REVIEW



Encapsulation of functional ingredients in lipidic nanocarriers and antimicrobial applications: a review

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Abstract

Global food demand and security are attracting stakeholders' attention to food quality and safety. In particular, there is an urgent need for efficient techniques to preserve food for a long time. This can be done by encapsulation in nanocarriers such as nanoemulsions, nanoliposomes and nanolipid carriers. These nanocarriers protect functional ingredients such as polyphenols, vitamins, minerals, flavors and antimicrobial agents. Nanocarriers improve stability, functionality, entrapment efficiency and controlled-release of functional ingredients. Antimicrobial ingredients are among the most promising tools for food preservation. The nanoencapsulated form of antimicrobial agents showed an increase in surface area, passive transport and sustained release, which enhance the antimicrobial efficiency by comparison with the direct application of antimicrobial agents. Here, we review lipid-based nanocarriers, nanoencapsulation of functional ingredients, and food application of lipid-based nanocarriers as antimicrobial agents.

 $\textbf{Keywords} \ \ Encapsulation \cdot Nanoemulsions \cdot Nanoliposomes \cdot Nanolipid \ carriers \cdot Functional \ ingredients \cdot Antimicrobial \ agents$

Introduction

The health awareness among consumers has increased the demand for the development of functional or novel food products containing bioactive compounds to impart certain health benefits. However, the utilization of bioactive compounds in food products has certain limitations in terms of decomposition, low stability during food processing conditions, which reduces their bioavailability as well as functional properties (Saini et al. 2019a). Such drawbacks can be overcome by a technique known as encapsulation to encase these compounds in suitable matrices or a combination thereof, which not only enhances their stability but also improves physicochemical properties (Lohith Kumar and Sarkar 2017). This technique has significant applications in the food as well as pharmaceutical industries and aims at preserving the sensitive compounds against undesirable circumstances until the controlled release of functional food

Microencapsulation is a broad category for the delivery of functional food ingredients and is defined as the technique to entrap the active components/agents such as antioxidant, vitamins, minerals, fatty acids, phytosterols, lycopene and living cells in another substance called wall material (Burey et al. 2008; Champagne and Fustier 2007; McClements et al. 2009a, b). These encapsulating/wall materials are also known as shell, capsules, carrier material, coating, membrane, matrix, or external phase (Wandrey et al. 2009; Fang and Bhandari 2010). Microencapsulation techniques involve the mechanical processes such as spray drying, fluidization bed coating, spray cooling/chilling and extrusion as well as chemical techniques such as molecular inclusion, interfacial polymerization, coacervation and co-crystallization (Gibbs et al. 1999; Zuidam and Shimoni 2009). Among different mechanical processes, approximately 80-90% of encapsulates are generally produced by spray drying (Porzio 2007;



ingredients. The most widely used technique is microencapsulation that increases the bioavailability of the components, enables the modification of ingredients' properties, masks the undesirable aroma as well as taste and prevents the interactions with other chemical structures (Barbosa-Cánovas et al. 2005; Ting et al. 2014; Assadpour and Jafari 2018; Jafari 2017).

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Milanovic et al. 2010). Spray cooling and chilling techniques operate at different melting points of lipids to fabricate the lipid-coated active agents, whereas in extrusion methods, the dripping tools such as a syringe, pipette, a vibrating nozzle or atomizing disk are used for releasing droplets of an aqueous solution of polymer into a gelling bath (Gouin 2004; Zuidam and Shimoni 2009; Wandrey et al. 2009). The fluidization bed technique is generally applied on the lightweight particles such as granules or powder particles either in drying or in encapsulation by fluid-bed coating (Dewettinck and Huyghebaert 1999). However, remarkable interest has been developed in nanoscale delivery systems owing to their better functional properties including more encapsulation efficiency, controlled release, improved stability, masking of undesirable flavors and enhanced bioavailability of various functional ingredients by reducing particle size as compared to microencapsulation (Shishir et al. 2018).

With the advancements of nanotechnology in the food sector, various other techniques are being devised to ensure the safe delivery and bioavailability of different functional compounds. At present, the traditional microencapsulation systems are being replaced with nanoencapsulation systems (having a size less than 1000 nm) that enhance bioavailability by increasing the surface-to-volume ratio without affecting the appearance of food products. These nanocarriers have a high possibility of muco-adhesiveness and interaction with metabolic factors and enzymes. Thus, these can easily penetrate into target cells and release their cargos (Jafari and McClements 2017; Katouzian et al. 2017; McClements and Jafari 2017).

Nanocarriers can be classified as lipid-based (nanoe-mulsions, nanostructured phospholipid carriers, nanolipid carriers), nature-inspired (caseins, cyclodextrins, amylose), special equipment-based (electrospinning, electrospraying, nanospray dryer, micro-/nanofluidics) and biopolymers that include single biopolymer nanoparticles, complex biopolymer nanoparticles, nanogels, nanotubes/nanofibrils (Assadpour and Jafari 2018). This review encompasses the important information regarding lipid-based nanocarriers for the delivery of different functional ingredients and their food application as antimicrobial agents.

Different types of lipid-based nanocarriers

Lipid-based nanocarriers are one of the major classes of nanoencapsulation for the delivery of polyphenols in different food systems. These are divided into three groups, which include nanoemulsions, nanoliposomes (nanostructured phospholipid carriers) and nanolipid carriers (Fig. 1). Lipid-based nanoemulsions are important nanocarriers formulated by the oil, water and emulsifiers or biopolymers. These systems are further divided into different subgroups

such as single (oil-in-water (O/W)), water-in-oil (W/O), double (oil-in-water-in-oil (O/W/O)), water-in-oil-in-water (W/O/W), pickering and structural (single interface layer, double interface layer) nanoemulsions (Jafari et al. 2017; Akhavan et al. 2018). Another group of lipid-based nanocarriers involves nanoliposomes (nanostructured phospholipid carriers), which are produced using oils, phospholipids and different solvents. Moreover, this group can be a monolayer, multilayer or in combination with coating as in the case of structured nanoliposomes/phytosomes (Demirci et al. 2017). Finally, the last group in lipid-based nanocarriers is nanolipid carriers, subgrouped into solid lipid nanoparticles, nanostructured lipid carriers and smart lipid nanocarriers that can be formulated by solid lipids or oils and solid lipids (Pyo et al. 2017; Katouzian et al. 2017). The overall classification of lipid-based nanocarriers along with their fabrication methods is shown in Table 1.

Nanoencapsulation of different functional ingredients

Functional ingredients such as antioxidants are the compounds that inhibit the oxidation for the prevention of cellular damage. These are classified as enzymatic and non-enzymatic antioxidants. The enzymatic class of antioxidants generally includes primary (catalase, superoxide dismutase, glutathione peroxidase) and secondary (glutathione reductase, glucose-6-phosphate) antioxidants. Non-enzymatic antioxidants involve vitamins, minerals, carotenoids and plant polyphenols. However, among these, polyphenols are considered as the main subgroup of nonenzymatic antioxidants (Esfanjani and Jafari 2017). These non-enzymatic antioxidants (hydrophobic and hydrophilic) are nanoencapsulated using different approaches to protect them from adverse environmental conditions, to facilitate gastrointestinal absorption and to enhance the bioavailability (Paroha et al. 2020). In the last few years, numerous studies have been reported on nanoencapsulation that observed this technique is very useful in the pharmaceutical, food and nutraceutical sectors where proper protection and controlled release of functional compounds are required (Sarkar et al. 2017). Different lipid-based nanocarriers used for the encapsulation of functional food ingredients have been discussed in subsequent sections.

Nanoemulsions

Nanoemulsions are nanosized emulsions that are produced using high and low energy approaches. Firstly, functional ingredients are dissolved in oil (oil phase), which is generally followed by mixing them with aqueous phase using blenders and/or high-speed homogenizers to obtain the



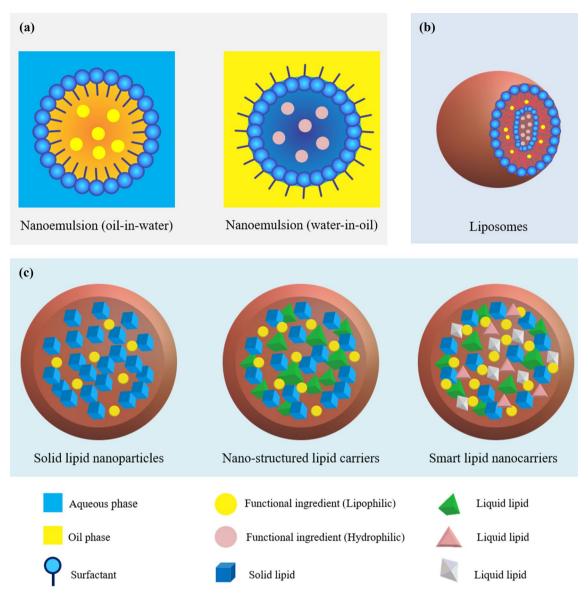


Fig. 1 Lipid-based nanocarriers for the delivery of functional ingredients. **a** Nanoemulsions indicating the formational ingredients such as surfactant, oil and aqueous phase with lipophilic or hydrophilic func-

tional ingredients. b Liposomes encapsulating the lipophilic as well as hydrophilic functional ingredients. c Various nanolipid carriers consisting of solid lipid, liquid lipid and functional ingredients

coarse emulsions. Finally, the formed coarse emulsions are further treated using high-energy approaches such as ultrasonication, high-pressure homogenization and high-speed homogenization. These nanoemulsions are used to encapsulate different functional compounds such as lutein (Surh et al. 2017), β -carotene (Teixé-Roig et al. 2020), lycopene (Li et al. 2018) and curcumin (Li et al. 2016a) as shown in Table 2. Also, these are used to improve the stability, texture, nutritive and sensorial attributes of different food products (Dasgupta et al. 2019a). Extensive studies have been reported on the O/W nanoemulsions for encapsulating the lipophilic compounds, in contrast to W/O nanoemulsions owing to their significant benefits in various commercial applications.

A recent study revealed that the presence of multilayers in nanoemulsions leads to an increase in hydrodynamic diameter along with loading capacity $(0.53\pm0.03\%, \text{w/w})$ and encapsulation efficiency of $99.8\pm0.8\%$, when the multilayered nanoemulsions are formed by electrostatic technique (layer-by-layer) to encapsulate the lipophilic compound (e.g., curcumin). Hence, these nanosystems have great potential to protect the functional properties of lipophilic compounds and are used in different applications (Silva et al. 2020). In another study, nanoemulsions loaded with limonene and carvone can be a propitious approach to protect the tissues from cadmium-induced oxidative damage (Shafaei et al. 2020). Some studies focused on the increase



Table 1 Techniques for the preparation of lipid-based nanocarriers for delivery of functional ingredients Source: Jafari (2017); Assadpour and Jafari (2018)

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Nanoencapsulation systems	Nanocarriers	Examples of nanocarriers	Preparation techniques	Summary
Nanoemulsions	Single nanoemulsions	Water-in-oil, oil-in-water	Hot emulsification, cold emulsification, solvent emulsification-	Typically, droplet size of dispersed phase is less than 500 nm
	Double nanoemulsions	Water-in-oil-in-water, oil-in-water-in-oil	evaporation, high-pressure homogenization, ultrasonication,	Kinetically stable and thermodynamically unstable
	Structural nanoemulsions	Single and double interface layer	microemulsion, melting disper- sion, solvent injection, solvent	Milky to optical clear in appearance
	Pickering nanoemulsions	1	emulsification-diffusion, double emulsion technique	
Nanostructured phospholipid car-	Nanoliposomes	Mono- and multilayer	Thin-film dispersion, ethanol/ether	Encapsulate both the hydrophilic and
liets	Nanophytosomes	Mono- and multilayer	tijection, probe/batii uittasonica- tion, membrane extrusion, freeze- dried rehydration vesicles reverse-	Spherical particles containing phos-
	Structural nanoliposomes/phyto-	With coating	phase evaporation, microfluidic channel, detergent depletion.	spidnoyd
	somes		high-pressure homogenization,	
			supercritical fluid injection & decompression, microfluidiza-	
			tion, dense gas, dual asymmetric centrifugation, heating method	
Nanolipid carriers	Solid lipid nanocarriers	I	Hot emulsification, cold emulsifica-	Average size is 10–500 nm
			tion, high-pressure homogeniza- tion, microemulsion, solvent	
			emulsification-evaporation, melt-	
			ing dispersion, solvent emulsifi-	
			cation-diffusion, ultrasonication,	
			solvent injection, double emulsion	
			ecumdne	
	Nanostructured lipid carriers			Formulation includes the binary mixture of solid lipids or solid lipids
				and liquid lipid which are spatially
	Smart linid nanocorriere			dinerent
	Silialt lipiu lialiocaliteis			



Table 2 Examples of lipid-based nanocarriers loaded with functional ingredients

Food ingredients	Encapsulated materials	References
Nanoemulsions		
Phenolic compounds	β-carotene	Chen et al. (2020a, b)
1	Lycopene	Zhao et al. (2020)
	β-carotene	Chen et al. (2020a, b)
	Tocopherol	Feng et al. (2020b)
	Carotenoids (Paprika)	Jimenez-Escobar et al. (2020)
	Capsanthin	Kulkarni et al. (2020)
	Resveratrol	Shehzad et al. (2019)
	Curcumin	Pinheiro et al. (2016)
	Eugenol	Majeed et al. (2016)
	Quercetin	Ni et al. (2017)
	Curcumin	Liu et al. (2020a)
	Rutin and anthocynin	Akhtar (2014)
	Olive leaf extract	Mohammadi et al. (2016)
	Resveratrol	Davidov-Pardo and McClements (2015)
Natural food colorants	Crocin	Mehrnia et al. (2016)
	β-carotene	Barman et al. (2020)
Food flavors	Peppermint	Liang et al. (2012)
	D-limonene	Jafari et al. (2007)
Essential oils	Thyme oil	Wu et al. (2014)
	Eugenol	Ma et al. (2016)
	Krill oil	El-Messery et al. (2020)
	Ricinus communis L. oil	Javanshir et al. (2020)
	Borage seed oil	Rehman et al. (2020)
	D-limonene	Feng et al. (2020a)
	Thyme oil	Guo et al. (2020)
	Bunium persicum Boiss & Zataria Multiflora Boiss oil	Keykhosravy et al. (2020)
	Araucaria heterophylla resin oil	
		Elshamy et al. (2020)
Vitamins	D_3	Schoener et al. (2019)
	E	Dasgupta et al. (2016)
	D	Guttoff et al. (2015)
	D_3	Ozturk et al. (2015)
	B_{9}	Assadpour et al. (2017)
	\mathbf{B}_2	Bou et al. (2014)
Nanostructured phospho		
Phenolic compounds	Curcumin	Mourtas et al. (2014)
-	Luteolin	Wu et al. (2018)
	Quercetin & resveratrol	Cadena et al. (2013)
	Epigallocatechin gallate	Zou et al. (2014b)
	Rutin	Babazadeh et al. (2017)
	Quercetin	Frenzel et al. (2015)
	Phenolic compounds of tea	Zou et al. (2014a)
	Catechin & epigallocatechin gallate	Rashidinejad et al. (2016)
	Hesperetin	Mukherjee et al. (2008)
Mineral ions/salts	FeSO ₄ .7H ₂ O	Kosaraju et al. (2005)
Essential oils	Anethum graveolens essential oil	Ortan et al. (2009)
	Rose essential oil	Wen et al. (2011)
	Cinnamon essential oil	Wu et al. (2015)
	Perilla oil	Zamani-Ghaleshahi et al. (2020)



Table 2 (continued)

Food ingredients	Encapsulated materials	References
Antimicrobial agents	Nisin	Taylor et al. (2008)
	Daptomycin	Li et al. (2013)
Vitamins	β-carotene	Tan et al. (2016)
	B_1	Fathima et al. (2016)
	A palmitate	Pezeshky et al. (2016)
	E & C	Marsanasco et al. (2011)
	A	Pezeshky et al. (2016)
	E, B_{12}, D_2	Bochicchio et al. (2016)
	C	Liu et al. (2017)
	C	Hamadou et al. (2020b)
Nanolipid carriers		
Phenolic compounds	Curcumin	Mulik et al. (2010)
	Resveratrol	Pandita et al. (2014)
	Quercetin	Liu et al. (2014)
	Myricetin	Gaber et al. (2017)
	Ferulic acid	Hassanzadeh et al. (2018)
	Epigallocatechin gallate	Radhakrishnan et al. (2016)
	Hesperetin	Fathi and Varshosaz (2013)
	Curcumin	Righeschi et al. (2016)
	Quercetin	Huang et al. (2017)
	β-carotene	Oliveira et al. (2016)
	Rutin	Babazadeh et al. (2016)
	Curcumin & genistein	Aditya et al. (2013)
Natural food colorants	α -tocopherol	de Carvalho et al. (2013)
	Lutein	Lacatusu et al. (2013)
	β-carotene	Zhang et al. (2013)
	Astaxanthin	Li et al. (2016b)
Essential oils	Cardamom essential oil	Nahr et al. (2018)
	Pomegranate seed oil	Soleimanian et al. (2018)
Vitamins	B_2	Couto et al. (2016)
	Е	Uraiwan and Satirapipathkul (2016)
	D_3	Mohammadi et al. (2017)

in shelf life of perishable products such as strawberry, meat and fish sausages through nanoemulsion-based films and coatings (Xiong et al. 2020; Chu et al. 2020; Feng et al. 2020b) as shown in Table 3. Chu et al. (2020) revealed that the pullulan-cinnamon essential oil nanoemulsions coating enhanced the shelf life of strawberry at room storage. Moreover, the better preservation (i.e., maintaining tenderness, minimizing the color and pH change, inhibiting the microbial growth and retarding the protein and lipid oxidation) of fresh pork loin under high oxygen-modified atmosphere packaging was reported using nanoemulsions of oregano essential oil and resveratrol loaded pectin edible coating (Xiong et al. 2020). The tocopherol-loaded nanoemulsions were formulated and added in fish sausages. The results indicated better fish sausage quality was obtained when nanoemulsions were incorporated at the concentration of 250 mg/kg (Feng et al. 2020b). In a study, Huang et al.

(2020) enhanced the shelf life of carbonado chicken (readyto-eat) with nanoemulsion-based edible coating loaded with ε-poly-l-lysine and rosemary extract. Also, an improvement was observed in the shelf life of Yao meat products (readyto-eat) through nanoemulsions-based coating containing the mixture of nisin, star anise essential oil and polylysine (Liu et al. 2020b). In addition, the nanoemulsions coating formed with Zataria multiflora Boiss essential oil and alginate (coating material) was used to increase the shelf life of fish fillets and inhibit the microbial flora than coarse emulsion (Khanzadi et al. 2020). Furthermore, the shelf life of edible oils could be enhanced by biopolymer nanoemulsions of Orchis mascula and Lepidium perfoliatum loaded with Hyssopus officinalis L. plant extract (Savadkouhi et al. 2020). However, in one study the authors reported that active films loaded with pickering emulsion of Marjoram essential oil showed strong antimicrobial and antioxidant activity



 Table 3
 Applications of nanocarriers as coating material for enhancing the functional properties of food products. The following abbreviations denote: solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC)

Functional food ingredients	Preparation techniques	Emulsifiers	Remarks	Target food products	References
Nanoemulsions					
Lemongrass	High-pressure homogenization	Tween-80	Improved texture and antimicrobial properties	Grape berry	Oh et al. (2017)
Carvacrol	High-pressure homogenization	Tween-20	Enhanced antioxidant & antimicrobial properties	Cucumber slices	Taştan et al. (2017)
Carvacrol	High-pressure homogenization	Tween-80	Enhanced antioxidant & antimicrobial properties	Shredded cabbages	Sow et al. (2017)
Oregano essential oil	Combination of high shear homogenization and micro- fluidization	Tween-80	Extend the shelf-life	Low-fat-cut cheese	Artiga-Artigas et al. (2017)
Trans-cinnamic acid	Low-energy method (mixing)	Tween-80	Improved antimicrobial properties	Fresh-cut lettuce	Letsididi et al. (2018)
Orange peel essential oil & pectin	Combination of ultrasonication & stirring	Tween-80	Improved texture and antimicrobial properties	Orange slices	Radi et al. (2018)
Zingiber officinale essential oil	Ultrasonication	Tween-80	Increased antimicrobial activity	Chicken breast fillets	Noori et al. (2018)
Citral	Ultrasonication	Tween-80	Reduction in respiration rate and microbial growth, long- lasting color retention	Fresh-cut pineapples	Prakash et al. (2019)
Zataria multiflora Boiss essential oil	Ultrasonication	Tween-80	Inhibit the microbial growth and increase in shelf life	Fish fillets	Khanzadi et al. (2020)
Ferulago angulata essential oil	Ultrasonication	Tween-80	Reduced the increase in lipid oxidation & total volatile basic nitrogen	Rainbow trout fillets	Shokri et al. (2020)
Polyphenols (gallic acid, curcumin and quercetin)	Combination of high-speed & high-pressure homogenizer	Hi-Cap 100	Increase in shelf life	Fresh broiler meat	Khan et al. (2020)
Cumin seed essential oil Nanostructured phospholipid carriers	Ultrasonication	Tween-80	Enhanced the shelf life	Beef Hamburger	Hemmatkhah et al. (2020)
Artemisia annua oil	Thin-film hydration	Soy lecithin and cholesterol	Antibacterial activity against E. coli O157:H7	Cherry tomatoes	Cui et al. (2017)
Satureja plant essential oil	Combination of thin-film hydration and sonication method	Lecithin and cholesterol	Inhibit the microbial and chemical spoilage	Lamb meat	Pabast et al. (2018)
Nettle (<i>Urtica dioica</i> L.) extract	Combination of thin-film hydration and sonication method	Soy lecithin	Decrease in antimicrobial activity, owing to the encapsulation that restricts the release of nettle extract from the matrix	1	Haghju et al. (2016)



Table 3 (continued)					
Functional food ingredients	Preparation techniques	Emulsifiers	Remarks	Target food products	References
Garlic essential oil	Combination of thin-film hydration and sonication method	Cholesterol & soybean phosphatidylcholine	Retarded microbial growth and lipid oxidation	Vacuum-packed sausages	Esmaeili et al. (2020)
Nanolipid carriers					
	Hot high-shear stirring method	Poloxamer 407	Lower the respiration rate and reduced the weight loss when fruit coated with 65 g/L of SLN	Guava (Psidium guajava L.) García-Betanzos et al. (2017)	García-Betanzos et al. (2017)
Pomegranate seed oil	Combination of melt-emulsifi- cation and ultrasonication	Tween-80 & lecithin	Excellent physical stability with particle range of NLC (71 to 366 nm)	1	Soleimanian et al. (2018)
Cardamom essential oil	Low-energy nanoemulsification	Tween-80	Protect the antimicrobial activity and provide good chemical & physical stability by NLC	1	Nahr et al. (2018)
Betasitosterol	Hot melt homogenization	Poloxame® 407 & poly ethylene glycol	Betasitosterol-loaded NLC incorporated in butter showed good stability during storage (3 months)	Butter	Bagherpouret al. (2017)
	Hot high-stirring method	Polyvinyl alcohol (Mowiol® 4–88, Mw ≈ 31,000)	The best results were obtained by 10 g/L of beeswax-SLN with lowest weight loss (6.1%), loss of firmness (34%) and decay index (31%) during storage	Strawberry	Zambrano-Zaragoza et al. (2020)



than loaded nanoemulsion-based films (Almasi et al. 2020). Moreover, functional food ingredients like omega-3 fatty acids are very susceptible to oxidation and have poor water solubility, although physical stability was maintained at 4 °C storage temperature through nanoemulsions formulated using lactoferrin concentrations higher than 2% (Nunes et al. 2020). Besides that, multiple nanoemulsions (e.g., W/O/W) that encapsulate both hydrophilic (caffeic acid) and hydrophobic (tocotrienols) bioactive ingredients were formulated using the microfluidizer and ultrasound technique. The results revealed that the ultrasound technique used lesser energy (~12 times) than the microfluidizer to produce the droplet size of ~235 nm (Raviadaran et al. 2020).

Valorization of various food industry wastes was done for the extraction of bioactive compounds (Saini et al. 2019b; Saini and Panesar 2020; Panwar et al. 2019) such as lutein (Saini et al. 2020) and β -carotene (Barman et al. 2020) and their use in the formation of nanoemulsions, which have better functional properties in food systems (Dasgupta et al. 2019b). The phenolic extracts of grape and apple pomace used for the formation of nanocapsules can be used as edible materials with improved antioxidant properties (Ahmed et al. 2020). In another research, β -carotene was extracted from orange (*Citrus reticulata*) peel waste and encapsulated in nanoemulsion-based delivery system. It was also reported that β -carotene-loaded nanoemulsion improved the color and enhanced the bioaccessibility of β -carotene when it was added in fruit juice (Barman et al. 2020).

Vitamins are lipophilic (vitamins A, E, K and D) and hydrophilic (vitamins C and B vitamins) in nature, and different nanocarriers are used for their improved delivery. These include nanoemulsions (Vit-D), nanodouble emulsion (folic acid), nanoliposomes (Vit-B₁₂), biopolymer nanoparticles (D₃), solid lipid nanoparticles (Vit-D₂), nanohydrogels (Vit-B₆) and nano-organogels (Vit-C) (Almajwal et al. 2016; Assadpour et al. 2017; Bochicchio et al. 2016; Lee et al. 2016; Patel and San Martin-Gonzalez 2012; Tsuchido et al. 2015; Lo Nostro et al. 2007). Vitamins are susceptible to different conditions such as temperature, oxygen and light and can be oxidized during processing and storage depending upon their types (Katouzian and Jafari 2016). Herein, vitamins usage in food supplements indicates shortcomings (e.g., low stability and poor bioavailability) in the gastrointestinal tract situations (Walia et al. 2019). However, these undesirable conditions can be circumvented using different encapsulation techniques, which can be further used in numerous food applications. O/W nanoemulsions of vitamin D₃ were formulated by quillaja saponin as a natural surfactant using different oils such as corn and fish oil, medium-chain triglycerides, orange and mineral oil where the highest bioaccessibility levels for vitamin D₃ were found in nanoemulsions prepared from corn and fish oil as compared to other oil phases (Ozturk et al. 2015). In another study, vitamin D nanoemulsions were successfully prepared and fed to different groups of healthy male albino rats. Noticeable changes were reported in the levels of phosphorus, parathyroid hormone, calcium and alkaline phosphatase (Almajwal et al. 2016). The formation of nanoemulsions loaded with vitamin D₃ and calcium citrate revealed that the presence of vitamin D₃ affects the size of oil core (dispersed oil phase), whereas the calcium ions showed the impact on the stability of nanoemulsions loaded with both oil- and water-soluble micronutrients in the aqueous phase (Demisli et al. 2020). Moreover, pea protein-stabilized nanoemulsions loaded with vitamin D were formulated and reported that transport efficiency of nanoencapsulated vitamin D across Caco-2 cells was ~ 5.3 times greater than the free form of vitamin D suspension (Walia and Chen 2020). These loaded nanoemulsions can be used for vitamin D fortifications in nondairy foods. In another study, the formation of vitamin D-encapsulated nanoemulsions by soya lecithin and Tween 80 reported that the mixed-surfactant-based nanoemulsions of vitamin D can be used in the food and beverage industry to overcome the deficiency of vitamin D (Mehmood and Ahmed 2020).

Various studies have been conducted on the fabrication of nanoemulsions for food colorants such as β -carotene (Qian et al. 2012) and lycopene (Li et al. 2018). Generally, most of the food colorants, which include flavonoids, carotenoids, betalains and chlorophylls, are unstable, hydrophobic and susceptible to degradation in nature (Akhavan and Jafari 2017) making their encapsulation desirable using suitable delivery systems such as nanoemulsions.

Food flavors such as allypyrazine, methoxypyrazines, 2-isobutyl-3-methoxypyrazine, acetyl-L-pyrazine, aldehydes, phenolics and terpenoids are important food ingredients, which improve the organoleptic properties of food to attract consumers (Asghari et al. 2017). Many of food flavor structures show instability due to different processing and environmental conditions. Therefore, it is a logical means that these compounds are encapsulated by nanoemulsions to preserve the functional and structural properties. Several studies have been reported for the formation of nanoemulsions containing food flavors such as peppermint, citral, β -carotene and D-limonene using different wall materials, which include the medium-chain triacylglycerol (MCT)-starch, MCT-buffer solution and maltodextrin (Liang et al. 2012; Zhao et al. 2013; Jafari et al. 2007).

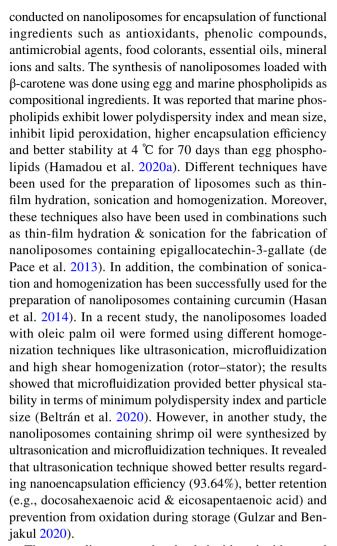
Minerals are valuable food ingredients, which cannot be synthesized by animals. Fruit and vegetables are the main sources of these nutrient ions that play a major role in the proper metabolic and biological activities to perform different functions in the body (Gharibzahedi and Jafari 2017b). These minerals are divided into two classes: macro-minerals (Ca, Mg, Na, K, P, Cl, S) and microminerals (Fe, Mn, Cu, I, Zn, Co, Mo, F, Se, Cr, B). Owing to their lack of solubility,



stability and liability to oxidative degradation, it is required to encapsulate these nutrient ions and salts in different nanocarriers and protect them from undesirable reactions with other components, thereby decreasing the sensory score of the food product (Gharibzahedi and Jafari 2017a). Numerous research studies for the nanoencapsulation of mineral ions and salts have been successfully reported. For example, Fe ions and C₄H₂FeO₄ were loaded in nanoemulsions using cholesterol, phosphatidylcholine and gelatin as wall materials (Tang and Sivakumar 2013; Naveen and Kanum 2014). Fe-loaded nanoemulsions showed the enhancement in bioavailability under in vivo studies when compared with the direct addition of Fe for milk enrichment (Naveen and Kanum 2014). These different functional ingredient-loaded nanoemulsions are characterized by various techniques such as physical (dynamic light scattering, zeta potential, nuclear magnetic resonance, X-ray diffraction, small-angle X-ray scattering), separation (chromatography, field flow fractionation) and imaging (transmission electron microscopy, scanning electron microscopy, atomic force microscopy) (Silva et al. 2012). Apart from enhancing the antioxidant properties of these functional food ingredients, various studies have also been reported on the nanoencapsulation of antimicrobial agents and essential oils to increase their antimicrobial properties (Ma et al. 2016; Xue et al. 2015). This application of loaded nanoemulsions is most suitable for the food industry. Some of the examples related to antimicrobial agents/essential oils containing nanoemulsions include peppermint oil (Liang et al. 2012), thyme oil (Xue et al. 2015) and sago oil (Moghimi et al. 2016). Moreover, nanoemulsions have a wide scope to modify the texture of food products. For example, a reduction in fat content from 16 to 1% of ice cream has been successfully done by food industries like Unilever through nanoemulsions. The phenomenon of gelation is possible in nanoemulsions at a low concentration of fat when compared with the emulsion. This functional property can be useful in food industries for producing products such as dressings, mayonnaise along with the desired texture and flavor. Numerous patents have been developed on the use of nanoemulsions for different applications such as the manufacturing of clear beverages (US20150030748, WO2011119228) and improved delivery of active ingredients (US20170246303) (Schultz and Monnier 2013; Bromley 2011; Wooster et al. 2017).

Nanostructured phospholipid carriers

At the nanoscale, nanoliposomes are colloidal structures, which are formed by the right combinations of phospholipids, oil and various solvents along with efficient energy input. These nanolipid vesicles are being used in numerous industries such as food, pharmaceutical and cosmetics (Mozafari et al. 2008). Various research studies have been



These nanoliposomes when loaded with antioxidants and phenolic compounds are improved the functional properties such as antioxidant capabilities and solubility. For instance, nanoliposomes loaded with quercetin and resveratrol (flavonoids) showed an increment in their antioxidant capabilities (Cadena et al. 2013). In one study, fish oil was encapsulated in nanoliposome, which was further incorporated in yogurt. That indicated a higher content of eicosapentaenoic acid and docosahexaenoic acid present in fortified yogurt. Also, fortified yogurt showed closer results in terms of sensory evaluation as compared to the control sample (Ghorbanzade et al. 2017). In a similar study, the olive leaf extract was loaded in nanoliposomes and added in yogurt. The results observed the enhanced antioxidant properties and no significant changes in sensory characteristics and minimized the syneresis rate in fortified yogurt. Therefore, these loaded nanoliposomes can be used in different food systems to increase their nutritive value and shelf life (Tavakoli et al. 2018).

Several studies also focused on the coating/films based on the nanoliposomes and used in various food applications. In a recent study, nanoliposomes doped with flaxseed—peptide



fractions were formed and coated with chitosan (0.4%) and showed an increase in encapsulation efficiency, antioxidant activity and physical stability after the reconstitution process of powder (Sarabandi and Jafari 2020).

Different coloring compounds such as β -carotene and astaxanthin loaded in nanoliposomes showed high solubility, high retention (> 90%) of encased β -carotene and high resistance against the thermal processing and UV rays (Moraes et al. 2013; Yoo et al. 2010). Furthermore, the incorporation of different carotenoids (e.g., lutein, β -carotene, lycopene, canthaxanthin) through nanoliposomes also improved their bioaccessibility (Tan et al. 2014).

Mineral ions/salts that include $FeSO_4$ and ferrous glycinate were encapsulated using different wall materials such as chitosan, soybean phosphatidylcholine, cholesterol, hydrogenated phosphatidylcholine, cationic phospholipids and egg-phosphatidylcholine (Ding et al. 2011a; Hermida et al. 2011). These nanoliposomes exhibited high barrier properties against the oxidative reactions, high stability, acceptable encapsulation efficiency (69.6–76.2%) and decreased deficiency of iron in rats more significantly than two free forms of iron (Ding et al. 2011a, 2011b; Hermida et al. 2011).

Nanoliposomes have a high potential for nanoencapsulation of essential oils and antimicrobial agents due to their high loading capacity, high penetration ability into cells and decreased potential toxicity of antimicrobial agents (Thamphiwatana et al. 2013; Halwani et al. 2008; Mugabe et al. 2006). Several studies have been done on nanoliposomes loaded with nisin (Taylor et al. 2008), daptomycin (Li et al. 2013), *Anethum graveolens* essential oil (Ortan et al. 2009), and it was revealed that these nanocarriers successfully improved the functional properties of antimicrobial agents and essential oils. Another study conducted on the encapsulation of rose essential oil in nanoliposomes reported the entrapment efficiency of 89.46% along with an average size of 94 nm (Wen et al. 2011).

Nanolipid carriers

The last group of lipid-based nanocarriers is nanolipid carriers. It is claimed that nanolipid carriers perform various functions more efficiently than classical nanoemulsions, for example, better control on release process, particle size and less leakage of encased functional compounds (Pyo et al. 2017; Katouzian et al. 2017). Various studies have been done on both subgroups of nanolipid carriers, which include solid lipid nanoparticles and nanostructured lipid carriers. These are formulated using different techniques such as hot homogenization, ultrasonication, emulsification-evaporation and cold homogenization or the combinations thereof. Solid lipid nanoparticles loaded with different phenolic compounds such as curcumin (Wang et al. 2015), resveratrol (Jose et al. 2014) and nanostructured lipid carriers

loaded with quercetin (Sun et al. 2014), curcumin (Aditya et al. 2014) and silymarin (Shangguan et al. 2014) have also been studied. It has been reported that solid lipid nanoparticles loaded with resveratrol formulated using Tween 80 or a combination of polyvinyl alcohol and Tween 80 sustainably release the compound and were found effective in the treatment of neoplastic diseases (Jose et al. 2014). As compared to solid lipid nanoparticles, nanostructured lipid carriers formed a combination of oil and fat having an 18% higher loading capacity for dermal applications (Gokce et al. 2012).

Recent studies related to nanolipid carriers were conducted to enhance various properties for extended shelf life of food products. For example, lipid carriers loaded with cinnamon essential oil and coated by chitosan showed stability against oxidation, when these nanocarriers were added into the milk (Bashiri et al. 2020). Besides, the nanostructured lipid carriers and solid lipid nanoparticles loaded with lycopene were formed using high shear homogenization and ultrasonication technique to incorporate in orange juice. It was reported that these nanocarriers can be used in liquid food samples after improving their solubility and homogeneity (Zardini et al. 2017). Therefore, these nanocarrier systems can be used in different food products like yogurt, fruit juices, etc., to extend their shelf life due to retardation in oxidation. In a recent study, a snack bar was formulated with sesame paste, date syrup and thymol-loaded nanostructured lipid carriers. It revealed that the addition of 100 ppm of thymol-loaded nanostructured lipid carriers showed better results in terms of oxidation stability of sesame paste/ date syrup mixture as compared to butylated hydroxytoluene (Bageri et al. 2020). Furthermore, the effects of different emulsifiers and pH conditions on the stability of nanostructured lipid carriers containing wheat germ oil were also studied. It was observed that poloxamer (nonionic surfactant) showed high oxidative stability at high pH, whereas sodium dodecyl sulfate (ionic surfactant) indicated at low pH (Mirtalebi et al. 2020).

Various food colorants like α-tocopherol (de Carvalho et al. 2013), astaxanthin (Li et al. 2016b) and anthocyanins (Ravanfar et al. 2016) have been successfully entrapped in solid lipid nanoparticles and nanostructured lipid carriers. Solid lipid nanoparticles containing anthocyanins have shown the 89.2% encapsulation efficiency, and the average size of the particle was 455 nm (Ravanfar et al. 2016). Also, nanostructured lipid carriers loaded with lutein was reported 89% entrapment efficiency along with a particle size of 200 nm (Lacatusu et al. 2013). Therefore, these loaded colorants in nanocarriers show better functional and structural properties as compared to their free form.

The study on the fabrication of solid lipid nanoparticles containing FeSO₄ was conducted using encapsulating material such as Compritol 888 ATO and lecithin, reported the encapsulation efficiency of 92.3% (Hosny et al. 2015). In



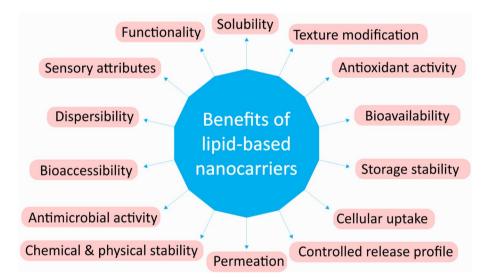
another study, FeSO₄-loaded solid lipid nanoparticles were formulated using chitosan-HCL, stearic acid and polyvinyl alcohol as compositional ingredients (Zariwala et al. 2013). These nanocarriers have also been used for the entrapment of nisin in solid lipid nanoparticles and inhibit the growth of *Lactobacillus plantarum* and *Listeria monocytogenes* over at least 15–20 days (Prombutara et al. 2012). Figure 2 shows the outcomes of these nanoencapsulated functional food ingredients in different lipid-based nanocarriers as shown in Fig. 1.

Application of lipid-based nanocarriers as antimicrobial agents

Nanoencapsulation of different functional ingredients is one of the most effective approaches used to enhance their functional properties such as antioxidant activity, thermal and storage stability, bioaccessibility, antimicrobial effect, anticarcinogenic activity and to improve the intestinal absorption. Lipid-based nanocarriers are currently used for a wide

range of applications as shown in Fig. 2. However, much focus is being recently given on the antimicrobial studies using different antimicrobial agents, which is used directly into the food systems required to ensure food safety. However, the direct use of antimicrobial agents in food systems has some disadvantages owing to the low solubility, low chemical stability and negative impact on the organoleptic properties of food. Therefore, the utilization of lipid-based nanocarriers as the delivery systems for the encapsulation of different antimicrobial ingredients is considered a promising tool for their improved properties in the food sector (Fig. 3). Various studies have been conducted on the antibacterial effect of functional food ingredients in their pure as well as encapsulated forms (nanocarriers) that were compared and analyzed based on three criteria such as minimum bacterial concentration, minimum inhibition concentration and inhibition zone as shown in Table 4. The majority of studies showed that values of minimum bacterial concentration and minimum inhibition concentration were lower in the case of encapsulated compounds as compared to their pure form. For example, Allium sativum essential oil encapsulated

Fig. 2 Benefits of nanoencapsulation of functional ingredients through lipid-based nanocarriers which are used in food and pharmaceutical industries



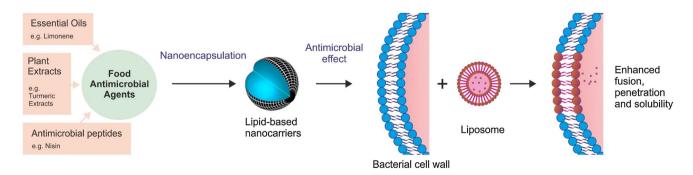


Fig. 3 Delivery of food antimicrobial agents through lipid-based nanocarriers (e.g., liposome) for improved antimicrobial effect on bacterial cell via better fusion, penetration and solubility



Table 4 Lipid-based nanocarriers as antimicrobial agents for food applications. The following abbreviations denote: minimum bacterial concentration (MBC); minimum inhibition concentration (MIC); inhibition zone (IZ); nanostructured lipid carriers (NLC); virgin coconut oil (VCO); and propylene glycol (PG)

Antimicrobial agents	Preparation techniques	Target microorganisms	Antimicrobial effects	effects	Remarks	References
			Pure	Encapsulated		
Nanoemulsions Thyme oil	Self-emulsification	Escherichia coli O157:H7 MIC: 0.4 g/L	MIC: 0.4 g/L	MIC: 0.2 g/L	Encapsulated thyme oil was more active than free thyme oil against target microorganisms when tested in tryptic	Zhang et al. (2020)
			MBC: 0.6 g/L	MBC: 0.2 g/L	Soy or our extraint Encapsulation effi- ciency: > 90%	
		Staphylococcus aureus	MIC: 0.6 g/L MBC: 0.6 g/L	MIC: 0.4 g/L MBC: 0.4 g/L		
Thyme oil		Escherichia coli O157:H7	MIC: 4.0 g/L	MIC: 3.5 g/L		
			MBC: 4.0 g/L	MBC: 3.5 g/L		
		Staphylococcus aureus	MIC: 8.0 g/L MBC: 8.0 g/L	MIC: 4.0 g/L MBC: 5.0 o/L		
			MDC. 8.0 g/L	MBC. 3.0 g/L		
Cinnamon essential oil	Ultrasonication	Aspergillus niger	IZ: 12.29 mm	IZ: 23.74 mm	Cinnamon essential oil containing nanoemulsions has higher antifungal activity than coarse emulsion	Pongsumpun et al. (2020)
		Rhizopus arrhizus	IZ: 10.43 mm	IZ: 22.12 mm		
		Penicillium sp.	IZ: 9.31 mm	IZ: 19.27 mm		
		Colletotrichum gloe- osporioides	IZ: 7.62 mm	IZ: 16.34 mm		
Lavandula x intermedia essential oil	Solvent displacement	Escherichia coli	MIC: 1.87 (v/v%)	MIC: 0.37 (v/v%)	Nanoemulsions of <i>Lavan-dula x intermedia</i> essential oil showed higher antibacterial activity than crude form	Garzoli et al. (2020)
			MBC: 1.87 (v/v%)	MBC: 0.37 (v/v%)		
		Bacillus cereus	MIC: 0.94 (v/v%)	MIC: 0.01 (v/v%) MBC: 0.02 (v/v%)		
Mangostin extract (VCO)	Combination of homogenization and ultrasonication	Escherichia coli	MIC: 3.13 mg/mL	MIC: 1.56 mg/mL	Nanoemulsions containing mangostin exhibited the high antioxidant and antimicrobial activities as compared to extract	Sungpud et al. (2020)



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Antimicrobial agents	Preparation techniques	Target microorganisms	Antimicrobial effects	effects	Remarks	References	
			Pure	Encapsulated			
		Staphylococcus aureus	MIC: 1.56 mg/mL	MIC: 0.79 mg/mL			
Mangostin extract (Mixed VCO-PG)		Escherichia coli	MIC: 1.56 mg/mL	MIC: 0.79 mg/mL			
		Staphylococcus aureus	MIC: 1.56 mg/mL	MIC: 0.79 mg/mL			
Mangostin extract (PG)		Escherichia coli	MIC: 1.56 mg/mL	MIC: 0.79 mg/mL			
		Staphylococcus aureus	MIC: 3.13 mg/mL	MIC: 1.56 mg/mL			
Lemon essential oil	Ultrasonication	Staphylococcus aureus	MIC: 12.50 mg/mL	MIC: 3.125 mg/mL	Nanoemulsions containing lemon essential oil was more effective for food pathogens (except <i>K. pneumoniae</i>) than pure form of lemon essential oil (100%)	Yazgan et al. (2019)	
			MBC: > 25 mg/mL	MBC:>25 mg/mL	MIC values indicated that nanoemulsions and 100% essential oil are more effective for bacterial pathogens as compared to fish spoilage bacteria		
		Klebsiella pneunonia	MIC: 12.50 mg/mL	MIC: 6.25 mg/mL	MBC values of nanoemulsions and 100% essential oil showed a noticeable bacterial activity against <i>S. paratyphi</i>		
			MBC: > 25 mg/mL	MBC: > 25 mg/mL			
		Salmonella Paratyphi A	MIC:1.56 mg/mL	MIC: 12.50 mg/mL			
			MBC: 3.125 mg/mL	MBC: 12.50 mg/mL			
		Enterococcus faecalis	MIC: 12.50 mg/mL	MIC: 12.50 mg/mL			
			MBC: > 25 mg/mL	MBC: > 25 mg/mL			
		Photobacterim damselae	$MIC: \ge 25 \text{ mg/mL}$	MIC:>25 mg/mL			
			MBC: > 25 mg/mL	MBC: > 25 mg/mL			
		Enterococcus faecalis	MIC:≥25 mg/mL	MIC: > 25 mg/mL			
			MBC: > 25 mg/mL	MBC: > 25 mg/mL			
		Vibrio vulnificus	MIC:>25 mg/mL	MIC: 25 mg/mL			
			MBC: > 25 mg/mL	MBC:>25 mg/mL			
		Proteus mirabilis	MIC:>25 mg/mL	MIC: > 25 mg/mL			
			MBC: > 25 mg/mL	MBC:>25 mg/mL			



lable 4 (continued)					
Antimicrobial agents	Preparation techniques	Target microorganisms	Antimicrobial effects	Remarks	References

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Antimicrobial agents	Preparation techniques	Target microorganisms	Antimicrobial effects	effects	Remarks	References
			Pure	Encapsulated		
		Serratia liquefaciens	MIC: 6.25 mg/mL MBC: 25 mg/mL	MIC: 6.25 mg/mL MBC: 25 mg/mL		
		Pseudomonas luteola	MIC: 3.125 mg/mL MBC: 1.56 mg/mL	MIC: 6.25 mg/mL MBC: 25 mg/mL		
Cinnamon oil	Ultrasonication	Different Salmonella strains) I	MIC: 0.039 v/v	0.5% nanoemulsions showed up to 7.7 & 5.5 log reductions in <i>Listeria monocytogenes</i> and <i>Salmonella</i> spp.	Paudel et al. (2019)
				MBC: 0.78%	Nanoemulsions can be used as natural antimi- crobial agent for melons	
		Different Listeria strains	I	MIC: 0.78 v/v MBC: 0.78%		
Clove oil	Ultrasonic emulsification	Staphylococcus aureus	МІС: 1908 µg/mL	MIC: 856 µg/mL	Nanoemulsions loaded with 7 mg/mL of clove oil showed the lowest MIC values as compared to free clove oil	Meneses et al. (2019)
		Staphylococcus epider- midis	1	MIC: 856 µg/mL	Microbial inhibition kinetics indicates the fast action of nanoemulsions with clove oil against the target microorganisms	
		Streptococcus mutans	I	MIC: 856 μg/mL		
		Escherichia coli	MIC: 2650 µg/mL	MIC: 999 μg/mL		
		Salmonella choleraesuis Klebsiella meumonia	MIC: 2650 µg/mL MIC: 1908 110/mL	MIC: 999 µg/mL		
Linalool	Ultrasonic homogenization	Salmonella Typhimurium	MIC: 1.25 v/v, %	MIC: 0.625 v/v, %	Linalool nanoemulsions showed the twofold higher antibacterial activity	Prakash et al. (2019)
			MBC: 1.25 v/v, %	MBC: 0.625 v/v, %		
Thymus capitatus essential oil	Thymus capitatus essential High-pressure homogenioil zation	Bacillus subtilis	MIC: 1.5 mg/mL	MIC: 0.0 mg/mL	Encapsulated essential oil exhibited the higher antibacterial activity than bulk one	Benjemaa et al. (2018)
			MBC: > 3 mg/mL	MBC: 0.1 mg/mL		



	References		
	Remarks		
	Antimicrobial effects	Encapsulated	
		Pure	
	Target microorganisms		
	Preparation techniques		
Table 4 (continued)	Antimicrobial agents		
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Antimicrobial agents	Preparation techniques	Target microorganisms	Antimicrobial effects	fects	Remarks	References
		,	Pure	Encapsulated		
Nanostructured phospho- lipid carriers						
Turmeric extract	Combination of thin-layer hydration, homogenization and sonication	Staphylococcus aureus	MIC: 20 mg/mL	MIC: 10 mg/mL	Turmeric extract nanoliposomes showed higher antibacterial as well as antioxidant activity as compared to free turmeric extract	Karimi et al. (2019)
		Escherichia coli	MIC: 5 mg/mL	MIC: 1.25 mg/mL	Encapsulation efficiency: 95%	
		Bacillus cereus	MIC: 20 mg/mL	MIC: 10 mg/mL		
		Streptococcus mutans	MIC: 20 mg/mL	MIC: 10 mg/mL		
		Acinetobacter junii	MIC: 20 mg/mL	MIC: 10 mg/mL		
		Pseudomonas aeruginosa	MIC: 40 mg/mL	MIC: 10 mg/mL		
		Candida albicans	MIC: 20 mg/mL	MIC: 10 mg/mL		
Garlic (Allium sativum L.) essential oil	Ethanol injection	Escherichia coli O157:H7	MIC: 0.03%	MIC: 0.02%	Nanoliposomal garlic essential oil showed higher antimicrobial activity than free form of essential oil	Zabihi et al. (2017)
			MBC: 0.04%	MBC: 0.03%	Encapsulation efficiency: 64.27%	
Zataria multiflora Boiss. essential oil	Thin film hydration	Escherichia coli O157:H7	MIC: 0.03% (v/v)	MIC: 0.015% (v/v)	Liposomal essential oil showed higher inhibitory effect on toxin titer than free oil	Khatibi et al. (2018)
Nisin and garlic extract	Thin-film hydration	Some G- & G+Bacteria (Listeria monocy- togenes, Salmonella Enteritidis, Escherichia coli, Staphylococcus aureus)	Viable count:	Viable count:	Nisin-garlic extract nanoliposome has potential for use as an antimicrobial agent	Pinilla and Brandelli (2016)
			4–5 log CFU/mL lower than control	4–5 log CFU/mL lower than control	Encapsulation efficiency: Nisin (82%) & garlic extract (90%)	
Carvacrol	Lipid film hydration	Staphylococcus aureus	MBC: 1.33 mg/mL	MBC: 5.30 mg/mL	Free carvacrol (control) showed better results than encapsulated for inactivation of given microorganisms	Cacciatore et al. (2020)



lable 4 (continued)						
Antimicrobial agents	Preparation techniques	Target microorganisms	Antimicrobial effects	Remarks	References	
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Antimicrobial agents	Preparation techniques	Target microorganisms	Antimicrobial effects	ects	Remarks	References
			Pure	Encapsulated		
		Listeria monocytogenes	MBC: 1.77 mg/mL	MBC: 5.30 mg/mL	Encapsulation efficiency: 98%	
		Escherichia coli Salmonella spp.	MBC: 1.33 mg/mL MBC: 1.77 mg/mL	MBC: 5.30 mg/mL MBC: 3.53 mg/mL		
Cardamom essential oil	Combination of thin-layer hydration, homogeniza- tion and sonication	Staphylococcus aureus	Emul-	MIC: 3000 µg/mL	Nanoliposome system showed the ability to protect the functional properties of cardamom essential oil	Nahr et al. (2019)
					Better antimicrobial properties at nanoscale	
		Escherichia coli	MIC: 2200 μg/mL (Emul- MIC: 1500 μg/mL sion)	MIC: 1500 µg/mL	Encapsulation efficiency: > 60	
Lupulon & xanthohumol	Ultrasonication	Clostridium perfringens	MIC: 64 mg/L	MIC: 32 mg/L	Nanoliposomal system has Khatib et al. (2019) the potential to replace the synthetic additives in real food systems	Khatib et al. (2019)
			MBC: 128 mg/L	MBC: 64 mg/L	Encapsulation efficiency: Lupulon (71.12%) & xanthohumol (67.81%)	
Nanolipid carriers						
Cardamom essential oil	Combination of low- energy nanoemulsi- fication, high shear homogenization and sonication	Escherichia coli	MIC: 2200 µg/mL (Emul- MIC: 1100 µg/mL sion)	МІС: 1100 µg/mL	High encapsulation effi- ciency: > 90%	Nahr et al. (2018)
					Loading capacity: > 25%	
		Staphylococcus aureus	MIC: 4400 µg/mL (Emul- MIC: 1100 µg/mL sion)	МІС: 1100 µg/mL	NLC delivery system shows good chemical and physical stability to cardamom essential oil	
Menthol	Hot-melt homogenization	Staphylococcus aureus	MIC: 1000 µg/mL	MIC: 125 μg/mL	Encapsulation efficiency: 98.73%	Piran et al. (2017)
			MBC: 4000 µg/ mL (Emulsion)	MBC: 500 µg/mL	Loading capacity: 9.8%	
					Menthol containing NLC indicated better effect on fungi as compared to bacteria	



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Antimicrobial agents	Preparation techniques	Target microorganisms	Antimicrobial effects	ects	Remarks	References
			Pure	Encapsulated		
		Bacillus cereus	MIC: 2000 µg/mL	MIC: 250 µg/mL	In bacteria, G+bacteria had higher antibacte- rial efficiency than G-bacteria	
			MBC: 4000 μg/ mL (Emulsion)	MBC: 1000 μg/mL		
		Escherichia coli	MIC: 2000 µg/mL	MIC: 500 µg/mL		
			MBC:>4000 μg/ mL (Emulsion)	MBC: > 4000 µg/mL		
		Candida albicans	MIC: 156 µg/mL	MIC: 78 µg/mL		
			MBC: 468 µg/mL (Emulsion)	MBC: 117 μg/mL		
Citral	Hot-melt homogenization	Staphylococcus aureus	MIC: 500 µg/mL	MIC: 125 µg/mL	Encapsulation efficiency: 99.84%	Mokarizadeh et al. (2017)
			MBC: 2000 μg/ mL (Emulsion)	MBC: 500 μg/mL	Loading capacity: 12.5%	
					Enhanced antimicrobial properties of citralloaded NLC than citral emulsion for all microorganisms	
		Bacillus cereus	MIC: 500 µg/mL	MIC: 31.25 µg/mL		
			MBC: 1000 μg/ mL (Emulsion)	MBC:125 µg/mL		
		Escherichia coli	MIC: 1000 μg/mL	MIC: 250 µg/mL		
			MBC: > 2000 μg/ mL (Emulsion)	MBC:>2000 μg/mL		
		Candida albicans	MIC: 125 µg/mL	ı		
			MBC: 250 µg/mL (Emulsion)			
Turmeric extract	High shear homogenization	Staphylococcus aureus	MIC: 20 mg/mL	MIC: 30 mg/mL	NLC loaded with turmeric Karimi et al. (2018) extract showed high antibacterial activity for Escherichia coli	Karimi et al. (2018)
		Escherichia coli	MIC: 5 mg/mL	MIC: 2.5 mg/mL	Turmeric extract—NLC indicated the characteristics of ideal functional food	
		Bacillus cereus	MIC: 20 mg/mL	MIC: 40 mg/mL		



Table 4 (continued)						
Antimicrobial agents	Antimicrobial agents Preparation techniques	Target microorganisms	Antimicrobial effects	effects	Remarks	References
			Pure	Encapsulated		
		Streptococcus mutans	MIC: 5 mg/mL	MIC: 30 mg/mL		
		Acinetobacter juni	MIC: 20 mg/mL	MIC: 7.5 mg/mL		
		Pseudomonas aeruginosa MIC: 40 mg/mL	MIC: 40 mg/mL	MIC: 30 mg/mL		
		Candida albicans	MIC: 20 mg/mL	MIC: 40 mg/mL		

through nanoliposomes exhibited the antibacterial effect against Escherichia coli at low concentration, whereas the pure form of essential oils produced an antibacterial effect at higher concentration (Zabihi et al. 2017). A recent study observed that the nanoemulsions containing cumin essential oil show a significant effect on Staphylococcus aureus. These nanoemulsions have been explored for their antibacterial and anticancer properties of the cumin seed oil (Nirmala et al. 2020). In another study, nanoemulsions prepared using Citrofortunella microcarpa essential oil were most effective against Staphylococcus aureus (Inhibition zone: 9.98 mm), Escherichia coli (Inhibition zone: 8.34) and Salmonella spp. (Inhibition zone: 7.71) as compared to other nanoemulsions formed by lime essential oil from Citrus aurantifolia and Citrus hystrix (Liew et al. 2020). However, in some studies, the pure form and encapsulated form of bioactive ingredients showed a similar additive effect. For example, the copaíba resin oil and its nanoemulsion along with amphotericin B showed the additive effect with a decrease in the values of minimum inhibition concentration ($\approx 50\%$) against the Paracoccidioides genus (Silva et al. 2020). Furthermore, the antibacterial activity was more effective toward the grampositive than gram-negative strains using the nanoemulsions doped with quercetin (Das et al. 2020).

Several studies were also conducted on the nanoliposomes and their function as antimicrobial agents. A study developed surface-modified nanoliposomes doped with cationic peptides (peptide + 2 & peptide + 5). It revealed that polymer-coated nanoliposomes loaded with peptides, increased the antimicrobial activity approximately 2000-fold against the *Listeria monocytogenes* (Cantor et al. 2019). Furthermore, the solid lipid nanoparticles loaded with *Eugenia caryophyllata* essential oil showed the lower values of minimum bacterial concentration and minimum inhibition concentration as compared to the pure form of oil alone against the *Salmonella typhi*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Candida albicans* (Fazly Bazzaz et al. 2018).

On the other hand, another important group of improved delivery systems is nanolipid carriers, which have some major advantages like high stability, high loading capacity with sustained release of functional ingredients. These functional properties were advantageous to overcome the limitations of nanoliposomes and nanoemulsions. Solid lipid nanoparticles and nanostructured lipid carriers are produced by similar techniques, but nanostructured lipid carriers have better functional properties along with the properties of solid lipid nanoparticles. The nanostructured lipid carriers revealed the lower crystallinity index, slower particle growth and polymorphic transition as compared to solid lipid nanoparticles (Gordillo-Galeano and Mora-Huertas 2018). Therefore, lipid-based nanocarriers improve the bioactivity of the various antibacterial agents like essential



oils, natural extracts from plant sources, natural, synthetic antibiotics, etc.

Among all the nanocarriers (nanoliposomes, nanoemulsions and nanolipid carriers), the utilization of nanoemulsions for encapsulation of antibacterial ingredients is maximum, which could be exploited in the food sector. This effect of nanoemulsions as antimicrobial agents have been explored mainly in three aspects, which include the utilization of nanoemulsions: a) in its pure form, i.e., nanoemulsions without incorporation of any functional compound, b) loaded with essential oils, c) loaded with a combination of one or more functional ingredients. For example, encapsulation of trans-cinnamic acid along with medium-chain triglycerides, Tween 80 & phosphate-buffered saline acetone as compositional ingredients were used against Salmonella typhimurium which reported the lower value of minimum inhibition concentration and minimum bacterial concentration (1.5 & 3.1 mg/mL) as compared to pure antibacterial type (12.5 & 25 mg/mL) (Letsididi et al. 2018). Moreover, nanoemulsions are known for several advantages such as targetability, large-scale production and encapsulation of both hydrophobic and hydrophilic compounds. However, nanoemulsions offer only one major limitation of the rapid release of functional ingredients due to their liquid nature. More studies on the antimicrobial effects of nanoemulsions containing soybean oil, black pepper oil, *Piper betle* L. essential oil have also been investigated against Bacillus subtilis, Pseudomonas aeruginosa, Klebsiella pneumonia, respectively (Benjemaa et al. 2018; Swathy et al. 2018; Roy and Guha 2018).

Conclusion

Among all the lipid-based nanocarriers, extensive research has been done on nanoliposomes due to their ability to carry hydrophilic, lipophilic and amphiphilic functional food ingredients. In contrast to all lipid-based nanoencapsulation techniques, nanolipid carriers (solid lipid nanoparticles, nanostructured lipid carriers and smart lipid nanocarriers) are one of the most predominant techniques in terms of loading capacity, sustained release and high stability (quality of functional compound over time). Further, nanolipid carriers showed the best results for the delivery of functional compounds due to their flexibility for the selection of compositional ingredients (solid lipid or solid lipid and oils) and increasing the capacity for holding functional ingredients. Besides, these are also considered as one of the most promising delivery systems to improve the solubility, physical stability, bioavailability as well as functionality of bioactive compounds along with high loading capacity. These nanocarriers can be used in the food industry for texture modification, improved food product quality, extended shelf life of food products and as coloring and antioxidant agents. Despite this, further research is required on the process optimization and engineering aspects to enhance different properties such as structural, physical and mass transfer to obtain productive results at the commercial level. Moreover, these can be loaded with polyphenolic compounds extracted from different natural sources and due to the increase in surface to volume ratio at nanoscale, these loaded nanocarriers can be used as effective preservatives at low concentrations. More in-depth research is also necessary for the safety concerns of these nanocarriers in the human body. Further, the focus should be given on the cost-effective processing operations for the synthesis of nanocarriers to be used in food industries at large scale.

Compliance with ethical standards

Conflicts of interest The authors have declared no conflict of interest.

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