.76% α-citral. 78.29% carvacrol and 6.11% ρ-cymene are active elements of oregano essential oil. Tahiti lemon essential oil comprises 63.45% limonene, 11.18% β-pinene, and 12.58% γ-terpinene. The major components of cinnamon and cardamom essential oils were represented before. The specific ratio of essential oils with Tween 80 was homogenized in Ultra-Turrax and then transferred to an ultrasonic homogenizer. The consequences disclosed that the mixture of these essential oils in the form of nanoemulsion was more effective than individual essential oils for the reduction of vegetative cells of *Clostridium sporogenes*, and the concentration of sodium nitrite in mortadella was dramatically reduced (75 ppm). After all, the design of nanoemulsion leads to a lower amount of essential oil utilization and prevents a negative effect on the sensorial attributes of mortadella (Pinelli et al., 2021). Fish with high nutritional value is perishable and deteriorates very rapidly. Rainbow trout (Oncorhynchus mykiss) is considered a good seafood worldwide. Therefore, the antibacterial activity of citrus essential oils such as grapefruit, orange, lemon, and mandarin on the shelf life of rainbow trout fillets at  $4 \pm 2$  °C was studied. Gram-negative psychrophilic bacteria are the major category of bacteria that trigger fresh fish spoilage in cold storage. The ultrasonic homogenizer with the power of 500 W and frequency of 20 kHz was applied for nanoemulsion formation. It was observed that these essential oil nanoemulsions were useful in postponing psychrophilic bacteria growth in fish fillets. It was emphasized that mandarin and



Table 2 The natural-based nanoemulsions as novel substitutes of artificial food additives, their formulations, fabrication methods, droplet sizes, and applications

Natural product- based nanoemulsion applications	Oil phase	Emulsifier	Fabrication technique	Average droplet size (nm)	Food matrices	Specific functions	References
Nanobio-preservatives (antibacterial)	Ginger, cinnamon, cardamom essential oils	Tween 80 (HLB 15), glycerol (HLB 4.5)	Self-emulsification method	<110 nm	ı	Antibacterial activity against Escherichia coli and Staphylo-coccus aureus	(Jafarizadeh-Malmiri et al., 2022)
	Thymus daenensis Celak (T. daenensis) essential oil	Tween 80	Ultrasonic homogenization	< 100 nm	Mayonnaise	Antibacterial activity against Listeria monocytogenes, Escherichia coli, and Salmonella Typhimurium (natural sodium benzoate substitute)	(Mansouri et al., 2021)
	Tahiti lemon, oregano, Tween 80 cinnamon, Chinese pepper, and cardamom essential oils	Tween 80	Ultrasonic homogeni- zation	ı	Mortadella	Antibacterial activity against Clostridium sporogenes (natural sodium nitrite substitute)	(Pinelli et al., 2021)
	Citrus essential oils	Tween 80	Ultrasonic homogeni- zation	47.40–94.66 nm	Rainbow trout fillets	Antibacterial activity against psychrophilic bacteria	(Durmus, 2020)
	Saffron essential oil	Tween 80, Tween 20	Ultrasonic homogeni- zation	10.5–10.8 nm	Shrimp	Antibacterial activity against Escherichia coli and Staphylo-coccus aureus	(Aboutorab et al., 2021)
	Cinnamon essential oil	Hydroxypropyl- β-cyclodextrin (HPCD), Tween 80	Ultrasonic homogenization	1	1	The CEO nanoemulsions made of HPCD and Tween 80 showed good antibacterial effects against Escherichia coli and Staphylococcus aureus	(Hou et al., 2021)
	Grape seed and cinnamon essential oils	Tween 80	Ultrasonic homogenization	Grape seed (42.90) Cinnamon (13.92)	Flathead mullet (Mugil cephalus)	Shelf life enhancement, prevent pH and TVB-N increment, postpone lipid oxidation, reduce total mesophilic, psychrophilic bacteria, Enterobacteria, events	(Ameur et al., 2022)



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Natural product- based nanoemulsion applications	Oil phase	Emulsifier	Fabrication technique	Average droplet size (nm)	Food matrices	Specific functions	References
	Cuminum cyminum L. extract	Tween 80, Tween 20	Ultrasonic homogeni- zation	24.5 nm	1	Higher antibacterial activity against Gram-negative than Gram-positive bacteria	(Asgari et al., 2021)
	Cinnamon essential oil	Tween 80	Phase inversion tem- perature	1	Asian seabass ( <i>Lates</i> calcarifer) fillets	ity and could be used as chemotherapeutic agents Antibacterial capacity against Escherichia coli, Salmonella Typhimurium, and Straphylococcus.	(Chuesiang et al., 2021)
	Thymol	Tween 80	Ultrasonic homogeni- zation	86.39 nm	Sausage	aureus Antibacterial activity against Escherichia coli, Staphylococ- cus aureus, and Clostridium perfrin-	(Sepahvand et al., 2021)
	Oregano (Origanum vulgare L.) essential oil	Tween 80	Ultrasonic homogeni- zation	72.26 nm	ı	gens (natural nitrite substitute) Antibacterial activity against Staphylo-coccus aureus and	(Enayatifard et al., 2021)
	Tarragon essential oil	Tween 80, Span 80	Ultrasonic homogeni- zation	50 nm	I	Antibacterial activity against Staphylococcus aureus, Listeria monocytogenes, and Shizella dysenteriae	(Azizkhani et al., 2021)
	Grapefruit peel essential oil	Tween 80	Ultrasonic homogeni- zation	204.5 nm	ſ	Bacteriostatic effect against Salmonella Paratyphi A, Pseu- domonas luteola, Photobacterium damselae, and Ser- ratia lianefaciens	(Özogul et al., 2021)
	Thyme essential oil	1	Ultrasonic homogenization	52 nm	UF labneh	Extend the labneh shelf life and enhanced its aroma	(El-Sayed and El-Sayed, 2021)



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Natural product- based nanoemulsion applications	Oil phase	Emulsifier	Fabrication technique	Average droplet size (nm)	Food matrices	Specific functions	References
	Cinnamaldehyde	EL (castor oil poly-oxyethylene ether)-90	ı	48 nm	1	Potent antibacterial activity against Escherichia coli and Staphylococcus aureus	(Gao et al., 2021)
	Finger citron essential Cremophor EL oil	Cremophor EL	Spontaneous emulsi- fication	20 nm <	1	Antibacterial activity against Escherichia coli, Staphylococcus aureus and Bacillus subrilis	(hua Li et al., 2018)
	Celery essential oil	Tween 80	Ultrasonic homogenization	23.4 nm	1	The nanoemulsion interacted with the pathogen and caused cytoplasmic leakage	(Nirmala et al., 2020)
	Ocimum basilicum essential oil	Sorbitan monooleate	Homogenization	120 nm	1	The antibacterial performance of basil essential oil with nanoemulsion form was potentiated against Escherichia coli, Staphylococcus aureus, Proteus mirabilis, Candida tropicalis, and Candida albicans	(da Silva Gündel et al., 2018)
	Citral	Tween 80	Ultrasonic homogenization	22.40–223.90 nm	Fresh cut pineapple	Reduction of Salmo- nella enterica Typh- imurium population	(Prakash et al., 2020)
	Rosemary, laurel, thyme, sage	Tween 80	Ultrasonic homogenization	Thyme: 112.82 nm	Rainbow trout fillets	The shelf life enhancement from 14 to 17	(Ozogul et al., 2017)
				Rosemary: 63.02 nm		Rosemary and thyme had the highest anti-bacterial activity	
				Laurel: 66.02 nm Sage: 59.48 nm			



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Table 2         (continued)							
Natural product- based nanoemulsion applications	Oil phase	Emulsifier	Fabrication technique	Average droplet size (nm)	Food matrices	Specific functions	References
	Sage essential oil	Tween 80	Ultrasonic homogenization	204.4 nm	ı	Effective on Staphylococcus aureus, Salmonella Pararyphi A, and Proteus mirabilis	(Yazgan, 2020)
	Thyme essential oil	Tween 20	Ultrasonic homogenization	163 nm	Rainbow trout fillets	The more thyme essential oil in nanoemulsion formulation showed more antibacterial activity against Pseudomonas aeruginosa, Escherichia coli, and Salmonella typhimurium	(Meral et al., 2019)
	Cumin and pepper essential oil	Tween 80	Ultrasonic homogenization	ı	Fresh fruits and vegetables	Effective on food- borne pathogens such as Escherichia coli and Salmonella enterica	(Amrutha et al., 2017)
Nanobio-preserva- tives (antifungal)	Oregano (Origanum vulgare L.) essential oil	Tween 80	Ultrasonic homogeni- zation	72.26 nm	I	Antifungal activity against Aspergillus niger	(Enayatifard et al., 2021)
	Origanum majorana essential oil	Tween 80	Ultrasonic homogeni- zation	1	Maize	Antifungal activity against Aspergillus flavus with disruption of membrane integrity and decrease AFB	(Chaudhari et al., 2020)
	Cleome viscosa essen- Triton-x-100 tial oil	Triton-x-100	Ultrasonic homogenization	<20 nm	I	Destroy Candida albicans cells and interfering cell wall biosynthesis	(Krishnamoorthy et al., 2021)
	Clove essential oil	1	High-pressure homogenization	I	I	Antifungal activity against Aspergillus niger and Candida albicans	(Shahbazi, 2019)
Nanobio-preserva- tives (antioxidant)	Cuminum cyminum L. extract	Tween 80, Tween 20	Ultrasonic homogeni- zation	24.5 nm	I	Antioxidant activity	(Asgari et al., 2021)



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Natural product- based nanoemulsion applications	Oil phase	Emulsifier	Fabrication technique	Average droplet size (nm)	Food matrices	Specific functions	References
	Ginger, cinnamon, cardamom	Tween 80 (HLB 15), glycerol (HLB 4.5)	Self-emulsification method	<110 nm	I	Antioxidant activity	(Jafarizadeh-Malmiri et al., 2022)
	Tarragon essential oil	Tween 80, Span 80	Ultrasonic homogenization	50 nm		Lower antioxidant capacity compared with gallic acid, while nanoemulsion had higher antiradical effect than free essential oil	(Azizkhani et al., 2021)
	Coconut oil and lycopene	Soy lecithin	Ultrasonic homogeni- zation	80 – 170 nm	Yogurt	Enhance antioxidant attributes	(Himanath et al., 2021)
	Sesame oil and sweet almond oil	Tween 80, Span 80	Ultrasonic homogeni- zation	1	Yogurt	The sesame oil nanoe- mulsion showed higher antioxidant activity	(Heydari Gharehcheshmeh et al., 2021)
	Tocopherol	Tween 80	Ultrasonic homogeni- zation	<500 nm	Fish sausages	250 mg/kg of tocopherol nanoemulsion indicated better antioxidant activity	(Feng et al., 2020)
	Zataria multiflora Boiss, Rosemary, and Cuminum essential oil	Tween 20, Span 80	Ultrasonic homog- enization/emulsion phase inversion	9.3–14.9 nm	Acipenser stellatus fillet	Cuminum nancemulsion formed by ultrasonic homogenizer showed optimum antioxidant activity compared to other nancemulsions	(Nasiri et al., 2020)
	Citrus peel (orange, grapefruit, manda- rin, lemon) essential oils	Tween 80	Ultrasonic homogeni- zation	Orange: 94.66 nm Grapefruit: 81.05 nm Mandarin: 79.14 nm Lemon: 47.40 nm	Rainbow trout (Oncorhynchus mykiss)	The citrus essential oil nanoemul-sions inhibited the oxidation of PUFA especially EPA and DHA	(Uçar, 2020)
	Quercetin	Tween 80 or Brij 30	Emulsion inversion point	180-200 nm	Chicken pâté	The quercetin nanoemulsion could inhibit lipid oxidation but could not prevent from protein oxidation	(de Carli et al., 2018)



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Natural product- Oil phased nanoemulsion applications  Whee	Oil phase	Emulsifier	Fabrication technique	Average droplet size (nm)	Food matrices	Specific functions	References
Whee				(			
Citru	Wheat germ oil	Tween 20	Ultrasonic homogeni- zation	1	Cooked fish (mackerel) fillets	The nanoemulsion has retarded the increase in TBAR, FFA, and PV of treated samples by 36.1%, 20.5%, and 32.2%, respectively	(Ceylan et al., 2020)
	Citrus medica L. var. sarcodactylis	Tween 80	Spontaneous emulsifi- cation method	I	Tofu	Nanoemulsions could scavenge the radi- cals more efficiently and showed higher reducing power	(Lou et al., 2017)
Curci	Curcumin	Tween 20	High-pressure homogenization	63–126 nm	Milk	Milk samples fortified by curcumin nanoemulsion could remarkably decrease the lipid oxidation than unfortified samples	(Joung et al., 2016)
Nanobio-flavors Ging offic	er (Zingiber cinale) essential	Tween 20, Arabic gum	Homogenization	68–1035 nm	ı	Bring about desired flavor	(Firoozi et al., 2020)
Ocim esse	Ocimum basilicum essential oil	Sorbitan monooleate	Homogenization	120 nm	ſ	Flavoring agent and stable during 90 days of storage	(da Silva Gündel et al., 2018)
Aron	Aroma compounds with olive oil	Tween 80	1	39.22 nm	1	The olive oil addition in nanoemulsion increases the stability of aroma components	(Ren et al., 2018)
D-lin	D-limonene oil	I	Ultrasonic homogeni- zation	116.60 nm	I	Induced pleasant citrus-like flavor to food products	(Sonu et al., 2018)
Nanobio-colorants Papri (Ca	ika oleoresin 1psicum annuum	Whey protein, soy lecithin	High-pressure homogenization	<160 nm	ı	Nanoemulsions could protect and stabilize carotenoids for their application in foodstuffs	(Flores-Andrade et al., 2021)
Beetr vul.	Beetroot (Beta vulgaris) extract: betalain	Whey protein concentrate	Ultrasonic homogeni- zation	701 nm		Improve color stability	(Mohammed et al., 2021)



Table 2   (continued)							
Natural product- based nanoemulsion applications	Oil phase	Emulsifier	Fabrication technique	Average droplet size (nm)	Food matrices	Specific functions	References
	Orange ( <i>Citrus reticulate</i> ) peel waste: β-carotene	Polyoxyethylene (20)	Ultrasonic homogeni- zation	143.7 nm	Fruit juice	Moderate color stability, enhance bioaccessibility and nutritional value	(Barman et al., 2020)
	β-Carotene	Tween 80, Span 80	Ultrasonic homogenization	260 nm	Nonsmoked sausage	The lowest lipid oxidation and β-carotene degradation were noticeable in the sausage with 10 g 100 g <sup>-1</sup> β-carotene-loaded nanoemulsion	(Chajjan et al., 2021)
Nanobio-nutritional additives	(Sesame oil or olive oil or grape seed oil)+vitamin D	Tween 80	High-pressure homogenization	137.6–171.6 nm	ı	Increase stability and bioavailability and controlled release of vitamin D	(Maurya and Aggarwal, 2019)
	Omega-3 fatty acids	Tween 80, Span 80	1	60 nm	Yogurt	Nanoemulsion is a suitable carrier of omega-3 fatty acids in food fortification	(Almasi et al., 2021)
	Vitamin D3 and saffron (Crocus sativus L.) petal bioactive compounds	Basil seed gum	High-pressure homogenization	115–385 nm	ı	Improve the bioavailability of vitamin D3 and saffron petal bioactive compounds	(Gahruie et al., 2020)
	Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA)	Tween 80, Span 80	Emulsion phase inversion	1	Apple juice	The results indicated that the nanoemulsion had good stability at low-temperature storage, near neutral pH	(Zhang et al., 2020)
	Canola oil + vitamin D	Soy lecithin, Tween 80	Ultrasonic homogenization	112.36 nm	I	Develop soya lecithin and Tween 80-based vitamin D delivery system for food additives and nutra- ceutical components	(Mehmood et al., 2019)



grapefruit outperformed other essential oils in reducing Enterobacteriaceae growth. The nanoemulsions eliminated the fishy odor and improved sensorial features (Durmus, 2020). As mentioned earlier, nitrite, a common synthetic food additive, reacts with amides and amines in food and produces N-nitrogen compounds, leading to human cancer. Thus, thymol nanoemulsion was applied as natural nitrite substitute in sausage products. Thymol recognizes as a monoterpene phenol ingredient with remarkable antibacterial capacity. The droplet size of provided nanoemulsion by ultrasonic homogenizer was reported 86.39 nm. The sausage samples treated with thymol nanoemulsion indicated low Escherichia coli, Staphylococcus aureus, and Clostridium perfringens counts compared to control and nitrite-comprising samples. The color quality of samples treated with thymol nanoemulsion and nitrite was identical to samples comprising 120 mg/kg nitrite. The achievements revealed that thymol nanoemulsion had an antimicrobial effect on sausages. Combining thymol and nitrite is advantageous in preserving the safety and color quality of sausages (Sepahvand et al., 2021).

#### Nanobio-Antifungal

Aflatoxin B<sub>1</sub> (AFB<sub>1</sub>) is deemed a carcinogenic and hepatotoxic mycotoxin produced by specific strains of Aspergillus flavus in foodstuffs (Manso et al., 2014; Nugraha et al., 2018). Moreover, AFB<sub>1</sub> underlies lipid peroxidation through free radical generation in food, which leads to off-odor and off-flavor (Eftekhari et al., 2018). Therefore, Origanum majorana essential oil with 28.92% terpinen-4-ol as a critical bioactive component was employed to prevent AFB<sub>1</sub> secretion in maize. This natural antifungal was nanoemulsified by Tween 80. Ultra-Turrax provided the preemulsion for 20 min at 4 °C. Afterward, the prepared emulsion was ultrasonicated for 10 min at 4 °C. The findings manifested that this natural nanoemulsion had a good inhibitory effect on AFB<sub>1</sub> and prevented lipid peroxidation from exerting negative impress on organoleptic properties (Chaudhari et al., 2020). Cleome viscosa essential oil encompasses different bioactive elements, which could be effective against food-borne pathogens. The nanoemulsion formulation of this essential oil is obtained by Triton-x-100 (polyoxyethylene isooctylphenyl ether) as a nonionic surfactant. The concentration of Cleome viscosa essential oil in nanoemulsion was 6% v/v. The provided emulsion was sonicated at 200 kHz and had a power output of 750 W. The nanoemulsion with a droplet diameter below 20 nm could effectively disrupt cell wall biosynthesis and demonstrate superior fungicidal performance against Candida albicans (Krishnamoorthy et al., 2021). Clove essential oil is one of the plant-based substances prone to be used as synthetic antifungal replacements in the food industry. The literature noted that the major elements of clove essential oil, which have various effects including anticarcinogenic, antimutagenic, antiinflammatory, and analgesic, are β-caryophyllene, eugenol, and eugenol acetate. The coarse emulsion was achieved by a high-speed mixer applying an Ultra-Turrax for 5 min at 24,000 rpm. After that, the obtained emulsion was passed through a specific valve of a high-pressure homogenizer at 300 MPa. The nanoemulsion of clove essential oil showed antifungal activity against Aspergillus niger and Candida albicans under the in vitro circumstances. The observation indicated that the inhibition zone was 2.13-3.19 mm. This result was due to different terpenoids that destroyed cell membranes or deterred the sporulation and germination of fungi. It is also presumed that clove essential oil could prevent enzyme synthesis, changing the cell wall morphology and consequently increasing cell membrane permeability (Shahbazi, 2019).

#### Nanobio-Antioxidants

Lipid oxidation is a radical-initiated reaction that leads to oxidative deterioration of polyunsaturated fatty acids, develops off-flavor, and degrades food quality. The fortification of foodstuffs with bioactive compounds comes up with many specialists as one of the pivotal measurements for health promotion. Heydari Gharehcheshmeh and coworkers in 2020 fortified yogurt with sweet almond and sesame oil nanoemulsions. It was proved that sesame oil and sweet almond oil contain polyunsaturated fatty acids, monounsaturated fatty acids, fibers, minerals, vitamins, phytochemicals, and several antioxidants, including tocotrienols, tocopherols, and gamma oryzanol. 0.5% of Tween 80 and 0.25% of Span 80 were selected as emulsifiers, and an ultrasonic homogenizer was used for the nanoemulsion production. The DPPH radical scavenging activity fortified yogurts were determined by IC<sub>50</sub> value. The IC<sub>50</sub> value of yogurts treated with sweet almond oil, sesame oil, and control samples was reported  $45 \pm 1.4$ ,  $31 \pm 2.1$ , and  $85 \pm 2.2 \mu g/ml$ , respectively. Therefore, the sesame oil nanoemulsion showed higher antioxidant activity and oxidative stability of yogurts. The present survey demonstrated that the sesame oil nanoemulsion with 0.25% emulsifier is an adequate substitute for synthetic antioxidants (Heydari Gharehcheshmeh et al., 2021). As fish sausages are highly vulnerable to lipid oxidation, which negatively affects sensory attributes, the tocopherol nanoemulsion and its coarse emulsion were established for evaluating lipid oxidation changes within 16 days of storage at 4 °C. The treatment of fish sausages with 250 and 500 mg/kg tocopherol nanoemulsions provided by an ultrasonic homogenizer indicated lower peroxide value and delayed lipid oxidation, whereas the coarse emulsion revealed higher peroxide value due to higher particle sizes ranging from 4 to 6 µm. The higher antioxidant activity of tocopherol nanoemulsion



arising from smaller droplet sizes (< 500 nm) gave rise to homogeneous droplet distribution and better stability. This study showed that 250 mg/kg of tocopherol nanoemulsion exhibited better antioxidants without changing textural properties during cold storage (Feng et al., 2020). Acipenser stellatus fillets were treated by three types of essential oils, such as Zataria multiflora Boiss, Rosemary, and Cuminum in the form of nanoemulsions. These essential oils were nanoemulsified by various procedures, including ultrasonic homogenization and emulsion phase inversion. 10 gr of fish fillets was immersed in nanoemulsions, and the antioxidant activity was evaluated at 4 and 10 °C. The peroxide value and malondialdehyde level were appraised to specify the antioxidant activity. The consequences revealed that the peroxide value of treated fish fillets with all nanoemulsions produced by both fabrication techniques was lower than control samples. It was also reported that malondialdehyde levels in untreated samples were remarkably higher than those in treated fish fillets. It was highlighted that Cuminum nanoemulsion at 3% and 5% produced by ultrasonic homogenizer indicated better antioxidant activity and could apply as flavoring agent (Nasiri et al., 2020). Chicken pâté has been known as a cooked chicken meat product that is highly sensitive to lipid oxidation reactions along the storage time. This process in poultry meat products underpins color, flavor, and nutritional value deterioration. The application of quercetin by researchers is an exciting strategy for the retardation of lipid oxidation in chicken pâté. Quercetin is a kind of flavonoid with significant antioxidant activity. The hydrophobic character of this natural antioxidant considers an obstacle to incorporation in chicken pâté. Therefore, the nanoemulsion of quercetin was produced with the emulsion inversion point method and Tween 80 or Brij 30. The mean droplet size of obtained nanoemulsion was in the range reported in the range of 180-200 nm. This novel antioxidant was more efficient than (about 60%) butylated hydroxytoluene and sodium nitrite as synthetic antioxidants during 24 weeks of storage. Meanwhile, Brij 30 formed nanoemulsions with more stability (de Carli et al., 2018).

#### **Nanobio-Flavors**

Flavor molecules and components are the major ingredients of food profile that influence desirability and consumer acceptance. Flavoring agents are generally categorized into natural and synthetic substances. Different essential oils, protein distillates, and oleoresins with plant or sometimes animal origins are natural-based flavors. At the same time, artificial flavors do not have vegetable or fruit sources and are obtained from chemical processing. Emulsions provided at the nanoscale consider suitable flavor carriers for improving

compatibility, solubility, oxidation sensitivity, and the moderately strong odor of natural flavors (Saffarionpour, 2019). Above all, the negligible turbidity of obtained nanoemulsion makes the flavor nanoemulsions suitable for application in clear beverages (Zhang et al., 2016).

Ginger (Zingiber officinale) essential oil, with various valuable attributes, including antimicrobial and antioxidant activities, could be used as a flavor ingredient in food and beverages. In contrast, low water solvability and susceptibility of bioactive components to heat, light, oxygen, and moisture consider major limitations in the direct utilization of this essential oil in food matrices. Firoozi and her team (2020) overwhelmed these challenges with the use of a bottom-up approach. Tween 20 and Arabic gum were applied as emulsifiers, and the average diameter size was obtained from 68 to 1035 nm (Firoozi et al., 2020). One of the most favorable flavoring agents with various therapeutic attributes that has been around for many years is Ocimum basilicum essential oil (common basil). This natural flavor is extensively utilized as seasoning. The nanoemulsion form could substantially prevent from photodegradation and oxidation of basil essential oil.

The stability of provided nanoemulsion was assessed over 90 days by one of the studies in 2018. It was observed that the mean droplet diameter of nanoemulsion (120 nm) produced by homogenization remains unchanged over the 60 days at different storage situations. After this duration, the temperature of the storage chamber increased to 160 nm and eventually to 200 nm in 90 days. The literature also corroborates that increasing the droplet size of essential oil nanoemulsion is associated with storage at high temperatures. The polydispersity index declined in the climatic chamber situation after 7 days. In contrast, this value increased at refrigeration temperature during 60 days. It was also pointed out that the polydispersity index achieved lower than 0.3 within 90 days in various storage conditions (da Silva Gündel et al., 2018). An interesting investigation studied the effect of olive oil on aroma retention in a nanoemulsion system. The oil phase was prepared with 31 mg of each aroma compound and a specific olive oil. The mean droplet size and polydispersity indexes were 39.22 nm and 0.242 nm, respectively. It was also expressed that the nanoemulsion stability was increased by the olive oil addition. Using 10% olive oil in nanoemulsion formulation decreased the release of ethyl acetate by 48% and adding 3% olive oil remarkably reduced the release of nonanal and a-pinene. The results indicated that the utilization of olive oil of more than 5% in nanoemulsion elevated the persistence of decanal, D-limonene,  $\beta$ -myrcene,  $\alpha$ -terpineol, and eugenol with 1-octanol, benzyl alcohol, and β-ionone being unchanged (Ren et al., 2018).



#### **Nanobio-Colorants**

Color is the most important attribute of food and beverages influencing market acceptance. Therefore, colorants and dyes are major additives to moderate food appearance (Fuenmayor et al., 2021). Natural pigments extracted from plant-food waste can replace artificial dyes (Ebrahimi & Parvinzadeh Gashti, 2016). The natural-based colorants can be categorized into various classes, such as flavonoids, carotenoids, chlorophylls, different pigments, and betalains (Akhavan & Jafari, 2017; Assadpour et al., 2017). These colorants are biodegradable, naturally accessible, and nontoxic and have antimicrobial/antioxidant performance (Micó-Vicent et al., 2020, 2021). The direct application of these pigments has several drawbacks, such as poor stability, low light fastness, and limited color array. Therefore, converting natural pigments to their nanostructure could overwhelm the limitations mentioned above (Ozogul et al., 2022).

One of the natural pigments with antioxidant and anticancer activity is carotenoids. Paprika oleoresin (Capsicum annuum L.) comprises yellow and red carotenoid fractions. It was pointed out that the yellow fraction contains antheraxanthin, β-cryptoxanthin, zeaxanthin, violaxanthin, capsolutein, and  $\beta$ -carotene and the red fraction involves capsorubin, ketocarotenoids, and capsanthin. These pigments are employed to color or restore color losses in beverages, sauces, salad dressings, ice cream, and mayonnaise. The carotenoids extracted from paprika are highly sensitive to light, pH, and heat within the process and storage period. Thus, the nanoemulsion of paprika oleoresin was produced in 2021 to conquer these challenges. The aqueous phase comprised whey protein, Arabic gum, and soy lecithin as emulsifiers. High-speed homogenizer entirely distributed paprika oleoresin throughout the aqueous phase at 11000 rpm for 6 min. Afterward, the obtained emulsion was crossed via a high-pressure homogenizer. Using soy lecithin and whey protein could efficiently produce nanosized droplets (smaller than 160 nm). Arabic gum indicated lower surface activity than soy lecithin and whey protein due to larger particles within emulsification. This issue may arise from the slow adsorption of large molecules of Arabic gum, lower surface activity, and higher interfacial tension. During five cycles, the pressure limit exerted on the emulsion was 103.42-158.57 MPa. The high pressure created the smaller particles' diameter. The observations showed that the smaller carotenoid droplets were more susceptible to chemical deterioration and could effectively utilize in food products (Flores-Andrade et al., 2021). The main red pigment of beetroot extract is betalain (betanidin 5-O-βglucoside). Betalain is a water-soluble nitrogen-containing colorant typically used in meat substitutes, confections, and dairy products. What is apparent is that this food colorant is susceptible to alkaline pH and high temperature. This gap is closed through nanoemulsification approach. Eventually, the betalain nanoemulsion was compared with its microemulsion for its stability and physicochemical and rheological attributes. Once the betalain has undergone the rotor-stator homogenization, the resulting microemulsion goes through ultrasonic homogenization. The obtained microemulsion and nanoemulsion of this natural pigment were compared for their stability and physicochemical and rheological attributes. The consequences confirmed that nanoemulsion indicated better pH and thermal stability within 15 days of storage. The resulting nanoemulsion slowed down the particle coarsening and moderated the color stability owing to nano-sized droplets (701  $\pm$  27.2 nm), low surface tension, and non-Newtonian behavior (Mohammed et al., 2021). The interest in converting agro-food waste into valuable products has existed for many years. One of the investigations extracts β-carotene from orange peel waste. The synthetic colors gave way to β-carotene with lipophilic attributes. The ultrasonic homogenizer fabricated a stable nanoemulsion of this natural pigment to increase its stability and bioaccessibility in fruit juice. The size of the droplet and surface charge of obtained nanoemulsion were 143.7 nm and -38.2 mV, respectively (Barman et al., 2020).

#### **Nanobio-Nutritional Additives**

There is an unequivocal relationship between vitamin consumption and normal body function, and also, the consumption of nutraceuticals enhances human health (Godswill et al., 2020). Their low stability, water solubility, and bioavailability are serious obstacles to direct incorporation into food products.

Vitamin D is crucial for accurate immune function and bone development. Vitamin D deficiency is prevalent throughout the world. The best strategy for overcoming this challenge is food fortification with vitamin D nanoemulsion. Jafarifar and coworkers used high-pressure homogenization in 7 cycles with a pressure of 1000 bar for this purpose due to the problem with sonication. It was declared that using an ultrasonic homogenizer might increase the probability of metal release during sonication and lead to metal contamination. The lipid phase includes a liquid vegetable oil and Tween 80 selected as an emulsifier. The range of nanosized particles was provided between 137.6 and 171.6 nm, and the nanoemulsion form released 26.9% vitamin D. This formulation also preserved vitamin D under acidic situations. The observations underscored that the nanoemulsion form could remarkably promote vitamin D bioavailability and facilitate food fortification (Maurya & Aggarwal, 2019). It is well established that the use of omega-3 fatty acids has positive effects on the human heart, skin, brain, eyes, and behavior. After all, omega-3 fatty acids inhibit high blood pressure, heart malfunction, arthritis, cancer, and diabetes.



Flaxseed oil is regarded as a rich source of omega-3 fatty acids. Its poor solubility and high tendency to oxidation trigger decreased flaxseed oil application in food formulation. One of the surveys employed a low-energy emulsification approach to produce a nanoemulsion of flaxseed oil to overwhelm the abovementioned limitations. The optimal formulation of nanoemulsion comprised 3% (w/w) flaxseed oil, 36%(w/w) surfactant, 10% (w/w) co-surfactant, and 51% (w/w) deionized water as the aqueous phase. The provided nanoemulsion was stable for 11 months at ambient temperature without phase separation and creaming. Eventually, the yogurt was fortified with this nanoemulsion. The pH and acidity of the resulting yogurt were reported 4.22 and 1.41 wt%, respectively (Almasi et al., 2021).

# **Gaps and Future Remarks**

Currently, special attention has been paid to nanoemulsions in food technology. The scientifically based evidence shows that food-grade nanoemulsions can decrease the dose, enhance the influence of natural-based compounds, and improve food attributes, including taste, texture, and stability. Food-grade nanoemulsions are thermodynamically unstable that may break down via different exterior agents. The larger surface area of nanoemulsion needs the most emulsifier, leading to off-flavor, toxicity, and high expenses. Therefore, the application of natural emulsifiers for forming natural-based nanoemulsions as an efficient and healthy substitute for synthetic food additives is more acceptable (Das et al., 2020). The reduction of droplet size of the nanoemulsions typically augments their stability while it may decrease chemical stability. According to recent findings, nanoemulsions could interact with biological systems and may have different roots in the gastrointestinal tract. Due to their smaller sizes, the nanodroplets simply pass via cell barriers and tissue. Toxic and allergic reactions are severe complications of nanoemulsion consumption. The accumulation of nanovitamins and nanonutraceuticals in different organs and tissues is an essential implication of their consumption. It can be suggested that the evaluating criteria, like the tolerable upper intake level and recommended daily allowance, should be revised, and risk assessments are required to evaluate the toxic effects of food containing nanoemulsions. The nanofood consumed by children and people with a health problems should be interpreted cautiously and specifically labeled (Li et al., 2021). The fabrication of natural-based nanofood additives, especially nanocolor and nano-antifungal, will need more attempts in the future. More in vivo studies turn out to be done for the understanding of nanofood effects on the human body.



#### **Conclusion**

The concern about food-related diseases has been around for many years. It is obvious that the long-term consumption of synthetic food additives has many complications. Thus, there is strong interest in using natural-based food additives to address this problem owing to their health effects and being environmentally friendly. This strategy's strength lies in the use of nanoemulsions that can decrease the amount of required bioactive compounds concomitant with the increase in their efficacy. The stability, bioavailability, flavor, color, and solubility of these natural compounds were improved by drawing on their nanoemulsion form. The production of bio-based food additives is an interdisciplinary research endeavor and represents a growing trend in the near future of food. More action mechanism of natural nanoemulsion as food additives and their probable side effects remain to be elucidated.

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Data Availability No data is available for this review article.

## **Declarations**

**Ethics Approval** This review article does not include any human or animal studies performed by any author.

**Competing Interests** The authors declare no competing interests.

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