Plant oils: From chemical composition to encapsulated form use

Narimane Lammari, Ouahida Louaer, Meniai Abdeslam-Hassen, Hatem Fessi, Abdelhamid Elaïssari

► To cite this version:

Narimane Lammari, Ouahida Louaer, Meniai Abdeslam-Hassen, Hatem Fessi, Abdelhamid Elaïssari. Plant oils: From chemical composition to encapsulated form use. *International Journal of Pharmaceutics*, 2021, 601, pp.120538. 10.1016/j.ijpharm.2021.120538 . hal-03200146

HAL Id: hal-03200146

<https://hal.science/hal-03200146>

Submitted on 16 Apr 2021

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Plant oils: From chemical composition to encapsulated form use

Narimane Lammari ^{1,2}, Ouahida Louaer ², Abdeslam Hassen Meniai ², Hatem Fessi ³,

Abdelhamid Elaissari ^{1*}

¹ Univ Lyon, University Claude Bernard Lyon-1, CNRS, ISA-UMR 5280, 69622 Villeurbanne, France

² Environmental Process Engineering Laboratory, University Constantine 3, Salah Boubnider, Constantine, Algeria.

³ Univ Lyon, Université Claude Bernard Lyon-1, CNRS, LAGEP UMR 5007, F-69622 Lyon, France

* **Corresponding author** : Abdelhamid Elaissari ; abdelhamid.elaissari@univ-lyon1.fr

Abbreviations

EO: Essential oil; VO: Vegetable oil; pNPs: Polymeric nanoparticles; SLN: Solid lipid nanoparticles; EE%: Encapsulation efficiency; HLB: Hydrophilic lipophilic balance; SUV: Small unilamellar vesicles; LUV: Large unilamellar vesicles; MLV: Multilamellar vesicles; NLC: Nanostructured lipid carriers; MIC: Minimum inhibitory concentration; AUC: Area under the curve.

Abstract

The last decade has witnessed a burgeoning global movement towards essential and vegetable oils in the food, agriculture, pharmaceutical, cosmetic, and textile industries thanks to their natural and safe status, broad acceptance by consumers, and versatile functional properties. However, efforts to develop new therapy or functional agents based on plant oils have met with challenges of limited stability and/or reduced efficacy. As a result, there has been increased research interest in the encapsulation of plant oils, whereby the nanocarriers serve as barrier between plant oils and the environment and control oil release leading to improved efficacy, reduced toxicity and enhanced patient compliance and convenience. In this review, special concern has been addressed to the encapsulation of essential and vegetable oils in three types of nanocarriers: polymeric nanoparticles, liposomes and solid lipid nanoparticles. First, the chemical composition of essential and vegetable oils was handled. Moreover, we gather together the research findings reported by the literature regarding the different techniques used to generate these nanocarriers with their significant findings. Finally, differences and similarities between these nanocarriers are discussed, along with current and future applications that are warranted by their structures and properties.

Key words: Essential oil, vegetable oil, encapsulation, polymeric nanoparticle, liposome, solid lipid nanoparticle.

Graphical abstract

1. Introduction

The last decade has evidently witnessed a tremendous surge in the use of herbal medicine as a form of complementary or replacement therapy (Mainardi et al., 2009). The global acceptance and public concern in the use of herbal medicines, phytonutrients or nutraceuticals continue to assume exponential increase. It has been estimated that up to 80% of people worldwide relying on them as a primary source of healthcare (Ekor, 2013). This concern in drugs of natural origin is related to numerous reasons, namely, the traditional medicine is more affordable, closer to the patient's ideology and receives greater public access than chemical synthesized treatment. Furthermore, abusive and/or incorrect use of conventional medicines results in some cases in harmful side effects (Wachtel-Galor and Benzie, 2011). The use of aromatic and medicinal plants is incessantly expanding due to increasing consumers demand and concern in these plants for several applications. In fact, consumers are becoming more and more aware of the benefits of inherent practice of medicinal and aromatic plants and their metabolites (Chikezie et al., 2015; Rates, 2001). These plants produce a large variety of secondary metabolites; among them, essential and vegetable oils deserve particular attention (Dhifi et al., 2016; Kumar et al., 2016; Pandey et al., 2016; Yara-Varón et al., 2017). Essential oils (EO) comprised volatile and semi-volatile organic compounds determining the specific aroma, flavor and fragrance of plants. They are volatile and instable at room-temperature. In the other hand, vegetable oils (VO) consist of esters of glycerol and fatty acids and are nonvolatile and stable at room temperature (Moghaddam and Mehdizadeh, 2017; Sagiri et al., 2016). Besides being edible in their refined or virgin form, VO play a crucial role in therapeutic and prophylactic prevention of diseases such as inflammation, diabetes, cancer and atherosclerosis (Ganesan et al., 2018; Kochikuzhyil et al., 2010; Saha and Ghosh, 2011; Yu et al., 2004). Subsequently, EO received significant attention in food, agricultural and pharmaceutical fields due to their antioxidant, antibacterial, antiviral and antifungal properties.

70 The diverse health benefits associated with the consumption of EO constitute an area of intense
71 research (Ali et al., 2015; Dhifi et al., 2016; Elshafie and Ippolito, 2017). Meantime, the benefits
72 linked to these bioactive agents is generally hampered by several obstacles. For instance, the
73 oxidation is the main problem limiting the use of VO in several fields. The unsaturated fatty
74 acids present in VO lead to increase the risk of lipid oxidation which in turn result in producing
75 numerous free radical species, primary oxidation products such as lipid hydroperoxides and
76 secondary oxidation products such as hydrocarbons, epoxides, ketones and aldehydes that
77 negatively impact aroma. Moreover, VO oxidation can generate toxic products that can largely
78 affect biological tissues (Chen et al., 2011; Matthäus, 2010). At the same time, numerous
79 studies have evidenced that EO are unstable and degraded easily if they are not protected from
80 external factors like oxidation, volatilization, heat and light (Turek and Stintzing, 2013).
81 Besides all these, the low water solubility, low permeation and low bioavailability of plant oils
82 in biological fluids and tissues constitute other factors that limit their rational use (Dima et al.,
83 2020; Rein et al., 2013). Therefore, designing suitable carriers by using nanoencapsulation
84 approach is crucial to overcome restrictions outlined (El-Asbahani et al., 2015; Sagiri et al.,
85 2016). Hoyos-leyva et al. (2019) revealed that the encapsulation of almond oil in starch
86 microcapsules conferred more protection against oxidation when compared to unencapsulated
87 oil. Similar results were already reported when investigating the stability of linseed, jasmine
88 and holy basil oils-loaded nanoparticles against heat, oxidation and volatilization as compared
89 to the free oils (Lv et al., 2014; Rubilar et al., 2012; Sutaphanit and Chitprasert, 2014).
90 Moreover, several studies have evidenced the amelioration of plant oils biological performance
91 after being incorporated in nanosystems. Alaarg et al. (2016) depicted that the encapsulation of
92 docosahexaenoic acid in liposomes improve its anticancer activity. Zhavah et al. (2015) related
93 the superior performance of *Cuminum cyminum* EO nanogels against *Aspergillus flavus* as
94 compared to the free oil to the increased surface area of the nanoparticles.

Depending on the preparation method, nanocarriers can be mainly classified into two main groups: polymer-based nanocarriers and lipid-based nanocarriers. Among the several colloidal systems investigated in drug delivery, polymeric nanoparticles (pNPs), liposomes and solid lipid nanoparticles (SLN) gained more interest (Allen and Cullis, 2013; El-say and El-sawy, 2017; Geszke-Moritz and Moritz, 2016; Immordino et al., 2006; Mehnert and Mäder, 2012; Rani et al., 2017). In this context, the present review covers literature data summarizing the current development of nanocarrier systems for plant oils delivery with a focus on the main properties and preparation technique of pNPs, liposomes and SLN. In addition, the chemical composition of both essential and vegetable oils along with the emerging and potential applications of plant oils loaded nanocarriers in several fields were explored.

2. Chemical composition of vegetable oils

Vegetable oils, also named non-essential or fixed oils, are fats usually extracted from plant seeds (e.g., soybean oil, rapeseed oil, sesame oil etc.), or less often from other parts of fruits (e.g., olive oil, palm oil etc.), by simple pressing and/or solvent extraction process (Yara-Varón et al., 2017). Depending on the origin, the crop, the season, and the producing methods, their composition is highly variable and complex (Lligadas et al., 2010).

2.1. Triglycerides

The main components of VO are triglycerides; they represent 95 to 98% of the global constituents depending on the source of oil (Yara-Varón et al., 2017). The word ‘oil’ hereby refers to triglycerides that are liquid at room temperature (Guner et al., 2006). Triglycerides are composed of three fatty acid molecules esterified to one glycerol molecule, as demonstrated in **Fig. 1** (Miao et al., 2014). Depending on the saturation degree of fatty acids, triglycerides are classified into saturated, mono- and poly-unsaturated fatty acids. The characteristics of VO depend on several parameters including; i) fatty acid chain length, ii) the degree of unsaturation, and iii) the stereochemistry of the double bonds (Meier et al., 2007). Additionally, varieties in

climatic, agronomic and cultivation may engender difference in fatty acid composition of triglycerides (Yara-Varón et al., 2017).

Fig. 1. Triglycerides composition of different vegetable oils.

2.2. Minor Components

Apart of triglycerides, VO contain also a diversity of non-triglyceride minor compounds (less than 5%) which present crucial biological properties and nutritional values for nutraceutical and pharmaceutical industries (**Fig. 2**) (Yara-Varón et al., 2017). They comprised two types: glycerolipids including monoglycerides, diglycerides and phospholipids; and non-glycerolipids such as tocopherols/tocotrienols, sterols, free fatty acids, pigments, vitamins, phenolic compounds, proteins and water (Xenakis et al., 2010).

Fig. 2. Minor components of vegetable oils.

3. Chemical composition of essential oils

Essential oils are oily aromatic liquids extracted from different plant organs as secondary metabolites like, leaves (eucalyptus, thym, salvia), zest (citrus), flowers (lavender, rose, jasmine), fruits (citrus), seeds (sesame), roots (ginger) and wood (sandal) (El-Asbahani et al., 2015). The EO are generally complex mixtures of individual aroma compounds. Even they are not strictly oils, they are poorly soluble in water (Calo et al., 2015). In last decades, innovative methods have been emerged to extract EO from plant raw materials (Boukroufa et al., 2015; Gavahian et al., 2015; Sodeifian et al., 2016; Zermane et al., 2016). The constituents of plant EO comprise mainly four main groups: terpenes, phenylpropanoids, straight-chain compounds and miscellaneous groups.

3.1. Terpenes

Terpenes are the most abundant compounds found in plant EO (Chizzola, 2013). They are synthesized via the mevalonic acid pathway in the cytoplasm of plant cells (Morsy, 2017).

Terpene compounds can be divided into two main categories: terpene hydrocarbons and oxygenated compounds (Moghaddam and Mehdizadeh, 2017).

3.1.1. Terpenes hydrocarbon

The essential building block of terpenes is the isoprene unit joined in a head-to-tail manner. Basing on the number of isoprene units, different terpenes can be found in EO, as demonstrated in **Fig. 3** (El-Asbahani et al., 2015; Morsy, 2017). Terpenes hydrocarbons are the first main group of components composed completely of carbon and hydrogen atoms and varied significantly in size and complexity (Moghaddam and Mehdizadeh, 2017). Monoterpenes and sesquiterpenes are the dominant terpenes found in plant EO. They are built up by two and three isoprene units, respectively. These terpenes could present acyclic, cyclic or aromatic structures. Cyclic terpenes can be classified depending on their ring size into monocyclic, bicyclic or tricyclic terpenes (**Table 1**). These compounds oxidize rapidly due to their fast reaction to heat and air sources (George et al., 2015). Diterpenes result by the combination of four isoprene units in a head-to-tail manner; they are essential constituents of plant resins (Langenheim, 2003). Commonly, diterpenes, triterpenes and tetraterpenes are present in EOs at a very low concentration. Their content may vary with the extraction method (Morsy, 2017).

3.1.2. Terpenoids

Terpene can be changed by adding functional groups and become terpenoid. When a monoterpene or a sesquiterpene has a functional group added to it, it is known as a monoterpenoid or sesquiterpenoid; respectively. The suffix “oid” means “derived from” or “like” therefore “terpenoid” can refer to all molecules with a terpene-like structure (Moghaddam and Mehdizadeh, 2017). They are classified into carboxylic acids, alcohols, aldehydes, esters, ethers, ketones, phenols, lactones, oxides, etc.

Fig. 3. Composition of terpenes.

3.2. Phenylpropanoid

This class of compounds, derived from phenylpropene, is synthesized from the amino acid phenylalanine and l-tyrosine via the shikimic acid pathway. Their name is derived from the aromatic phenyl group and the propene tail. The propyl side chain may contain hydroxyl or carboxyl group; while the aromatic ring may carry methoxy, hydroxyl and methylene dioxy groups (Morsy, 2017). Phenylpropanoids give a specific flavor and odor to the plant when they are present (Moghaddam and Mehdizadeh, 2017). Eugenol and cinnamaldehyde are example of this group of constituents (**Fig. 4**).

3.3. Straight-chain compounds

This group contains only straight-chain compounds, not containing any side branches. They range from n-heptane, to compounds with 35 carbon atoms. The leaf alcohol (3(Z)-hexen-1-ol) (**Fig. 4**) represents an example of this class; it gives an intense grassy-green odor upon cutting green grass and leaves (Morsy, 2017).

3.4. Miscellaneous group

They issue from the degradation of unsaturated fatty acids, lactones, terpenes, glycosides and represent sulfur- and nitrogen-containing compounds. Diallyl disulfide and indole are example of this class of compounds (**Fig. 4**) (Morsy, 2017).

Fig. 4. Examples of phenylpropanoids, straight chain compounds and miscellaneous groups.

4. Limitation in clinical use of plant oils

Since ancient times, EO have been recommended all over the world for a variety of health problems and diseases (Moghaddam and Mehdizadeh, 2017). Enormous studies have investigated the biological properties of EO, including antimicrobial, antifungal (Ceole et al., 2017; Garcia-Rellán et al., 2016), antiviral (Zeghib et al., 2017), insecticidal (Chen et al., 2016; Jassbi et al., 2017), antioxidant (Hassanen et al., 2015; Limaverde et al., 2017), anticancer (Carneiro et al., 2017; Thakre et al., 2016), antidiabetic (Tahir et al., 2016), anti-inflammatory (Chansang et al., 2018; Nonato et al., 2012), antihypertensive (Cherkaoui-Tangi et al., 2016) and immunomodulatory (Orhan et al., 2016; Ozek et al., 2017). In medical field, EO have been used against nosocomial infections, as a cleaning liquid for disinfection of medical equipment and surfaces (Warnke et al., 2009) or as an aerosol in operating blocks and waiting rooms for air cleaning to limit contaminations (De Billerbeck, 2007). The application of EO has emerged to food and agriculture fields. They are used as antioxidants and preservatives in food (Khosravi, 2013; Pandey et al., 2016), as plant and crop protectants (Abdullah et al., 2018) and incorporated into foodstuff packaging (Ribeiro-Santos et al., 2017).

In the other side, VO is a source of everlasting components which are responsible of pertinent biological properties. Many of the fatty acids and other compounds present in VO have long been known to benefit our health. Numerous experimental studies approved that a dietary intake of omega-3 polyunsaturated fatty acids can reduce inflammation and may prevent the risk of chronic diseases like heart disease, cancer, and arthritis (Gammone et al., 2019; Hardman and Fakas, 2016; Kris-Etherton et al., 2003). In addition, polyphenols, medium chain fatty acids and tocopherol present in some VO were the reason of their antioxidant and antistress activities (Duthie et al., 2016; Yaep et al., 2015). Current animal studies have indicated that palmitic acid had a potent antiviral property against HIV-1 and HIV-2 (Özçelik et al., 2005). Linoleic and oleic acids were considered as effective antibacterial agents (Dilika et al., 2000). Further experimental studies highlighted other biological benefits of VO such as anti-inflammatory (Hsu and Parthasarathy, 2017), analgesic and antipyretic (Intahphuak et al., 2010), hypolipidemic (Ali and El-Anany, 2017), antibacterial (Tabassum and Vidyasagar, 2014), antiviral (Orhan et al., 2011), hepatoprotective and gastroprotective properties (Cheng et al., 2015).

In the pharmaceutical field, plant oils entered in the composition of many dosage forms through several pathways, including the cutaneous route (creams, ointments, massage oils, gels), the oral route (tablets, syrup, capsules), the rectal route (suppositories) and the pulmonary route (aerosols, nasal drops, sprays) (El-Asbahani et al., 2015). Despite that, the preparations based on plant oil have some important constraints. The VO oral delivery is always confronted to their low solubility in biological fluids, low permeation and poor bioavailability because of their possible oxidation in the gastrointestinal tract (Márquez-Ruiz et al., 2008). For instance, Kanner and Lapidot (2001) suggested that the adsorbed oxygen and low pH of the human gastric fluid may enhance the oxidation of VO in the presence of catalysts found in foods. Moreover, it was reported that hydroperoxide resulted from the hydrolysis of triacylglycerol

contained in VO by pancreatic lipase are not likely to be absorbed in their intact form (Suomela et al., 2004).

Additionally, the toxicity and irritation effects of EO on the oesophageal and gastrointestinal mucosa limit also their uses. EO could be the reason of potential allergic reactions of the skin if they are undiluted or insufficiently diluted (Pedro et al., 2013; Warshaw et al., 2015). For instance, applying excessive amounts of cinnamaldehyde rich-EO to a large surface of the skin can result in significant allergic reaction and anaphylactic shock, which in turn may be fatal (Diba and Statham, 2003). Some oils like those extracted from cumin, bergamot, verbena and lemon can cause photosensitization and induce malignant skin changes like redness, itching, burns, hyperpigmentation, pigmentary changes or berloque dermatitis (Zammit, 2010). Moreover, the high volatility and the high risk of deterioration of EO upon their direct exposure to heat, humidity, light, or oxygen discourages their free use, *i.e.* without a pharmaceutical vehicle (Turek and Stintzing, 2013). Therefore, the nanoncapsulation has been considered as a key to overcome the mentioned limitations (El-Asbahani et al., 2015; Sagiri et al., 2016).

Encapsulation strategies help in converting oils into several dosage forms including, liquid, solid or semi-solid dosage forms and thus enables retention of their activity for longer periods of time (Sagiri et al., 2016). Nanocarriers protect plant oils from environmental factors such as pH, oxygen, light etc., serving as barrier between the molecule and the environment. They also shield the oils from oxidative degradation, evaporation and photo-degradation (Bilia et al., 2014). Their ability to control oil release confers improved efficacy, reduced toxicity, improved patient compliance and convenience (El-Asbahani et al., 2015; Zhao et al., 2017).

5. Plant oils-loaded nanodelivery systems

Nanodelivery systems is an area of intense research as they provide a number of benefits for therapy, such as (i) high drug efficacy, specificity and tolerability, (ii) sustained and controlled release of drugs (iii) less risk of toxicity (iv) deep tissue diffusion due to the

nanometric size, and (iv) protection of drugs at both extracellular and intracellular levels (Bilia et al., 2014; Kumari et al., 2010). In this paper, we highlighted the different experimental strategies designed to encapsulate plants oils into two main groups of organic nanocarriers; polymer based-nanocarriers (including polymeric nanoparticles) and lipid based-nanocarriers (including liposomes and solid lipid nanoparticles).

5.1. Encapsulation in polymer-based nanocarriers

Polymeric nanoparticles (pNP) are submicronic core-shell spherical systems prepared from natural or synthetic polymers (Mattheolabakis et al., 2012). Depending on the nanoparticle preparation process, nanocapsule or nanosphere can be obtained. Nanospheres have a matrix-like form in which the drug is evenly distributed. Nanocapsules are, however, vesicular structures in which the drug is confined in an inner core surrounded by a polymeric membrane (Crucho and Barros, 2017) (**Fig. 5**). Many polymers were used for this purpose, notably, biodegradable polyesters like poly(lactide-co-glycolide), polylactide and poly (ϵ -caprolactone) were widely used (Froio et al., 2020). Recently, pNP are extensively studied for plant oil delivery in view of their ability to entrap and protect oils, biodegradability, bioavailability and their high stability. The plant oil may be conjugated with the polymer (matrix or wall) or entrapped in the oily core (Bilia et al., 2014). Several methods have been reported for developing pNP while the nanoprecipitation, the ionic gelation, the emulsification/solvent evaporation and spray drying methods, are extensively used and **Fig. 5** demonstrates the principle of each technique.

Fig. 5. Schematic illustration of the techniques used to produce polymeric nanoparticles.

5.1.1. Spray drying

Spray-drying technique has been used for decades to encapsulate plant oils in micro- and nano polymeric particles. It is based on the conversion of an infeed (solution, emulsion or suspension) into a dry powder in a single and continuous step. With respect to the encapsulation of plant oil, oil in water emulsion was atomized into fine drops in a drying chamber where hot air is passed (150-250°C). A fast evaporation of water occurred leading to the instantaneous formation of powder (**Fig.5.d**) (Encina et al., 2016; Matos et al., 2019). Spray drying technique is extensively used to encapsulate both essential and vegetable oils in micro and nanoparticles, as illustrated in **Table 1**.

Regarding the particle size and the encapsulation efficiency (EE%) of the particles produced by spray drying technique, high average diameter with moderate oil entrapment amount have been reported by numerous work studies, as depicted in **Table 1**. Hoyos-leyva et al. (2019) reported that almond oil loaded taro starch particles had an average size ranging from 1.4 to 31.1 μm with an EE% of 37.5%. In addition, De-Oliveira et al. (2014) found that *Lippia sidoides* EO loaded alginate : cashew gum nanoparticles exhibited a spherical shape with size ranging from 223 to 399 nm, zeta potential values in range of -30 to -36 mV and EE% of about 50 %. In another work, the same EO was encapsulated in chitosan : cashew gum based nanoparticles owning an EE% of 70% with an average particle sizes in the range 335–558 nm (Abreu et al., 2012). Furthermore, the mixture maltodextrin : soy protein was used to encapsulate walnut oil and the resultant particles showed an average diameter of 4 to 10 μm with an EE% equal to 60% (González et al., 2016).

The main feature of spray drying method is the formation of special particles. Indeed, the scanning electron microscopy carried by Tonon et al. (2011) on flaxseed oil loaded microparticles revealed the formation of hollow particles, i.e. particles with concave and shriveled surfaces. Same images were found by Gallardo et al. when visualizing linseed oil-loaded gum arabic microcapsules. They ascribed this form to vacuoles formation inside the particles after the crust development. The magnitude of this process is inversely related to solid concentration in the emulsion (Gallardo et al., 2013). Moreover, Wang et al. (2018) carrying out confocal scanning laser microscopy on peony seed oil microparticles stated that the spray dried particles had a complete core-shell structure with smooth surface and no apparent fissures or cracks.

In vitro release profile of plant oils from particles prepared by spray drying technique generally exhibit a controlled manner. In a study carried out by De-Oliveira et al. (2014) the nanoparticles have reached a level of maximal release around 30–50 h. In that time, the content

of *Lippia sidoides* EO from alginate : cashew gum particles varied from 45 and 95% depending on the ratio of used polymers. Higher and faster release rate was achieved with high amount of cashew gum due to its greater hydrophilic character which allows greater diffusion of EO through the polymeric wall. Conversely, a smaller and more controlled release was assessed when increasing alginate content; after 50h, only 45% of oil was released. This was related to the formation of compact network which in turn slow down the diffusion of EO to the external medium (De-Oliveira et al., 2014).

Particles produced by spray drying process provides a high stability for encapsulated oils. In this context, Hoyos-leyva et al. (2019) investigated the oxidative stability of almond oil before and after encapsulation into taro starch microcapsules. They found that these systems conferred more protection against oxidation when compared to unencapsulated almond oil due to the relatively reduced porosity of the material, which in turn limits the exposure of the oil to stress conditions during storage.

Several parameters have to be taken into consideration to efficiently entrap plant oils in polymeric micro- and nanoparticles by spray drying technique. The influence of type and amount of wall material on plant oils-loaded particles characteristics has been extensively studied in the literature (Bae and Lee, 2008; Chin et al., 2018; Gallardo et al., 2013; Laohasongkram et al., 2011; Lozano et al., 2012; Rodea-gonzález et al., 2012; Rubilar et al., 2012; Shamaei et al., 2017). Carneiro et al. (2013) investigated the microencapsulation of flaxseed oil by spray drying technique. They studied the potential of maltodextrin mixed with different wall materials: arabic gum, whey protein concentrate and two types of modified starch (Hi-Cap 100TM and Capsul TA) on droplets size. Results showed that the highest viscosity presented by maltodextrin : arabic gum emulsion implies a higher resistance to droplets movement, thus preventing coalescence and leading to smaller droplets size. Shamaei et al. (2017) related the differences in the mean droplet size of the emulsions using different wall

material to the surface activity and molecular weight of wall material constituents. They found that as the ratio of tween 80 to skim milk powder increases, the mean droplet size decreases. This in turn was attributed to the fact that tween 80 mitigated droplet coalescence and Ostwald ripening phenomena in the emulsion by reducing the surface tension and interfacial free energy of the emulsion. In another study, emulsion droplet size was found to decrease as the ratio of wall to core material increases due to the fact that at low ratio, there may not be enough coating materials to cover the whole surface of the droplets in order to prevent them from coalescence which in turn increases the droplet size (Rodea-gonzález et al., 2012). Same result was also reported for chia seed oil-loaded microcapsules prepared by spray drying process (Laohasongkram et al., 2011). Moreover, Chew et al. (2018) spotlighted that adding β -cyclodextrin to the wall matrix increases the EE% of refined kenaf seed oil due to its host-guest character. In fact, its interior cavity acts as a host which can fix the guest (hydrophobic oil), while the exterior surface can bind with water or hydrophilic head of other wall materials. Furthermore, Us-medina and coworkers (2018) stated that adding chia mucilage to sodium caseinate : maltodextrin wall matrix increases the EE% of chia seed oil from 71.26 to 86.65%. They attributed this result to the fact that chia mucilage, used as thickener agent, increases the viscosity of the system which in turn promotes a greater physical stability of the emulsion during the spray drying process.

With respect to the oil content, Rubilar et al. (2012) revealed that increasing the oil concentration provokes a significant increase in droplet emulsion size and viscosity, which in turn reduces the EE% and increases the surface oil content of the powder leading to potential lipid oxidation. Similar result was already published (Tonon et al., 2012).

Air inlet temperature is another factor to take into account for the development of plant oil-loaded particles; and it was widely investigated in the literature (Frascareli et al., 2011; Laohasongkram et al., 2011; Roccia et al., 2014; Shamaei et al., 2017). Frascareli et al. (2011)

studied the encapsulation of coffee oil and observed that as the air flow temperature increases the EE% decreases due to the fact that higher temperature leads to faster drying of the external phase which creates cracks in the particle wall, resulting in oil loss. Moisture content is an important variable for the shelf life of powders. It was reported that increasing the inlet temperature reduced the moisture content (Mohammed et al., 2017). However, higher values (more than 175 °C) resulted in an increase in moisture content due to the formation of rapid crust which hampered the water evaporation leading to particles with more moisture content. The particle size is another parameter which vary when modifying the air inlet temperature. In 2017, Mohammed and coworkers pointed out that an increased inlet air temperature produced larger-sized *Nigella sativa* EO particles and ascribed this result to the microcapsule structure. Indeed, high temperature enable the particles to form early which in turn prevents the shrinkage of particles during drying (Mohammed et al., 2017).

To sum up, despite of the high temperature required, the spray drying method is widely used to encapsulate either essential or vegetable oils. This was related to the fact that short time of contact between hot air and plant oil occurred, and thus the evaporation happens between 15 and 30 seconds and takes place at the surface of the particle; hence , the oils never reach the inlet temperature of drying gas (Fang and Bhandari, 2012). According to **Table 1**, natural polymers like maltodextrin, gums and chitosan are the mostly used wall materials. Currently, this technique is widely used in nutraceutical and food industry due to its benefits including i) ease of scaling up, ii) simplicity, iii) low production costs, and iv) ability to produce microparticles facile to the transport and storage. Many drawbacks are associated to the use of this process including the lack of uniformity; high particle size, low oil loading and possibility of oil loss. Moreover, the wall material used must have good water solubility as most formulations used by the food industry are aqueous-based and simultaneously impart a suitable viscosity in order to enable the drying process (Corrêa-Filho et al., 2019).

5.1.2. Emulsion evaporation

Emulsion evaporation method has been proposed by Vanderhoff and Asser (1979) to develop pNPs. In this process, an organic solution consisting of polymer and oil is emulsified with a non-solvent mixture under a high shear stress (e.g. by high-shear homogenization or ultrasonication). After that, the organic solvent is evaporated either by continuous magnetic stirring at room temperature or under reduced pressure leading to nanoparticles formation (**Fig.5.b**) (Rao and Geckeler, 2011; Rodríguez et al., 2016). This technique has been used to encapsulate both essential and vegetable oils in pNPs, as depicted in **Table 1**.

The emulsion evaporation technique produces nanoparticles with higher EE% and smaller average diameter, as compared to the spray drying technique. In this context, Gomes et al. (2011a) reported a particle size of 179.3 and 173.8 nm with an EE% of 98 and 92% for eugenol- and trans-cinnamaldehyde loaded poly (lactide-co-glycolide) nanoparticles, respectively. Similarly, chia seed oil loaded nanoparticles using chia mucilage as wall material exhibited a small particle size (205 nm) with negative zeta potential (-11.58 mv) and high EE% (82.8%) (Campo et al., 2017). Moreover, poly (lactide-co-glycolide) nanoparticles were prepared to encapsulate clove EO, rich in eugenol which has potent antimicrobial activities (Priyadarshini et al., 2018). The average size of the resultant nanoparticles was about 237 nm with negative zeta potential of -40 mv and an EE% equal to 93%.

The nanoparticles prepared by emulsion evaporation process exhibited *in vitro* release pattern similar to that of particles produced by spray drying. In 2018, Priyadarshini et al. pointed out that *in vitro* cumulative clove EO release from poly (lactide-co-glycolide) nanoparticles followed a biphasic profile with an initial burst release at the first 4h due to the release of clove EO found near the nanoparticles surface (Priyadarshini et al., 2018). A cumulative amount of 75% was progressively released up to ~15 days. Similar *in vitro* release kinetics were governed by eugenol and trans-cinnamaldehyde from poly (lactide-co-glycolide) nanoparticles where 64

and 87% of the initial load was released in the medium within 72 h, respectively (Gomes et al., 2011a).

The stability of the pNPs formulated by this technique was investigated in the literature. In 2017, Campo et al. studied the oxidation of chia seed oil by gas chromatography with flame ionization detector in both emulsions and chia seed mucilage based-nanoparticles at accelerated conditions ($40\pm1^{\circ}\text{C}$) during 28 days of storage (Campo et al., 2017). No significant change was shown in term of particle size, zeta potential or polydispersity index. However, the fatty acid methyl esters content reduction in pNPs was smaller than in emulsions; therefore, the chia seed mucilage provided a high protection against oil oxidation (Campo et al., 2017).

With respect to the emulsification evaporation process, several parameters may affect the nanoparticles properties. Freiburger et al. (2015) investigated the effect of polymer type (poly(3-hydroxybutyrate-co-3-hydroxyvalerate)/polylactide); dispersion mechanism (ultrasonication / high shear homogenization) and polymer : oil ratio on the average size and oil recovery of biocompatible nanoparticles containing coffee oil. The statistical analysis showed non-significant effect of the experimental factors on the nanoparticle size within the experimental range. While for the coffee oil recovery, regression analysis produced a significant model. Less oil was lost by volatilization when sonication was used, because the required dispersion time (3min) was smaller when compared to the ultraturrax time (10min). Results showed also that less coffee oil loss was pronounced when using poly(3-hydroxybutyrate-co-3-hydroxyvalerate) combined to the high shear homogenization as well as using polylactide combined with sonication. This was explained by the high viscosity of poly(3-hydroxybutyrate-co-3-hydroxyvalerate)-dichloromethane solution which could avoid oil volatilization even with high shear homogenization (Freiburger et al., 2015). Regarding the polymer:oil ratio, an increase in polymer amount lead to increase the viscosity of the solution resulting in efficient oil protection from the heat generated by the homogenizer.

To sum up, the emulsification evaporation method can be used to encapsulate both essential and vegetable oils. Although it provides high EE%, this method is less used to encapsulate plant oils, as compared to the spray drying technique. The possible reason behind this is the possible coalescence of droplets during evaporation which may lead to polydisperse particles and the need for a high shear process.

5.1.3. Nanoprecipitation

Nanoprecipitation is a simple, fast and increasingly trending technique for nanoparticles preparation (Almoustafa et al., 2017). It was firstly reported by Fessi et al. (1989) and it is based on the interfacial deposition of polymers as a result of the displacement of a water miscible solvent from a lipophilic solution (**Fig.5.a**) (Miladi et al., 2016). This method has been widely used to encapsulate plants oils in pNPs and **Table 1** summarizes some work studies using the nanoprecipitation process to encapsulate either essential or vegetable oils during the last decade.

According to **Table 1**, the nanoparticles produced by nanoprecipitation process owned small particle size, narrow distribution with high EE%. Iannitelli et al. (2011) developed carvacrol loaded poly (lactide-co-glycolide) based-nanocapsules with a spherical shape, small particle size (209.8 nm) and regular distribution (poly dispersibility index=0.26). Similarly, *Cymbopogon martini* EO was efficiently entrapped in poly (ϵ -caprolactone) based-nanoparticles with an average size of 282.1 nm, zeta potential equal to -27.2 mV and EE% of about 99.54 % (Khoobdel et al., 2017). Furthermore, Babassu tree nut oil loaded- poly (lactide-co-glycolide) nanoparticles exhibited an average diameter about 209.2 nm with a negative zeta potential of -15.8 mV (Sousa et al., 2013).

In term of particle size, Esfandyari-Manesh and coworkers (2013) compared the nanoprecipitation to the emulsification solvent evaporation method to design carvone/anethole loaded poly (lactide-co-glycolide) nanoparticles and found that the particles produced by

nanoprecipitation had smaller average diameter (158 and 126 nm for anethole and carvone, respectively) and narrower size distribution (0.08). Additionally, the amount of carvone and anethole were determined respectively by HPLC and UV analysis and results showed higher oil loading for the particles produced by nanoprecipitation (14.73 and 12.32% for anethole and carvone, respectively). The authors related the low EO loading for the emulsification method to its loss during the evaporation step which has taken a long time (about 3h). In addition, the high particle diameter of the nanoparticles prepared by this method was attributed to the difficulty for the mutual dispersion of the phase which is viscous due to the presence of high amount of oil and polymer.

According to the literature, to develop pNPs with suitable physicochemical properties, numerous factors had to be taken into consideration. The polymer type and amount have a critical effect on nanoparticles average size. In 2017, Khoobdel et al. (2017) developing poly (ϵ -caprolactone) -based nanoparticles loaded with rosemary EO reported that increasing polymer quantity, leads in increasing the thickness of the particles shell and thus increasing their mean diameter, instead of increasing their number. Moreover, low values of EE% were observed when using Eudragit L100 as polymer for the encapsulation of *Siberian cedar* seed oil or free fatty acids due to its porous structure which enabled oil leakage (Averina and Allémann, 2013). Regarding the type of the EO, Liakos et al. (2018) studied the influence of EO chemical composition on the particle size of three types of pNPs: Peppermint, cinnamon and lemongrass EOs loaded-cellulose acetate nanocapsules. The average size was increasing as follow: Cinnamon-pNPs <Peppermint-pNPs <Lemongrass pNPs. The larger pNPs were those containing lemongrass EO, due to the presence of high percentage of geranial and neral which have long carbon chains (≈ 10 C atoms) leading to larger pNPs when attached to cellulose acetate. While, peppermint contains mainly 35% menthol and 27% menthone leading to the creation of less uniform, complex and large nanoparticles. In the other hand, cinnamon EO

consists essentially of cinnamaldehyde which reacts with hydroxyl group of cellulose acetate giving hemiacetal bound and hence combats the nanocapsules. Liakos and his coworkers assessed also in their study higher zeta-potential upon increasing lemongrass EO concentration, suggesting that some EO molecules are present onto the outer surface of the particles (Liakos et al., 2018). Similarly, it was reported that the presence of lime EO decreased the zeta potential and the values were 61.1 and 57.0 mV for free- and loaded- chitosan nanocapsules, respectively. They attributed this result to the diminution of free NH_3^+ groups of chitosan following their interaction with lime EO (Sotelo-Boyás et al., 2017b). However, in another work study, the presence of rosemary EO did not affect the zeta potential of poly (ϵ -caprolactone) nanoparticles which confirm its presence in the core of the nanoparticles instead of being adsorbed on their surface (Khoobdel et al., 2017).

In term of surfactant type and amount, Badri et al. (2015) pointed out that the amount of polyvinyl alcohol used as surfactant had no significant effect on the average diameter of poly (ϵ -caprolactone) nanoparticles but at higher concentration (more than 0.1mg/mL), a significant increase was assessed due to the deposition of extra polyvinyl alcohol on the nanoparticle surface. Furthermore, it was reported that the use of span 20 instead of tween 20 gave smaller rosemary EO-loaded nanocapsules, lower polydispersity index and limited loss of the oil during the solvent evaporation step. In the presence of span 20, the hydrophilic lipophilic balance (HLB) was between 12 and 15 (14.3), which was in the range of HLB necessary for rosemary EO nanoemulsion stability (Ephrem et al., 2014). Furthermore, the effect of the ratio between organic and aqueous phase may affect the particle size. Indeed, an increase in argan oil loaded nanoparticles was assessed when increasing the organic to aqueous phase ratio due to the slow diffusion of the organic solvent (acetone) to water resulting slow polymer precipitation and thus, larger pNPs were obtained (Badri et al., 2015).

Regarding the effect of operating conditions, Badri et al. (2015) investigated the effect of stirring speed and organic phase addition rate consisting of poly (ϵ -caprolactone), acetone, argan oil, indomethacin and span20 on the physicochemical properties of the obtained pNPs. Results revealed a decrease in particle size by increasing the stirring speed. While, it increases when decreasing the organic phase addition speed due to the difficulty to get a homogenous mixture of phases. Furthermore, Ephrem et al. (2014) studied the influence of the evaporation method on the pNPs properties and rosemary EO loss and found that the evaporation of acetone under normal pressure at room temperature was the best since it avoided heat and low pressure, giving negligible loss of the encapsulated EO.

Recently, a novel form of pNPs was developed called lipid-core nanocapsules which is composed of a mixture of oil and solid lipid surrounded by a polymeric wall (Ourique et al., 2010). For instance, the oily core of pNP may consist of a liquid lipid, a mixture of liquid lipids, or a mixture of liquid lipid and solid lipid. The latter concerns a specific form of nanocapsules called lipid-core nanocapsules (Frank et al., 2015). Several research works have been already published investigated the feasibility to entrap VO into lipid core NPs (Almeida et al., 2009; Drozdek and Bazyli, 2016; Friedrich et al., 2008; Marchiori et al., 2017; Rigo et al., 2013; Weber et al., 2016). In this context, nanoprecipitation technique was efficiently carried out to develop borage oil : betamethasone co-loaded lipid-core nanocapsules with a mean size around 210 nm, negative zeta potential (-16.6mv), low polydispersity index (<0.05) and high EE% (up to 100%) (Weber et al., 2016). Furthermore, Rigo et al. (2013) studied the influence of the type of VO on the release kinetic of clobetasol propionate, selected as model drug, from the lipid core nanoparticles. Results revealed a biphasic drug release profiles for all the formulations. After 168 h, the concentration of clobetasol propionate released from the formulation was in the following order: Sunflower oil-pNPs < Soybean oil-pNPs < Rice ban-pNPs. The authors related these results to the consistency indices of the mixture oil : sorbitan monostearate, used

as solid lipid; and a greater control of the drug release was observed with higher consistency index of the VO-sorbitan monostearate.

Regarding the nanoparticles stability, Badri et al. (2018) investigated the stability of poly (ϵ -caprolactone) based nanoparticles containing *Nigella sativa* EO coupled with indomethacin during one month under three different conditions (4°C, 25°C and 40°C). The samples were analyzed at predefined times and results demonstrated no significant change in either size or zeta potential for all the tested particles. Similarly, the photodegradation study of the lipid-core nanocapsules containing borage oil and betamethasone was carried out to demonstrate the ability of nanocapsules in the photoprotection of the drug. In brief, nanoparticles suspensions were placed in transparent quartz cell and exposed to UVC radiation and the total concentration of drug was quantified. Results revealed a degradation of 61% from the nanocapsules suspension at the end of the experiment (10 h), while 58% of drug was degraded in 2 h from drug solution. This confirmed the property of polymeric wall to protect the bioactive molecules (Weber et al., 2016).

Regarding the scalability and reproducibility of the nanoprecipitation process, it was noticed no significant difference between rosemary EO loaded poly (ϵ -caprolactone) nanocapsules prepared at small and large scales in term of shape, particle size, polydispersity index zeta potential and EE% (Ephrem et al., 2014).

Overall, the nanoprecipitation or solvent displacement method is widely used to develop pNPs for plants oils encapsulation. According to the **Table 1**, the polymers commonly used to design the polymeric matrix are synthetic polyesters like poly (lactide-co-glycolide) (Esfandyari-Manesh et al., 2013; Iannitelli et al., 2011; Sousa et al., 2013), poly (ϵ -caprolactone) (Badri et al., 2018; Christofoli et al., 2015; Ephrem et al., 2014; Jummes et al., 2020; Khoobdel et al., 2017), polylactide (Liakos et al., 2016), Eudragit®L100 (Averina and Allémann, 2013), S100 (Averina and Allémann, 2013), L100-55 (Pina-Barrera et al., 2019) and

RS100 (El-Asbahani et al., 2015; Froiio et al., 2019). Synthetic polymers are more used than natural ones like chitosan (Luque-Alcaraz et al., 2016; Sotelo-Boyás et al., 2015, 2017a, 2017b) and cellulose derivatives (Liakos et al., 2018; Marchiori et al., 2017) because they have higher purity and better reproducibility. The benefits associated to this encapsulation method are rapidity, simplicity, reproducibility, and scalability. Moreover, NPs with narrow size distribution, high EE% and high stability could be obtained. In addition, the use of surfactant or high production energy is avoided. The main drawback of this method in encapsulating plant oils is the use of organic solvents which may be toxic for health.

5.1.4. Ionic gelation

In order to avoid the use of toxic organic solvent or high shear forces, Calco et al. (1997) proposed a novel approach called ionic gelation or coacervation. Alginate, an anionic polysaccharide, and chitosan, a cationic polyelectrolyte, are extensively used for ionic gelation purpose. These polyelectrolytes can interact with crosslinking agents like tripolyphosphate having an opposite charge via electrostatic interaction and aggregate into nanoparticles (J. Yang et al., 2015). The coacervation consists on the transition from liquid to gel state upon complexation between the oppositely charged molecules at determined pH values leading to the formation of nano-sized particles (Nagavarma et al., 2012) (**Fig.5.c**). A number of studies have been carried out using this technique to encapsulate plant oils, as displayed in **Table 1**.

Recently, cinnamon EO-loaded chitosan nanoparticles crosslinked with tripolyphosphate were prepared by using coacervation method and the obtained particles owned small average diameter (80-100 nm) with good zeta potential values (-11.2 to -22.4 mV) (Liu et al., 2017). In addition, cardamom EO was successfully entrapped into chitosan based nanoparticles with an average particle size ranging between 50 and 100 nm, zeta potential more than +50 mV and a high EE% which was more than 90% (Jamil et al., 2016). Furthermore, Woranuch and his coworker (2013) reported that the thermal stability of eugenol was enhanced

by encapsulation in chitosan: tripolyphosphate- nanoparticles. According to some research works depicted in Table 2, the ionic gelation technique may produce microparticles with moderate EE% as compared to the nanoprecipitation process (Feyzioglu and Tornuk, 2016; López-meneses et al., 2018; Sutaphanit and Chitprasert, 2014; Yang et al., 2014; K. Zhang et al., 2012).

Currently, several research works have been reported to investigate the effect of pNPs composition and operating conditions on physicochemical properties of particles prepared by ionic gelation method. The optimization of the type and amount of polymer and crosslinking agent is crucial to develop pNPs with suitable characteristics. In this approach, *Carum copticum* EO-loaded chitosan nanoparticles were prepared by ionic gelation method using two types of crosslinking agents: tripolyphosphate and hexametaphosphate (Esmaeili and Asgari, 2015). The efficacy of crosslinking agent type and tripolyphosphate concentration on the EE% were evaluated. The particles prepared using hexametaphosphate (0.5% (w/v)) had significantly lower loading capacity and EE% than those prepared using tripolyphosphate (0.5% (w/v)). This was attributed to the ring structure and bigger size of hexametaphosphate which in turn lead to decrease the crosslinking phenomenon. In the same work, different nanoparticles were prepared using different tripolyphosphate concentrations (0.25, 0.5, 0.75 and 1% (w/v)) and results indicated that maximum EE% was obtained with the concentration of 0.5% (w/v). The low value of EE% obtained with the concentration of 0.25% (w/v) was explained by the shortage of tripolyphosphate concentration to crosslink the nanoparticles; while the low values shown with 0.75 and 1% (w/v) tripolyphosphate concentrations were related to the particle shrinkage (Esmaeili and Asgari, 2015).

With respect to the polymer effect, the viscosity of chitosan was optimized for fabrication of vanilla oil loaded microcapsules using the coacervation method (Yang et al., 2014). Results showed that at low chitosan viscosity, no microcapsules were formed because

chitosan at low viscosity could not form hard membrane wall. On the other hand, when using high viscosity chitosan, aggregation problem was observed (Yang et al., 2014).

Regarding the EO concentration, Hasheminejad et al. (2019) stated that both particle size and zeta potential decreased significantly when increasing clove EO concentration. The reduction in particle size was explained by the great packing of polymer chains, due to the high number of amino groups in chitosan responsible for the interaction with the oil. Additionally, the thermogravimetric analysis performed by Hosseini et al. (2013) on oregano EO loaded-chitosan nanoparticles demonstrated that as the initial EO content increases from 0.1 to 0.8 g/g chitosan, loading capacity increases too from 3 to 8%, but the EE% decreases from 47 to 21%. This was explained by the saturation of oregano EO loaded into chitosan nanoparticles. The EO concentration was found to affect also the *in vitro* release profile. Indeed, Hosseini and his coworkers reported that low concentration of oregano EO (0.1 g/g chitosan) leads to burst release (82% of encapsulated EO was released from the nanoparticles within 3 h). While, as oregano EO amount increased, the burst effect was dramatically alleviated and the cumulative release was reduced from 82 to 12% after 3h. This phenomenon was attributed to the fact that chitosan nanoparticles with smaller particle size would have bigger surface-to-volume ratio which may result in fast release of oregano EO adsorbed on their surfaces (Hosseini et al., 2013). Another factor affecting the release profile was found to be the composition of the encapsulated material. In 2014, Dima et al. investigating the release of *Pimenta dioica* EO found that chitosan microspheres covered with k-carrageenan are more fragile and exhibit higher swelling degree with zero order release kinetics, as compared to the chitosan : k-carrageenan microspheres hardened by glutaraldehyde crosslinking which show non-Fickian release mechanism (Dima et al., 2014).

Numerous research works noticed the stability of pNPs produced by ionic gelation method. In 2014, Sutaphanit et al. reported that the encapsulation of holy basil EO into gelatin

by simple coacervation method could prevent its volatility and oxidation (Sutaphanit and Chitprasert, 2014). Indeed, the particles stored under accelerated conditions at 60 °C for 49 days exhibited small decreases in the holy basil EO retention rate and antioxidant activity (Sutaphanit and Chitprasert, 2014). Moreover, the stability studies performed on peppermint oil loaded capsules showed that only 7% of the oil was released during the storage of 40 days in cold water (Dong et al., 2011). In another work study, jasmine EO nanoparticles exhibited high heat-stability against humid heat (80°C for 7h) (Lv et al., 2014).

On the whole, ionic gelation method is broadly used to encapsulate plants oils when compared to simple emulsion evaporation method. Gelatin (Devi et al., 2012; Dong et al., 2011; Sutaphanit and Chitprasert, 2014; K. Zhang et al., 2012), arabic gum (Dong et al., 2011; Lv et al., 2014; X. Yang et al., 2015; K. Zhang et al., 2012), alginate (Devi et al., 2012; Natrajan et al., 2015) and chitosan (Feyzioglu and Tornuk, 2016; Hosseini et al., 2013; Jamil et al., 2016; Liu et al., 2017; López-meneses et al., 2018) are the most commonly used wall materials. In addition, tripolyphosphate (Hasheminejad et al., 2019; Hosseini et al., 2013; Hu et al., 2015; Liu et al., 2017; Woranuch and Yoksan, 2013) and glutaraldehyde (Devi et al., 2012; Dima et al., 2014; Natrajan et al., 2015; Sutaphanit and Chitprasert, 2014) are widely used as crosslinking agents. The main advantages of ionic gelation method are, in particular; the avoidance of high shear forces and the use of aqueous solvents instead of organic ones. Moreover, ionic gelation is simple, economic and reproducible. However, moderate EE% and larger particle size were assessed using this method as compared to the nanoprecipitation technique.

658 **Table 1.** Preparation methods for plant oils encapsulation in polymeric nanoparticles and fine applications.

Encapsulated oil	Plant (origin)	Wall material	Physicochemical properties			Biological properties	Application	Ref.
			Size (nm)	Z.pot (mv)	EE (%)			
Nanoprecipitation method								
Costus	Saussurea lappa	Eudragit RS 100	145	+45	/	Anticholinesterase, anti-inflammatory	Medicine	(Lammari et al., 2021)
Baccharis dracunculifolia	Baccharis dracunculifolia DC	Eudragit RS 100	151.6	+51.7	99.4	Antibacterial	Food	(Timbe et al., 2020)
Oregano	Origanum vulgare L.	PCL	158-300	-13.8 to -28.5		Antibacterial	Food	(Souza et al., 2020)
Palmorasa	Cymbopogon martini Roxb.	PCL	282.1	-27.2	99.54	Antioxidant, antimicrobial	Cosmetic	(Jummes et al., 2020)
Geraniol	/	PCL	289.3	-26.6	99.88	Antioxidant, antimicrobial	Cosmetics	(Jummes et al., 2020)
Zataria	Zataria multiflora Boiss.	PCL	192-398	+13.9 to +29.2	75-79	Insecticide	Agriculture	(Ahsaei et al., 2020)
Thyme	Thymus vulgaris L.	Eudragit L 100-55	153.9	-4.11	52.81	Antioxidant	Food	(Pina-Barrera et al., 2019)
	Thymus leptobotrys L.	Eudragit RS 100	144	+80.9	/	Bacteriostatic, fungistatic	Medicine	(El-Asbahani et al., 2015)
	Thymus satureoides L.	Eudragit RS 100	132	81.6	/	Bacteriostatic, fungistatic	Medicine	(El-Asbahani et al., 2015)
	Thymus serpyllum L.	Chitosan	117-226	+27	/	Antimicrobial	Agriculture	(Sotelo-Boyás et al., 2015)
		Chitosan	/	/	68	Antimicrobial	Agriculture	(Sotelo-Boyás et al., 2017a)
Sweet orange	Citrus sinensis L.	Eudragit RS100	57- 208	+39 to +74	56-96	Antimicrobial	Food	(Froiio et al., 2019)
Bergamot	Citrus bergamia Risso.	Eudragit RS100	57- 208	+39 to +74	28-84	Antimicrobial	Food	(Froiio et al., 2019)
Rosemary	Rosmarinus officinalis L.	PCL	181-407	+11.6 to +28.3	82.9-84.3	Insecticide	Agriculture	(Ahsaei et al., 2020)
		Eudragit EPO	200	/	59	Antioxidant	Cosmetics	(Silva-Flores et al., 2019)
		PCL	145	-11.0	78.2	Insecticide	Agriculture	(Khoobdel et al., 2017)
		PCL	220	-19.9	99	Antioxidant, antimicrobial	Medicine	(Ephrem et al., 2014)
Lavender	Lavandula dentate L.	Eudragit EPO	200	/	41	Antioxidant	Cosmetics	(Silva-Flores et al., 2019)
		PEO-b-PLA	10-75	/	70-75	Antimicrobial	Textile	(Popielski et al., 2016)
Peppermint	Mentha piperita L.	Cellulose acetate	180	-38	/	Antimicrobial	Medicine	(Liakos et al., 2018)
Cinnamon	Cinnamomum cassia persl.	Cellulose acetate	150	-40	/	Antimicrobial	Medicine	(Liakos et al., 2018)
Lemongrass	Cymbopogon citratus DC.	PLA	96.4	/	99	Antifungal	Medicine	(Antonioli et al., 2020)
		Cellulose acetate	200	-36	/	Antimicrobial	Medicine	(Liakos et al., 2018)
		PLA	300	-6	/	Antimicrobial	Medicine	(Liakos et al., 2016)
Black seed oil + Indometacin	Nigella sativa L.	PCL	230–260	–20 to–30	Oil=84 Drug=70	Anti-inflammatory	Cosmetics	(Badri et al., 2018)

Lime	<i>Citrus aurantiifolia</i> Christm.	Chitosan	100-300	+57	/	Antimicrobial	Food	(Sotelo-Boyás et al., 2017b)
		Chitosan	250-1000	+20.2	/	Antimicrobial	Agriculture	(Sotelo-Boyás et al., 2015)
Pepper tree	<i>Schinus molle</i> L.	Chitosan	754	+9.1	/	Antifungal	Food	(Luque-Alcaraz et al., 2016)
<i>Zanthoxylum rhoifolium</i>	<i>Zanthoxylum rhoifolium</i> L.	PCL	500	-20	96	Insecticide	Agriculture	(Christofoli et al., 2015)
Argan oil +Indometacin	<i>Argania spinosa</i> L.	PCL	290 - 350	-40 to-50	65 - 75	Anti-inflammatory	Cosmetics	(Badri et al., 2015)
<i>Pelargonium graveolens</i>	<i>Pelargonium graveolens</i> L.	Eudragit RS 100	113	+80.6	/	Bacteriostatic, fungistatic	Medicine	(El-Asbahani et al., 2015)
<i>Eugenia caryophyllata</i>	<i>Eugenia caryophyllata</i> C.	Eudragit RS 100	131	+80.7	/	Bacteriostatic, fungistatic	Medicine	(El-Asbahani et al., 2015)
Carvacrol	/	PLA	114.7	+54.7	53.9	Antimicrobial	Food	(Niza et al., 2020)
	/	PHB	146	-26	21	Antimicrobial	/	(Shakeri et al., 2014)
	/	PLGA	209.8	/	26	Antimicrobial	Medicine	(Iannitelli et al., 2011)
Carvone	/	PLGA	126	/	/	Antimicrobial	Food	(Esfandiyari-Manesh et al., 2013)
Anethole	/	PLGA	158	/	/	Antimicrobial	Food	(Esfandiyari-Manesh et al., 2013)
Date seed	<i>Phoenix dactylifera</i> L.	Eudragit RS 100	207	+59	97	Antidiabetic	Medicine	(Lammari et al., 2020)
Pomegranate oil+ Silibinin	<i>Punica granatum</i> L.	Ethylcellulose	/	/	/	Anti-inflammatory for skin damage UVB	Cosmetics	(Marchiori et al., 2017)
Rosehip	<i>Rosa rugosa</i> Thunb.	Eudragit RS100	158	+9.8	/	Accelerate the skin regenerating process	Cosmetics	(Contri et al., 2016)
Castor	<i>Ricin commun</i> L.	TAD	260-150	/	/	Source of PUFA	/	(Chattopadhyay and Prez, 2016)
Olive	<i>Olea europaea</i> L.	TAD	185	-30	/	Source of PUFA	/	(Chattopadhyay and Prez, 2016)
Pumpkin	<i>Cucurbita pepo</i> L.	TAD	172	-35	/	Source of PUFA	/	(Chattopadhyay and Prez, 2016)
Sunflower	<i>Helianthus annuus</i> L.	TAD	178	-33	/	Source of PUFA	/	(Chattopadhyay and Prez, 2016)
Hazelnut	<i>Corylus avellana</i> L.	TAD	175	-35	/	Source of PUFA	/	(Chattopadhyay and Prez, 2016)

Borage oil+ Betamethason e dipropionate	<i>Borago officinalis</i> L.	PCL	210	-16.6	100	Treatment of atopic dermatitis	Cosmetics	(Weber et al., 2016)
Rice bran	<i>Oryza sativa</i> L.	PCL	200	-9	/	Sunscreen (treatment of inflammatory disorders of skin)	Cosmetics	(Rigo et al., 2015)
Pine seed	<i>Pinus pinea</i> L.	Eudragit L 100-55	236-296	/	85-91	Source of PUFA	Medicine	(Averina and Allémann, 2013)
Free fatty acid	/	/ Eudragit L100 / Eudragit S100	260-319	/	83-99			
Babassu	<i>Attalea speciosa</i> Mart.	PLGA	209.2	−15.8	/	Treatment of benign prostatic hyperplasia	Medicine	(Sousa et al., 2013)
Emulsion evaporation method								
Mastic tree of Chios	<i>Pistacia lentiscus</i> L. var. chia	PLA	239-286	-29.1 to −34.5	9-37	Antimicrobial	Cosmetic	(Vrouvaki et al., 2020)
Clove	<i>Syzygium aromaticum</i> L.	PLGA	237.6	−40	93.95	Antimicrobial	Medicine	(Priyadarshini et al., 2018)
Eugenol	/	PLGA	179.3	/	98	Antimicrobial	Food	(Gomes et al., 2011a)
Trans-cinnamaldehyde	/	PLGA	173.8	/	92	Antimicrobial	Food	(Gomes et al., 2011a)
Chia seed	<i>Salvia hispanica</i> L.	Chia seed mucilage	205	-11.58	82.8	Source of PUFA	/	(Campo et al., 2017)
Coffee	<i>Coffea arabica</i> L.	PLA	263	/	112.7	Flavoring agent	Food	(Freiberger et al., 2015)
		PHBV	271		94.5	Flavoring agent	Food	(Freiberger et al., 2015)
Ionic gelation method								
Homalomena pineodora	<i>Homalomena pineodora</i> L.	Chitosan	70	+24.1		Wound healing	Medicine	(Rozman et al., 2020)
Piper nigrum	<i>Piper nigrum</i> L.	Chitosan	527.5	-5.3	35-40	Pesticide	Agriculture	(Rajkumar et al., 2020)
Nettle	<i>Urtica dioica</i> L.	Chitosan	208.3–369.4	/	59.5-68.2	Antimicrobial	Food; Medicine	(Bagheri et al., 2020)
Tarragon	<i>Artemisia dracunculus</i> L.	Gelatin+Chitosan	246–505	27.1–37.1	9.8–35.6	Preservative	Food	(Zhang et al., 2020)
Camelthorn	<i>Alhagi maurorum</i> L.	Chitosan	172	+28.6	/	Antimicrobial	Medicine	(Hassanshahian et al., 2020)
Great morinda	<i>Morinda citrifolia</i> L.	Chitosan	1006	+43.5	/	Anticancer	Medicine	(Rajivgandhi et al., 2020)
Clove	<i>Syzygium aromaticum</i> L.	Chitosan	268.5	+22.4	/	Antifungal	Agriculture; Food	(Hasheminejad et al., 2019)
Pepper tree	<i>Schinus molle</i> L.	Chitosan	516.9	+40.2	26.6	Antifungal, anti-aflatoxigenic	Medicine	(López-meneses et al., 2018)

Cinnamon	<i>Cinnamomum cassia</i> persl.	Chitosan	80–100	-11.2 to -22.4	47.67 - 55.64	Antimicrobial	Food	(Liu et al., 2017)
		Chitosan	215	/	/	Antimicrobial	Food	(Hu et al., 2015)
Cardamon	<i>Elettaria cardamomum</i> L.	Chitosan	50–100	>+50	>90	Antimicrobial	Medicine	(Jamil et al., 2016)
	<i>Summer savory</i>	Chitosan	135.5-237.4	-9.68 to -21.12	35.1 –40.7	Antioxidant, antimicrobial	Food	(Feyzioglu and Tornuk, 2016)
	<i>Carum copticum</i>	Chitosan	/	/	36.2	Antioxidant, antimicrobial	Cosmetics; Medicine	(Esmacili and Asgari, 2015)
Tumeric	<i>Curcuma longa</i> L.	Alginate+Chitosan	<300	/	71	Anticancer	Medicine	(Natrajan et al., 2015)
Lemongrass	<i>Cymbopogon citratus</i> DC.	Chitosan	58	/	/	Antimicrobial	Food	(Sameen et al., 2020)
		Alginate+Chitosan	<300	/	86.9	Anticancer	Medicine	(Natrajan et al., 2015)
Jasmine	<i>Jasminum polyanthum</i> L.	Gelatin+Gum arabic		/	/	Flavor agent	Food; Textile	(Lv et al., 2014)
Holy basil	<i>Ocimum tenuiflorum</i> L.	Gelatin	392.30 .10 ³	/	95.41	Antioxidant	Medicine	(Sutaphanit and Chitprasert, 2014)
Pimenta	<i>Pimenta dioica</i> L.	Chitosan + k-carrageenan	/	/	/	Antioxidant, antifungal	Food	(Dima et al., 2014)
Eugenol	/	Chitosan	80–100	+16.2 to +33.5	1.1–20.2	Antioxidant	Food	(Woranuch and Yoksan, 2013)
Oregano	<i>Origanum vulgare</i> L.	Chitosan	40 - 80	/	/	Antioxidant, antimicrobial	/	(Hosseini et al., 2013)
Poppy seed	<i>Papaver somniferum</i> L.	Gelatin+arabic gum	<5000	/	76.8	Anti-cancer, anti-tumor, anti-diabetic	Medicine	(X. Yang et al., 2015)
Vanilla	<i>Vanilla planifolia</i> L.	Chitosan+arabic gum	7500	/	94.2	Flavor agent	Food	(Yang et al., 2014)
Olive	<i>Olea europaea</i> L.	Gelatin + Sodium alginate	/	/	/	Source of vitamins and fatty acids	Medicine	(Devi et al., 2012)
Peppermint	<i>Mentha piperita</i> L.	Gelatin+Arabic gum	/	/	/	/	/	(Dong et al., 2011)
Spray drying method								
Carvacrol	/	Pectin+sodium alginate	2580-5300	/	/	Antioxidant, antimicrobial	/	(Sun et al., 2020)
Black seed	<i>Nigella sativa</i> L.	Sodium caseinate + maltodextrin DE10	18500	/	95.4	Antioxidant	Medicine	(Mohammed et al., 2017)
Eucalyptus	<i>Eucalyptus staigeriana</i> L.	Cashew gum	27.7-432.6	+24.5 to +10.4	24.89 - 26.80	Antimicrobial	Food	(Herculano et al., 2015)
<i>Lippia sidoides</i>	<i>Lippia sidoides</i> L.	Alginate:cashew gum	223- 399	-30 to -36	50	Larvicide	Agriculture	(De-Oliveira et al., 2014)
		Chitosan+cashew gum	335–558	/	70	Larvicide	Agriculture	(Abreu et al., 2012)
		Chitosan	25	-17.3	77.8	Larvicide	Agriculture	(Paula et al., 2010)

Oregano	<i>Origanum vulgare</i> L.	Inulin	3000 - 4500	/	/	Antioxidant	Food	(Beirão da costa et al., 2013)
		Rice starch	3000 – 4500	/	/	Antioxidant, antimicrobial	Food	(Beirão da costa et al., 2012)
		Gelatine/sucrose	3000 – 4500	/	/	Antioxidant, antimicrobial	Food	(Beirão da costa et al., 2012)
Soybean	<i>Glycine max</i> L.	Kafirin + sodium caseinate	10450	/	/	Source of PUFA	Food	(X. Bai et al., 2019)
Almond	<i>Prunus dulcis</i> L.	Taro starch	1600–31.1.10 ³	/	37.5	Prevention of colon cancer and cardiovascular diseases	Medicine	(Hoyos-leyva et al., 2019)
Peony	<i>Paeonia lactiflora</i> L.	Whey protein+Corn syrup + Lecithin	/	/	93.6	Source of PUFA	Food	(Wang et al., 2018)
Refined kenaf seed	<i>Hibiscus cannabinus</i> L.	β-cyclodextrin + gum arabic + sodium caseinate	/	/	/	Source of MUFA and PUFA	/	(Chew et al., 2020)
		β-cyclodextrin + Arabic gum	(25.4–37.3). 10 ³	/	90.0-95.3	Source of MUFA and PUFA	/	(Chew et al., 2018)
		β-cyclodextrin +sodium caseinate						
		β-cyclodextrin + gum arabic + sodium caseinate						
Chia seed	<i>Salvia hispanica</i> L.	Sodium caseinate + maltodextrin + chia protein rich fraction + chia mucilage	/	/	53.4- 96.2	Source of omega 3	Food	(Us-medina et al., 2018)
		Maltodextrin + soy protein	4000-10000	/	≈ 60	Source of omega 3	Food	(González et al., 2016)
Walnut	<i>Juglans cinerea</i> L.	Skim milk powder + Tween 80	/	/	/	Source of PUFA, tocopherols and phytosterols.	Food; Medicine	(Shamaei et al., 2017)
Sunflower	<i>Helianthus annuus</i> L.	Maltodextrin + HPMC	/	/	79.43	Source of PUFA	/	(Roccia et al., 2014)
Linseed	<i>Linum usitatissimum</i> L.	Alginate+ whey protein	/	-44	84	Source of omega 3	Food	(Fioramonti et al., 2019)
		Maltodextrin +	600 -26000		62.3-95.7	Source of omega 3	Food	(Carneiro et al., 2013)

		Gum arabic					
		Gum arabic	/	/	≈ 90	Source of omega 3	Food (Gallardo et al., 2013)
		Gum arabic + Maltodextrin + whey protein	/	/	≈ 90	Source of omega 3	Food (Gallardo et al., 2013)
		Maltodextrin + methylcellulose	/	/	≈ 90	Source of omega 3	Food (Gallardo et al., 2013)
		Gum arabic	/	/	54.9 - 90.7	Source of omega 3	Food (Rubilar et al., 2012)
		Gum arabic + Maltodextrin	/	/	54.9 – 90.7	Source of omega 3	Food (Rubilar et al., 2012)
<i>Macadamia integrifolia</i>		Sodium caseinate + maltodextrin	9750	/	88.75	Source of MUFA	Medicine (Laohasongkram et al., 2011)
Coffee	<i>Coffea arabica</i> L.	Arabic gum	4000-11.10 ³	/	10-30	Antioxidant	Cosmetic (Nosari et al., 2015)
		Arabic gum	7880-13.10 ³	/	48-88	Flavoring agent	Food (Frascareli et al., 2011)

659 PLGA: Polylactic glycolic acid; PCL: Polycaprolactone; PLA: Poly lactic acid; PHB: Poly(3-hydroxybutyrate); PEO: poly (ethylene oxide); TAD: 1,2,4-Triazoline-3,5-dione; PHBV: Poly(3-hydroxybutyrate-co-3-hydroxyvalerate);

660 HPC: Hydroxypropylcellulose; HPMC: Hydroxypropylmethylcellulose; PVA: Poly vinyl alcohol; PUFA: Poly unsaturated fatty acids; MUFA: Mono unsaturated fatty acids.

661

5.2. Encapsulation in lipid based nanocarriers

5.2.1. Liposomes

Liposomes were first developed for drug delivery purposes by Bangham et al. in 1965 (1965). Liposomes are vesicles formed by one or more lipid bilayers defining one or several aqueous compartments. They can be classified depending on their size and lamellarity to: i) small unilamellar vesicles (SUV) with a size between 20nm and 100 nm, ii) large unilamellar vesicles (LUV) with a size greater than 100 nm and iii) multilamellar vesicles (MLV) with a size greater than 0.5µm, as demonstrated in **Fig. 6** (El-Asbahani et al., 2015). Generally, the liposome bilayer consists of natural and/or synthetic phospholipids like phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine, phosphatidylglycerol and phosphatidylinositol. Cholesterol may also be incorporated to the lipidic bilayer to reduce the permeability of water-soluble molecules through the membrane and improve its fluidity, and stability (Laouini et al., 2012). Due to the lipophilic character of the liposome bilayer, plant oils like essential or vegetable oils are highly entrapped to enhance their bioavailability and hurdle their physicochemical instability upon exposure to light, oxygen and temperature (El-Asbahani et al., 2015). Several methods have been used to develop liposomes containing plants oils, while the thin film hydration, solvent injection and heating methods were widely used in the last decade.

Fig. 6. Schematic illustration of the techniques used to produce liposomes.

5.2.1.1. Thin lipid film hydration

Thin lipid film hydration or thin membrane hydration is the first process which was initially used for liposomes production (Bangham et al., 1965). A mixture of lipid ingredients was dispersed in organic solvent in a round-bottom flask. Subsequent evaporation of the organic solvent was performed using a rotary evaporator at reduced pressure. Finally, the hydration of the formed lipid film by water or buffer solution under agitation at temperature above the lipid transition temperature allows the formation of MLVs dispersion (**Fig.6.a**) (Laouini et al., 2012). Liposome size reduction techniques, such as sonication or extrusion were applied to ensure size reduction and particles uniformity (Patil and Jadhav, 2014). Thin hydration method was extensively used to develop plant oils-loaded liposomes, as illustrated in **Table 2**.

Regarding the size of liposomes prepared by this method, several work studies reported a small average diameter with a spherical shape. Cui et al. (2015) revealed that clove EO loaded-liposomes had small size of 149.2 nm, a high zeta potential (-24.5 mV) with an entrapment efficiency of 20.41%, for 5.0 mg/mL clove oil concentration. Accordingly, Cui et al. (2016) used the same method to limit the volatility of salvia EO by encapsulation in soy lecithin/cholesterol based liposomes. Atomic force microscopy images showed that the obtained liposomes were spherical in shape, uniformly dispersed without any aggregation with an average size ranging from 100 to 700 nm. Furthermore, bergamot EO and its fraction (bergapten) were entrapped in phospholipids based-liposomes using thin lipid hydration process (Celia et al., 2013). The prepared liposomes had an average size of 188.25 and 185.14 nm, a zeta potential of -2.95 and -2.57 mV and a high EE% of 75.0 and 77.0% for bergamot EO and its fraction, respectively (Celia et al., 2013).

Several authors have compared the size of empty liposomes to EO-loaded liposomes prepared by thin hydration method. Ge and his coworker (2016) revealed a significant difference in the average size between empty- and *Melaleuca alternifolia* EO loaded-liposomes. Empty liposomes had an average size of 142 nm, while loaded liposomes were smaller with size around 75 nm. Similar results were found by Yoshida et al. (Yoshida et al., 2010). Risaliti et al. (2019) attributed this to the high cohesion package of oil components to the bilayer constituents. On the other hand, Detoni et al. (2012) reported no difference in liposomes size between empty and *Zanthoxylum tingoassuiba* EO-loading MLVs and SUVs, respectively. Moreover, nerolidol- and cyclodextrin/nerolidol-loaded liposomes prepared by thin lipid hydration method showed larger mean particle size than blank liposomes (Azzi et al., 2018). Cui et al. studying the encapsulation of curry EO in liposomes, revealed that the oil concentration had a positive effect on vesicles size (Cui et al., 2017a). For instance, the vesicles size was increased from 103.86 to 257.36 nm as a consequence of an increase in the oil

concentration from 2.0 to 6.0 mg/ml. Similar behavior was pointed for the encapsulation of cinnamon EO in soy lecithin/cholesterol based liposomes prepared by thin hydration method (Cui et al., 2016a). Accompanying the increase of cinnamon oil concentration from 3.0 to 6.0 mg/mL, the vesicles size was progressively increased from 133 to 157 nm. Similar results were also reported when increasing cardamom EO (Nahr et al., 2019), thyme EO (Cui et al., 2017b) and chrysanthemum EO (Lin et al., 2019b).

The liposome size was not only affected by the EO concentration. In fact, Nazari et al., (2019) developing garlic EO nanophytosomes by thin hydration method, investigated the effect of the preparation method. For instance, nanophytosomes were a novel lipid based vesicular delivery systems where stable hydrogen bonds are formed between the phosphatidylcholine molecules and nutraceuticals leading to the formation of stable complex (Ghanbarzadeh et al., 2016). In this study, MLVs reduction size was performed using three different types of methods: sonication, homogenization and the combination of sonication and homogenization. Results showed that the combination of two methods produced the smallest liposomes (115 nm) with transparent suspension view. Homogenization produced larger particles than probe sonication method and the average size was around 161 and 135 nm, respectively. Considering the zeta potential, all the prepared phytosomes had lower values (-12.36 to -3.86 mV) than the expected and reported values for soy bean phosphatidylcholine made nanovesicular systems (around -26 mV). This was linked to the interaction between the positively charged allicin (the main component of garlic EO) and the negatively charged phosphate group of phosphatidylcholine (Nazari et al., 2019). In another work study, Salari and his colleague (2019) developing rosemary EO loaded- L- α -phosphatidylethanolamine dioleoyl : cholesteryl hemisuccinate liposomes found that sonication method produced smaller liposome than filtration method. The average sizes were 142.5 and 437.2 nm, respectively. Results showed also that increasing the

lipid ratio of L- α -phosphatidylethanolamine dioleoyl to cholesteryl hemisuccinate from 3:2 to 7:3 resulted in much larger liposomes with more negative zeta potential.

As there are several types of phospholipids, it is reliable to alter the size, charge and EE%, upon variation of type or addition of new ingredients to the lipid mixture. In this approach, the effect of lipid composition on the EE% of *Anethum graveolens* EO-loaded liposomes was investigated by Ortan et. al (2009). Liposomes with different lipids; fresh egg yolk, dimiristroylphosphatidyl choline, dipalmitoylphosphatidyl choline, dimiristroylphosphatidyl glycerol and dioleoylphosphatidyl choline, were prepared by thin hydration method. Results showed that oil entrapment varied in this way: dimiristroylphosphatidyl glycerol (55.2%) < dimiristroylphosphatidyl choline (58.9%) < dioleoylphosphatidyl choline (77%) < dipalmitoylphosphatidyl choline (97%) < fresh egg yolk (98%). Although dipalmitoylphosphatidyl choline showed good entrapment efficiency, its use was difficult as it required high temperature due to its high transition temperature. The authors related the low values of EE% of dioleoylphosphatidyl choline, dimiristroylphosphatidyl glycerol and dimiristroylphosphatidyl choline to their unsaturation.

In addition to the factors mentioned above, other parameters may affect the physicochemical properties of liposomes prepared by thin hydration process. In this context, Plackett–Burman design was applied in order to investigate the effect of the mass ratio of phosphatidylcholine and cholesterol, tree tea EO concentration, tween 80 concentration, hydration medium pH, temperature, sonication time and power on physicochemical properties of tree tea EO-loaded liposomes (Ge & Ge, 2015). Results revealed that only three factors (the ratio of phosphatidylcholine and cholesterol, EO concentration and tween 80) exhibited a significant impact on the entrapment efficiency of tree tea EO. Increasing the lipid ratio with EO amount and decreasing tween 80 had a positive effect on EO encapsulation efficiency. Good EE% (97.18%) was obtained with the following parameters: the mass ratio of fresh egg yolk

and cholesterol (5:51); EO concentration (1.21%); tween 80 concentration (0.79%); pH 7.4; temperature (55 °C); sonication time (15 min) and sonication power (300w) (Ge & Ge, 2015).

Regarding the stability of EO loaded in liposomes, Liolios et al. (2009) investigated the oxidative stability of carvacrol and thymol isolated from *Origanum dictamnus* L. EO and their mixtures, before and after their encapsulation in egg L- α phosphatidylcholine/cholesterol-based liposomes by differential scanning calorimetry analysis. Results showed the appearance of exothermic peaks related to the auto-oxidation process of the samples. The onset temperatures at which the auto-oxidation process starts were in the following order: Carvacrol (258°C)<Thymol (273°C)<Carvacrol : Thymol (302°C) <Empty liposomes (362°C) <Liposomes +Carvacrol : Thymol (392°C). One can conclude that carvacrol and thymol presented better antioxidant action when encapsulated than when in pure form. The antioxidant activity of empty liposomes is lower than that of oil loaded- liposome, suggesting that the liposome membranes were stabilized by the link of the lipophilic compounds with lipid bilayers (Liolios et al., 2009).

Beyond EO, liposomes can potentially enable the encapsulation of VO and their derivatives, as illustrated in **Table 3**. Recently, numerous studies have been investigated to encapsulate fatty acids in liposomes. Among the several polyunsaturated fatty acids (PUFAs), dietary ω 3 like eicosapentaenoic and docosahexaenoic acids have been extensively investigated for their beneficial effects (Hadian, 2016). Alaarg et al. (2016) developed docosahexaenoic acid- loaded liposomes by thin hydration method. The obtained liposomes exhibited small average diameter around 100 nm, narrow size distributions, negative zeta potential (15.7 ± 2.5 mv) and high EE% of 81.35 %. Moreover, eicosapentaenoic and docosahexaenoic acids were entrapped in nanoliposomes (i.e. nanoscale lipid vesicles) developed by thin hydration followed by either extrusion ultrasonic irradiation; bath sonication; probe sonication; or combined probe and bath sonication (Hadian et al., 2014). Results showed that probe sonication

produced liposomes with higher EE% for both investigated fatty acids. Results displayed also that EE% differs from a VO to another for liposomes prepared in the same experimental conditions. Indeed, the EE% value was higher for docosahexaenoic acid than for eicosapentaenoic acid. This was ascribed to the fact that docosahexaenoic acid may change the physical properties of 1, 2-dipalmitoyl-sn-glycero-3-phosphocholine bilayer, as it would provide a tightly packed conformation because of the coiled configuration (Hadian et al., 2014).

In overall, thin hydration method is widely employed to develop plant oils loaded liposomes due to its simplicity. Several phospholipids are used in the literature including soybean phosphatidylcholine (Ge & Ge, 2016; Ge & Ge, 2015; Khatibi et al., 2017; Nazari et al., 2019; Rasti et al., 2012; Q. Wang et al., 2015), dipalmitoyl phosphatidylcholine (Detoni et al., 2012), egg phosphatidylcholine (Saffari et al., 2016), phospholipon®90G (Risaliti et al., 2019). Cholesterol is the most used fluidifying agent (Alikhani-Koupaei, 2015; H. Cui, Yuan, et al., 2017; Y. Cui et al., 2010; Y. Ge & Ge, 2016; Ge & Ge, 2015; Khatibi et al., 2017; Lin et al., 2018; Lin, Chen, et al., 2019; Q. Wang et al., 2015); in other cases, tween 80 (Y. Ge et al., 2019; Y. Ge & Ge, 2016; Ge & Ge, 2015; Lin, Chen, et al., 2019) and poly vinyl pyrrolidone (Cui et al., 2017a, 2017b, 2016a, 2016b, 2015; Lin et al., 2019b, 2018) were incorporated as surfactants.

Using this method, heterogeneous vesicles of large sizes may be produced which requires additional steps like sonication and extrusion to reduce and homogenize the vesicle size and thus, the process consumes more time. Besides, thin hydration method is difficult to scale up and requires organic solvents which in turn represent the major drawback. In fact, their residues may remain in the final liposome preparation resulting in potential toxicity and reduced stability of the lipid vesicles (Cortesi et al., 1999; Vemuri and Rhodes, 1995).

5.2.1.2 Solvent injection

The solvent injection method, firstly described in 1973 (Batzri and Korn, 1973), implies the dissolution of the lipid into an organic phase such as ethanol or ether, followed by the injection of the lipid solution into aqueous solution resulting in liposomes dispersion (Laouini et al., 2012). After that, the organic solvent was evaporated under reduced pressure (**Fig. 6.b**). This technique is widely used for plant oil encapsulation, as demonstrated in **Table 2**. The solvent injection' main feature is that narrow size distribution of submicron liposomes (under 100 nm) could be produced without extrusion or sonication (Stano et al., 2004). Moreover, compared with thin hydration method, the ethanol injection technique was found to be scalable. In fact, clove EO-liposomes were successfully scaled-up using a membrane contactor (600ml) and a pilot plant (3L) (Sebaaly et al., 2015a). Furthermore, various eugenol- and clove EO-liposomes were prepared at laboratory (ethanol injection) and large scale (membrane contactor): free hydroxypropyl- β -cyclodextrin loaded liposomes; drug in hydroxypropyl- β -cyclodextrin in liposomes (DCL) and DCL₂ obtained by double loading technique, where the drug is added in the organic phase and the inclusion complex in the aqueous phase (Sebaaly et al., 2016a). Results showed that eugenol and clove EO loaded DCL and DCL₂ developed at large scale had a mean size similar to those obtained by laboratory scale. Besides, Eugenol and clove EO loaded DCL and DCL₂ had a mean particle size significantly smaller than that of free hydroxypropyl- β -cyclodextrin liposomes containing either eugenol or clove EO at both laboratory and large scales. This was explained by the complete incorporation of the aromatic cycle of eugenol inside the hydrophobic cavity of hydroxypropyl- β -cyclodextrin, resulting in limit interaction between eugenol and lipidic bilayers. Regarding the polydispersity index and zeta potential, no difference was assessed between all the tested liposomes.

Currently, several studies have been reported to investigate the effect of liposome composition and operating conditions on physicochemical properties of liposomes prepared by ethanol injection method (Hammoud et al., 2019; Rushmi et al., 2017; Sebaaly et al., 2016b).

840 The effect of oil concentration, injection rate, stirring speed on the average diameter of black
841 seed oil-liposomes was studied (Rushmi et al., 2017). Results showed that liposomes decrease
842 in size from 520.70 to 51.48 nm after oil incorporation. As the concentration of oil increases
843 from 0.17 to 0.67% v/v, liposomes size reduced significantly due to the antioxidant activity of
844 the oil which could decrease phospholipid bilayer oxidation, preventing liposomes growth;
845 while, no change in average size of liposomes was noticed upon further increase in oil (0.67%
846 v/v). Thus, the oil concentration of 0.67% v/v was found to be optimum for its antioxidant
847 activity. Results showed also that small sized liposomes were formed under 1mL/min injection
848 rate and 2200 rpm stirring speed. Low injection rates result in faster lipids oxidation while high
849 rates may cause a variable distribution of particle size. Similar results were already reported
850 (Sebaaly et al., 2016b). In regards of the phospholipid:cholesterol ratio effect, the EE% was
851 improved from 39.8 to 49.9 % after increasing the ratio of egg extract to cholesterol from 3:1
852 to 3:2 (Rushmi et al., 2017). This was related to the fact that cholesterol may reduce the
853 flexibility and mobility of lipidic layer which in turn lead to enhance liposomes stability.
854 Moreover, another study performed by Hammoud et al. (2019) spotlighted that the type of
855 encapsulated EO affects significantly the phospholipid and cholesterol incorporation rates into
856 the lipid layer. Lower phospholipids incorporation rates were observed when encapsulating
857 isoeugenol, pulegone or thymol. While, high cholesterol incorporation rates were measured in
858 presence of estragole or terpineole. Additionally, the oil entrapment efficiency was found to be
859 affected by the chemical structure of encapsulated EO. In fact, EO bearing hydroxyl groups in
860 their structure are more greatly to fluidize the lipid layer than those without a hydroxyl group
861 leading to higher EE%. The authors concluded that EO bearing hydroxyl groups had low
862 aqueous solubility with low Henry constant value and higher liposomal EE% (Hammoud et al.,
863 2019).

Regarding the stability of liposomes prepared by ethanol injection process, Liu et al. (2016) investigated the stability of galanga EO-loaded liposomes at low temperature (4°C) and dark conditions and results revealed minor change in mean particle size and polydispersity index. Furthermore, the photostability of eugenol in aqueous solution and in liposome formulations (Phospholipon 80H, Phospholipon 90H and Lipoid S100) was investigated under UV light irradiation for 96hours (Sebaaly et al., 2015b). Results revealed that liposomes formulations protect eugenol more than aqueous solutions. The percentages of remaining eugenol were 58, 82, 91 and 95% for aqueous solution, Phospholipon 80H-, 90H- and S100-liposomes, respectively. The highest value of remaining eugenol for lipoid S100 was related to the flexibility of the membrane resulting in a deep insertion of eugenol into the lipid bilayer leading to better protection from any UV light effect (Sebaaly et al., 2015b).

Despite using ethanol injection for EO encapsulation in liposomes, a few reports have been published during the last decade regarding the encapsulation of VO. Recently, Huang et al. (2020) developed co-loaded linseed oil with quercetin in liposomes with the aim of enhancing their solubility and stability. The produced liposomes owned a spherical shape with a small average size (262.2 nm). In 2019, Bai and his coworkers investigated the effect of different coix seed oil: β -carotene ratios on the physiochemical properties, stability and antioxidant activity of coix seed oil : β -carotene co-loaded-liposomes (C. Bai et al., 2019). Results showed that by increasing coix seed oil, the EE% of β -carotene in the liposomes decreased. The values of EE% for 1:1, 1:5, and 1:10, β -carotene:coix seed oil liposomes were 83.8, 81.3, and 80.8 %, respectively, which were slightly lower than that of liposomes containing β -carotene alone (86.0%). This was ascribed to the ability of coix seed oil to compete for the available hydrophobic domains within the phospholipid bilayers.

To sum up, ethanol injection method is widely employed for plant oils encapsulation as it is simple, easy to scalable and it does not require any additional process for vesicle size

reduction. According to the previous work studies, phospholipon[®]90H (Sebaaly et al., 2016a, 2016b), phospholipon[®]80H (Sebaaly et al., 2016b), lipoid[®] S100 (Hammoud et al., 2019; Sebaaly et al., 2016b) and egg phospholipids (C. Bai et al., 2019; Rushmi et al., 2017) are widely used as bilayer forming lipids. Ethanol injection method suffers from several drawbacks including continuous exposure of plant oils to high temperature and organic solvents which may affect both the safety and stability of the liposomes (Nkanga et al., 2019).

5.2.1.3. Heating method

The heating method, called also Mozafari method, was first developed in 2005. It is known to be the most attractive method for liposomes preparation due to its organic solvent/detergents free characteristics (Mozafari & Mortazavi, 2005). In this technique, lipids are hydrated in the presence of hydrating agent (glycerin or propylene glycol) and heated at 40–120°C (at the temperature which is above the transition temperature of the phospholipids) depending on the properties of the ingredients, the presence or absence of cholesterol, and the type of material to be entrapped (**Fig.6.c**) (Mozafari et al., 2008).

Currently, Mozafari method is widely used to encapsulate VO and polyunsaturated fatty acids (**Table 2**). When compared to thin hydration process, Mozafari method produce liposomes with higher stability. Rsati et al. (2012) investigated the difference between the oxidative stability of liposomes (before sonication) and nanoliposomes (after sonication) produced by Mozafari and conventional thin hydration techniques. For both methods, polyunsaturated fatty acids entrapment efficiency values of nanoliposomes were higher than those of liposomes. Authors related this result to the fact that size reduction increases the surface area of the liposomes resulting in increasing the contact and bond between the fatty acids and phospholipids in the bilayers. Moreover, liposomes prepared by Mozafari process showed higher physical stability than those prepared by conventional method (Rasti et al., 2012). In

another work study, the effect of formulation strategies on phytosterol, extracted from canola oil, loaded-liposomes was investigated (Poudel et al., 2019). The results showed that Mozafari method produce liposomes with high average size (260 nm) as compared to those obtained by thin film hydration homogenization (186 nm) and thin film hydration ultrasonication (196 nm). This result was attributed to the high shear force and cavitation involved in size reduction during the ultrasonication and homogenization process; while in Mozafari method, less intense magnetic stirring will probably yield to larger particles. In term of polydispersity index and zeta potential, no difference was found for all the formulations (Poudel et al., 2019).

Like the methods discussed above, Mozafari method was affected by several operating conditions. In 2013, Rasti et al. investigated the effect of shear rate, mixing and sonication times on colloidal properties of polyunsaturated fatty acids (docosahexaenoic acid and eicosapentaenoic acid) nanoliposomes (Rasti et al., 2013). In their study, response surface methodology was applied to predict the optimum levels of liposome preparation condition producing maximum EE% and minimum average size. According to ANOVA analysis, all the independent variables and their interactions were found significant; while, the main significant effect on liposome size and EE% was found to be the shear rate. After optimizing the operating parameters; shear rate (795 rpm), mixing time (60 min) and sonication time (10 min), the nanoliposome exhibited an average diameter of 81.4nm with an EE% of 100% (Rasti et al., 2013).

Besides using heating method to encapsulate VO in liposomes, no report was found regarding the encapsulation of EO maybe due to their high sensitivity and volatility upon exposure at high temperature. Thus, this technique is not suitable for thermosensitive bioactive agents. In closing, Mozafari method showed to be a fast, simple, scalable, and non-toxic technique for liposome preparation with high EE%. In addition, the obtained liposomes can be freely used without any further sterilization treatments as they were prepared under heating

938 conditions which in turn could minimize both formulation timing and complexity (Nkanga et
939 al., 2019).

940 **Table 2.** Preparation methods for plant oils encapsulation in liposomes with their fine applications.

Encapsulated oil	Plant (origin)	Phospholipid used	Physicochemical properties			Biological properties	Application	Ref.
			Size (nm)	Z.pot (mV)	EE (%)			
<i>Thin hydration method</i>								
Myristica	<i>Myristica fragrans</i> Houtt.	Soybean phospholipid	/	/	/	Antimicrobial, antioxidant	Food	(Zhu et al., 2020)
<i>Ferula gummosa</i> Boiss.	<i>Ferula gummosa</i> Boiss.	Phospholipid	74.3 -99.9	/	/	Antibacterial		(Najafi et al., 2020)
Laurel	<i>Laurelia sempervirens</i> Tul.	L- α -PCH	200	/	/	Antibacterial, antioxidant	Food	(Wu et al., 2020)
Cardamon	<i>Elettaria cardamomum</i> L.	Phospholipid	71.8–147.9	-17.4 to -10.7	< 60	Antimicrobial, antioxidant	Food	(Nahr et al., 2019)
Chrysanthemum	<i>Chrysanthemum pacificum</i> L.	Soybean phospholipid	132.4	-37.6	42.7	Antibacterial	Food	(Lin et al., 2019b)
Sage	<i>Salvia triloba</i> L.	Phospholipon 90G	≈200	-20 to -35	57	Antioxidant, antibacterial	Medicine	(Risaliti et al., 2019)
		Soybean phospholipid	188.5	-48.38	46.5	Anti-inflammatory	Food	(Cui et al., 2016b)
Rosemary	<i>Rosmarinus officinalis</i> L.	L- α -PEA dioleoyl	79	-2.77	45	Anticancer	Medicine	(Salari and Salari, 2019)
		Phospholipon 90G	≈200	-20 to -35	65	Antioxidant; antibacterial	Medicine	(Risaliti et al., 2019)
		PCH	/	/	/	Preservative	Food	(Alikhani-Koupaei, 2015)
Garlic	<i>Allium sativum</i> L.	Soybean PCH	115	-12.36	86.00	Antibacterial, antioxidant	Food	(Nazari et al., 2019)
Tea tree	<i>Melaleuca alternifolia</i> Cheel.	Soybean PCH	50-100	/	98.49	Antimicrobial	/	(Ge et al., 2019)
		Soybean PCH	58	/	97.18	Antimicrobial	/	(Ge & Ge, 2015)
Ajwain	<i>Trachyspermum copticum</i> L.	Soybean PCH	75	-7.45	96.08	Antimicrobial	/	(Ge and Ge, 2016)
		Soybean PCH	170.8	/	85.9	Antimicrobial	Cosmetics	(Tabatabai et al., 2018)
Thyme	<i>Thymus vulgaris</i> L.	Soybean phospholipid	182.60	-40.90	35.35	Antibacterial	Food	(Lin et al., 2018)
		Soybean phospholipid	208.1	-52.2	38.16	Antibacterial	Food	(Cui et al., 2017b)
Eucalyptus	<i>Eucalyptus globulus</i> L’Hér.	Soybean phospholipid	/	/	97.35	Antimicrobial	Medicine	(Tang and Ge, 2017)
	<i>Eucalyptus citriodora</i> L.	Soybean phospholipid	266.56	-33.73	22.47	Antimicrobial	/	(Lin et al., 2019a)

Cineole	/	Egg yolk PCH	128	6.8	67.7	Permeation enhancers	Medicine	(Saffari et al., 2016)
Thymol	+	Soybean PCH	270.20	+39.99	/	Antibacterial	Food	(Engel et al., 2017)
Carvacrol		L- α -PCH	/	/	/	Antimicrobial	Food	(Liolios et al., 2009)
<i>Zataria multiflora</i>	<i>Zataria multiflora</i> Boiss.	Soybean PCH	99.9	/	18.4	Antimicrobial	Food	(Khatibi et al., 2017)
							Cosmetics	
							Medicine	
Curry	<i>Helichrysum italicum</i> G.	Soybean phospholipid	196.6	-31.1	56.3	Antibacterial	Food	(Cui et al., 2017a)
Limonene	/	Egg yolk PCH	102	6.1	71.0	Permeation enhancers	Medicine	(Saffari et al., 2016)
Cinnamon	<i>Cinnamomum cassia</i> persl.	Soybean phospholipid	144.3	-54.7	29.2	Antibacterial	Medicine	(Cui et al., 2016a)
Clove	<i>Syzygium aromaticum</i> L.	Soybean phospholipid	149	-24.5	20.4	Antibacterial	Food	(Cui et al., 2015)
<i>Bergamot</i>	<i>Monarda didyma</i> L.	Phospholipid	185.1	-2.95	75.0	Anticancer	Medicine	(Celia et al., 2013)
Bergapten	/	Phospholipid	185.1	-2.95	75.0	Anticancer	Medicine	(Celia et al., 2013)
Macassar kernels	<i>Brucea javanica</i> L.	Phospholipid	108.2	-57.0	92.4	Anticancer	Medicine	(Cui et al., 2010)
Dill	<i>Anethum graveolens</i> L.	PCH	/	/	98	Antimicrobial	/	(Ortan et al., 2009)
<i>Zanthoxylum tingoassuiba</i>	<i>Zanthoxylum tingoassuiba</i> L.	1,2-Dipalmitoyl PCH	210-3630	/	68.5-79.2	Anticancer	Medicine	(Detoni et al., 2012)
Sterol	/	PCH	< 200	-9 to -14	>89	Antioxidant	Food	(Poudel et al., 2019)
DHA	/	1,2-Dipalmitoyl PCH	99	-15.7	81.4	Anticancer; anti-inflammatory	Medicine	(Alaarg et al., 2016)
		PCH	/	/	38.6	Anticancer; anti-inflammatory	Medicine	(Hadian et al., 2014)
EPA	/	1,2-Dipalmitoyl PCH	/	/	56.9	Anticancer; anti-inflammatory	Medicine	(Hadian et al., 2014)
EPA+DHA	/	Soybean phospholipid	<100	-48.4	/	Anticancer; anti-inflammatory	Medicine	(Rasti et al., 2012)

Solvent injection method

Anethole	/	Lipoid S100	/	/	/	Antibacterial	/	(Auezova et al., 2020)
Cinnamaldehyde	/	Egg yolk phospholipid	1000-2500	/	/	Antimicrobial	/	(Wang et al., 2019)
Isoeugenol	/	Lipoid S100	/	/	96.4	/	/	(Hammoud et al., 2019)
Pulegone	/	Lipoid S100	/	/	90.5	/	/	(Hammoud et al., 2019)
Terpineol	/	Lipoid S100	/	/	73.7	/	/	(Hammoud et al., 2019)
Thymol	/	Lipoid S100	/	/	79.1	/	/	(Hammoud et al., 2019)
Estragole	/	Lipoid S100	/	/	90.9	/	/	(Hammoud et al., 2019)
Eucalyptol	/	Lipoid S100	/	/	61.9	/	/	(Hammoud et al., 2019)
Black seed	<i>Nigella sativa</i> L.	Egg yolk PCH	50–900	/	34–87	Analgesic	Medicine	(Rushmi et al., 2017)

Garlic	<i>Allium sativum</i> L.	Phospholipid	131.7	/	64.3	Antimicrobial	Food	(Zabihi et al., 2017)
Galangal	<i>Alpinia officinarum</i> L.	Phospholipid	61.9	-16	/	Antimicrobial; antioxidant	Medicine	(Liu et al., 2016)
		Phospholipid	125.6	- 35.5	35.6	Antimicrobial; antioxidant	Medicine	(Cao et al., 2016)
Clove	<i>Syzygium aromaticum</i> L.	Phospholipon 90H	/	/	54.2 - 59.7	Anti-inflammatory	Medicine	(Sebaaly et al., 2016a)
		Phospholipid	/	/	/	Anti-inflammatory	Medicine	(Sebaaly et al., 2015b)
Eugenol	/	Lipoid S100	74.6	/	24.2	Anti-cancer	Medicine	(Mishra et al., 2019)
		Phospholipon 90H	/	/	63.1 - 63.5	Anti-inflammatory	Medicine	(Sebaaly et al., 2016a)
		Phospholipid S75	58.6	/	59.2	Antibacterial	Food	(Peng et al., 2015)
		Phospholipid	/	/	/	Anti-inflammatory	Medicine	(Sebaaly et al., 2015b)
Linseed oil + quercetin	<i>Linum usitatissimum</i> L.	Soybean phospholipid	262.2	/	/	Source of PUFA	Food	(Huang et al., 2020)
Coix seed oil + B-carotene	<i>Coix lacryma-jobi</i> L.	Egg yolk PCH	156.7- 193.1	-47.8 to -32.4	80.8 – 83.8	Anticancer	Medicine	(C. Bai et al., 2019)
Linoleic acid	/	Soybean PCH	266	/	83.3	/	Food	(Vélez et al., 2019)
Heating method								
Sterol	/	Soybean phospholipid	> 200	-9 to -14	>89	Antioxidant	Food	(Poudel et al., 2019)
EPA + DHA	/	Soybean phospholipid	<200	-48.3	/	/	/	(Rasti et al., 2012)

941 EPA: Eicosapentaenoic acid; DHA: Docosahexaenoic acid; PUFA: Polyunsaturated fatty acids; PCH: phosphatidylcholine; PEA: phosphatidylethanolamine.

942

5.2.2. Solid lipid nanoparticles and nanostructured lipid carriers

Solid lipid nanoparticles (SLN) are other lipid-based carriers that have emerged as they combine the benefits of liposomes and polymeric nanoparticles (Sarangi and Padhi, 2016). Solid lipid nanoparticles, developed since 1990, are suspensions of nanosized solid lipid particles dispersed in an aqueous media (Patel, 2013). They are composed of surfactants and a lipid matrix that acquires a solid-state lipid at ambient temperature (Bayón-Cordero et al., 2019). The commonly used materials to structure the lipid core are fatty acids (stearic acid, palmitic acid, decanoic acid and benzoic acid), triacylglycerols (trimyristin, trilaurin, tristearin and tripalmitin) and acyl glycerols (glycerol monostearate, glycerol palmitostearate and glycerol benzoate). These lipids are characterized by their purity, low price, safety and biodegradability. In the other hand, phospholipids (phosphatidylcholine, soy and egg lecithins), poloxamer, pluronic[®]F127, bile salts, tween 80 and polyvinyl alcohol are example of commonly used surfactants (Kaliyannurthi and Selvaraj, 2016).

In the aim of enhancing the loading capacity of SLN, a second generation of lipid nanoparticles was developed in 1999; so called nanostructured lipid carriers (NLC) in which the matrix is composed not only of a solid lipid, but of a blend of a solid and a liquid lipid oil, as illustrated in **Fig. 7**. These carriers may provide an additional space for the loading of bioactive agents, improving in this way the amount of the active compounds entrapped and minimizing the probability of expulsion from the lipid phase (Patel, 2013).

Considering the delivery of plant oil, the main reason to use SLN or NLC as nanocarriers is the improvement of entrapment efficiency. Since the oils are mostly lipophilic, they present a good miscibility with the lipid matrix, resulting high amount of oil could be entrapped (Falcao et al., 2015). In addition, these lipid-based carriers protect the labile and sensitive oil components from chemical, photochemical or oxidative degradation, due to the immobilization by solid lipids. Different methods are employed to produce SLN, however, high pressure

homogenization and high-speed homogenization (ultrasonication) are commonly used due to their simplicity and facility of scaling up.

Fig. 7. Schematic illustration of solid lipid nanoparticles and nanostructured lipid carriers' preparation methods.

5.2.2.1. High pressure homogenization

The high-pressure homogenization method was extensively used to encapsulate plant oils in SLN since it produces particles with small size and higher homogeneity. Using a high-pressure homogenizer, liquids were pushed with high pressure (100-2000 bar) through a narrow gap (micron size) creating fluid acceleration over a very short distance at very high viscosity of

over 1000 km/h which in turn result in disrupting the particles down to submicron range (Garud et al., 2012).

Using the high-pressure homogenization to encapsulate plants oils, the lipid is heated at 5 to 10°C above its melting point, and the oil is dissolved within (**Fig.7.a**). After that two approaches are involved: hot or cold homogenization. In hot homogenization, hot aqueous surfactant solution is dispersed with the plant oil-lipid melt under stirring at the same temperature creating the pre-emulsion. The resultant pre-emulsion was pushed through a piston-gap homogenizer creating a hot oil-in-water (O/W) nanoemulsion which is cooled after at room temperature allowing the crystallization of the lipid and the formation of SLN.

Using the cold homogenization approach the oil-lipid melt was cooled down creating solid lipid microparticles that are dispersed after in a cold aqueous surfactant solution forming a pre-suspension. The subsequent homogenization of this pre-suspension creates SLN (**Fig.7.b**). Several studies have been already published investigating the use of high-pressure homogenization process to encapsulate plant oils (see **Table 3**).

Regarding the size of SLN prepared by this technique, numerous research works reported a small average diameter with good stability and high EE%. For example, SLN containing frankincense and myhrr EO in a ratio 1:1 were developed using hot homogenization process by Wang et al. (Wang, 2012). An average mean size of 113.3 nm, a zeta potential of -16.8 mV and an EE% of 80.60% were assessed for the obtained SLN. The same process was used to prepare SLN encapsulating the VO: copaiba oil with and without allantoin which is widely used in cosmetology for its keratolytic, moisturizing, soothing and wound healing properties (Svetlichny et al., 2015). The dynamic light scattering analysis revealed an average particle size of 126.06 nm and 118.63 nm for the copaiba oil-loaded SLN and copaiba oil: allantoin-co-loaded SLN, respectively.

Concerning the stability of SLN, previous works highlighted their efficiency in preserving the quality of encapsulated oil during long-term storage as compared to un-encapsulated-form (Tian et al., 2018; Zielinska et al., 2019). Tian et al. (2018) reported that SLN can enhance the stability of citral in acidic surroundings. Gas-chromatography analysis showed that after 12 days storage, 67% of citral remained in the citral loaded-SLN formulations, while only 8% remained in the control. In addition, the overall flavour of the degradation products generated from citral-SLN were assessed and results demonstrated that the off-flavours had little effect on the whole flavour of citral-SLN in the system sample as compared with the control (Tian et al., 2018).

Several factors such as the kind of lipid, surfactant and the operating process conditions could influence the physicochemical properties of the particles obtained by high-pressure homogenization. In this context, Mai et al. (2018) investigated the influence of homogenization conditions on gac fruit EO-loaded SLN prepared by hot and cold homogenization. Results showed that increasing hot homogenization speed from 5000 to 10000 rpm was accompanied with a decrease in particle size from 3297 to 201 nm. However, further increase in speed leads to increase the particle size due to the fact that the oil particles are more likely to collide and aggregate with others. Concerning hot homogenization time, short time was found not enough for active ingredient encapsulation while more homogenization time result in small particles which in turn lead to reduce the volume containing active ingredients (Mai et al., 2018).

In another work study, the impact of the surfactant content, the ratio of citral to lipid, and their total content on the physicochemical characteristics of citral-loaded SLN has been explored (Tian et al., 2018). As the surfactant amount increases the EE% decreases due to the fact that the surface of the formed SLN was not large enough to absorb the excess of surfactant which in turn form micelles, resulting a partitioning phenomenon of citral between micelles and SLN; therefore, a decrease in entrapment efficiency was noticed. Results revealed also an

increase in particle size and a decrease in EE% when increasing the content of the mixture citral : glyceryl monostearate, used as lipid matrix, from 1 to 5%. The increase in the content of citral : lipid leads to increase the viscosity of the system which in turn reduce the efficiency of the high-pressure homogenization process to decrease the particle size. Additionally, too much citral and lipid cannot be emulsified when the surfactant content is kept constant this is why the EE% decreased. The same behavior of EE% was observed when increasing the ratio of citral to glycerol monostearate. In fact, the excess of citral cannot be entrapped when the content of the mixture citral : lipid was kept constant (Tian et al., 2018).

In recent years, NLC were introduced to bypass the potential problems associated with the use of SLN. They were widely used for plant oils encapsulation, as depicted in **Table 3**. The main feature of these nanocarriers is to enhance the drug loading and prevent drug expulsion during long term storage (Sailaja et al., 2011) and this was confirmed by several research works. In 2019, using the high-pressure homogenization technique, Miranda and his colleagues developed *Ridolfia segetum* EO loaded-NLC with a small particle size (148.1 nm), a high zeta potential (16.3 mV) with excellent loading capacity (EE%=100%) (Miranda et al., 2019). In another research work, NLC containing sucupira EO produced by hot homogenization process owning an average diameter of 143 nm with an EE% of 99.98% (Vieira et al., 2020).

Another characteristic intended by using either SLN or NLC as plant oils carrier is providing a controlled released pattern. For this context, *in vitro* release profile of sucupira oil from NLC was assessed by means of Franz glass diffusion cells and the recorded release profile was fitted into four mathematical models i.e., zero order, first order, Higuchi and Korsmeyer-Peppas (Vieira et al., 2020). Results showed that the release profile of sucupira oil followed a sustained manner over the course of 8 h. About 17.5% was released within the first hour, while the cumulative amount reached 30% at the end of the 8 h (Vieira et al., 2020). Results showed also that the best model describing the release of sucupira oil from NLC was the first order with

a regression coefficient close to 1. In contrary to SLN, the release profile of plant oils from NLC does not follow Higuchi or Korsmeyers–Peppas model. Indeed, the release was governed by sucupira oil concentration inside the particles rather than the physicochemical properties of the carriers and this was expected as NLC are made of blend of solid and liquid lipids. Higuchi and Korsmeyers–Peppas are typically followed in the case of SLN formulations as these have a higher degree of crystallinity which controls better the release profile.

With respect to vegetable oils, NLC were employed for co-delivery of VO with another bioactive molecule (Badea et al., 2015; Lacatusu et al., 2015; Rahman et al., 2013, 2014; Sidding et al., 2013). The benefit of these nanocarriers is that the VO can complement or even enhance the biological activity of the synthetic drug (Lacatusu et al., 2015). For this context, diethylamino hydroxybenzoyl hexyl benzoate used as UVA filter was co-encapsulated with various vegetable oils and their combinations (pomegranate seed oil, wheat germ oil, blackcurrant seed oil, sesame seed oil, carrot root oil, raspberry seed oil and rice bran oil) in NLC by high pressure homogenization method in order to enhance its antioxidant activity and UV protection performance (Badea et al., 2015). All the prepared NLC owned a mean particle size in the range of 108 to 145 nm with narrow size distribution, high zeta potential ranging from -34.4 to -44.3 mV and an entrapment efficiency between 51 and 70% (Badea et al., 2015). In another work study, in the aim of enhancing the anti-inflammatory properties, olive oil was co entrapped with thymoquinone in NLC and the resultant particles owned an average diameter around 75 nm with negative zeta potential of -31 mV (Sidding et al., 2013). Olive oil was further encapsulated in hydrogenated palm oil-NLC for co-delivery with synthetic drug purpose. The resultant particles had a mean diameter, polydispersity index, zeta potential, specific surface area, and crystallinity index of 61.14 nm, 0.461, -25.4 mV, 49.07 m² and 27.12% respectively (How et al., 2013).

Besides the synthesized drugs, VO may be co-encapsulated with EO in NLC. For instance, Lacatusu et al. (2015) highlighted the possible blend of plant and animal oils – grape seed oil or fish oil with laurel leaf EO in NLC. The mean average diameter of obtained NLC reduces after increase of grape seed oil or fish oil content. This was ascribed to the role of the long fatty chains of these oils which lead to a more confined lipid core.

On the whole the high-pressure homogenization technique is largely employed thanks to its benefits including low cost, good scalability and high stability of particles. While, with respect to the encapsulation of plant oils hot homogenization is more used as compared to the cold homogenization method. Lipids like tristearin (Salminen et al., 2017), n-hexadecyl palmitate (Lacatusu et al., 2015), myritol®318 (caprylic/capric triglyceride) (Lacatusu et al., 2015), compritol®888 ATO (Wang, 2012), glyceryl monolinoleate (Shi et al., 2013; Tian et al., 2018), oleoyl macrogolglycerides (Shi et al., 2013), lipoid®S100 (Sidding et al., 2013), cetyl palmitate (Svetlichny et al., 2015) and glycerol monostearate (Shi et al., 2013) are usually used to structure either SLN or NLC. Soybean lecithin (Salminen et al., 2017; Wang, 2012), tween 80 (Shi et al., 2013; Sidding et al., 2013; Svetlichny et al., 2015; Wang, 2012), tween 20 (Badea et al., 2015; Lacatusu et al., 2015), span 80 (Mai et al., 2018; Tian et al., 2018) poloxamer (Badea et al., 2015) and sodium taurodeoxycholate hydrate (Salminen et al., 2017) are example of used emulsifiers.

The use of high-speed homogenization process is often limited by the need of high energy input and the high temperature which cause oil loss.

5.2.2.2. Ultrasonication / high speed homogenization

Solid lipid nanoparticles may also be prepared by ultrasonication or high-speed homogenization technique. In brief, the heated aqueous phase was added to the melted lipid phase and emulsified by high speed stirrer, probe sonication or by adding the aqueous phase drop by drop to the lipid phase under magnetic stirring. The obtained pre-emulsion was

ultrasonicated using probe sonicator with water bath (**Fig.7.c**). In order to prevent re-crystallization during the process, the production temperature was kept at least 5°C above the lipid melting point (Ramteke et al., 2012; Yadav et al., 2013).

With respect to the encapsulation of plant oils, the ultrasonication technique is widely used, as described in **Table 3**. *Zataria multiflora* EO-loaded SLN were developed using Precirol® ATO 5 (Glyceryl monostearate) as lipidic matrix and tween 80 with poloxamer 188 as surfactants (Nasseri et al., 2016). The obtained SLN owned a particle size around 255.5 nm with zeta potential of -37.8 mV and high EE% of 84 %. The same technique was used to develop cardamom EO loaded-NLC using cocoa butter (as solid lipid), olive oil (as liquid lipid) and tween 80 (as surfactant); and the resultant particles had round shape, smooth surface with particle size less than 100 nm (Nahr et al., 2018). Similarly, NLC were developed using palm stearin as solid lipid and lecithin as emulsifier and the resultant particles were physically and chemically stable during 70-day storage at room temperature and 4°C (Zhu et al., 2015). Furthermore, Noor et al. (2013) successfully loaded coconut VO into SLN by the same process and reported high EE% (99.97%).

Like all the colloidal formulations discussed above, both SLN and NLC prepared by high-speed homogenization provide a controlled release profile of plant oils (Pivetta et al., 2018; Zhao et al., 2017). The release profile of EO from these nanocarriers may be affected by several factors such as the particle size and the composition of lipidic matrix. In 2011, Garg and his coworkers compared the release profile of eugenol from SLN and NLC formulations made from stearic acid and the mixture stearic acid: caprylic triglyceride, respectively (Garg and Singh, 2011). Results revealed a biphasic release pattern from both nanocarriers. After initial burst release, the cumulative amounts of eugenol released within 12 h were 65 and 78% from SLN and NLC, respectively. This was related to the structure of the nanocarrier's matrix. The addition of liquid lipid in the case of NLC provides fewer barriers to partitioning of eugenol to

the dissolution media. The authors ascribed also this result to the small particle size of NLC (87.7 nm) as compared to that of SLN (332 nm). Indeed, the addition of liquid lipid decreases the viscosity of the organic phase (lipid solution) to be dispersed in the aqueous one resulting in smaller particles. Moreover, liquid lipid may inhibit the crystallization of solid lipid leading to smaller particle size (Garg and Singh, 2011). One may conclude that the incorporation of liquid lipid improves the EE% but decreases the barrier provided by lipid matrix for the diffusion of bioactive molecule in the dissolution medium.

The particle size and zeta potential of NLC were influenced by several parameters including solid lipid composition, oil and surfactant (type and concentration), lipid:surfactant ratio, etc. The impact of these factors was extensively studied in the literature (Krasodomska et al., 2016; Lacatusu et al., 2013; Soleimanian et al., 2018). It was found that increasing stearic acid concentration results in increasing the size of *Eugenia caryophyllata* EO-loaded SLN prepared by ultrasonication method (Bazzaz et al., 2018). Moreover, Soleimanian et al. (2018) developing pomegranate seed oil-loaded NLC using two types of natural waxes: beeswax and propolis wax, investigated the influence of solid lipid composition, surfactant blend concentration and oil content on NLC physicochemical properties. Results demonstrated that increasing oil amount resulted in a decrease in particle size of beeswax NLC. This was related to the reduction of core viscosity and enhancement of fluidity which results in a decrease in particle size. The opposite behavior was observed in the case of propolis wax NLC. The particle size increases by increasing the oil content. The authors ascribed that to enhanced interfacial tension or swelling rate of the core as result of greater oil concentration. Concerning the impact of solid lipid type, Soleimanian et al. (2018) reported that small differences in the lipid composition (particularly, the melting point) might have considerable impact on size and quality of nano lipid carriers. Beeswax consisting of a longer series of carboxylic acid homologues, alcohols and hydrocarbons exhibits higher melting point, leading to higher

viscosity of the dispersed phase which in turn results in increasing particle size (203 nm). On the other hand, propolis wax having lower proportion of components produced smaller NLC (143 nm). Regarding the zeta potential, the same authors reported that increasing the concentration of surfactant mixture (Lecithin:Tween 80) results in decreasing the zeta potential of NLC. They related this result to the differences in mobility and redistribution of used surfactants. In fact, high amounts of surfactant decrease the surface tension and enhance the particle partition during homogenization, resulting to a decrease in particle size and thus new NLC appear. The time required for the redistribution of surfactant molecules to cover the new surfaces differ. Indeed, low molecular weight surfactants such as tween 80 adsorb rapidly at the interface, while lecithin, as high molecular weight surfactant, needs more time to be adsorbed. Therefore, tween 80, external hydrophilic non-ionic surfactant, will cover the internal lipophilic surfactant (i.e. lecithin), and thus the zeta potential decreases (Soleimanian et al., 2018).

In summary, the ultrasonication is chosen by scientists to design both SLN and NLC systems to entrap plant oils. The commonly used lipid are glyceryl behenate (Zhao et al., 2017), stearic acid (Bazzaz et al., 2018; Garg and Singh, 2013, 2011), carnauba wax (Lacatusu et al., 2013), whey protein isolate (Azizi et al., 2019), glycerol stearate (Lacatusu et al., 2013), palmitic acid (Azizi et al., 2019), propolis (Soleimanian et al., 2018), palm stearin (Zhu et al., 2015), beeswax (Shakeri et al., 2019; Soleimanian et al., 2018), illipe butter (Pivetta et al., 2018), cocoa butter (Nahr et al., 2018), Precirol® ATO 5 (glyceryl palmitostearate) (Ghodrati et al., 2019), miglyol®812 (caprylic/capric triglycerides) (Ghodrati et al., 2019) and myverol® RX GMS 95P (mixture of glycerol palmitic (57,8%) stearic (37.3%) and myristic (1.3%) acid) (Krasodomska et al., 2016). Lecithin (Soleimanian et al., 2018; Zhu et al., 2015), poly vinyl alcohol (Zhao et al., 2017), tween 80 (Lacatusu et al., 2013; Nahr et al., 2018; Noor et al., 2013), poloxamer (Ghodrati et al., 2019; Lacatusu et al., 2013) and pluronic® F68 (Pivetta et al., 2018) are example of used emulsifiers. The main features of the ultrasonication process including

1176 facility, simplicity and reduced high shear. However, it is limited by the high metal
1177 contamination potential, unproven scalability and high energy requirement.

1178 **Table 3.** Preparation methods for plant oils encapsulation in solid lipid nanoparticles and nanostructured lipid carriers with their fine applications.

Encapsulated oil	Plant (origin)	Lipid used	Physicochemical properties			Biological properties	Application	Ref.
			Size (nm)	Z.pot (mV)	EE (%)			
Solid lipid nanoparticles								
High pressure homogenization								
Carvacrol	/	Cocoa butter	/	/	/	Antioxidant	Medicine	(Carvalho et al., 2020)
Geranial	/	Monoterpene	120.1	0	/	/	/	(Zielińska et al., 2020)
Ziziphora	Ziziphora clinopodioides	Imwitor® 900K						
		Percirol ATO5	241.1	-22.6	93	Insecticide	Agriculture	(Jajarm et al., 2020)
Eugenol	/	Campritrol 888						
		Caprylic triglyceride	332	-18.7	91.8	Anticancer	Medicine	(Garg and Singh, 2011)
	/	Stearic acid						
	/	Hydrogenated palm oil	164.5-172.9	/	/	Antifungal	Food	(McDaniel et al., 2019)
		Coconut oil						
Thymol	/	Hydrogenated	166.4-170.5	/	/	Antifungal	Food	(McDaniel et al., 2019)
Cinnamaldehyde	/	palm oil	198.0-202.1					
		Coconut oil						
Sclareol	/	Compritol	128	-29.3	/	Treatment of metabolic disorder	Medicine	(Cerri et al., 2019)
Chamomile	Matricaria chamomilla L.	Stearic acid	542	-35.9	/	Wound healing	Cosmetics	(Gad et al., 2019)
α-pinene	/	Imwitor® 900K	136.7	/	/	Antimicrobial, antioxidant	/	(Zielinska et al., 2019)
		Monoterpene	89.7	0	/	/	/	(Zielińska et al., 2020)
		Imwitor® 900K						
Citral	/	Glyceryl monostearate	215.4	/	/	Flavoring agent	Food	(Tian et al., 2018)
		Monoterpene	125.4	0		/	/	(Zielińska et al., 2020)
		Imwitor® 900K						
Gac fruit EO	Momordica cochinchinensis L.	Emulgade	200	/	90	Antioxidant; Anti-aging Skin tanning, skin care and skin protection	Cosmetics	(Mai et al., 2018)
Frankincense + Myhr oil	Commiphora myrrha L.	Compritol888 ATO	113.3	-16.8	80-60	Antitumor	Medicine	(Wang, 2012)
Copaiba oil	Copaifera officinalis L.	Cetyl palmitate	126.06	/	/	Antifungal	Cosmetics	(Svetlichny et al., 2015)

Copaiba oil+ Allantoin	<i>Copaifera officinalis</i> L.	Cetyl palmitate	118.63	/	/	Antifungal	Cosmetics	(Svetlichny et al., 2015)
Ultrasonication method								
<i>Zataria multiflora</i>	<i>Zataria multiflora</i> Boiss.	Precirol ATO 5	220-486	-37.8 to -27.2	85.3-95.2	Fungicide Pesticide	Food Medicine Agriculture	(Nasseri et al., 2020)
		Stearic acid						
		Glyceryl monostearate						
		Glyceryl monostearate	255.5	-37.8	84	Antifungal	Medicine	(Nasseri et al., 2016)
		Precirol® ATO 5						
β-elemene	/	Glyceryl monostearate	128.4	-3.07	/	Antitumor	Medicine	(He et al., 2019)
		Glyceryl tristearate						
Clove	<i>Syzygium aromaticum</i> L.	Precirol® ATO 5	397.2	-20.9	/	Antimicrobial	Medicine	(Bazzaz et al., 2018)
		Stearic acid						
		Glyceryl monostearate						
Linalool	/	Myristyl myristate Cetyl esters	90-130	-4	>80	Anticancer	Medicine	(Rodenak-Kladniew et al., 2017)
		Cetyl palmitate						
Eugenol	/	Stearic acid/Compritol	363– 423	/	/	Antifungal	Medicine	(Garg and Singh, 2013)
		Stearic acid	87.7	-19.2	98.5	Antifungal	Medicine	(Garg and Singh, 2011)
		Caprylic triglyceride						
Coconut	<i>Cocos nucifera</i> L.	Stearic acid	608	-47.5	99.9	Moisturizing lotion	Cosmetics	(Noor et al., 2013)
Nanostructured lipid carriers								
High pressure homogenization								
Cinnamon	<i>Cinnamomum cassia</i> persl.	Cocoa butter	100-120	-14.9 to -17.5	>82.1	Antimicrobial, antioxidant	Food	(Bashiri et al., 2020b)
		Almond oil						
Sucupira	<i>Pterodon emarginatus</i> L.	Imwitor® 900 K	148.1	/	99.9	Antidiabetic	Medicine	(Vieira et al., 2020)
		Tripalmitin						
Squaw mint	<i>Mentha pulegium</i> L.	Precirol® ATO 5	40-250	-10 to -15	/	Wound healing	Cosmetics	(Khezri et al., 2020)
		Miglyol®812						

Rosemary	<i>Rosmarinus officinalis</i> L.	Precirol®ATO 5 Miglyol®812	100-250	-15.7	92.1	Wound healing	Cosmetics	(Khezri et al., 2019)
Peppermint	<i>Mentha piperita</i> L.	Precirol®ATO 5 Miglyol®812	40-250	-10 to -15	/	Wound healing	Cosmetics	(Ghodrati et al., 2019)
Clove	<i>Syzygium aromaticum</i> L.	Beeswax Coconut oil	121-367	/	≈60	Cholinesterase enzyme inhibition	Medicine	(de Meneses et al., 2019)
<i>Ridolfia segetum</i>	<i>Ridolfia segetum</i> L.	Precirol®ATO 5	143	16.3	100	Antioxidant; anti-inflammatory	Medicine	(Miranda et al., 2019)
B-elemene	/	Glycerol monostearate Glyceryl monolinoleate Oleoyl macrogolglycerides	138.9	-20.2	82.11	Antitumor	Medicine	(Shi et al., 2013)
Thymoquinone	/	Hydrogenated palm oil Olive oil Lipoid®S100	75	-31	/	Antiulcer	Medicine	(Sidding et al., 2013)
Sunflower	<i>Helianthus annuus</i> L.	Sunflower oil	48.23 - 342.10	-22.3 to -29.7	/	Source of phytosterols	Food	(Santos et al., 2019)
Crambe	<i>Crambe maritima</i> L.	Crambe oil						
Canola	<i>Brassica napus</i> L.	Canola oil						
Pomegranate seed	<i>Punica granatum</i> L.	Glycerol monostearate	108 -145	34.4 to -44.3	51 – 70	Antioxidant UVA protector	Cosmetics	(Badea et al., 2015)
Wheat germ	<i>Triticum aestivum</i> L.	Emulgade						
Blackcurrant seed	<i>Ribes nigrum</i> L.							
Sesame	<i>Sesamum indicum</i> L.							
Carrot root	<i>Daucus carota</i> subsp. <i>Sativus</i>							
Raspberry seed	<i>Rubus idaeus</i> L.							
Rice bran	<i>Oryza sativa</i> L.							
Olive	<i>Olea europaea</i> L.	Hydrogenated palm oil	61.14	-25.4	/	Source of PUFA	Medicine	(How et al., 2013)
Grape seed + Laurel	<i>Vitis vinifera</i> L.	n-Hexadecyl palmitate	< 150	/	/	Antitumor; antioxidant	Medicine	(Lacatusu et al., 2015)

Ultrasonication method

Cinnamon	<i>Cinnamomum cassia</i> persl.	Cocoa butter	119.4	+21.4	84.6	Antioxidant	Food	(Bashiri et al., 2020a)
<i>Lippia sidoides</i>	<i>Lippia sidoides</i> L.	Gelucire® Labrasol®	214.4–423.2	–40.6 to –23.0	/	Antifungal	/	(Baldim et al., 2019)
Carvacrol + Astaxanthin	/	Lecithin Beeswax	58.8	–36	Asta=95 Car=88	Antioxidant Antibiofilm	Medicine	(Shakeri et al., 2019)
Eucalyptus	<i>Eucalyptus globulus</i> L.	Olive oil	50 – 60	–22.07	101.7	Wound healing	Cosmetics	(Saporito et al., 2018)
Peppermint	<i>Mentha piperita</i> L.	Miglyol-812 Precirol-ATO 5	40-250	-10 to -15	93.2	Wound healing	Cosmetics	(Ghodraty et al., 2019)
Cardamon	<i>Elettaria cardamomum</i> L.	Cocoa butter Olive oil	<150	/	>90	Antimicrobial	Food	(Nahr et al., 2018)
Thymol	/	Illipe butter Calendula oil	107.7	–11.6	89.1	Anti-inflammatory Antipsoriatic	Cosmetics	(Pivetta et al., 2018)
Houttuynia cordata	<i>Houttuynia cordata</i> Thunb.	Glyceryl behenate	171	-19.3	90.20	Treatment of pneumonia, respiratory and urinary tract infections	Medicine	(Zhao et al., 2017)
Pomegranate seed	<i>Punica granatum</i> L.	Propolis Beeswax	71.4 - 366.3	–18.3 to –27.2	96–99	Antioxidant	Food	(Soleimani et al., 2018)
Blackcurrant	<i>Ribes nigrum</i> L.	Myverol RX	/	/	/	Source of PUFA	Medicine	(Krasodomska et al., 2016)
Blackberry	<i>Rubus fruticosus</i> L.	GMS 95P						
Raspberry	<i>Rubus idaeus</i> L.	Chemal EO-20						
Strawberry	<i>Fragaria ananassa</i> Duchesne.							
Plum	<i>Prunus domestica</i> L.							

6. Application

6.1. Agriculture field

The indiscriminate use of chemicals in field as well as during postharvest poses serious problems for the environment and the human health. The excessive application of synthetic fungicides can also have other negative side effects. The appearance of resistance in the pathogen populations has been notified for many fungi (Saharan et al., 2013). In addition, over the last few years increasing consumers concern regarding contamination of crops with fungicidal residues has been reported (Shukla, 2018). Therefore, low toxicity and more environmentally friendly compounds as an alternative to chemical fungicides was brought to the forefront. Among them, GRAS (generally regarded as safe) antifungal compounds such as EO have been reported (Shukla, 2018; Sotelo-Boyás et al., 2015). Due to their broad spectrum of activity against plant pathogenic fungi and insects-pests, EO have been used as antifungal, insecticidal, repellent, antifeedant and oviposition deterrent (De Souza et al., 2005; Shukla, 2018). However, the replacement of synthetic compounds is not easy due to the poor stability shown by EOs during the processing steps. Therefore, nanoencapsulation has been proposed for this purpose (Maryam et al., 2015). According to the literature, pNPs are widely used for EO encapsulation in agriculture industry.

Recently, Khoobdel et al. (2017) investigated the insecticidal activity of *Rosmarinus officinalis* EO-loaded pNPs against the red flour beetle, *Tribolium castaneum*. Fumigant and contact toxicity assays revealed that the developed particles had significant increase in fumigant and contact toxicity as compared to the pure EO. At the 72 h exposure for fumigant toxicity, the mortality of *Tribolium castaneum* adults was 83.3 % for free EO at a concentration of 27.76 $\mu\text{L/L}$ air and 100 % for EO-loaded nanoparticles at concentration of 19.12 $\mu\text{L/L}$ air (Khoobdel et al., 2017). Moreover, Zhavah et al. (2015) related the superior performance of *Cuminum cyminum* EO nanogels against *Aspergillus flavus* as compared to the free oil to the encapsulation

in chitosan : caffeic acid nanoparticles. Similar results were already reported when investigating insecticidal activity against *Bemisia tabaci* for *Zanthoxylum rhoifolium* EO-loaded nanoparticles as compared to the free oil (Christofoli et al., 2015). Therefore, the nanoencapsulation can enhance the insecticidal potential of EO due to the controlled and slow release of EO and increased surface area of the nanoparticles.

Sotelo-Boyas and his coworkers (2015) combined the bacterial efficiency of chitosan with those of lime and thyme EO in pNPs to eradicate *Pectobacterium carotovorum*, plant phytopathogenic bacteria, involved in the decay of fresh vegetables and fruits like radishes, onions, potatoes, cucumbers, carrots, eggplant, squash, peppers, tomato and cabbage. For instance, chitosan was highly used for its potential effect in the control of phytopathogenic fungi Gram-negative and Gram positive bacteria (Benhabiles et al., 2012; Kaur et al., 2012; Zhu et al., 2016). The antibacterial study demonstrated that thyme based-nanoparticles showed the highest inhibitory effect on the growth of *Pectobacterium carotovorum* than free chitosan nanoparticles and lime based- nanoparticles. The inhibition halo diameters were found 15, 13 and 24 mm for chitosan free nanoparticles, lime-chitosan nanoparticles and Thyme-chitosan nanoparticles, respectively. Moreover, the number of colonies forming units (CFU) could not be determined (countless colonies) for chitosan free nanoparticles. While for lime- and thyme-chitosan nanoparticles, CFU were found 450 and 240, respectively (Sotelo-Boyás et al., 2015). Furthermore, the results of antifungal assay carried out on chitosan:pepper tree EO nanoparticles revealed that higher activity was assessed for the nanoparticles on the viability of *Aspergillus parasiticus* spores as compared to that of chitosan and pepper tree oil present individually. One may conclude that the antifungal effect of chitosan nanoparticles was attributed to two reasons: 1) the small size of nanoparticles will increase the contact area with fungus; 2) The cationic nature of chitosan allows electrostatic interaction with proteins and

phospholipids of the plasmatic membrane of the microorganism which in turn cause membrane destabilization and death.

With respect to the use of lipid based-nanocarriers in agriculture industry, few reports have been investigated in the last decade. Liposomes were used for the first time for rosemary EO encapsulation to inhibit the seed germination of invasive alien species (*Acacia saligna*) (Maccioni et al., 2019). The incorporation of rosemary EO in liposomes limited the loss of EO volatile components and delivering them into the seed resulting in enhancing EO efficacy. Similarly, Adel et al. (2015) pointed out that *Pelargonium graveolens* EO loaded-SLN were stable under field conditions and exhibit higher larvicidal activity against *Phthorimaea operaculella* as compared to the free oil.

6.2. Food field

In recent years, consumer demands in eating healthy and less processed foods have boosted remarkably. Functional foods play a pivotal role in promoting health and preventing degenerative diseases such as heart disease, cancer and diabetes, which account for almost two thirds of deaths in the world (Conto et al., 2012; Rubilar et al., 2012). Foods enriched with long chain omega-3 polyunsaturated fatty acids are classified as functional foods by acting on human health. The ingestion of omega-3 fatty acids is accompanied with a prevention of cardiovascular diseases, a decreased risk of cancer, autoimmune and inflammatory diseases (Azizi et al., 2019; Conto et al., 2012; Gallardo et al., 2013). However, polyunsaturated fatty acids are very susceptible to oxidation during processing and storage resulting in decreased nutritional value and sensory quality. Thus, micro and nanoencapsulation of lipids have been used in this concern (Gökmen et al., 2011).

Currently, several nanocarriers have been designed in the literature to encapsulate several healthful oils like chia seed oil (Campo et al., 2017), walnut oil (Shamaei et al., 2017),

flaxseed oil (Carneiro et al., 2013; Gallardo et al., 2013; Pu et al., 2010), pomegranate oil (Soleimanian et al., 2018), roasted coffee oil (Freiberger et al., 2015) and fruit seed oil (blackcurrant, blackberry, raspberry, strawberry and plum) (Krasodomska et al., 2016). In 2012, Rubilar et al. developed a soup fortified with linseed oil microcapsules and depicted that microencapsulation protected linseed oil from oxidation with respect to free oil (Rubilar et al., 2012). Similarly, Gökmen et al. (2011) demonstrated the feasibility to include flaxseed oil nanoparticles in bread without affecting the sensorial properties.

At the same time, foods are paramount carriers of many damaging agents like virus, bacteria, parasites, and toxins which can cause food-borne diseases (Dussault et al., 2014). Every year, around 30% of people suffer from foodborne diseases in developed countries (Lee et al., 2014). Meanwhile, due to the increased consumer awareness to the use of synthetic food preservatives or aromatic agents, the tendency toward natural ones is gaining more and more attention (Alikhani-Koupaei, 2015). In light of that, using EO with antioxidant, antibacterial and antifungal properties and applying nanoparticulate systems are effective approaches in this regard (Bazzaz et al., 2018; Khatibi et al., 2017). In 2017, Cui and his coworkers developed thyme EO-loaded liposomes to treat salmonellosis, an important food-borne disease, usually associated with direct consumption or cross contamination of animal origin foods, especially poultry, and poultry related products (Cui et al., 2017b). They investigated in their study the time-kill analysis of liposome-encapsulated thyme oil on fresh chicken contaminated with *Salmonella enteritidis*. Results demonstrated that *Salmonella enteritidis* colonies reduced by 71.16, 90.45, 83.02, 89.53 and 97.71% after exposure to 300 mg/mL liposomes for 3, 4, 5, 6, and 7 days, respectively (Cui et al., 2017b). In another work study, the antimicrobial activity of curry plant EO loaded-liposomes against *Bacillus cereus* in rice flour was investigated (Cui et al., 2017a). Results showed that the antibacterial activity and active time of curry plant EO loaded-liposomes were significantly boosted when compared to the free EO. For instance, the

population of *Bacillus cereus* in rice flour was almost unchanged or even increased after EO treatment. However, it reduced significantly after 4 days liposomes treatment (Cui et al., 2017a). Gomes et al. (2011b) related the boosting in trans cinnamaldehyde or –eugenol against both *Salmonella* and *Listeria Spp* activity to three reasons: the improved hydrophilicity, the sustained release, and the small size of pNPs. In 2018, Lin et al. investigated the antimicrobial activity of thyme EO-loaded liposomes against *Escherichia coli* O157:H7 in four vegetable juices: tomato, carrot, cucumber and lettuce juices (Lin et al., 2018). Indeed, Enterohaemorrhagic *Escherichia coli* serotype O157:H7 as a main human pathogen may cause food borne outbreaks, bloody diarrhea, hemorrhagic colitis and hemolytic uremic syndrome and even death (Khatibi et al., 2017). Results showed that solid liposomes exhibited significant reduction in *Escherichia coli* O157:H7 when compared to group control. For instance, no bacterial growth was observed on nutrient agar plate in the case of cucumber juice and lettuce juice treated with 5 mg/mL liposomes. While, treating tomato juice and carrot juice with the same concentration of liposomes lead to 99.99 and 99.80% reduction of *Escherichia coli* O157:H7 (Lin et al., 2018). Moreover, Khatibi et al. (2017) found that the relative transcriptional level of Stx2A gene of *Escherichia coli* O157:H7 was decreased from 0.721 to 0.646 when using 75% minimum inhibitory concentration (MIC) of *Zataria multiflora* EO loaded-nanoliposomes.

The antibacterial mechanism of EOs loaded-nanocarriers has been investigated. In 2015, Cui et al. investigated the antibacterial mechanism of liposomes containing clove EO against *Staphylococcus aureus* in Tofu (Cui et al., 2015). A selective antimicrobial activity for *Staphylococcus aureus* by means of pore-forming toxins to activate clove oil release from liposomes was noticed. In fact, the liposomes did not fuse with biological membranes but release clove oil after toxins secretion by the bacteria. About 99.87% reduction in population was observed in *Staphylococcus aureus* after 24 h of liposome treatment. However, no

reduction was observed in *Escherichia coli* population after liposome treatment due to the fact that these bacteria did not secrete toxins and therefore clove oil could not reach them (Cui et al., 2015).

The antioxidant and antimicrobial activities of EO-loaded nanocarriers were found to be conserved for long period. In this context, the physicochemical qualities of fresh-cut bananas in contact with free rosemary EO, rosemary oil plus mucilage and rosemary oil liposomes were evaluated during 9 days storage at 5°C (Alikhani-Koupaei, 2015). Sensory analysis revealed that liposomal formulations was more efficient in enhancing the quality of fresh-cut bananas and extending their shelf life (Alikhani-Koupaei, 2015). Likewise, the conversion of cardamom EO to NLC (Nahr et al., 2018) and nanoliposomes (Nahr et al., 2019) greatly conserves its antioxidant and antimicrobial activities for long period. The NLC showed MIC values around 1100 µg/ml for both bacteria after 30 days compared to that of cardamom oil emulsion. The MIC values were around 4400 and 2200 µg/ml for *Staphylococcus aureus* and *Escherichia coli*, respectively (Nahr et al., 2018).

The biological activity of nanocarriers encapsulated plant oils was affected by operating parameters and particles ingredients. In 2017, Mohammed and his coworkers depicted that a high antioxidant efficiency of *Nigella sativa* EO-loaded microparticles prepared by spray drying process was associated with high ratio of wall material (30%), medium of oil concentration (10%) and low inlet temperature (160°C) (Mohammed et al., 2017). Furthermore, Bazzaz et al. (2018) investigated the antimicrobial activity of SLN encapsulated *Eugenia caryophyllata* EO against *Salmonella typhi*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Candida albicans* using time-kill methods. Results demonstrated that the SLN formulations were effective in Gram negative bacteria and fungi killing, especially those containing stearic acid compared to glycerol monostearate (Bazzaz et al., 2018).

In recent years, the use of EO has emerged to the food packaging industry as reported by several work studies (Cui et al., 2016a, 2016b; Engel et al., 2017; Liu et al., 2017). Cinnamon EO, known for its antimicrobial properties, has been formulated in chitosan/poly lactic acid fibers for food packaging application as an alternative for synthetic chemicals due to consumer concerns over food safety (Liu et al., 2017). Results showed high long-term inactivation rates against *Escherichia coli* and *Staphylococcus aureus* (Liu et al., 2017). Cinnamon EO was further formulated in liposomes and tested for its Methicillin-resistant *Staphylococcus aureus* antibiofilm properties on the surfaces of different materials like stainless steel, gauze, nylon membrane, and non-woven fabrics (Cui et al., 2016a). Results revealed a significant enhancement of the anti-biofilm activities and active time for liposome-encapsulated cinnamon EO when compared to the free oil. For instance, the counts of viable *Staphylococcus aureus* in biofilms formed were reduced by 2.08 and 2.82 logs on gauze and 4.55 and 5.42 logs on non-woven fabrics after five days treatment with free cinnamon oil and liposome containing cinnamon oil, respectively (Cui et al., 2016a). Additionally, the antibacterial effect of salvia EO nanoliposomes against *Staphylococcus aureus* biofilms attached on milk container was explored by scanning electron microscopy and confocal laser scanning microscopy and results revealed that salvia EO nanoliposomes have high anti-biofilm activity against *Staphylococcus aureus* biofilms on milk container (Cui et al., 2016b). Furthermore, Engel et al. (2017) noticed the antimicrobial potential of liposome-encapsulated thymol and carvacrol against pools of *Staphylococcus aureus* and *Salmonella* adhered to stainless steel.

6.3. Medicinal field

6.3.1. Antimicrobial activity

The management of bacterial infection is raising serious concern across the globe. The emergence of multi-drug-resistant bacterial pathogens and the ability of microorganisms to form biofilms result high tolerance to high amounts of antibiotics and to all host defense

mechanisms (Mandal et al., 2014). Faced with this challenge, the scientists throughout the world search for new antimicrobial agents, such as plant oils based formulations which are economic and ecologic antimicrobial agents; and combine them with nanotechnology (Liakos et al., 2018). In this context, Iannitelli et al. (2011) investigated the effects of carvacrol-loaded poly (lactide-co-glycolide)-nanocapsules on the viscoelastic features of *Staphylococcus epidermidis* biofilms by rheological measurements. Results revealed the ability of carvacrol loaded nanoparticles to reduce the elasticity and mechanical stability of preformed biofilms which in turn enable the penetration of antimicrobial agents into the deep core of biofilms (Iannitelli et al., 2011). Liakos et al. (2016) tested the antibiofilm activity of poly lactide nanoparticles encapsulating lemongrass EO against *Candida albicans*, *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Results showed higher anti-biofilm effect for *Candida albicans* and *Escherichia coli* tested strains. The cytotoxicity of the prepared nanoparticles was further analyzed and results revealed a high cell viability and good growth of human cells (Liakos et al., 2016). Subsequently, in 2018, the same research team tested the antibiofilm activity of cellulose acetate pNPs containing either lemongrass, peppermint or cinnamon EO and the results showed high antibiofilm activity against *Candida albicans* and *Staphylococcus aureus* (Liakos et al., 2018). Manconi et al. (2018) proposed the use of liposomes containing *Thymus capitatus* EO as antibacterial-antioxidant mouthwash for the treatment of oral cavity diseases. The liposomes were biocompatible, able to prevent oxidative stress and favor wound repair in keratinocytes. Their antibacterial activity was evidenced against commensal *Streptococcus sanguinis* and cariogenic *Streptococcus mutans* and *Lactobacillus acidophilus* (Manconi et al., 2018). Similarly, Priyadarshini et al. (2018) proposed the use of poly (lactide-co-glycolide)-nanoparticles containing clove EO as antibacterial systems for dental purposes by removing bacterial plaque and reducing dental diseases. Confocal microscopy demonstrated successful delivery and position of clove oil

loaded-nanoparticles inside dentinal tubules. In another work study, the antiviral activity of *Santolina insularis* EO loaded-liposomes against Herpes simplex virus-type 1 was investigated (Valenti et al., 2001). Although the *in vitro* activity of free oil was higher than liposomal oil, the high stability of liposomes make them an interesting delivery system for antiviral treatment; they could be administered in drops for ocular herpetic infection, parenterally for diffused systemic infections or topically on lips and mucosae from gel or cream formulations (Valenti et al., 2001). Furthermore, Zhao et al. (2017) highlighted the use of SLN as a carrier for the encapsulation and sustained inhalation delivery of yuxingcago EO for the treatment of respiratory infectious diseases. Besides prolonging pulmonary retention up to 24h after intratracheal administration to rats, yuxingcago EO loaded-SLN enhance the area under the curve (AUC) values by 4.5-7.7 folds compared to the intratracheally dosed EO solution and by 257–438 folds to the intravenously dosed EO solution (Zhao et al., 2017).

6.3.2. Antifungal activity

Considering the antifungal properties of *Zataria multiflora* EO, Nasser et al. developed *Zataria multiflora* EO loaded-SLN to enhance its activity against *Aspergillus ochraceus*, *Aspergillus niger*, *Aspergillus flavus*, *Alternaria solani*, *Rhizoctonia solani*, and *Rhizopus stolonifera* (Nasser et al., 2016). Results showed that the encapsulated oil was more efficient than the free one. For instance, the MIC for the encapsulated oil on the fungal pathogens of *Aspergillus ochraceus*, *Aspergillus niger*, *Aspergillus flavus*, *Alternaria solani*, *Rhizoctonia solani*, and *Rhizopus stolonifer* was 200, 200, 200, 100, 50 and 50 ppm, respectively; while for un-encapsulated oil, it was 300, 200, 300, 200, 200 and 200 ppm (Nasser et al., 2016). Furthermore, the nanoencapsulation enhanced the antifungal properties of copaiba oil against *Candida krusei*, *Microsporum canis*, *Candida parapsilosis* and *Trichophyton rubrum* with MIC₉₀ values of 250, 1.95, 7.8 and 1.95µg/mL, respectively. In another work study, microparticles encapsulating *Lippia sidoides* EO were found more efficient than ketaconazole,

used as positive control, in eradicating *Candida albicans*, *Candida glabrata*, *Candida krusei* and *Candida parapsilosis* (Fernandes et al., 2008).

Recently, many studies related the occurrence of some diseases like teratogenesis, mutation and hepatocellular carcinoma to the high exposure to aflatoxin which is secondary metabolites synthesized by toxigenic fungi: *Aspergillus flavus*, *Aspergillus parasiticus* and *Aspergillus nomius*. López-meneses et al. (2018) investigated the antifungal and antiaflatoxigenic activities against *Aspergillus parasiticus* of *Shinus molle* EO-loaded chitosan nanoparticles. Results showed that the prepared nanoparticles affected the spore's germination and viability, delayed mycelial growth and reduced aflatoxin production.

6.3.3. Larvicidal activity

Currently, several reports has demonstrated the larvicidal activity of *Lippia sidoides* EO against larvae of *Aedes (Stegomyia aegypti)*, the dengue vector which is responsible for many diseases, and even deaths, in tropical countries like Brazil (Carvalho et al., 2003). In order to boost its larvicidal effect, Paula et al. (2010) developed angico gum : chitosan nanoparticles containing *Lippia Sidoides* EO and investigated the *in vivo* activity on 20 third instar *Stegomyia aegypti* larvae. Results demonstrated that the larval mortality was proportional to the oil loading. For instance, the sample oil: angico gum-chitosan 1:20 showed the lowest loading (3.3%) and consequently the lowest mortality, with 52 % after 24 h and 60 % after 48 h. Sample oil: angico gum-chitosan 1:10 showed 85 and 92 % mortality after 24 and 48 h, respectively (Paula et al., 2010). Similar results were found by Abreu et al. when studying the larvicidal activity of *Lippia Sidoides* EO loaded-cashew gum : chitosan nanoparticles (Abreu et al., 2012).

6.3.4. Antitumor activity

The antitumor activity of frankincense and myrrh oil loaded-SLN was assessed on H22 tumor-bearing mice and results revealed an enhancement in antitumor efficiency of SLN when compared to that of suspension and cyclodextrine inclusion (Wang, 2012). The inhibition rates

were 31.23, 34.81 and 43.66% for oil suspension, oil- β -cyclodextrin and oil-SLN, respectively. Similarly, Celia et al. (2013) found that liposomal formulations encapsulating bergamot EO showed a greater reduction in human SH-SY5Y neuroblastoma cells viability and a greater increase in cell mortality at various concentrations and time points as compared to their free drug counterparts. Same results were also reported by Detoni et al. (2012) where MLVs and SUVs containing *Zanthoxylum tingoassuiba* EO were more efficient in reducing the viability of glioma cells than free EO. In another work study, docosahexaenoic acid was encapsulated in liposomes and investigated for its anticancer activity and results showed a strong inhibition of FaDu head, neck squamous carcinoma and 4T1 breast cancer cells in *in vitro* cultures (Alaarg et al., 2016). In 2013, Shi and his coworkers developed NLC containing β -elemene and investigated their pharmacokinetics, anti-tumor effects, and venous irritation (Shi et al., 2013). In this study, β -elemene-NLC suspensions were injected in an ear vein test, and compared with elemene injection and saline solution used as positive and negative controls, respectively. Results demonstrated no obvious discoloration or damage at the injection site in either β -elemene-NLC groups or saline solution group, two days after the injection. However, unencapsulated β -elemene caused macroscopic edema and erythema at the injection site. Additionally, the pharmacokinetic study revealed that the availability of the β -elemene was increased by formulation into NLC since they showed higher AUC and slower clearance as compared to elemene injection. Furthermore, the anti-tumor efficacy of β -elemene-NLC was significantly higher than that of elemene injections with inhibition rates of 34.36 and 24.11%, respectively (Shi et al., 2013).

6.4. Cosmetic field

Wound healing is one of the most complicated physiological processes. Indeed, tissue regeneration enhancement and infection prevention are key factors to reduce pain, discomfort, and scar formation (Jahromi et al., 2018). Several chemical products have been proposed for

wound repair; however, their uses are limited due to the complications and side effects (Purohit et al., 2012). Recently, researchers have paid great attention to the effectiveness of plant oils thanks to their antioxidant, antimicrobial, and anti-inflammatory properties (Raut and Karuppayil, 2014). In this context, Ghodrati et al. (2019) investigated the therapeutic effect of NLC containing peppermint EO on infected wound. For *in vivo* study, two full-thickness wounds with the size of 5mm were created in each mouse and inoculated with *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Results showed that peppermint EO-NLC could accelerate wound healing in the infected wound model by reducing the total bacterial count, and increasing neovascularization, fibroblast infiltration, collagen deposition, re-epithelization, and levels of FGF-2 and EGF mRNA expressions when compared to control group. Similarly, Zhang et al. reported a decrease in TGF- β 1, MMP-1, collagen I and collagen III levels and an increase in apoptosis cells, caspase -3 and -9 levels after application of *Ligusticum chuanxiong* EO-loaded liposomes on formed hypertrophic scars in the rabbit ear model (H. Zhang et al., 2012). Furthermore, NLC based on olive oil and loaded with eucalyptus oil promote wound healing in rat burn model by cell proliferation enhancement, good bioadhesion, cell biocompatibility and antimicrobial properties (Saporito et al., 2018). In 2018, Pivetta et al. prepared carbopol-gels containing thymol loaded-NLC as promising approach for treating skin inflammatory disorders (Pivetta et al., 2018). In their study, they investigated the anti-inflammatory effects of thymol-NLC gel on two mouse models: the cutaneous acute inflammation model induced by croton oil and ear edema model induced by anthralin. Results showed that thymol encapsulated in NLC provided better anti-inflammatory effect than free thymol (Pivetta et al., 2018).

Chronic skin infections in immunocompromised patients has become an important public health issue because they can become serious, resulting in invasive infections (Svetlichny et al., 2015). In this context, Ortan et al. (2013) developed hydrogels containing

Anethum graveolens oil entrapped in liposomes to treat fungal infections in skin. The *in vitro* release kinetics study using Franz diffusion cell showed that the designed hydrogels follow a zero order kinetic model after a period of three hours from the beginning of the experiment (Ortan et al., 2013). Moreover, hydrogel containing eugenol entrapped in either stearic acid- or compritol-SLN were designed for epidermal targeting to treat fungal infections in skin (Garg and Singh, 2013). *Ex vivo* permeation and retention studies for almond oil solution of eugenol and three types of hydrogels containing: eugenol-stearic acid-SLN, eugenol-compritol-SLN or eugenol-hydroxypropyl- β -cyclodextrin complex; were established with full thickness human cadaver skin using Franz diffusion cell. Results revealed higher accumulation of eugenol in the epidermis (62.65 and 52.86 $\mu\text{g}/\text{cm}^2$ for eugenol-stearic acid-SLN and eugenol-compritol-SLN, respectively) when compared to that of almond oil solution of eugenol (3.45 $\mu\text{g}/\text{cm}^2$) and eugenol-hydroxypropyl- β -cyclodextrine complex (9.77 $\mu\text{g}/\text{cm}^2$) (Garg and Singh, 2013).

Currently, VO exhibit a great concern as raw materials in the development of natural and eco-friendly cosmetics due to their benefits including antioxidant, moisturizers and emollients properties. In addition, they provide skin protection against reactive oxygen species and prevent oxidative stress (Dhavamani et al., 2014; Saraf et al., 2010). In order to obtain efficient formulations with UV protection performance and antioxidant activity, Badea et al. (2015) formulated creams containing NLC entrapping various VO and their combinations (pomegranate seed oil, wheat germ oil, blackcurrant seed oil, sesame seed oil, carrot root oil, raspberry seed oil and rice bran oil) with a synthetic UVA filter (diethylamino hydroxy benzoyl hexyl benzoate). The UV protection factors were evaluated on the individual VO and on cream formulations based on NLC and results showed that the best UV protection was assured by pomegranate seed oil combined with wheat germ-loaded NLC based cream resulting in a SPF of 5.1 and an UVAPF of 9.5 (Badea et al., 2015).

6.5. Textiles

Nowadays, functional textiles fascinated consumers interest due to their crucial benefits as they enhance the native properties and promote new functions in the textile products like flame retardency, UV resistance, photo-catalytic, antimicrobial, antibiotic and wrinkle recovery to the fabrics (Javid et al., 2014). In medical field, textile consumers are becoming more aware and conscious of the deleterious effect that microorganisms may have upon textile materials like drapes, bed sheets, pillow cases, gowns and masks which are frequently used in hospitals (Thelagavath and Kannaian, 2008). In this context, Li et al. (2013) grafted moxa oil microcapsules made with gelatin and arabic gum on cotton fabric and investigated their antibacterial activity against *Staphylococcus aureus* and the results showed strong antibacterial effect. Similarly, ozonated red pepper seed oil antimicrobial microcapsules were applied on 100% polypropylene non-woven fabric and showed good antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli* and *Candida albicans* (Ozyıldız et al., 2012). Furthermore, Rajendran et al. (2013) reported that *Ocimum sanctum* oil loaded alginate-nanoparticles possessed remarkable antibacterial activities with excellent wash durability. After 20 washes, the inhibition percentage was 100% for *Bacillus cereus*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* except for *Escherichia coli* (90%). After 30 washes, the bacterial inhibition was reduced to 95, 87, 98 and 98% for *Bacillus cereus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Staphylococcus aureus*, respectively (Rajendran et al., 2013). In 2013, Javid et al. reported that antibacterial activity of cotton fabric grafted with chitosan capsules containing eucalyptus and sandal wood oils increased with the increase in chitosan and EO concentrations (Javid et al., 2014).

Recent developments in textile industry were conducted to perfumed textiles in jackets, sweaters, T-shirts and undershirts to meet consumers' needs for comfort and wellbeing. During wearing, the mechanical forces on the capsules result in opening of the capsules and releasing of the designed aroma and deodorant (Ghayempour and Montazer, 2016). In this context, Liu

et al. (2015) treated methyl methacrylate–styrene nanoparticles containing cologne EO on the cotton fabric through immersion and the release study revealed that 6.8% cologne EO remained in fabrics after being washed 15 times. In another work, Wang et al. reported that ethyl cellulose microcapsule can retain 50% of the lavender oil after 2 months, while almost no EO persisted on the direct sprayed fabric after 7 days (Wang et al., 2009). Additionally, Li et al. (2013) found that orange oil retention of microcapsules on the cotton and polyester fabrics was 8 days longer than free oil.

7. Conclusion and perspectives

In the last two decades, the growing demand for natural bioactive products especially essential and vegetable oils with the same efficiency or even more than chemical synthesized drugs has urged researchers to focalize most of their efforts on developing new approaches of extending the shelf life of these bioactive agents. In fact, plant oils are very sensitive to external factors when used as such. The encapsulation of these bioactive agents represents a relevant alternative to extend their physical stabilities, protecting them from oxidation and other deleterious environmental factors like light, heat, oxygen and humidity, besides improving their efficacy mainly owing to their nanometer size range. In this bibliographic paper, we emphasize recent advances of both polymer and lipid based-nanocarriers including polymeric nanoparticles, liposomes and solid lipid nanoparticles in the emergence of new concepts for the effective use of plant oils. A number of benefits and drawbacks are linked to each carrier. For instance, both solid lipid nanoparticles and polymeric nanoparticles have more oil stability and prolonged release than liposomes; while liposomes offer wide application spectrum especially to the skin delivery thanks to their chemical nature which is very close to that of the skin layers. Although solid lipid nanoparticles are safer than polymeric nanoparticles since the avoidance of organic solvents, they were less used to encapsulate both essential and vegetable oils, according to the investigations discussed above. This may be related to the high

temperature requirements which in turn cause oil loss and thus decrease the encapsulation efficiency. Several preparation methods have been reported for each nanocarrier; they are differentiated by the complexity of their execution and the characteristic of their final product; nonetheless, the right selection of the suitable carrier with the appropriate preparation method is the crucial key to determine the carrier features responsible for the best attainment of the final goal. The discussed nanostructured systems provide pertinent perspectives for applications in several fields like medicinal, cosmetic, culinary, agriculture and textiles. Nowadays, the association of plants oils and active molecules is attracting special attention. Lipid core nanocapsules and nanostructured lipid carriers represent promising carriers to entrap both plant oil and synthetic drugs. The appropriate selection of plant oil is very important for achieving the high loading capacity and physical stability of the hydrophobic drugs. In addition, the oil may complement or even enhance the biological activities of these drugs. Hence, the research in the field of plants oils encapsulation can make an important contribution to the development of new methodologies in the treatment and diagnosis of major chronic diseases.

Experimental advances are necessary in engineering plant oils loaded nanocarriers with broader applications and functionalities. Some techniques discussed in this review provide poor control over the final structure and stability of the obtained colloidal systems. Others lack from scalability and reproducibility; therefore, new techniques with improved control and reproducibility are crucial to design nanocarriers with predictable properties.

Even if several advances have been already reported in the literature regarding the application of plants oils nanocarriers for pharmaceutical and cosmetics purposes, more *in vivo* studies are required to provide reliable results. Additionally, plant oils mechanism of action, toxic effects, pharmacokinetic parameters, biodistribution in biological systems and removal mechanisms must be investigated. Moreover, with the aim of improving the biodistribution of colloidal systems, scientists throughout the world are currently focalizing their efforts on the

functionalization of the particle surface with special ligands to target specific organs and tissues. However, to our knowledge, there are no reports in the literature that deal with targeting delivery of plant oils loaded nanocarriers. Such demonstrations would provide a blueprint for the development of new concepts and products in large-scale for broader application.

CRedit authorship contribution statement

Narimane Lammari: Conceptualization, Writing - original draft, Investigation, Visualization.

Ouahida Louaer: Supervision, Writing - review & editing. **Abdeslam Hassen Meniai:** Writing - review & editing. **Hatem Fessi:** Conceptualization. **Abdelhamid Elaissari:** Supervision, Writing - review & editing, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

- Abdullah, S.W., Ahmed, K.S.D., Khidher, K.Q., 2018. Plant essential oils as grain protectants against *Rhizopertha dominica* (Coleoptera:Bostrichidae) during storage. *Tikrit J. Pure Sci.* 23, 41–44.
- Abreu, F.O.M.S., Oliveira, E.F., Paula, H.C.B., Paula, R.C.M., 2012. Chitosan/cashew gum nanogels for essential oil encapsulation. *Carbohydr. Polym.* 89, 1277–1282. <https://doi.org/10.1016/j.carbpol.2012.04.048>
- Adel, M., Atwa, W., Hassan, M., Salem, N., Farghaly, D.S., Ibrahim, S., 2015. Biological activity and field persistence of *Pelargonium graveolens* (Geraniales : Geraniaceae) loaded solid lipid nanoparticles (SLNs) on *Phthorimaea operculella* (Zeller) (PTM)

1602 (Lepidoptera : Gelechiidae). Int. J. Sci. Res. 4, 514–520.

1603 Ahsaei, S.M., Talebi-Jahromi, K., Amoabediny, G., 2020. Insecticidal activity of
 1604 polycaprolactone nanoparticles decorated with chitosan containing two essential oils
 1605 against *Tribolium confusum*. Int. J. Pest Manag.
 1606 <https://doi.org/10.1080/09670874.2020.1825875>

1607 Alaarg, A., Jordan, N.Y., Verhoef, J.J.F., Metselaar, J.M., Storm, G., Kok, R.J., 2016.
 1608 Docosahexaenoic acid liposomes for targeting chronic inflammatory diseases and cancer :
 1609 an *in vitro* assessment. Int. J. Nanomedicine 11, 5027–5040.

1610 Ali, B., Al-Wabel, N.A., Shams, S., Ahamad, A., Khan, S.A., Anwar, F., 2015. Essential oils
 1611 used in aromatherapy: A systemic review. Asian Pac. J. Trop. Biomed. 5, 601–611.

1612 Ali, F.R., El-Anany, A.M., 2017. Hypolipidemic and hypocholesterolemic effect of roselle
 1613 (*Hibiscus sabdariffa* L.) seeds oil in experimental male rats. J. Oleo Sci. 66, 41–49.

1614 Alikhani-Koupaei, M., 2015. Liposomal and edible coating as control release delivery systems
 1615 for essential oils : comparison of application on storage life of fresh-cut banana. Qual.
 1616 Assur. Saf. Crop. Foods 7, 175–185. <https://doi.org/10.3920/QAS2013.0297>

1617 Allen, T.M., Cullis, P.R., 2013. Liposomal drug delivery systems: from concept to clinical
 1618 applications. Adv. Drug Deliv. Rev. 65, 36–48.

1619 Almeida, J.S., Jezur, L., Fontana, M.C., Paese, K., Silva, C.B., Pohlmann, A.R., Guterres, S.S.,
 1620 Beck, R.C.R., 2009. Oil-based nanoparticles containing alternative vegetable oils (grape
 1621 seed oil and almond kernel oil): Preparation and characterization. Lat. Am. J. Pharm. 28,
 1622 165–172.

1623 Almoustafa, H.A., Alshawsh, M.A., Chik, Z., 2017. Technical aspects of preparing PEG-PLGA
 1624 nanoparticles as carrier for chemotherapeutic agents by nanoprecipitation method. Int. J.
 1625 Pharm. 533, 275–284.

1626 Antonioli, G., Fontanella, G., Echeverrigaray, S., Delamare, A.P.L., Pauletti, G.F., Barcellos,

1627 T., 2020. Poly(lactic acid) nanocapsules containing lemongrass essential oil for
 1628 postharvest decay control: *In vitro* and *in vivo* evaluation against phytopathogenic fungi.
 1629 Food Chem. 326, 126997.

1630 Auezova, L., Najjar, A., Kfoury, M., Fourmentin, S., Greige-Gerges, H., 2020. Antibacterial
 1631 activity of free or encapsulated selected phenylpropanoids against *Escherichia coli* and
 1632 *Staphylococcus epidermidis*. J. Appl. Microbiol. 128, 710–720.

1633 Averina, E., Allémann, E., 2013. Encapsulation of alimentary bioactive oils of the Baikal Lake
 1634 area into pH-sensitive micro- and nanoparticles. LWT - Food Sci. Technol. 53, 271–277.
 1635 <https://doi.org/10.1016/j.lwt.2013.01.020>

1636 Azizi, M., Li, Y., Kaul, N., Abbaspourrad, A., 2019. Study of the physicochemical properties
 1637 of fish oil solid lipid nanoparticle in the presence of palmitic acid and quercetin. J. Agric.
 1638 Food Chem. 67, 671–679. <https://doi.org/10.1021/acs.jafc.8b02246>

1639 Azzi, J., Auezova, L., Danjou, P., Fourmentin, S., Greige-Gerges, H., 2018. First evaluation of
 1640 drug-in-cyclodextrin-in-liposomes as an encapsulating system for nerolidol. Food Chem.
 1641 255, 399–404. <https://doi.org/10.1016/j.foodchem.2018.02.055>

1642 Badea, G., Ioana, L., Badea, N., Ott, C., Meghea, A., 2015. Use of various vegetable oils in
 1643 designing photoprotective nanostructured formulations for UV protection and antioxidant
 1644 activity. Ind. Crop. Prod. 67, 18–24. <https://doi.org/10.1016/j.indcrop.2014.12.049>

1645 Badri, W., Asbahani, A. El, Miladi, K., Baraket, A., Agusti, G., Agha, Q., Errachid, A., Fessi,
 1646 H., Elaissari, A., 2018. Poly (ϵ -caprolactone) nanoparticles loaded with indomethacin and
 1647 *Nigella Sativa* L. essential oil for the topical treatment of inflammation. J. Drug Deliv. Sci.
 1648 Technol. 46, 234–242. <https://doi.org/10.1016/j.jddst.2018.05.022>

1649 Badri, W., Miladi, K., Eddabra, R., Fessi, H., Elaissari, A., 2015. Elaboration of nanoparticles
 1650 containing indomethacin: Argan oil for transdermal local and cosmetic application. J.
 1651 Nanomater. 2015, 1–9. <https://doi.org/10.1155/2015/935439>

1652 Bae, E.K., Lee, S.J., 2008. Microencapsulation of avocado oil by spray drying using whey
 1653 protein and maltodextrin. J. Microencapsul. 25, 549–560.
 1654 <https://doi.org/10.1080/02652040802075682>

1655 Bagheri, R., Ariaii, P., Motamedzadegan, A., 2020. Characterization, antioxidant and
 1656 antibacterial activities of chitosan nanoparticles loaded with nettle essential oil. Food
 1657 Meas. <https://doi.org/10.1007/s11694-020-00738-0>

1658 Bai, C., Zheng, J., Zhao, L., Chen, L., Xiong, H., Mcclements, D.J., 2019. Development of oral
 1659 delivery Systems with enhanced antioxidant and anticancer activity : coix seed oil and β -
 1660 carotene coloaded liposomes. J. Agric. Food Chem. 67, 406–414.
 1661 <https://doi.org/10.1021/acs.jafc.8b04879>

1662 Bai, X., Li, C., Yu, L., Jiang, Y., Wang, M., Lang, S., Liu, D., 2019. Development and
 1663 characterization of soybean oil microcapsules employing kafirin and sodium caseinate as
 1664 wall materials. LWT 111, 235–241. <https://doi.org/10.1016/j.lwt.2019.05.032>

1665 Baldim, I., Tonani, L., von Zeska Kress, M.R., Pereira Oliveira, W., 2019. *Lippia sidoides*
 1666 essential oil encapsulated in lipid nanosystem as an anti-candida agent. Ind. Crops Prod.
 1667 127, 73–81. <https://doi.org/10.1016/j.indcrop.2018.10.064>

1668 Bangham, A.D., Standish, M.M., Watkins, J.C., 1965. Diffusion of univalent ions across the
 1669 lamellae of swollen phospholipids. J. Mol. Biol. 13, 238–252.

1670 Bashiri, S., Ghanbarzadeh, B., Ayaseh, A., Dehghannya, J., Ehsani, A., 2020a. Preparation and
 1671 characterization of chitosan-coated nanostructured lipid carriers (CH-NLC) containing
 1672 cinnamon essential oil for enriching milk and anti-oxidant activity. LWT - Food Sci.
 1673 Technol. 119, 108836.

1674 Bashiri, S., Ghanbarzadeh, B., Ayaseh, A., Dehghannya, J., Ehsani, A., Adun, P., 2020b.
 1675 Essential oil-loaded nanostructured lipid carriers: The effects of liquid lipid type on the
 1676 physicochemical properties in beverage models. Food Biosci. 35, 100526.

1677 <https://doi.org/10.1016/j.fbio.2020.100526>

1678 Batzri, S., Korn, E.D., 1973. Single bilayer liposomes prepared without sonication. *Biochim.*
1679 *Biophys. Acta - Biomembr.* 298, 1015–1019.

1680 Bayón-Cordero, L., Alkorta, I., Arana, L., 2019. Application of solid lipid nanoparticles to
1681 improve the efficiency of anticancer drugs. *Nanomaterials* 9, 474.

1682 Bazzaz, B.S.F., Khameneh, B., Namazi, N., Iranshahi, M., Davoodi, D., Golmohammadzadeh,
1683 S., 2018. Solid lipid nanoparticles carrying *Eugenia caryophyllata* essential oil : the novel
1684 nanoparticulate systems with broad-spectrum antimicrobial activity. *Lett. Appl.*
1685 *Microbiol.* 66, 506–513. <https://doi.org/10.1111/lam.12886>

1686 Beirão da costa, S., Duarte, C., Bourbon, A.I., Pinheiro, A.C., Januário, M.I.N., Vicente, A.A.,
1687 Beirão-da-costa, M.L., Delgadillo, I., 2013. Inulin potential for encapsulation and
1688 controlled delivery of oregano essential oil. *Food hydrocolloids.* 33, 199–206.
1689 <https://doi.org/10.1016/j.foodhyd.2013.03.009>

1690 Beirão da costa, S., Duarte, Claudia, Bourbon, A.I., Pinheiro, A.C., Teresa, A., Moldão, M.,
1691 Isabel, M., Januário, N., Vicente, A.A., Delgadillo, I., Duarte, Catarina, Luísa, M., 2012.
1692 Effect of the matrix system in the delivery and *in vitro* bioactivity of microencapsulated
1693 oregano essential oil. *J. Food Eng.* 110, 190–199.
1694 <https://doi.org/10.1016/j.jfoodeng.2011.05.043>

1695 Benhabiles, M.S., Salah, R., Lounici, H., Drouiche, N., Goosen, M.F.A., Mameri, N., 2012.
1696 Antibacterial activity of chitin, chitosan and its oligomers prepared from shrimp shell
1697 waste. *Food Hydrocoll.* 29, 48–56.

1698 Bilia, A.R., Guccione, C., Isacchi, B., Righeschi, C., Firenzuoli, F., Bergonzi, M.C., 2014.
1699 Essential oils loaded in nanosystems : A developing strategy for a successful therapeutic
1700 approach. *Evidence-Based Complement. Altern. Med.* 2014, 1–14.

1701 Boukroufa, M., Boutekedjiret, C., Petigny, L., Rakotomanomana, N., Chemat, F., 2015. Bio-

refinery of orange peels waste: A new concept based on integrated green and solvent free extraction processes using ultrasound and microwave techniques to obtain essential oil, polyphenols and pectin. *Ultrason. Sonochem.* 24, 72–79.

Calo, J.R., Crandall, P.G., O'Bryan, C.A., Ricke, S.C., 2015. Essential oils as antimicrobials in food systems – A review. *Food Control* 54, 111–119.

Calvo, P., Remunan Lopez, J.L., Vila-Jato, Alonso, M.J., 1997. Novel hydrophilic chitosan – polyethylene oxide nanoparticles as protein carriers. *J. Appl. Polym. Sci.* 63, 125–132.

Campo, C. De, Pereira, P., Maria, T., Costa, H., Guterres, S.S., Rios, A.D.O., Flôres, H., 2017. Nanoencapsulation of chia seed oil with chia mucilage (*Salvia hispanica* L.) as wall material: characterization and stability evaluation. *Food Chem.* 234, 1–9. <https://doi.org/10.1016/j.foodchem.2017.04.153>

Cao, Y., Zhou, W., Li, J., Huang, X., Yuan, Y., Lin, L., 2016. Preparation and stability evaluation of pectin coated galanga essential oil liposomes, in: 2nd International Conference on Architectural, Civil and Hydraulics Engineering (ICACHE 2016) Preparation. pp. 285–290.

Carneiro, H.C.F., Tonon, R. V, Grosso, C.R.F., Hubinger, M.D., 2013. Encapsulation efficiency and oxidative stability of flaxseed oil microencapsulated by spray drying using different combinations of wall materials. *J. Food Eng.* 115, 443–451. <https://doi.org/10.1016/j.jfoodeng.2012.03.033>

Carneiro, N.S., Alves, C.C., Alves, J.M., Egea, M.B., Martins, C.H., Silva, T.S., Bretanha, L.C., Balleste, M.P., Mlicke, G.A., Silveira, E. V, Miranda, M.L., 2017. Chemical composition, antioxidant and antibacterial activities of essential oils from leaves and flowers of *Eugenia klotzschiana* Berg (Myrtaceae). *An. Acad. Bras. Cienc.* 89.

Carvalho, A., Melo, V., Craveiro, A., Machado, M., Bantim, M., Rabelo, E., 2003. Larvicidal activity of the essential oil from *Lippia sidoides* Cham. against *Aedes aegypti* Linn. *Mem.*

1727 Inst. Oswaldo Cruz 98, 569–571.

1728 Carvalho, F.O., Silva, É.R., Nunes, P.S., Felipe, F.A., Ramos, K.P.P., Ferreira, L.A.S., Lima,
 1729 V.N.B., Shanmugam, S., Oliveira, A.S., Guterres, S.S., Camargo, E.A., Cravalho Olivera,
 1730 T.V., de Albuquerque Júnior, R.L.C., de Lucca Junior, W., Quintans-Júnior, L.J., Araújo,
 1731 A.A.S., 2020. Effects of the solid lipid nanoparticle of carvacrol on rodents with lung
 1732 injury from smoke inhalation. *Naunyn. Schmiedeberg's Arch. Pharmacol.* 393, 445–455.
 1733 <https://doi.org/10.1007/s00210-019-01731-1>

1734 Celia, C., Trapasso, E., Locatelli, M., Navarra, M., Anna, C., Wolfram, J., Carafa, M., Maria,
 1735 V., Britti, D., Di, L., Paolino, D., 2013. Anticancer activity of liposomal bergamot essential
 1736 oil (BEO) on human neuroblastoma cells. *Colloids Surfaces B Biointerfaces* 112, 548–
 1737 553. <https://doi.org/10.1016/j.colsurfb.2013.09.017>

1738 Ceole, L.F., Cardoso, M.D.G., Soares, M.J., 2017. Nerolidol, the main constituent of *Piper*
 1739 *aduncum* essential oil, has anti-Leishmania braziliensis activity. *Parasitology* 144, 1179–
 1740 1190.

1741 Cerri, G.C., Lima, L.C.F., Lelis, D. de F., Barcelos, L. da S., Feltenberger, J.D., Mussi, S.V.,
 1742 Monteiro-Junior, R.S., Santos, R.A.S. dos, Ferreira, L.A.M., Santos, S.H.S., 2019.
 1743 Sclareol-loaded lipid nanoparticles improved metabolic profile in obese mice. *Life Sci.*
 1744 218, 292–299. <https://doi.org/10.1016/j.lfs.2018.12.063>

1745 Chansang, A., Champakaew, D., Junkum, A., Amornlerdpison, D., Chaithong, U., Jitpakdi, A.,
 1746 Riyong, D., Wannasan, A., Intirach, J., Muangmoon, R., Pitasawat, B., 2018. Potential of
 1747 natural essential oils and cinnamaldehyde as insecticides against the dengue vector *Aedes*
 1748 *Aegypti* (Diptera: Culicidae). *Southeast Asian J. Trop. Med. Public Health* 49, 6–22.

1749 Chattopadhyay, S., Prez, F. Du, 2016. Simple design of chemically crosslinked plant oil
 1750 nanoparticles by triazolidione- ene chemistry. *Eur. Polym. J.* 81, 77–85.
 1751 <https://doi.org/10.1016/j.eurpolymj.2016.05.022>

1752 Chen, B., McClements, D.J., Decker, E.A., 2011. Minor components in food oils : A critical
 1753 review of their roles on lipid oxidation chemistry in bulk oils and emulsions. Crit. Rev.
 1754 Food Sci. Nutr. 51, 901–916. <https://doi.org/10.1080/10408398.2011.606379>

1755 Chen, Y.-F., Wang, Y.-W., Huang, W.-S., Lee, M.-M., Wood, W.G., Leung, Y.-M., Tsai, H.-
 1756 Y., 2016. Trans-cinnamaldehyde, an essential oil in cinnamon powder, ameliorates
 1757 cerebral ischemia-induced brain injury via inhibition of neuroinflammation through
 1758 attenuation of iNOS, COX-2 expression and NFκ-B signaling pathway. NeuroMolecular
 1759 Med. 18, 322-333.

1760 Cheng, Y.-T., Lu, C.-C., Yen, G. chin, 2015. Beneficial effects of camellia oil (*Camellia*
 1761 *oleifera* Abel.) on hepatoprotective and gastroprotective activities. J. Nutr. Sci. Vitaminol.
 1762 61, S100–S102.

1763 Cherkaoui-Tangi, K., Israili, Z.H., Lyoussi, B., 2016. Vasorelaxant effect of essential oil
 1764 isolated from *Nigella sativa* L. seeds in rat aorta: Proposed mechanism. Pak. J. Pharm. Sci.
 1765 29, 1–8.

1766 Chew, S.-C., Tan, C.-P., Tan, C.-H., Nyam, K.-L., 2020. *In vitro* bioaccessibility of spray dried
 1767 refined kenaf (*Hibiscus cannabinus*) seed oil applied in coffee drink. J. Food Sci. Technol.
 1768 57, 2507–2515. <https://doi.org/10.1007/s13197-020-04286-9>

1769 Chew, S.C., PingTan, C., Nyam, K.L., 2018. Microencapsulation of refined kenaf (*Hibiscus*
 1770 *cannabinus* L.) seed oil by spray drying using β -cyclodextrin / gum arabic / sodium
 1771 caseinate. J. Food Eng. J. 237, 78–85. <https://doi.org/10.1016/j.jfoodeng.2018.05.016>

1772 Chikezie, P.C., Ibegbulem, C.O., Mbagwu, F.N., 2015. Bioactive principles from medicinal
 1773 plants. Res. J. Phytochem. 9, 88–115. <https://doi.org/10.3923/rjphyto.2015.88.115>

1774 Chin, S., Ping, C., Lin, K., 2018. Microencapsulation of refined kenaf (*Hibiscus cannabinus*
 1775 L.) seed oil by spray drying using β -cyclodextrin / gum arabic / sodium caseinate. J. Food
 1776 Eng. 237, 78–85. <https://doi.org/10.1016/j.jfoodeng.2018.05.016>

1777 Chizzola, R., 2013. Regular monoterpenes and sesquiterpenes (essential oils), in: K. G.
 1778 Ramawat & J. M. Mérillon (Eds.), Natural products. Springer-Verlag Berlin Heidelberg,
 1779 pp. 2973–3008. <https://doi.org/10.1007/978-3-642-22144-6>
 1780 Christofoli, M., Cristina, E., Costa, C., Bicalho, K.U., Cássia, V. De, Fernandes, M., Cristina,
 1781 C., Alves, F., Araújo, W.L., Melo, C. De, 2015. Insecticidal effect of nanoencapsulated
 1782 essential oils from *Zanthoxylum rhoifolium* (Rutaceae) in *Bemisia tabaci* populations. Ind.
 1783 Crop. Prod. 70, 301–308. <https://doi.org/10.1016/j.indcrop.2015.03.025>
 1784 Conto, L.C. de, Oliveira, R.S.P., Martin, L.G.P., Chang, Y.K., Steel, C.J., 2012. Effects of the
 1785 addition of microencapsulated omega-3 and rosemary extract on the technological and
 1786 sensory quality of white pan bread. LWT - Food Sci. Technol. 45, 103–109.
 1787 Contri, R. V, Kulkamp-guerreiro, I.C., Janine, S., Frank, L.A., Pohlmann, A.R., Guterres, S.S.,
 1788 2016. Nanoencapsulation of Rose-Hip oil prevents oil oxidation and allows obtainment of
 1789 gel and film topical formulations. AAPS PharmSciTech 17, 863–871.
 1790 <https://doi.org/10.1208/s12249-015-0379-9>
 1791 Corrêa-Filho, L.C., Moldao-Martins, M., Alves, V.D., 2019. Advances in the application of
 1792 microcapsules as carriers of functional compounds for food products. Appl. Sci. 9, 571.
 1793 <https://doi.org/10.3390/app9030571>
 1794 Cortesi, R., Esposito, E., Gambarin, S., Telloli, P., Menegatti, E., Nastruzzi, C., 1999.
 1795 Preparation of liposomes by reverse-phase evaporation using alternative organic solvents.
 1796 J. Microencapsul. 16, 251–256.
 1797 Crucho, C.I.C., Barros, M.T., 2017. Polymeric nanoparticles: A study on the preparation
 1798 variables and characterization methods. Mater. Sci. Eng. C 80, 771–784.
 1799 Cui, H., Li, W., Li, C., Vittayapadung, S., Lin, L., 2016a. Liposome containing cinnamon oil
 1800 with antibacterial activity against methicillin-resistant *Staphylococcus aureus* biofilm.
 1801 Biofouling. 32, 215–225. <https://doi.org/10.1080/08927014.2015.1134516>

1802 Cui, H., Li, W., Lin, L., 2017a. Antibacterial activity of liposome containing curry plant
 1803 essential oil against *Bacillus cereus* in rice. J. food Saf. 37, 3–7.
 1804 <https://doi.org/10.1111/jfs.12302>

1805 Cui, H., Yuan, L., Ma, C., Li, C., Lin, L., 2017b. Effect of nianoliposome-encapsulated thyme
 1806 oil on growth of *Salmonella enteritidis* in chicken. J. food Process. Preserv. 41, 1–9.
 1807 <https://doi.org/10.1111/jfpp.13299>

1808 Cui, H., Zhao, C., Lin, L., 2015. The specific antibacterial activity of liposome-encapsulated
 1809 clove oil and its application in tofu. Food Control 56, 128–134.
 1810 <https://doi.org/10.1016/j.foodcont.2015.03.026>

1811 Cui, H., Zhou, H., Lin, L., 2016b. The specific antibacterial effect of the salvia oil
 1812 nanoliposomes against *Staphylococcus aureus* bio films on milk container. Food Control
 1813 61, 92–98. <https://doi.org/10.1016/j.foodcont.2015.09.034>

1814 Cui, Y., Wu, Z., Liu, X., Ni, R., Zhu, X., Ma, L., Liu, J., 2010. Preparation , safety ,
 1815 pharmacokinetics , and pharmacodynamics of liposomes containing *Brucea javanica* oil.
 1816 AAPS PharmSciTech 11, 878–884. <https://doi.org/10.1208/s12249-010-9454-4>

1817 De-Oliveira, E.F., Paula, H.C.B., De Paula, R.C.M., 2014. Alginate / cashew gum nanoparticles
 1818 for essential oil encapsulation. Colloids Surfaces B Biointerfaces. 113, 146–151.
 1819 <https://doi.org/10.1016/j.colsurfb.2013.08.038>

1820 De Billerbeck, V., 2007. Huiles essentielles et bactéries résistantes aux antibiotiques.
 1821 Phytothérapie 5, 249–253.

1822 De Meneses, A.C., Marques, E.B.P., Leimann, F.V., Gonçalves, O.H., Ineu, R.P., de Araújo,
 1823 P.H.H., de Oliveira, D., Sayer, C., 2019. Encapsulation of clove oil in nanostructured lipid
 1824 carriers from natural waxes: Preparation, characterization and *in vitro* evaluation of the
 1825 cholinesterase enzymes. Colloids Surfaces A Physicochem. Eng. Asp. 583, 123879.
 1826 <https://doi.org/10.1016/j.colsurfa.2019.123879>

1827 De Souza, E., De Lima, K.L., Freire, K., De Sousa, C., 2005. Inhibitory action of some essential
 1828 oils and phytochemicals on the growth of various moulds isolated from foods. Brazilian
 1829 Arch. Biol. Technol. 48, 245–250.

1830 Detoni, C.B., Oliveira, D.M. De, Santo, I.E., São Pedro, A., El-bacha, R., Velozo, E. da S.,
 1831 Ferreira, D., Elaine, C., Cabral-albuquerque, D.M., 2012. Evaluation of thermal-oxidative
 1832 stability and antiglioma activity of *Zanthoxylum tingoassuiba* essential oil entrapped into
 1833 multi- and unilamellar liposomes. J. Liposome Res. 22, 1–7.
 1834 <https://doi.org/10.3109/08982104.2011.573793>

1835 Devi, N., Deka, C., Hazarika, D., Kakati, D., 2012. Study of complex coacervation of gelatin
 1836 A and sodium alginate for microencapsulation of olive oil. J. Macromol. Sci. Part A 49,
 1837 936–945. <https://doi.org/10.1080/10601325.2012.722854>

1838 Dhavamani, S., Rao, Y.P.C., Lokesh, B.R., 2014. Total antioxidant activity of selected
 1839 vegetable oils and their influence on total antioxidant values in vivo. Food Chem. 164,
 1840 551–555.

1841 Dhifi, W., Bellili, S., Jazi, S., Bahloul, N., Mnif, W., 2016. Essential oils’ chemical
 1842 characterization and investigation of some biological activities: A critical review. Med. 3,
 1843 25.

1844 Diba, V.C., Statham, B.N., 2003. Contact urticaria from cinnamal leading to anaphylaxis.
 1845 Contact Dermatitis 48, 119.

1846 Dilika, F., Bremner, P., Meyer, J., 2000. Antibacterial activity of linoleic and oleic acids
 1847 isolated from *Helichrysum pedunculatum*: a plant used during circumcision rites.
 1848 Fitoterapia 71, 450–2.

1849 Dima, C., Assadpour, E., Dima, S., Jafari, S.M., 2020. Bioavailability and bioaccessibility of
 1850 food bioactive compounds; overview and assessment by *in vitro* methods. Compr. Rev.
 1851 Food Sci. Food Saf. 19, 2862–2884. <https://doi.org/10.1111/1541-4337.12623>

1852 Dima, C., Cotârlet, M., Alexe, P., Dima, S., 2014. Reprint of “ Microencapsulation of
1853 essential oil of pimento [*Pimenta dioica* (L) Merr .] by chitosan / k-carrageenan
1854 complex coacervation method”. Innov. Food Sci. Emerg. Technol. 25, 97–105.
1855 <https://doi.org/10.1016/j.ifset.2014.07.008>

1856 Dong, Z., Ma, Y., Hayat, K., Jia, C., Xia, S., Zhang, X., 2011. Morphology and release profile
1857 of microcapsules encapsulating peppermint oil by complex coacervation. J. Food Eng.
1858 104, 455–460. <https://doi.org/10.1016/j.jfoodeng.2011.01.011>

1859 Drozdek, S., Bazyli, U., 2016. Biocompatible oil core nanocapsules as potential co-carriers of
1860 paclitaxel and fluorescent markers : preparation, characterization and bioimaging. Colloid
1861 Polym. Sci. 294, 225–237. <https://doi.org/10.1007/s00396-015-3767-5>

1862 Dussault, D., Vu, K.D., Lacroix, M., 2014. *In vitro* evaluation of antimicrobial activities of
1863 various commercial essential oils, oleoresin and pure compounds against food pathogens
1864 and application in ham. Meat Sci. 96, 514–520.

1865 Duthie, G.G., Gardner, P.T., Morrice, P.C., McPhail, D.B., 2016. The Contribution of d α -
1866 tocopherol and d γ -tocopherol to the antioxidant capacity of several edible plant oil. Nat.
1867 Sci. 8, 41–48.

1868 Ekor, M., 2013. The growing use of herbal medicines: issues relating to adverse reactions and
1869 challenges in monitoring safety. Front. Pharmacol. 4, 177.

1870 El-Asbahani, Abdelhafed, Miladi, K., Addi, H., Bitar, A., Casabianca, H., Abdelhamid, E.M.,
1871 Hartmann, D., Jilale, A., Renaud, F., Elaissari, A., 2015. Antimicrobial activity of nano-
1872 encapsulated essential oils: comparison to non-encapsulated essential oils. J. Colloid Sci.
1873 Biotechnol. 4, 39–48.

1874 El-Asbahani, A, Miladi, K., Badri, W., Sala, M., Addi, E.H.A., Casabianca, H., Mousadik, A.
1875 El, Hartmann, D., Jilale, A., Renaud, F.N.R., Elaissari, A., 2015. Essential oils: From
1876 extraction to encapsulation. Int. J. Pharm. 483, 220-243.

1877 <https://doi.org/10.1016/j.ijpharm.2014.12.069>

1878 El-say, K.M., El-sawy, H.S., 2017. Polymeric nanoparticles : Promising platform for drug
1879 delivery. *Int. J. Pharm.* 528, 675–691. <https://doi.org/10.1016/j.ijpharm.2017.06.052>

1880 Elshafie, H.S., Ippolito, C., 2017. An overview of the biological effects of some mediterranean
1881 essential oils on human health. *Biomed Res. Int.* 2017, e9268468.

1882 Encina, C., Vergara, C., Gimenez, B., Oyarzún-ampuero, F., Robert, P., 2016. Conventional
1883 spray-drying and future trends for the microencapsulation of fish oil. *Trends Food Sci.*
1884 *Technol.* 56, 46–60. <https://doi.org/10.1016/j.tifs.2016.07.014>

1885 Engel, J.B., Heckler, C., Tondo, E.C., Daroit, D.J., Malheiros, P. ia da S., 2017. Antimicrobial
1886 activity of free and liposome-encapsulated thymol and carvacrol against *Salmonella* and
1887 *Staphylococcus aureus* adhered to stainless steel. *Int. J. Food Microbiol.* 252, 18–23.
1888 <https://doi.org/10.1016/j.ijfoodmicro.2017.04.003>

1889 Ephrem, E., Greige-Gerges, H., Fessi, H., Charcosset, C., 2014. Optimisation of rosemary oil
1890 encapsulation in polycaprolactone and scale-up of the process. *J. Microencapsul.* 31, 746–
1891 753. <https://doi.org/10.3109/02652048.2014.918669>

1892 Esfandyari-Manesh, M., Ghaedi, Z., Asemi, M., Khanavi, M., Manayi, A., Jamalifar, H.,
1893 Atyabi, F., Dinarvand, R., 2013. Study of antimicrobial activity of anethole and carvone
1894 loaded PLGA nanoparticles. *J. Pharm. Res.* 7, 290–295.
1895 <https://doi.org/10.1016/j.jopr.2013.04.019>

1896 Esmaeili, A., Asgari, A., 2015. In vitro release and biological activities of *Carum copticum*
1897 essential oil (CEO) loaded chitosan nanoparticles. *Int. J. Biol. Macromol.* 81, 283–290.
1898 <https://doi.org/10.1016/j.ijbiomac.2015.08.010>

1899 Falcao, D.Q., Mourao, S.C., Araujo, J.L. de, Pereira, P.A.K., Cardoso, A.C.A., Almeida, K.B.
1900 de, Zibetti, F.M., Lima, B.G., 2015. Chapter 23: Challenges in development of essential
1901 oil nanodelivery systems and future prospects, in Naik, J. (Ed.), *Nano Based Drug*

1902 Delivery. *Zagreb: IAPC*, pp. 557–578.. .

1903 Fang, Z., Bhandari, B., 2012. Spray drying , freeze drying and related processes for food
 1904 ingredient and nutraceutical encapsulation, in: Garti, N., McClements, D.J., (Eds.),
 1905 Encapsulation technologies and delivery systems for food ingredients and nutraceuticals.
 1906 Oxford: WP Woodhead Publishing, pp. 73 109.
 1907 <https://doi.org/10.1533/9780857095909.2.73>

1908 Fernandes, L.P., Turatti, I.C.C., Lopes, N.P., Ferreira, J.C., Candido, R.C., Oliveira, W.P.,
 1909 Fernandes, L.P., Turatti, I.C.C., Lopes, N.P., Ferreira, J.C., 2008. Volatile retention and
 1910 antifungal properties of spray- dried microparticles of *Lippia sidoides* essential oil. Dry.
 1911 Technol. 26, 1534–42. <https://doi.org/10.1080/07373930802464034>

1912 Fessi, H., Puisieux, F., Devissaguet, J.P., Ammoury, N., Benita, S., 1989. Nanocapsule
 1913 formation by interfacial polymer deposition following solvent displacement. Int. J. Pharm.
 1914 55, R1–R4.

1915 Feyzioglu, G.C., Tornuk, F., 2016. Development of chitosan nanoparticles loaded with summer
 1916 savory (*Satureja hortensis* L.) essential oil for antimicrobial and antioxidant delivery
 1917 applications. LWT - Food Sci. Technol. 70, 104–110.
 1918 <https://doi.org/10.1016/j.lwt.2016.02.037>

1919 Fioramonti, S.A., Stepanic, E.M., Tibaldo, A.M., Pavón, Y.L., Santiago, L.G., 2019. Spray
 1920 dried flaxseed oil powdered microcapsules obtained using milk whey proteins-alginate
 1921 double layer emulsions. Food Res. Int. 119, 931–940.
 1922 <https://doi.org/10.1016/j.foodres.2018.10.079>

1923 Frank, L.A., Contri, R. V, Beck, R.C.R., Pohlmann, A.R., Guterres, S.S., 2015. Improving drug
 1924 biological effects by encapsulation into polymeric nanocapsules. Adv. Rev. 7, 623–639.
 1925 <https://doi.org/10.1002/wnan.1334>

1926 Frascareli, E.C., Silva, V.M., Tonon, R. V, Hubinger, M.D., 2011. Effect of process conditions

1927 on the microencapsulation of coffee oil by spray drying. *Food Bioprod. Process.* 90, 413–
 1928 424. <https://doi.org/10.1016/j.fbp.2011.12.002>
 1929 Freiburger, E.B., Kaufmann, K.C., Bona, E., Araújo, P.H.H. de, Sayer, C., Leimann, F.V.,
 1930 Gonçalves, O.H., 2015. Encapsulation of roasted coffee oil in biocompatible
 1931 nanoparticles. *LWT - Food Sci. Technol.* 64, 381–359.
 1932 <https://doi.org/10.1016/j.lwt.2015.05.039>
 1933 Friedrich, R.B., Fontana, M.C., Beck, R.C.R., 2008. Development and physicochemical
 1934 characterization of dexamethasone-loaded polymeric nanocapsule suspensions. *Quim.*
 1935 *Nova* 31, 1131–1136.
 1936 Froiio, F., Ginot, L., Paolino, D., Lebaz, N., Bentaher, A., Fessi, H., Elaissari, A., 2019.
 1937 Essential oils-loaded polymer particles: Preparation, characterization and antimicrobial
 1938 property. *Polymers (Basel)*. 11, 1017. <https://doi.org/10.3390/polym11061017>
 1939 Froiio, F., Lammari, N., Tarhini, M., Alomari, M., Louaer, W., Meniai, A.H., Paolino, D., Fessi,
 1940 H., Elaissari, A., 2020. Chapter 16 - Polymer-based nanocontainers for drug delivery, in:
 1941 Tri, P.N., Do. T.O., Nguyen, T.A. (Eds.), *Smart Nanocontainers Micro and Nano*
 1942 *Technologies*. Elsevier Science Publishing Co Inc.: New York, USA. pp. 271–285.
 1943 Gad, H.A., Abd El-Rahman, F.A.A., Hamdy, G.M., 2019. Chamomile oil loaded solid lipid
 1944 nanoparticles: A naturally formulated remedy to enhance the wound healing. *J. Drug*
 1945 *Deliv. Sci. Technol.* 50, 329–338. <https://doi.org/10.1016/j.jddst.2019.01.008>
 1946 Gallardo, G., Guida, L., Martinez, V., López, M.C., Bernhardt, D., Blasco, R., Pedroza-islas,
 1947 R., Hermida, L.G., 2013. Microencapsulation of linseed oil by spray drying for functional
 1948 food application. *Food reseach Int.* 52, 473–482.
 1949 <https://doi.org/10.1016/j.foodres.2013.01.020>
 1950 Gammone, M.A., Riccioni, G., Parrinello, G., D’Orazio, N., 2019. Omega-3 polyunsaturated
 1951 fatty scids: Benefits and endpoints in Sport. *Nutrients* 11, 1–16.

1952 Ganesan, K., Sukalingam, K., Xu, B., 2018. Impact of consumption and cooking manners of
 1953 vegetable oils on cardiovascular diseases-A critical review. Trends Food Sci. Technol. 71,
 1954 132–154.

1955 Garcia-Rellán, D., Verdeguer, M., Salamone, A., Blázquez, M.A., Boira, H., 2016. Chemical
 1956 composition, herbicidal and antifungal activity of *Satureja cuneifolia* essential oils from
 1957 Spain. Nat. Prod. Commun. 2, 11-19.

1958 Garg, A., Singh, S., 2013. Targeting of eugenol-loaded solid lipid nanoparticles to the epidermal
 1959 layer of human skin. Nanomedicine 9, 1223–1238.

1960 Garg, A., Singh, S., 2011. Enhancement in antifungal activity of eugenol in immunosuppressed
 1961 rats through lipid nanocarriers. Colloids Surfaces B Biointerfaces 87, 280–288.
 1962 <https://doi.org/10.1016/j.colsurfb.2011.05.030>

1963 Garud, A., Singh, D., Garud, N., 2012. Solid lipid nanoparticles (SLN): Method ,
 1964 characterization and applications. Int. Curr. Pharm. J. 1, 384–393.

1965 Gavahian, M., Farahnaky, A., Farhoosh, R., Javidnia, K., Shahidi, F., 2015. Extraction of
 1966 essential oils from *Mentha piperita* using advanced techniques: Microwave versus ohmic
 1967 assisted hydrodistillation. Food Bioprod. Process. 94, 50–58.

1968 Ge, Y., Ge, M., 2016. Distribution of *Melaleuca alternifolia* essential oil in liposomes with
 1969 Tween 80 addition and enhancement of *in vitro* antimicrobial effect. J. Exp. Nanosci. 11,
 1970 345–358. <https://doi.org/10.1080/17458080.2015.1065013>

1971 Ge, Y. of tea tree oil-loaded liposomal formulation using response surface methodology D. of
 1972 tea tree oil-loaded liposomal formulation using response surface methodology, Ge, M.,
 1973 2015. Development of tea tree oil-loaded liposomal formulation using response surface
 1974 methodology. J. Liposome Res. 25, 222–231.
 1975 <https://doi.org/10.3109/08982104.2014.987786>

1976 Ge, Y., Tang, J., Fu, H., Fu, Y., Wu, Y., 2019. Characteristics , controlled-release and

1977 antimicrobial properties of Tea tree oil liposomes-incorporated chitosan-based electrospun
 1978 nanofiber mats. *Fibers Polym.* 20, 698–708. <https://doi.org/10.1007/s12221-019-1092-1>

1979 George, K.W., Alonso-gutierrez, J., Keasling, J.D., Lee, T.S., 2015. Isoprenoid drugs , biofuels
 1980 , and chemicals — Artemisinin , Farnesene and Beyond. *Adv. Biochem. Eng. Biotechnol.*
 1981 148, 355–89. <https://doi.org/10.1007/10>

1982 Geszke-Moritz, M., Moritz, M., 2016. Solid lipid nanoparticles as attractive drug vehicles:
 1983 Composition, properties and therapeutic strategies. *Mater. Sci. Eng. C* 68, 982–944.

1984 Ghanbarzadeh, B., Babazadeh, A., Hamishehkar, H., 2016. Nano-phytosome as a potential
 1985 food-grade delivery system. *Food Biosci.* 15, 126–135.

1986 Ghayempour, S., Montazer, M., 2016. Micro/nanoencapsulation of essential oils and
 1987 fragrances: Focus on perfumed, antimicrobial, mosquito-repellent and medical textiles. *J.*
 1988 *Microencapsul.* 33, 497–510. <https://doi.org/10.1080/02652048.2016.1216187>

1989 Ghodrati, M., Reza, M., Hamishehkar, H., 2019. Encapsulation of Peppermint essential oil in
 1990 nanostructured lipid carriers : *In vitro* antibacterial activity and accelerative effect on
 1991 infected wound healing. *Colloids Surfaces A* 564, 161–169.
 1992 <https://doi.org/10.1016/j.colsurfa.2018.12.043>

1993 Gökmen, V., Ataç, B., Barone, R., Fogliano, V., Kaplun, Z., Shimoni, E., 2011. Development
 1994 of functional bread containing nanoencapsulated omega-3 fatty acids. *J. Food Eng.* 105,
 1995 585–591. <https://doi.org/10.1016/j.jfoodeng.2011.03.021>

1996 Gomes, C., Moreira, R.G., Castell-perez, E., 2011a. Nanoparticles with entrapped trans -
 1997 cinnamaldehyde and eugenol for antimicrobial delivery applications. *J. Food Sci.* 76, 16–
 1998 24. <https://doi.org/10.1111/j.1750-3841.2010.01985.x>

1999 Gomes, C., Moreira, R.G., Castell-perez, E., 2011b. Poly (DL-lactide-co-glycolide) (PLGA)
 2000 nanoparticles with entrapped trans-cinnamaldehyde and eugenol for antimicrobial delivery
 2001 applications. *J. Food Sci.* 76, 16–24.

2002 González, A., Martínez, M.L., Paredes, A.J., León, A.E., Ribotta, P.D., 2016. Study of the
 2003 preparation process and variation of wall components in chia (*Salvia hispanica* L.) oil
 2004 microencapsulation. Powder Technol. 301, 868–875.
 2005 <https://doi.org/10.1016/j.powtec.2016.07.026>

2006 Guner, S.F., Yagci, Y., Erciyes, T.A., 2006. Polymers from triglyceride oils 31, 633–670.
 2007 <https://doi.org/10.1016/j.progpolymsci.2006.07.001>

2008 Hadian, Z., 2016. A review of nanoliposomal delivery system for stabilization of bioactive
 2009 omega-3 fatty acids. Electron. Physician 8, 1776–1785.

2010 Hadian, Z., Ali, M., Moghimi, H.R., Barzegar, M., 2014. Formulation , characterization and
 2011 optimization of liposomes containing eicosapentaenoic and docosahexaenoic acids ; A
 2012 methodology approach. Iran. J. Pharm. Res. 13, 393–404.

2013 Hammoud, Z., Gharib, R., Fourmentin, S., Elaissari, A., Greige-Gerges, H., 2019. New findings
 2014 on the incorporation of essential oil components into liposomes composed of lipoid S100
 2015 and cholesterol. Int. J. Pharm. 561, 161–170.
 2016 <https://doi.org/10.1016/j.ijpharm.2019.02.022>

2017 Hardman, D., Fakas, S., 2016. Polyunsaturated fatty acids as dietary supplements: Biological
 2018 activities and sources. Int. J. Clin. Nutr. Diet. 2, 2.

2019 Hasheminejad, N., Khodaiyan, F., Safari, M., 2019. Improving the antifungal activity of clove
 2020 essential oil encapsulated by chitosan nanoparticles. Food Chem. 275, 113–122.
 2021 <https://doi.org/10.1016/j.foodchem.2018.09.085>

2022 Hassanen, N.H.M., Eissa, A.M.F., Sa'eb A. M Hafez, Mosa, E.A.M., 2015. Antioxidant and
 2023 antimicrobial activity of celery (*Apium graveolens*) and coriander (*Coriandrum sativum*)
 2024 herb and seed essential oils. Int. J. Curr. Microbiol. Appl. Sci. 4, 284–296.

2025 Hassanshahian, M., Saadatfar, A., Masoumipour, F., 2020. Formulation and characterization of
 2026 nanoemulsion from *Alhagi maurorum* essential oil and study of its antimicrobial,

antibiofilm, and plasmid curing activity against antibiotic-resistant pathogenic bacteria. J. Environ. Heal. Sci. Eng. 18, 1015–1027.

He, H., Yao, J., Zhang, Y., Chen, Y., Wang, K., Lee, R.J., Yu, B., Zhang, X., 2019. Solid lipid nanoparticles as a drug delivery system to across the blood-brain barrier. Biochem. Biophys. Res. Commun. 519, 385–390. <https://doi.org/10.1016/j.bbrc.2019.09.017>

Herculano, E.D., Paula, H.C.B. De, Dias, F.G.B., Pereira, V.D.A., 2015. Physicochemical and antimicrobial properties of nanoencapsulated *Eucalyptus staigeriana* essential oil. LWT - Food Sci. Technol. 61, 484–491. <https://doi.org/10.1016/j.lwt.2014.12.001>

Hosseini, S.F., Zandi, M., Rezaei, M., Farahmandghavi, F., 2013. Two-step method for encapsulation of oregano essential oil in chitosan nanoparticles: Preparation , characterization and *in vitro* release study. Carbohydr. Polym. 95, 50–56. <https://doi.org/10.1016/j.carbpol.2013.02.031>

How, C.W., Rasedee, A., Abbasalipourkabir, R., 2013. Characterization and cytotoxicity of nanostructured lipid carriers formulated with olive oil, hydrogenated palm oil, and polysorbate 80. IEEE Trans. Nanobioscience 12, 72–78.

Hoyos-leyva, J.D., Bello-perez, L.A., Agama-acevedo, J.E., Alvarez-ramirez, J., Jaramillo-Echeverry, L.M., 2019. Characterization of spray drying microencapsulation of almond oil into taro starch spherical aggregates. LWT - Food Sci. Technol. 101, 526–533. <https://doi.org/10.1016/j.lwt.2018.11.079>

Hsu, E., Parthasarathy, S., 2017. Anti-inflammatory and antioxidant effects of sesame oil on atherosclerosis: A descriptive literature review. Cureus 9, 1438.

Hu, J., Wang, X., Xiao, Z., Bi, W., 2015. Effect of chitosan nanoparticles loaded with cinnamon essential oil on the quality of chilled pork. LWT - Food Sci. Technol. 63, 519–526. <https://doi.org/10.1016/j.lwt.2015.03.049>

Huang, J., Wang, Q., Chu, L., Xia, Q., 2020. Liposome-chitosan hydrogel bead delivery system

for the encapsulation of linseed oil and quercetin: Preparation and *in vitro* characterization studies. LWT - Food Sci. Technol. 117, 108615.

Iannitelli, A., Grande, R., di Stefano, A., di Giulio, M., Sozio, P., Bessa, L.J., Laserra, S., Paolini, C., Protasi, F., Cellini, L., 2011. Potential antibacterial activity of carvacrol-loaded poly(DL-lactide-co-glycolide) (PLGA) nanoparticles against microbial biofilm. Int. J. Mol. Sci. 12, 5039–5051. <https://doi.org/10.3390/ijms12085039>

Immordino, M.L., Dosio, F., Cattel, L., 2006. Stealth liposomes: Review of the basic science, rationale, and clinical applications, existing and potential. Int. J. Nanomedicine 1, 297–315.

Intahphuak, S., Khonsung, P., Panthong, A., 2010. Anti-inflammatory, analgesic, and antipyretic activities of virgin coconut oil. Pharm. Biol. 48, 151–157.

Jahromi, M.M., Zangabad, P.S., Basri, S.M., Zangabad, M.S., Ghamarypour, A., Aref, A., Karimi, M., Hamblin, M., 2018. Nanomedicine and advanced technologies for burns: preventing infection and facilitating wound healing. Adv. Drug Deliv. Rev. 123, 33–64.

Jajarm, F.H., Moravvej, G., Awal, M.M., Golmohammadzadeh, S., 2020. Insecticidal activity of solid lipid nanoparticle loaded by *Ziziphora clinopodioides* Lam. against *Tribolium castaneum* (Herbst, 1797) (Coleoptera: Tenebrionidae). Int. J. Pest Manag. <https://doi.org/10.1080/09670874.2020.1713420>.

Jamil, B., Abbasi, R., Abbasi, S., Imran, M., Khan, S.U., Ihsan, A., Javed, S., Bokhari, H., Imran, M., 2016. Encapsulation of cardamom essential oil in chitosan nano-composites : In-vitro efficacy on antibiotic-resistant bacterial pathogens and cytotoxicity studies. Front. Microbiol. 7, 1–10. <https://doi.org/10.3389/fmicb.2016.01580>

Jassbi, A.R., Zare, M., Jamebozorgi, F.H., 2017. Chemical composition and biological activity of the essential oil and solvent extracts of Scaligeria nodosa. Open Bioact. Compd. J. 5, 16–22.

2077 Javid, A., Raza, Z.A., Hussain, T., Rehman, A., Javid, A., Raza, Z.A., Hussain, T., Rehman,
 2078 A., 2014. Chitosan microencapsulation of various essential oils to enhance the functional
 2079 properties of cotton fabric chitosan microencapsulation of various essential oils to enhance
 2080 the functional properties of cotton fabric. J. Microencapsul. 31, 461–468.
 2081 <https://doi.org/10.3109/02652048.2013.879927>

2082 Jummes, B., Sganzerla, W.G., da Rosa, C.G., Noronha, C.M., Nunes, M.R., Bertoldi, F.C.,
 2083 Barreto, P.L.M., 2020. Antioxidant and antimicrobial poly-ε-caprolactone nanoparticles
 2084 loaded with *Cymbopogon martinii* essential oil. Biocatal. Agric. Biotechnol. 23, 101499.
 2085 <https://doi.org/10.1016/j.bcab.2020.101499>

2086 Kalamurthi, S., Selvaraj, G., 2016. Insight on solid lipid nanoparticles: characterization and
 2087 application in diabetes mellitus. J. Crit. Rev. 3, 11–16.

2088 Kanner, J., Lapidot, T., 2001. The stomach as a bioreactor: dietary lipid peroxidation in the
 2089 gastric fluid and the effects of plant-derived antioxidants. Free Radic. Biol. Med. 31, 1388–
 2090 1395. [https://doi.org/10.1016/S0891-5849\(01\)00718-3](https://doi.org/10.1016/S0891-5849(01)00718-3)

2091 Kaur, P., Thakur, R., Choudhary, A., 2012. An in vitro study of the antifungal activity of
 2092 silver/chitosan nanoformulations against important seed borne pathogens. Int. J. Sci.
 2093 Technol. Res. 1, 83–86.

2094 Khatibi, S.A., Misaghi, A., Moosavy, M.H., Basti, A.A., Mohamadian, S., Khanjari, A., 2017.
 2095 Effect of nanoliposomes containing *Zataria multiflora* Boiss . essential oil on gene
 2096 expression of Shiga toxin 2 in *Escherichia coli* O157 : H7. J. Appl. Microbiol. 124, 389–
 2097 397. <https://doi.org/10.1111/jam.13641>

2098 Khezri, K., Farahpour, M.R., Mounesi Rad, S., 2020. Efficacy of *Mentha pulegium* essential
 2099 oil encapsulated into nanostructured lipid carriers as an *in vitro* antibacterial and infected
 2100 wound healing agent. Colloids Surfaces A Physicochem. Eng. Asp. 589, 124414.
 2101 <https://doi.org/10.1016/j.colsurfa.2020.124414>

2102 Khezri, K., Farahpour, M.R., Rad, S.M., 2019. Accelerated infected wound healing by topical
 2103 application of encapsulated rosemary essential oil into nanostructured lipid carriers. *Artif.*
 2104 *Cells, Nanomedicine, Biotechnol.* 47, 980–988.

2105 Khoobdel, M., Ahsaei, S.M., Farzaneh, M., 2017. Insecticidal activity of polycaprolactone
 2106 nanocapsules loaded with *Rosmarinus officinalis* essential oil in *Tribolium castaneum*
 2107 (Herbst). *Entomol. Res.* 47, 175–184.

2108 Khosravi, K., 2013. Essential oils as natural food preservatives: Antimicrobial and antioxidant
 2109 applications, in: Doughari, J.H. (Ed.), *Antimicrobials from nature: effective control agents*
 2110 *for drug resistant pathogens*. Transworld research network, India. pp. 15–37.

2111 Kochikuzhyil, B.M., Devi, K., Fattepur, S.R., 2010. Effect of saturated fatty acid-rich dietary
 2112 vegetable oils on lipid profile, antioxidant enzymes and glucose tolerance in diabetic rats.
 2113 *Indian J. Pharmacol.* 42, 142–145.

2114 Krasodomska, O., Paolicelli, P., Cesa, S., Antonietta, M., Jungnickel, C., 2016. Protection and
 2115 viability of fruit seeds oils by nanostructured lipid carrier (NLC) nanosuspensions. *J.*
 2116 *Colloid Interface Sci.* 479, 25–33. <https://doi.org/10.1016/j.jcis.2016.06.041>

2117 Kris-Etherton, P.M., Harris, W.S., Appel, L.J., 2003. Omega-3 fatty acids and cardiovascular
 2118 disease: New recommendations from the american heart association. *J. Am. Heal. Assoc.*
 2119 23, 151–152.

2120 Kumar, A., Sharma, A., Upadhyaya, K.C., 2016. Vegetable oil: Nutritional and industrial
 2121 perspective. *Curr. Genomics* 17, 230–240.

2122 Kumari, A., Yadav, S.K., Yadav, S.C., 2010. Biodegradable polymeric nanoparticles based
 2123 drug delivery systems. *Colloids Surfaces B Biointerfaces* 75, 1–18.

2124 Lacatusu, I., Badea, N., Badea, G., Oprea, O., Mihaila, M.A., Kaya, D.A., Stan, R., Meghea,
 2125 A., 2015. Lipid nanocarriers based on natural oils with high activity against oxygen free
 2126 radicals and tumor cell proliferation. *Mater. Sci. Eng. C.* 56, 88–94.

2127 <https://doi.org/10.1016/j.msec.2015.06.019>

2128 Lacatusu, I., Mitrea, E., Badea, N., Stan, R., Oprea, O., Meghea, A., 2013. Lipid nanoparticles
 2129 based on omega-3 fatty acids as effective carriers for lutein delivery . Preparation and *in*
 2130 *vitro* characterization studies. J. Funct. Foods 5, 1260–1269.
 2131 <https://doi.org/10.1016/j.jff.2013.04.010>

2132 Lammari, N., Demautis, T., Louaer, O., Hassen, A., Bentaher, A., Elaissari, A., 2021.
 2133 Nanocapsules containing *Saussurea lappa* essential oil : Formulation, characterization,
 2134 antidiabetic, anti-cholinesterase and anti-inflammatory potentials. Int. J. Pharm. 593,
 2135 120138. <https://doi.org/10.1016/j.ijpharm.2020.120138>

2136 Lammari, N., Froiio, F., Louaer, M., Cristiano, M.C., Bensouici, C., Paolino, D., Louaer, W.,
 2137 Meniai, A.H., Elaissari, A., 2020. Poly (ethyl acrylate-co-methyl methacrylate-co-
 2138 trimethylammoniumethyl methacrylate chloride) (Eudragit RS 100) nanocapsules as
 2139 nanovector carriers for *Phoenix dactylifera* L. seeds oil: a versatile antidiabetic agent.
 2140 Biomacromolecules DOI: <https://dx.doi.org/10.1021/acs.biomac.0c00255>.
 2141 <https://doi.org/10.1021/acs.biomac.0c00255>

2142 Langenheim, J.H., 2003. *Plant resins: chemistry, evolution, ecology and ethnobotany*. Timber
 2143 Press, Portland, OR.

2144 Laohasongkram, K., Mahamaktudsanee, T., Chaiwanichsiri, S., 2011. Microencapsulation of
 2145 macadamia oil by spray drying. Ital. Oral Surg. 1, 1660–1665.
 2146 <https://doi.org/10.1016/j.profoo.2011.09.245>

2147 Laouini, A., Jaafer-Maalej, C., Limayem-Blouza, I., Sfar, S., Charcosset, C., Fessi, H., 2012.
 2148 Preparation , characterization and applications of liposomes : State of the art. J. Colloid
 2149 Sci. Biotechnol. 1, 147–168. <https://doi.org/10.1166/jcsb.2012.1020>

2150 Lee, S.Y., Kim, K.B.W.R., Lim, S.I., Ahn, D.H., 2014. Antibacterial mechanism of *Myagropsis*
 2151 *myagroides* extract on *Listeria monocytogenes*. Food Control 42, 23–28.

2152 Li, L., Au, W., Hua, T., Zhao, D., Wong, K., 2013. Improvement in antibacterial activity of
 2153 moxa oil containing gelatin-arabic gum microcapsules. Text. Res. J. 83, 1236–1241.

2154 Li, Y., Ai, L., Yokoyama, W., Shoemaker, C., Wei, D., Ma, J., Zhong, F., 2013. Properties of
 2155 chitosan-microencapsulated orange oil prepared by spray-drying and its stability to
 2156 detergents. J. Agric. Food Chem. 61, 3311–3319.

2157 Liakos, I.L., Grumezescu, A.M., Holban, A.M., Florin, I., D’Autilia, F., Carzino, R., Bianchini,
 2158 P., Athanassiou, A., 2016. Polylactic acid-lemongrass essential oil nanocapsules with
 2159 antimicrobial properties. Pharmaceuticals 9, 42. <https://doi.org/10.3390/ph9030042>

2160 Liakos, I.L., Iordache, F., Carzino, R., Scarpellini, A., Oneto, M., Bianchini, P., Grumezescu,
 2161 A.M., Holban, A.M., Mihai, A., Maria, A., 2018. Cellulose acetate - essential oil
 2162 nanocapsules with antimicrobial activity for biomedical applications. Colloids Surfaces B
 2163 Biointerfaces 172, 471–479. <https://doi.org/10.1016/j.colsurfb.2018.08.069>

2164 Limaverde, P.W., Campina, F.F., Cunha, F.A.. da, Crispim, F.D., Figueredo, F.G., Lima, L.F.,
 2165 Oliveira-Tintino, C.D. de M., Matos, Y.M.L.S. de, Morais-Braga, M.F.B., Menezes, I.R.,
 2166 Balbino, V.Q., Coutinho, H.D., Siqueira-Júnior, J.P., Almeida, J.R.G., Tintino, S.R.,
 2167 2017. Inhibition of the TetK efflux-pump by the essential oil of *Chenopodium*
 2168 *ambrosioides* L. and α -terpinene against *Staphylococcus aureus* IS-58. Food Chem.
 2169 Toxicol. 109, 957–961.

2170 Lin, L., Chen, W., Li, C., Cui, H., 2019a. Enhancing stability of *Eucalyptus citriodora* essential
 2171 oil by solid nanoliposomes encapsulation. Ind. Crops Prod. 140, 111615.
 2172 <https://doi.org/10.1016/j.indcrop.2019.111615>

2173 Lin, L., Gu, Y., Sun, Y., Cui, H., 2019b. Characterization of chrysanthemum essential oil triple-
 2174 layer liposomes and its application against *Campylobacter jejuni* on chicken. LWT - Food
 2175 Sci. Technol. 107, 16–24. <https://doi.org/10.1016/j.lwt.2019.02.079>

2176 Lin, L., Zhu, Y., Thangaraj, B., Abdel-samie, M.A.S., Cui, H., 2018. Improving the stability of

2177 thyme essential oil solid liposome by using β - cyclodextrin as a cryoprotectant.
 2178 Carbohydr. Polym. 188, 243–251. <https://doi.org/10.1016/j.carbpol.2018.02.010>
 2179 Liolios, C.C., Gortzi, O., Lalas, S., Tsaknis, J., Chinou, I., 2009. Liposomal incorporation of
 2180 carvacrol and thymol isolated from the essential oil of *Origanum dictamnus* L . and in
 2181 vitro antimicrobial activity. Food Chem. 112, 77–83.
 2182 <https://doi.org/10.1016/j.foodchem.2008.05.060>
 2183 Liu, C., Liang, B., Shi, G., Li, Z., Zheng, X., 2015. Preparation and characteristics of
 2184 nanocapsules containing essential oil for textile application. Flavour Fragr. J. 30, 295–301.
 2185 <https://doi.org/10.1002/ffj.3245>
 2186 Liu, N., Guan, T., Zhou, W., Li, J., Cao, Y., Lin, L., 2016. Preparation and characterization of
 2187 Galanga essential oil liposomes. In: The 2016 International Conference on Advances in
 2188 Energy, Environment and Chemical Science (AEECS 2016). pp. 99–105.
 2189 Liu, Y., Wang, S., Zhang, R., Lan, W., Qin, W., 2017. Development of poly (lactic acid)/
 2190 chitosan fibers loaded with essential oil for antimicrobial applications. Nanomaterials. 7,
 2191 194. <https://doi.org/10.3390/nano7070194>
 2192 Lligadas, G., Ronda, J.C., Galia, M., Cadiz, V., 2010. Plant oils as platform chemicals for
 2193 polyurethane synthesis : current state-of-the-art. Biomacromolecules. 11, 2825–2835.
 2194 López-meneses, A.K., Plascencia-jatomea, M., Lizardi-mendoza, J., Fernández-quiroz, D.,
 2195 2018. *Schinus molle* L . essential oil-loaded chitosan nanoparticles : Preparation,
 2196 characterization, antifungal and anti-aflatoxigenic properties. LWT - Food Sci. Technol.
 2197 96, 597–603. <https://doi.org/10.1016/j.lwt.2018.06.013>
 2198 Lozano, M., Gonza, D., Calvo, P., Herna, T., 2012. Microencapsulation of extra-virgin olive
 2199 oil by spray-drying : Influence of wall material and olive quality. Eur. J. lipid Sci. Technol.
 2200 112, 852–858. <https://doi.org/10.1002/ejlt.201000059>
 2201 Luque-Alcaraz, A.G., Cortez-Rocha, M.O., Velázquez-Contreras, C.A., Acosta-Silva, A.L.,

2202 Santacruz-Ortega, H.D.C., Burgos-Hernández, A., Argüelles-Monal, W.M., Plascencia-
 2203 Jatomea, M., 2016. Enhanced antifungal effect of chitosan/Pepper tree (*Schinus molle*)
 2204 essential oil bionanocomposites on the viability of *Aspergillus parasiticus* spores. J.
 2205 Nanomater. 2016, 6060137. <https://doi.org/10.1155/2016/6060137>
 2206 Lv, Y., Yang, F., Li, X., Zhang, X., Abbas, S., 2014. Formation of heat-resistant nanocapsules
 2207 of jasmine essential oil via gelatin / gum arabic based complex coacervation. Food
 2208 Hydrocolloids. 35, 305–314. <https://doi.org/10.1016/j.foodhyd.2013.06.003>
 2209 Maccioni, A., Santo, A., Falconieri, D., Piras, A., Manconi, M., Maxia, A., Bacchetta, G., 2019.
 2210 Inhibitory effect of rosemary essential oil, loaded in liposomes, on seed germination of
 2211 *Acacia saligna* (Labill.) Wendl., an invasive species in Mediterranean ecosystems. Botany
 2212 97, 283–291.
 2213 Mai, C.H., LE, T.T.T., Diep, T.T., Le, T.H.N., Nguyen, D.T., Bach, L.G., 2018. Development
 2214 of solid lipid nanoparticles of Gac (*Momordica cochinchinensis* Spreng) oil by nano-
 2215 emulsion technique. Asian J. Chem. 30, 293–297.
 2216 <https://doi.org/10.14233/ajchem.2018.20902>
 2217 Mainardi, T., Kapoor, S., Bielory, L., 2009. Complementary and alternative medicine: herbs,
 2218 phytochemicals and vitamins and their immunologic effects. J. allergu cinical Immunol.
 2219 123, 283–94.
 2220 Manconi, M., Petretto, G., Guy, D., Escibano, E., Milia, E., Pinna, R., Palmieri, A.,
 2221 Firoznezhad, M., Peris, J.E., Usach, I., Fadda, A.M., Caddeo, C., Manca, M.L., 2018.
 2222 Thymus essential oil extraction, characterization and incorporation in phospholipid
 2223 vesicles for the antioxidant / antibacterial treatment of oral cavity diseases. Colloids
 2224 Surfaces B Biointerfaces 171, 115–122. <https://doi.org/10.1016/j.colsurfb.2018.07.021>
 2225 Mandal, S.M., Roy, A., Ghosh, A.K., Hazra, T.K., Basak, A., Franco, O.L., 2014. Challenges
 2226 and future prospects of antibiotic therapy: from peptides to phages utilization. Front.

2227 Pharmacol. 5, 105.

2228 Marchiori, M.C.L., Rigon, C., Camponogara, C., Oliveira, S.M., Cruz, L., 2017. Hydrogel
 2229 containing silibinin-loaded pomegranate oil based nanocapsules exhibits anti-
 2230 inflammatory effects on skin damage UVB radiation-induced in mice. J. Photochem.
 2231 Photobiol. ,B Biol. 170, 25–32. <https://doi.org/10.1016/j.jphotobiol.2017.03.015>

2232 Márquez-Ruiz, G., García-Martínez, M.C., Holgado, F., 2008. Changes and effects of dietary
 2233 oxidized lipids in the gastrointestinal tract. Lipids insights 11–19.

2234 Maryam, I., Huzaifa, U., Hindatu, H., Zubaida, S., 2015. Nanoencapsulation of essential oils
 2235 with enhanced antimicrobial activity : A new way of combating antimicrobial Resistance.
 2236 J. Pharmacogn. Phytochem. 4, 165–170.

2237 Matos, S.P. De, Lucca, L.G., Koester, L.S., 2019. Essential oils in nanostructured systems :
 2238 Challenges in preparation and analytical methods. Talanta 195, 204–214.
 2239 <https://doi.org/10.1016/j.talanta.2018.11.029>

2240 Matthäus, B., 2010. Oxidation of edible oils, in: Decker, E.A., Elias, R.J., McClements, D.J.
 2241 (Eds.), Oxidation in foods and beverages and antioxidant applications. Woodhead
 2242 Publishing Limited, pp. 183–283.

2243 Mattheolabakis, G., Rigas, B., Constantinides, P, A., 2012. Nanodelivery strategies in cancer
 2244 chemotherapy: biological rationale and pharmaceutical perspectives. Nanomedicine 10,
 2245 1577-1590.

2246 McDaniel, A., Tonyali, B., Yucel, U., Trinetta, V., 2019. Formulation and development of lipid
 2247 nanoparticle antifungal packaging films to control postharvest disease. J. Agric. Food Res.
 2248 1, 100013. <https://doi.org/10.1016/j.jafr.2019.100013>

2249 Mehnert, W., Mäder, K., 2012. Solid lipid nanoparticles: Production, characterization and
 2250 applications. Adv. Drug Deliv. Rev. 64, 83–101.

2251 Meier, M.A.R., Jurgen, M.O., Schubert, U.S., 2007. Plant oil renewable resources as green

2252 alternatives in polymer science. Chem. Soc. Rev. 36, 1788–1802.
 2253 <https://doi.org/10.1039/b703294c>

2254 Miao, S., Wang, P., Su, Z., Zhang, S., 2014. Vegetable-oil-based polymers as future polymeric
 2255 biomaterials. Acta Biomater. 10, 1692–1704. <https://doi.org/10.1016/j.actbio.2013.08.040>

2256 Miladi, K., Sfar, S., Fessi, H., Elaissari, A., 2016. Nanoprecipitation process : From particle
 2257 preparation to in vivo applications, in: Vauthier, C., Ponchel, G. (Eds.), Polymer
 2258 Nanoparticles for Nanomedicines. Springer: Cham, Switzerland, pp. 17–53.
 2259 <https://doi.org/10.1007/978-3-319-41421-8>

2260 Miranda, M., Cruz, M.T., Vitorino, C., Cabral, C., 2019. Nanostructuring lipid carriers using
 2261 *Ridolfia segetum* (L.) Moris essential oil. Mater. Sci. Eng. C 103, 109804.
 2262 <https://doi.org/10.1016/j.msec.2019.109804>

2263 Mishra, H., Mishra, P.K., Iqbal, Z., Jaggi, M., Madaan, A., Bhuyan, K., Gupta, Namita, Gupta,
 2264 Neha, Vats, K., Verma, R., Talegaonkar, S., 2019. Co-delivery of eugenol and dacarbazine
 2265 by hyaluronic acid-coated liposomes for targeted inhibition of survivin in treatment of
 2266 resistant metastatic melanoma. Pharmaceutics 11, 163.

2267 Moghaddam, M., Mehdizadeh, L., 2017. Chemistry of essential oils and factors influencing
 2268 their constituents, in: Grumezescu, A.M., Holban, A.M. (Eds.), Soft Chemistry and Food
 2269 Fermentation. Elsevier Science Publishing Co Inc., New York., pp. 379–419.
 2270 <https://doi.org/10.1016/B978-0-12-811412-4.00013-8>

2271 Mohammed, N.K., Tan, C., Manap, Y.A., Alhelli, A.M., Hussin, A.S.M., 2017. Process
 2272 conditions of spray drying microencapsulation of *Nigella sativa* oil. Powder Technol. 315,
 2273 1–14. <https://doi.org/10.1016/j.powtec.2017.03.045>

2274 Morsy, N.F.S., 2017. Chemical structure, quality indices and bioactivity of essential oil
 2275 constituents, in: El-Shemy, H. (Ed.), Active Ingredients from Aromatic and Medicinal
 2276 Plants. IntechOpen, Spain, pp. 175–206.

2277 Mozafari, M.R., Khosravi-Darani, K., Borazan, G.G., Cui, J., Pardakhty, A., Yurdugul, S.,
 2278 2008. Encapsulation of food ingredients using nanoliposome technology. *Int. J. Food Prop.*
 2279 11, 833-844.

2280 Mozafari, M.R., Mortazavi, S.M., 2005. A new technique for the preparation of non-toxic
 2281 liposomes and nanoliposomes: The heating method, in: *Nanoliposomes: From*
 2282 *Fundamentals to Recent Developments..* Trafford Publishing Ltd., Oxford, UK.. pp. 91–
 2283 98.

2284 Nagavarma, B.V.N., Yadav, H.K.S., Ayaz, A., Vasudha, L.S., Shivakumar, H.G., 2012.
 2285 Different techniques for preparation of polymeric nanoparticles-A review. *Asian J. Pharm.*
 2286 *Clin. Res.* 5, e33413145.

2287 Nahr, F.K., Ghanbarzadeh, B., Hamishehkar, H., Kafil, H.S., 2018. Food grade nanostructured
 2288 lipid carrier for cardamom essential oil : Preparation, characterization and antimicrobial
 2289 activity. *J. Funct. Foods* 40, 1–8. <https://doi.org/10.1016/j.jff.2017.09.028>

2290 Nahr, F.K., Ghanbarzadeh, B., Hamishehkar, H., Samadi, H., Hoseini, M., Esmailnejad, B.,
 2291 2019. Investigation of physicochemical properties of essential oil loaded nanoliposome for
 2292 enrichment purposes. *LWT - Food Sci. Technol.* 105, 282–289.
 2293 <https://doi.org/10.1016/j.lwt.2019.02.010>

2294 Najafi, M.N., Arianmehr, A., Sani, A.M., 2020. Preparation of Barije (*Ferula gummosa*)
 2295 essential oil-loaded liposomes and evaluation of physical and antibacterial effect on
 2296 *Escherichia coli* O157:H7. *J. Food Prot.* 83, 511–517.

2297 Nasser, M., Golmohammadzadeh, S., Arouiee, H., Jaafari, M.R., Neamati, H., 2020.
 2298 Preparation and comparison of various formulations of solid lipid nanoparticles (SLNs)
 2299 containing the essential oil of *Zataria multiflora*. *J. Hortic. postharvest Res.* 3, 73–84.

2300 Nasser, M., Golmohammadzadeh, S., Arouiee, H., Reza, M., Neamati, H., 2016. Antifungal
 2301 activity of *Zataria multiflora* essential oil-loaded solid lipid nanoparticles *in-vitro*

2302 condition. Iran. J. Basic Med. Sci. 19, 1231–1237.

2303 Natrajan, D., Srinivasan, S., Sundar, K., Ravindran, A., 2015. Formulation of essential oil-

2304 loaded chitosan alginate nanocapsules. J. Food Drug Anal. 23, 560–568.

2305 <https://doi.org/10.1016/j.jfda.2015.01.001>

2306 Nazari, M., Ghanbarzadeh, B., Kafil, H.S., Zeinali, M., 2019. Garlic essential oil

2307 nanophytosomes as a natural food preservative : Its application in yogurt as food model.

2308 Colloid interface Sci. Commun. 30, 1–7. <https://doi.org/10.1016/j.colcom.2019.100176>

2309 Niza, E., Božik, M., Bravo, I., Clemente-Casares, P., Lara-Sanchez, A., Juan, A., Klouček, P.,

2310 Alonso-Moreno, C., 2020. PEI-coated PLA nanoparticles to enhance the antimicrobial

2311 activity of carvacrol. Food Chem. 328, 127131.

2312 Nkanga, C.I., Bapolisi, A.M., Okafor, N.I., Krause, R.W.M., 2019. General perception of

2313 liposomes : Formation, manufacturing and applications, in: Catala, A. (Ed.), Liposomes -

2314 Advances and Perspectives. IntechOpen, Spain., pp. 1–24.

2315 Nonato, F.R., Santana, D.G., Melo, F.M. de, Santos, G.G.L. dos, Brustolim, D., Camargo, E.A.,

2316 Sousa, D.P. de, Soares, M.B.P., Villarreal, C.F., 2012. Anti-inflammatory properties of

2317 rose oxide. Int. Immunopharmacol. 14, 4(4):779-84.

2318 Noor, N.M., Aziz, A.A., Sarmidi, M.R., Aziz, R., 2013. The effect of virgin coconut oil loaded

2319 solid lipid particles (VCO-SLPs) on skin hydration and skin elasticity. J. Teknol. 62, 39–

2320 43.

2321 Nosari, A.B.F.L., Lima, J.F., Serra, O.A., Alexandre, L., Freitas, P., 2015. Improved green

2322 coffee oil antioxidant activity for cosmetical purpose by spray drying microencapsulation.

2323 Rev. Bras. Farmacogn. 25, 307–311. <https://doi.org/10.1016/j.bjp.2015.04.006>

2324 Orhan, I.E., Mesaik, M.A., Jabeen, A., Kan, Y., 2016. Immunomodulatory properties of various

2325 natural compounds and essential oils through modulation of human cellular immune

2326 response. Ind. Crops Prod. 81, 117–122.

- 2327 Orhan, I.R., Özçelik, B., Şener, B., 2011. Evaluation of antibacterial, antifungal, antiviral, and
2328 antioxidant potentials of some edible oils and their fatty acid profiles. *Turkish J. Biol.* 35,
2329 251–258.
- 2330 Ortan, A., Câmpeanu, G., Dinu-Pîrvu, C., Popescu, L., 2009. Studies concerning the entrapment
2331 of *Anethum graveolens* essential oil in liposomes. *Roum. Biotechnol. Lett.* 14, 4411–4417.
- 2332 Ortan, A., Ferdes, M., Rodino, S., Pîrvu, C.D., Drăganescu, D., 2013. Topical delivery system
2333 of liposomally encapsulated volatile oil of *Anethum Graveolens*. *Farmacia* 61, 361–370.
- 2334 Ourique, A., Azoubel, S., Ferreira, C., Silva, C., Marchiori, M., Pohlmann, A., Guterres, S.,
2335 Beck, R., 2010. Lipid-core nanocapsules as a nanomedicine for parenteral administration
2336 of tretinoin: development and in vitro antitumor activity on human myeloid leukaemia
2337 cells. *J. Biomed. Nanotechnol.* 6, 214–23.
- 2338 Özçelik, B., Aslan, M., Orhan, I., Karaoglu, T., 2005. Antibacterial, antifungal, and antiviral
2339 activities of the lipophylic extracts of *Pistacia vera* L. *Microbiol. Res.* 160, 159–64.
- 2340 Ozek, G., Schepetkin, I.A., Utegenova, G.A., Kirpotina, L.N., Andrei, S.R., Ozek, T., Baser,
2341 K.H.C., Abidkulova, K.T., Kushnarenko, S. V, Khlebnikov, A.I., Damron, D.S., Quinn,
2342 M.T., 2017. Chemical composition and phagocyteimmunomodulatory activity of *Ferula*
2343 *iliensis* essential oils. *J. Leukoc. Biol.* 101, 1361–1371.
- 2344 Ozyıldız, F., Karagonlu, S., Basal, G., Uzel, A., Bayraktar, O., 2012. Micro-encapsulation of
2345 ozonated red pepper seed oil with antimicrobial activity and application to nonwoven
2346 fabric. *Lett. Appl. Microbiol.* 56, 168–179. <https://doi.org/10.1111/lam.12028>
- 2347 Pandey, A.K., Kumar, P., Singh, P., Tripathi, N.N., Bajpai, V.K., 2016. Essential oils: Sources
2348 of antimicrobials and food preservatives. *Front. Microbiol.* 7, 1–14.
- 2349 Patel, D., 2013. Development & screening approach for lipid nanoparticle: A review. *Int. J.*
2350 *Innov. Pharm. Sci.* 2, 27–32.
- 2351 Patil, Y., Jadhav, S., 2014. Novel methods for liposome preparation. *Chem. Phys. Lipids* 177,

2352 8–18.

2353 Paula, H.C.B., Sombra, F.M., Abreu, F.O.M.S., Paula, R.C.M., 2010. *Lippia sidoides* essential
 2354 oil encapsulation by angico gum/chitosan nanoparticles. J. Braz. Chem. Soc. 21, 2359–
 2355 2366.

2356 Pedro, A.S., Santo, I.E., Silva, C. V, Detoni, C., Albuquerque, E., 2013. The use of
 2357 nanotechnology as an approach for essential oil-based formulations with antimicrobial
 2358 activity. In: Méndez-vilas, A. (Ed.), Microbial pathogens and strategies for combating
 2359 them: science, technology and education. Badajoz : Formatex Research Center, pp. 1364–
 2360 1374.

2361 Peng, S., Zhou, L., Liu, Wei, Gan, L., Liu, Weilin, Liang, R., Liu, C., Niu, J., Cao, Y., Liu, Z.,
 2362 Chen, X., 2015. Strage stability and actibacterial activity of eugenol nanoliposomes
 2363 prepared by an ethanol injection-dynamic high pressure microfluidization method. J. o f
 2364 Food Prot. 78, 22–30. <https://doi.org/10.4315/0362-028X>

2365 Pina-Barrera, A.M., Alvarez-Roman, R., Baez-Gonzalez, J.G., Amaya-Guerra, C.A., Rivas-
 2366 Morales, C., Gallardo-Rivera, C.T., Galindo-Rodriguez, S.A., 2019. Application of a
 2367 multisystem coating based on polymeric nanocapsules containing essential oil of *Thymus*
 2368 *vulgaris* L. to increase the shelf life of table grapes (*Vitis vinifera* L.). IEEE Trans.
 2369 Nanobioscience 18, 549–557. <https://doi.org/10.1109/TNB.2019.2941931>

2370 Pivetta, T.P., Simões, S., Araújo, M.M., Carvalho, T., Arruda, C., Marcato, P.D., 2018.
 2371 Development of nanoparticles from natural lipids for topical delivery of thymol :
 2372 Investigation of its anti-inflammatory properties. Colloids Surfaces B Biointerfaces 164,
 2373 281–290. <https://doi.org/10.1016/j.colsurfb.2018.01.053>

2374 Popiolski, T.M., Otsuka, I., Halila, S., Muniz, E.C., Soldi, V., Borsali, R., Catarina, F.D.S.,
 2375 2016. Preparation of polymeric micelles of poly (Ethylene oxide- b -lactic acid) and their
 2376 encapsulation with lavender oil. Mater. Res. 19, 1356–1365.

2377 Poudel, A., Gachumi, G., Wasan, K.M., Bashi, Z.D., El Aneed, A., Badea, I., 2019.
 2378 Development and characterization of liposomal formulations containing phytosterols
 2379 extracted from canola oil deodorizer distillate along with tocopherols as food additives.
 2380 Pharmaceutics 11, 185. <https://doi.org/10.3390/pharmaceutics11040185>

2381 Priyadarshini, B.M., Antipina, M.N., Fawzy, A.S., 2018. Formulation and characterisation of
 2382 poly (lactic-co-glycolic acid) encapsulated clove oil nanoparticles for dental applications.
 2383 Inst. Eng. Technol. 12, 311–317. <https://doi.org/10.1049/iet-nbt.2017.0141>

2384 Pu, J., Bankston, J.D., Sathivel, S., 2010. Developing microencapsulated flaxseed oil containing
 2385 shrimp (*Litopenaeus setiferus*) astaxanthin using a pilot scale spray. Biosyst. Eng. 108,
 2386 121–132. <https://doi.org/10.1016/j.biosystemseng.2010.11.005>

2387 Purohit, S., Solanki, R., Soni, M., 2012. Experimental evaluation of *Aloe vera* leaves pulp as
 2388 topical medicament on wound healing. Int. J. Pharmacol. Res. 2, 110–112.

2389 Rahman, H.S., Rasedee, A., How, C.W., Abdul, A.B., Zeenathul, A.N., Othman, H.H., Saeed,
 2390 M.I., Yeap, S.K., 2013. Zerumbone-loaded nanostructured lipid carriers : preparation,
 2391 characterization, and antileukemic effect. Int. J. Nanomedicine 8, 2769–2781.

2392 Rahman, H.S., Rasedee, A., Othman, H.H., Chartrand, M.S., Namvar, F., Yeap, S.K., Samad,
 2393 N.A., Andas, R.J., Nadzri, N.M., Anasamy, T., Ng, K., How, C.W., 2014. Acute toxicity
 2394 study of zerumbone-loaded nanostructured lipid carrier on BALB/c mice model. Biomed
 2395 Res. Int. 2014, 1–15.

2396 Rajendran, R., Radhai, R., Kotresh, T.M., Csiszar, E., 2013. Development of antimicrobial
 2397 cotton fabrics using herb loaded nanoparticles. Carbohydr. Polym. 91, 613–617.
 2398 <https://doi.org/10.1016/j.carbpol.2012.08.064>

2399 Rajivgandhi, G., Saravanan, K., Ramachandran, G., Li, J., Yin, L., Quero, F., Alharbi, N.S.,
 2400 Kadaikunnan, S., Khaled, J.M., Manoharan, N., Li, W., 2020. Enhanced anti-cancer
 2401 activity of chitosan loaded *Morinda citrifolia* essential oil against A549 human lung cancer

cells. Int. J. Biol. Macromol. 164, 4010–4021.

Rajkumar, V., Gunasekaran, C., Dharmaraj, J., Chinnaraj, P., Paul, C.A., Kanithachristy, I., 2020. Structural characterization of chitosan nanoparticle loaded with *Piper nigrum* essential oil for biological efficacy against the stored grain pest control. Pestic. Biochem. Physiol. 166, 104566.

Ramteke, K.H., Joshi, S.A., Dhole, S.N., 2012. Solid lipid nanoparticle : A review. IOSR J. Pharm. 2, 34–44.

Rani, S., Sharma, A.K., Khan, I., Gothwal, A., 2017. Polymeric nanoparticles in targeting and delivery of drugs, in Nanotechnology-Based Approaches for Targeting and delivery of Drugs and Genes. Elsevier Science Publishing Co Inc.: New York, USA. <https://doi.org/10.1016/B978-0-12-809717-5.00008-7>

Rao, J.P., Geckeler, K.E., 2011. Polymer nanoparticles : Preparation techniques and size-control parameters. Prog. Polym. Sci. 36, 887–913. <https://doi.org/10.1016/j.progpolymsci.2011.01.001>

Rasti, B., Jinap, S., Mozafari, M.R., 2013. Optimization on preparation condition of polyunsaturated fatty acids nanoliposome prepared by Mozafari method. J. Liposome Res. 2104, 1–7. <https://doi.org/10.3109/08982104.2013.839702>

Rasti, B., Jinap, S., Mozafari, M.R., Yazid, A.M., 2012. Comparative study of the oxidative and physical stability of liposomal and nanoliposomal polyunsaturated fatty acids prepared with conventional and Mozafari methods. Food Chem. 135, 2761–2770. <https://doi.org/10.1016/j.foodchem.2012.07.016>

Rates, S.M.K., 2001. Plants as source of drugs. Toxicon 39, 603–613.

Raut, J.S., Karuppayil, S.M., 2014. Experimental evaluation of *Aloe vera* leaves pulp as topical medicament on wound healing. Ind. Crop. Prod. 62, 250–264.

Rein, M.J., Renouf, M., Cruz-Hernandez, C., Actis-Goretta, L., Thakkar, S.K., da Silva Pinto,

2427 M., 2013. Bioavailability of bioactive food compounds: a challenging journey to
 2428 bioefficacy. Br. J. Clin. Pharmacol. 75, 588–602. <https://doi.org/10.1111/j.1365->
 2429 2125.2012.04425.x

2430 Ribeiro-Santos, R., Andrade, M., Melo, N.R. de, Sanches-Silva, A., 2017. Use of essential oils
 2431 in active food packaging: Recent advances and future trends. Trends Food Sci. Technol.
 2432 61, 132–140.

2433 Rigo, L.A., Frescura, V., Fiel, L., Coradini, K., Ourique, A.F., Emanuelli, T., Tedesco, S., Silva,
 2434 C.B., Stanic, S., Pohlmann, A.R., Carlos, R., Beck, R., 2013. Influence of the type of
 2435 vegetable oil on the drug release profile from lipid-core nanocapsules and in vivo
 2436 genotoxicity study. Pharm. Technol. Dev. 1–10.
 2437 <https://doi.org/10.3109/10837450.2013.829097>

2438 Rigo, L.A., Silva, C.R., Oliveira, S.M., Cabreira, T.N., Silva, C.B., Ferreira, J., Beck, R.C.R.,
 2439 2015. Nanoencapsulation of rice bran oil increases its protective effects against UVB
 2440 radiation-induced skin injury in mice. Eur. J. Pharm. Biopharm. 93, 11–17.
 2441 <https://doi.org/10.1016/j.ejpb.2015.03.020>

2442 Risaliti, L., Kehagia, A., Daoultzi, E., Lazari, D., Bergonzi, M.C., Vergkizi-nikolakaki, S.,
 2443 Hadjipavlou-litina, D., Bilia, A.R., 2019. Liposomes loaded with *Salvia triloba* and
 2444 *Rosmarinus officinalis* essential oils : *In vitro* assessment of antioxidant , antiinflammatory
 2445 and antibacterial activities. J. Drug Deliv. Sci. Technol. 51, 493–498.
 2446 <https://doi.org/10.1016/j.jddst.2019.03.034>

2447 Roccia, P., Martínez, M.L., Llabot, J.M., Ribotta, P.D., 2014. Influence of spray-drying
 2448 operating conditions on sunflower oil powder qualities. Powd 254, 307–313.
 2449 <https://doi.org/10.1016/j.powtec.2014.01.044>

2450 Rodea-gonzález, D.A., Cruz-olivares, J., Román-guerrero, A., Rodríguez-huezo, M.E., Vernon-
 2451 carter, E.J., Pérez-alonso, C., 2012. Spray-dried encapsulation of chia essential oil (*Salvia*

2452 *hispanica* L.) in whey protein concentrate-polysaccharide matrices. J. Food Eng. 111,
 2453 102–109. <https://doi.org/10.1016/j.jfoodeng.2012.01.020>

2454 Rodenak-Kladniew, B., Islan, G.A., de Bravo, M.G., Durán, N., Castro, G.R., 2017. Design,
 2455 characterization and *in vitro* evaluation of linalool-loaded solid lipid nanoparticles as
 2456 potent tool in cancer therapy. Colloids Surfaces B Biointerfaces 154, 123–132.
 2457 <https://doi.org/10.1016/j.colsurfb.2017.03.021>

2458 Rodríguez, J., Martín, M.J., Ruiz, M.A., Clares, B., 2016. Current encapsulation strategies for
 2459 bioactive oils : From alimentary to pharmaceutical perspectives. Food Reseach Int. 83, 41–
 2460 59. <https://doi.org/10.1016/j.foodres.2016.01.032>

2461 Rozman, N.A.S., Tong, W.Y., Leong, C.R., Anuar, M.R., Karim, S., Ong, S.K., Yusof, F.A.M.,
 2462 Tan, W.-N., Sulaiman, B., Ooi, M.L., Lee, K.C., 2020. *Homalomena pineodora* essential
 2463 oil nanoparticle inhibits diabetic wound pathogens. Sci. Rep. 10, 3307.

2464 Rubilar, M., Morales, E., Contreras, K., Ceballos, C., Acevedo, F., Villarroel, M., Shene, C.,
 2465 2012. Development of a soup powder enriched with microencapsulated linseed oil as a
 2466 source of omega-3 fatty acids. Eur. J. Lipid Sci. Technol. 114, 423–433.
 2467 <https://doi.org/10.1002/ejlt.201100378>

2468 Rushmi, Z.T., Akter, N., Mow, R.J., Afroz, M., Kazi, M., Matas, M. De, Rahman, M., Shariare,
 2469 M.H., 2017. The impact of formulation attributes and process parameters on black seed oil
 2470 loaded liposomes and their performance in animal models of analgesia. Saudi Pharm. J.
 2471 25, 404–412. <https://doi.org/10.1016/j.jsps.2016.09.011>

2472 Saffari, M., Shirazi, F.H., Moghimi, H.R., 2016. Terpene-loaded liposomes and isopropyl
 2473 myristate as chemical permeation enhancers toward liposomal gene delivery in lung cancer
 2474 cells ; A comparative study. Iran. J. Pharm. Res. 15, 261–267.

2475 Sagiri, S.S., Anis, A., Pal, K., 2016. A Review on encapsulation of vegetable oils : Strategies,
 2476 preparation methods and application. Polym. Plast. Technol. Eng. 55, 37–41.

2477 <https://doi.org/10.1080/03602559.2015.1050521>

2478 Saha, S., Ghosh, M., 2011. Antioxidant effect of vegetable oils containing conjugated linolenic
 2479 acid isomers against induced tissue lipid peroxidation and inflammation in rat model.
 2480 Chem. Biol. Interact. 190, 109–120.

2481 Saharan, V., Mehrotra, A., Khatik, R., Rawal, P., Sharma, S.S., Pal, A., 2013. Synthesis of
 2482 chitosan based nanoparticles and their *in vitro* evaluation against phytopathogenic fungi.
 2483 Int. J. Biol. Macromol. 62, 677–683.

2484 Sailaja, A.K., Amareshwar, P., Chakravarty, P., 2011. Formulation of solid lipid nanoparticles
 2485 and their applications. Curr. pharma Res. 1, 197–203.

2486 Salari, S., Salari, R., 2019. Nanoliposomal system of rosemary essential oil made by specific
 2487 human cell phospholipids and evaluation of its anti-cancer properties. Appl. Nanosci. 9,
 2488 2085–2089. <https://doi.org/10.1007/s13204-019-01009-1>

2489 Salminen, H., Helgason, T., Kristinsson, B., Kristbergsson, K., Weiss, J., 2017. Tuning of shell
 2490 thickness of solid lipid particles impacts the chemical stability of encapsulated x-3 fish oil.
 2491 J. Colloid Interface Sci. 490, 207–216. <https://doi.org/10.1016/j.jcis.2016.11.063>

2492 Sameen, D.E., Ahmed, S., Qin, W., Zhang, Q., Chen, H., Dai, J., He, L., Liu, Y., 2020.
 2493 Preparation and characterization of grass carp collagen-chitosan-lemon essential oil
 2494 composite films for application as food packaging. Int. J. Biol. Macromol. 160, 340–351.

2495 Santos, V. da S., Braz, B.B., Silva, A.Á., Cardoso, L.P., Ribeiro, A.P.B., Santana, M.H.A.,
 2496 2019. Nanostructured lipid carriers loaded with free phytosterols for food applications.
 2497 Food Chem. 298, 125053. <https://doi.org/10.1016/j.foodchem.2019.125053>

2498 Saporito, F., Sandri, G., Bonferoni, M.C., Rossi, S., Boselli, C., Cornaglia, A.I., Mannucci, B.,
 2499 Grisoli, P., Vigani, B., Ferrari, F., 2018. Essential oil-loaded lipid nanoparticles for wound
 2500 healing. Int. J. Nanomedicine 13, 175–186.

2501 Saraf, S., Sahu, S., Kaur, C., Saraf, S., 2010. Comparative measurement of hydration effects of

herbal moisturizers. *Pharmacognosy Res.* 2, 146–151.

Sarangi, M.K., Padhi, S., 2016. Solid lipid nanoparticles- A review. *J. critica Rev.* 3, 5–12.
<https://doi.org/10.5958/0975-4377.2016.00030.6>

Sebaaly, C., Charcosset, C., Stainmesse, S., Fessi, H., Greige-gerges, H., 2016a. Clove essential oil-in-cyclodextrin-in-liposomes in the aqueous and lyophilized states : From laboratory to large scale using a membrane contactor. *Carbohydr. Polym.* 138, 75–85.

Sebaaly, C., Greige-Gerges, H., Agusti, G., Fessi, H., Charcosset, C., 2015a. Large-scale preparation of clove essential oil and eugenol-loaded liposomes using a membrane contactor and a pilot plant. *J. Liposome Res.* 26, 126-38.
<https://doi.org/10.3109/08982104.2015.1057849>

Sebaaly, C., Greige-gerges, H., Stainmesse, S., Fessi, H., Charcosset, C., 2016b. Effect of composition , hydrogenation of phospholipids and lyophilization on the characteristics of eugenol-loaded liposomes prepared by ethanol injection method. *Food Biosci.* 15, 1–10.
<https://doi.org/10.1016/j.fbio.2016.04.005>

Sebaaly, C., Jraij, A., Fessi, H., Charcosset, C., Greige-gerges, H., 2015b. Preparation and characterization of clove essential oil-loaded liposomes. *Food Chem.* 178, 52–62.
<https://doi.org/10.1016/j.foodchem.2015.01.067>

Shakeri, F., Shakeri, S., Hojjatoleslami, M., 2014. Preparation and characterization of carvacrol loaded polyhydroxybutyrate nanoparticles by nanoprecipitation and dialysis methods. *J. Food Sci.* 79, 697–705. <https://doi.org/10.1111/1750-3841.12406>

Shakeri, M., Hadi, S., Shakeri, S., 2019. Carvacrol and astaxanthin co-entrapment in beeswax solid lipid nanoparticles as an efficient nano-system with dual antioxidant and anti-biofilm activities. *LWT - Food Sci. Technol.* 107, 280–290.
<https://doi.org/10.1016/j.lwt.2019.03.031>

Shamaei, S., Sadegh, S., Aghbashlo, M., Tsotsas, E., Kharaghani, A., 2017. Microencapsulation

2527 of walnut oil by spray drying: Effects of wall material and drying conditions on
 2528 physicochemical properties of microcapsules. *Innov. Food Sci. Emerg. Technol.* 39, 101–
 2529 112. <https://doi.org/10.1016/j.ifset.2016.11.011>
 2530 Shi, F., Yang, G., Ren, J., Guo, T., Du, Y., Feng, N., 2013. Formulation design, preparation,
 2531 and in vitro and in vivo characterizations of β -elemene- loaded nanostructured lipid
 2532 carriers. *Int. J. Nanomedicine* 8, 2533–2541.
 2533 Shukla, A.C., 2018. Essential oils as green pesticides for postharvest disease management. *Acta*
 2534 *Hortic.* 1210, 199–206.
 2535 Sidding, Abdelwahab, I., Sheikh, B.Y., Taha, M.M.E., How, C.W., Abdullah, R., Yagoub, U.,
 2536 El-sunousi, R., Eid, E.E., 2013. Thymoquinone-loaded nanostructured lipid carriers :
 2537 preparation, gastroprotection, in vitro toxicity, and pharmacokinetic properties after
 2538 extravascular administration. *Int. J. Nanomedicine* 8, 2163–2172.
 2539 Silva-Flores, P.G., Opez, L.A.P.-L., Rivas-Galindo, V.M., Paniagua-Vega, D., Galindo-
 2540 Rodríguez, S.A., Alvarez-Roman, R., 2019. Simultaneous GC-FID quantification of main
 2541 components of *Rosmarinus officinalis* L . and *Lavandula dentata* essential oils in
 2542 polymeric nanocapsules for antioxidant application. *J. Anal. Methods Chem.* 2019, 1–9.
 2543 Sodeifian, G. hossein, Nedasadat, S., Seyed, Sajadian, A.A., Ghorbandoost, S., 2016.
 2544 Application of supercritical carbon dioxide to extract essential oil from *Cleome*
 2545 *coluteoides* Boiss: Experimental, response surface and grey wolf optimization
 2546 methodology. *J. Supercrit. Fluids* 114, 55–63.
 2547 Soleimanian, Y., Amir, S., Goli, H., Varshosaz, J., Sahafi, S.M., 2018. Formulation and
 2548 characterization of novel nanostructured lipid carriers made from beeswax , propolis wax
 2549 and pomegranate seed oil. *Food Chem.* 244, 83–92.
 2550 <https://doi.org/10.1016/j.foodchem.2017.10.010>
 2551 Sotelo-Boyás, M., Valverde-Aguilar, G., Plascencia-Jatomea, M., Correa Pacheco, Z.,

2552 Jiménez-Aparicio, A., Solorza-Feria, J., Barrera-Necha, L., Bautista-Baños, S., 2015.
 2553 Characterization of chitosan nanoparticles added with essential oils. *In vitro* effect on
 2554 *Pectobacterium carotovorum*. *Rev. Mex. Ing. química* 14, 589–599.
 2555 Sotelo-Boyás, M.E., Correa-Pacheco, Z., Bautista-Banos, S., Gómez, Y.G. y, 2017a. Release
 2556 study and inhibitory activity of thyme essential oil-loaded chitosan nanoparticles and
 2557 nanocapsules against foodborne bacteria. *Int. J. Biol. Macromol.* 103, 409–414.
 2558 <https://doi.org/10.1016/j.ijbiomac.2017.05.063>
 2559 Sotelo-Boyás, M.E., Correa-Pacheco, Z.N., Bautista-Baños, S., Corona-Rangel, M.L., 2017b.
 2560 Physicochemical characterization of chitosan nanoparticles and nanocapsules incorporated
 2561 with lime essential oil and their antibacterial activity against food-borne pathogens. *LWT*
 2562 - *Food Sci. Technol.* 77, 15–20. <https://doi.org/10.1016/j.lwt.2016.11.022>
 2563 Sousa, V.P. de, Crean, J., Borges, V.R. de A., Rodrigues, C.R., Tajber, L., Boylan, F., Cabral,
 2564 L.M., 2013. Nanostructured systems containing babassu (*Orbignya speciosa*) oil as a
 2565 potential alternative therapy for benign prostatic hyperplasia. *Int. J. Nanomedicine* 8,
 2566 3129–3139.
 2567 Souza, J.R., Bonfim, K.S., Lorevice, M.V., Correa, D.S., Mattoso, L.H.C., Moura, M.R. de,
 2568 2020. Antibacterial properties of oregano essential oil encapsulated in poly(ε-
 2569 Caprolactone) nanoparticles. *Adv. Sci. Eng. Med.* 12, 7.
 2570 Stano, P., Bufali, S., Pisano, C., Bucci, F., Barbarino, M., Santaniello, M., Carminati, P., Luisi,
 2571 P.L., 2004. Novel camptothecin analogue (gimatecan)-containing liposomes prepared by
 2572 the ethanol injection method. *J. Liposome Res.* 14, 87–109.
 2573 Sun, X., Cameron, R.G., Bai, J., 2020. Effect of spray-drying temperature on physicochemical,
 2574 antioxidant and antimicrobial properties of pectin/sodium alginate microencapsulated
 2575 carvacrol. *Food Hydrocoll.* 100, 105420. <https://doi.org/10.1016/j.foodhyd.2019.105420>
 2576 Suomela, J.-P., Ahotupa, M., Sjövall, O., Kurvinen, J.-P., Kallio, H., 2004. Diet and lipoprotein

2577 oxidation: Analysis of oxidized triacylglycerols in pig lipoproteins. *Lipids* 39, 639–647.
 2578 <https://doi.org/10.1007/s11745-004-1277-4>

2579 Sutaphanit, P., Chitprasert, P., 2014. Optimisation of microencapsulation of holy basil essential
 2580 oil in gelatin by response surface methodology. *Food Chem.* 150, 313–320.
 2581 <https://doi.org/10.1016/j.foodchem.2013.10.159>

2582 Svetlichny, G., Kulkamp-Guerreiro, I.C., Cunha, S.L., Silva, F.E.K., Bueno, K., Pohlmann,
 2583 A.R., Fuentefria, A.M., Guterres, S.S., 2015. Solid lipid nanoparticles containing copaiba
 2584 oil and allantoin : development and role of nanoencapsulation on the antifungal activity.
 2585 *Pharmazie* 70, 155–164. <https://doi.org/10.1691/ph.2015.4116>

2586 Tabassum, N., Vidyasagar, G., 2014. *In vitro* antimicrobial activity of edible oils against
 2587 human pathogens causing skin infections. *Int. J. Pharm. Sci. Res.* 5, 4493–4498.
 2588 [https://doi.org/10.13040/IJPSR.0975-8232.5\(10\).4493-98](https://doi.org/10.13040/IJPSR.0975-8232.5(10).4493-98)

2589 Tabatabai, M.B., Mirjalili, M., Yazdiyan, F., Hekmatimoghaddam, S., 2018. Antibacterial
 2590 activity and cytotoxicity of nanoliposomic and nanoniosomic essential oil of
 2591 *Trachyspermum copticum*. *Proc. Natl. Acad. Sci. India Sect. B - Biol. Sci.* 89, 1109–1116.
 2592 <https://doi.org/10.1007/s40011-018-1025-6>

2593 Tahir, H.U., Sarfraz, R.A., Ashraf, A., Adil, S., 2016. Chemical composition and antidiabetic
 2594 activity of essential oils obtained from two spices (*Syzygium aromaticum* and *Cuminum*
 2595 *cyminum*). *Int. J. Food Prop.* 19, 2156-2164.

2596 Tang, J., Ge, Y., 2017. Development and evaluation of novel eucalyptus essential oil liposomes
 2597 /chitosan composite sponges for medical use. *Fibers Polym.* 18, 424–433.
 2598 <https://doi.org/10.1007/s12221-017-6983-4>

2599 Thakre, A.D., Mulange, S. V, Kodgire, S.S., Zore, G.B., Karuppayil, S.M., 2016. Effects of
 2600 cinnamaldehyde , ocimene , camphene , curcumin and farnesene on *Candida albicans*.
 2601 *Adv. Microbiol.* 6, 627–643.

2602 Thelagavath, G., Kannaian, T., 2008. Dual antimicrobial and blood repellent finishes for cotton
 2603 hospital fabrics. *Ind J. Fibre Text. Res.* 33, 23–9.

2604 Tian, H., Lu, Z., Li, D., Hu, J., 2018. Preparation and characterization of citral-loaded solid
 2605 lipid nanoparticles. *Food Chem.* 248, 78–85.
 2606 <https://doi.org/10.1016/j.foodchem.2017.11.091>

2607 Timbe, P.P.R., Motta, A. de S., Isaia, H.A., Brandelli, A., 2020. Polymeric nanoparticles loaded
 2608 with *Baccharis dracunculifolia* DC essential oil: Preparation, characterization, and
 2609 antibacterial activity in milk. *J. Food Process. Preserv.* 44, e14712.
 2610 <https://doi.org/10.1111/jfpp.14712>

2611 Tonon, R. V, Grosso, C.R.F., Hubinger, M.D., 2011. Influence of emulsion composition and
 2612 inlet air temperature on the microencapsulation of flaxseed oil by spray drying. *Food Res.*
 2613 *Int.* 44, 282–289. <https://doi.org/10.1016/j.foodres.2010.10.018>

2614 Tonon, R. V, Pedro, R.B., Grosso, C.R.F., Hubinger, M.D., 2012. Microencapsulation of
 2615 flaxseed oil by spray drying : Effect of oil load and type of wall material. *Dry. Technol.*
 2616 30, 1491–1501. <https://doi.org/10.1080/07373937.2012.696227>

2617 Turek, C., Stintzing, F.C., 2013. Stability of essential oils: A review. *Compr. Rev. Food Sci.*
 2618 *Food Saf.* 12, 40–53.

2619 Us-medina, U., Julio, L.M., Segura-campos, M.R., Ixtaina, V.Y., Tomás, M.C., 2018.
 2620 Development and characterization of spray-dried chia oil microcapsules using by-products
 2621 from chia as wall material. *Powder Technol.* 334, 1–8.
 2622 <https://doi.org/10.1016/j.powtec.2018.04.060>

2623 Valenti, D., Logu, A. De, Loy, G., Sinico, C., Bonsignore, L., Cottiglia, F., Grarau, D., Fadda,
 2624 A.M., 2001. Liposome-incorporated *Santolina insularis* essential oil: Preparation,
 2625 characterization and in vitro antiviral activity. *J. Liposome Res.* 11, 73–90.

2626 Vanderhoff, J.W., Asser, M.S. El, 1979. Polymer emulsification process.

2627 Vélez, M.A., Perotti, M.C., Hynes, E.R., Gennaro, A.M., 2019. Effect of lyophilization on food
 2628 grade liposomes loaded with conjugated linoleic acid. *J. Food Eng.* 240, 199–206.
 2629 <https://doi.org/10.1016/j.jfoodeng.2018.07.033>
 2630 Vemuri, S., Rhodes, C.T., 1995. Preparation and characterization of liposomes as therapeutic
 2631 delivery systems: a review. *Pharm. Acta Helv.* 70, 95–111.
 2632 Vieira, R., Severino, P., Nalone, L.A., Souto, S.B., Silva, A.M., Lucarini, M., Durazzo, A.,
 2633 Santini, A., Souto, E.B., 2020. Sucupira oil-loaded nanostructured lipid carriers (NLC):
 2634 Lipid screening, factorial design, release profile, and cytotoxicity. *Molecules* 25, 1–22.
 2635 <https://doi.org/10.3390/molecules25030685>
 2636 Vrouvaki, I., Koutra, E., Kornaros, M., Avgoustakis, K., Lamari, F.N., Hatziantoniou, S., 2020.
 2637 Polymeric nanoparticles of *Pistacia lentiscus* var. chia essential oil for cutaneous
 2638 applications. *Pharmaceutics* 12, 353.
 2639 Wachtel-Galor, S., Benzie, I.F.F., 2011. Herbal medicine: An introduction to its history, usage,
 2640 regulation, current trends, and research needs, in: Benzie, I.F.F., Wachtel-Galor, S. (Eds.),
 2641 Herbal Medicine: Biomolecular and Clinical Aspects. CRC Press, pp. 1–10.
 2642 Wang, J.M., Zheng, W., Song, Q.W., Zhu, H., Zhou, Y., 2009. Preparation and characterization
 2643 of natural fragrant microcapsules. *J. Fiber Bioeng. Informatics* 1, 293–300.
 2644 Wang, Q., Lv, S., Lu, J., Jiang, S., Lin, L., 2015. Evaluation of carboxymethyl chitosan coated
 2645 liposomes containing fish oil. *J. Food Sci.* 80, 1460–1467. [https://doi.org/10.1111/1750-](https://doi.org/10.1111/1750-3841.12929)
 2646 [3841.12929](https://doi.org/10.1111/1750-3841.12929)
 2647 Wang, S., Shi, Y., Han, L., 2018. Development and evaluation of microencapsulated peony
 2648 seed oil prepared by spray drying : Oxidative stability and its release behavior during in-
 2649 vitro digestion. *J. Food Eng.* 231, 1–9. <https://doi.org/10.1016/j.jfoodeng.2018.03.007>
 2650 Wang, X., Liu, L., Xia, S., Muhoza, B., Cai, J., Zhang, X., Duhoranimana, E., Su, J., 2019.
 2651 Sodium carboxymethyl cellulose modulates the stability of cinnamaldehyde-loaded

liposomes at high ionic strength. Food Hydrocoll. 93, 10–18.

Wang, Z., 2012. Preparation and characterization of solid lipid nanoparticles loaded with frankincense and myrrh oil. Int. J. Nanomedicine 7, 2033–2043. <https://doi.org/10.2147/IJN.S30085>

Warnke, P., Becker, S., Podschun, R., Sivananthan, S., Springer, I., Russo, P., Wiltfang, J., Fickenscher, H., Sherry, E., 2009. The battle against multi-resistant strains: Renaissance of antimicrobial essential oils as a promising force to fight hospital-acquired infections. J. Craniomaxillofac. Surg. 37, 392–7.

Warshaw, E.M., Maibach, H.I., Taylor, J.S., Sasseville, D., DeKoven, F., Zirwas, M., Fransway, A., Mathias, C., Zug, K., DeLeo, V., Fowler, J., Marks, J., Pratt, M., Storrs, F., Belsito, D., 2015. North American contact dermatitis group patch test results: 2011-2012. Dermatitis 26, 49–59.

Weber, J., Funk, N.L., Motta, M.H., Guedes, A.M., Visintainer, A.P.C., Tedesco, S.B., Silva, C.D.B., Chalmers, H., 2016. Association of borage oil and betamethasone dipropionate in lipid-core nanocapsules: characterization, photostability and *in vitro* irritation test. J. Nanosci. Nanotechnol. 16, 1354–1362. <https://doi.org/10.1166/jnn.2016.11674>

Woranuch, S., Yoksan, R., 2013. Eugenol-loaded chitosan nanoparticles : I . Thermal stability improvement of eugenol through encapsulation. Carbohydr. Polym. 96, 578–585. <https://doi.org/10.1016/j.carbpol.2012.08.117>

Wu, Z., Zhou, W., Pang, C., Deng, W., Xu, C., Wang, X., 2020. Multifunctional chitosan-based coating with liposomes containing laurel essential oils and nanosilver for pork preservation. Food Chem. 295, 16–25.

Xenakis, A., Papadimitriou, V., Sotiroudis, T.G., 2010. Colloidal structures in natural oils. Curr. Opin. Colloid Interface Sci. 15, 55–60. <https://doi.org/10.1016/j.cocis.2009.11.007>

Yadav, N., Khatak, S., Sara, U.V.S., 2013. Solid lipid nanoparticles- A review. Int. J. Appl.

Pharm. 5, 8–18.

Yaep, S., Beh, B., Ali, N., Yusof, H., 2015. Antistress and antioxidant effects of virgin coconut oil *in vivo*. Exp. Ther. Med. 9, 39–42.

Yang, J., Han, S., Zheng, H., Dong, H., Liu, J., 2015. Preparation and application of micro/nanoparticles based on natural polysaccharides. Carbohydr. Polym. 123, 53–66.

Yang, X., Gao, N., Hu, L., Li, J., Sun, Y., 2015. Development and evaluation of novel microcapsules containing poppy-seed oil using complex coacervation. J. Food Eng. 161, 87–93. <https://doi.org/10.1016/j.jfoodeng.2015.03.027>

Yang, Z., Peng, Z., Li, J., Li, S., Kong, L., Li, P., Wang, Q., 2014. Development and evaluation of novel flavour microcapsules containing vanilla oil using complex coacervation approach. Food Chem. 145, 272–277. <https://doi.org/10.1016/j.foodchem.2013.08.074>

Yara-Varón, E., Li, Y., Balcells, M., Canela-Garayoa, R., Fabiano-Tixier, A.-S., Chemat, F., 2017. Vegetable oils as alternative solvents for green oleo-extraction, purification and formulation of food and natural products. Molecules 22, 1474. <https://doi.org/10.3390/molecules22091474>

Yoshida, P.A., Yokota, D., Foglio, M.A., Rodrigues, R.A.F., Pinho, S.C., 2010. Liposomes incorporating essential oil of Brazilian cherry (*Eugenia uniflora* L.): Characterization of aqueous dispersions and lyophilized formulations. J. Microencapsul. 27, 416–425. <https://doi.org/10.3109/02652040903367327>

Yu, F.L., Greenlaw, R., Fang, Q., Bender, W., Yamaguchi, K., Xue, B.H., Yu, C.C., 2004. Studies on the chemopreventive potentials of vegetable oils and unsaturated fatty acids against breast cancer carcinogenesis at initiation. Eur. J. Cancer Prev. 13, 239–248.

Zabihi, A., Basti, A.A., Amoabediny, G., Khanjari, A., Bazzaz, J.T., Mohammadkhan, F., Bargh, A.H., Vanaki, E., 2017. Physicochemical characteristics of nanoliposome garlic (*Allium sativum* L.) essential oil and its antibacterial effect on Escherichia coli O157 : H7.

2702 J. Food Qual. Hazards Control 4, 24–28.

2703 Zammit, M.L., 2010. Photosensitivity : Light , sun and pharmacy. J. Malta Coll. Pharm. Pract.

2704 16, 12–17.

2705 Zeghib, A., Kabouche, A., Laggoune, S., Calliste, C.-A., Simon, A., Bressolier, P., Aouni, M.,

2706 Duroux, J.-L., Kabouche, Z., 2017. Antibacterial, antiviral, Antioxidant and

2707 antiproliferative activities of *Thymus guyonii* essential oil. Nat. Prod. Commun. 12, 1651-

2708 1654.

2709 Zermane, A., Larkeche, O., Meniai, A.-H., Crampon, C., Badens, E., 2016. Optimization of

2710 Algerian rosemary essential oil extraction yield by supercritical CO₂ using response

2711 surface methodology. Comptes Rendus Chim. 19, 538–543.

2712 Zhang, H., Li, X., Liang, Y., Kang, H., 2020. Effect of chitosan-gelatin coating containing

2713 nano-encapsulated tarragon essential oil on the preservation of pork slices. Meat Sci. 166,

2714 108137.

2715 Zhang, H., Ran, X., Hu, C., Qin, L., Lu, Y., Peng, C., 2012. Therapeutic effects of liposome-

2716 enveloped *Ligusticum chuanxiong* essential oil on hypertrophic scars in the rabbit ear

2717 model. PLoS One 7, 1–8. <https://doi.org/10.1371/journal.pone.0031157>

2718 Zhang, K., Zhang, H., Hu, X., Bao, S., Huang, H., 2012. Synthesis and release studies of

2719 microalgal oil-containing microcapsules prepared by complex coacervation. Colloids

2720 Surfaces B Biointerfaces 89, 61–66. <https://doi.org/10.1016/j.colsurfb.2011.08.023>

2721 Zhao, Y., Chang, Y.-X., Hu, X., Liu, C.-Y., Quan, L.-H., Liao, Y.-H., 2017. Solid lipid

2722 nanoparticles for sustained pulmonary delivery of Yuxingcao essential oil: Preparation,

2723 characterization and *in vivo* evaluation. Int. J. Pharm. 516, 364–371.

2724 Zhavah, S., Mohsenifar, A., Beiki, M., Tahereh, S., Abdollahi, A., Rahmani-cherati, T.,

2725 Tabatabaei, M., 2015. Encapsulation of *Cuminum cyminum* essential oils in chitosan-

2726 caffeic acid nanogel with enhanced antimicrobial activity against *Aspergillus flavus*. Ind.

2727 Crop. Prod. 69, 251–256. <https://doi.org/10.1016/j.indcrop.2015.02.028>

2728 Zhu, D., Chenga, H., Li, J., Zhang, W., Shen, Y., Chen, Shaojun, Ge, Z., Chen, Shiguo, 2016.

2729 Enhanced water-solubility and antibacterial activity of novel chitosan derivatives modified

2730 with quaternary phosphonium salt. Mater. Sci. Eng. C 61, 79–84.

2731 Zhu, J., Zhuang, P., Luan, L., Sun, Q., Cao, F., 2015. Preparation and characterization of novel

2732 nanocarriers containing krill oil for food application. J. Funct. Foods 19, 902–912.

2733 <https://doi.org/10.1016/j.jff.2015.06.017>

2734 Zhu, Y., Li, C., Cui, H., Lin, L., 2020. Plasma enhanced-nutmeg essential oil solid liposome

2735 treatment on the gelling and storage properties of pork meat batters. J. Food Eng. 266,

2736 109696.

2737 Zielińska, A., Ferreira, N.R., Icon, A.F.-G., Nowak, I., Souto, E.B., 2020. Loading, release

2738 profile and accelerated stability assessment of monoterpenes-loaded solid lipid

2739 nanoparticles (SLN). Pharm. Dev. Technol. 25, 832-844.

2740 Zielinska, A., R.Ferreira, N., Durazzo, A., Lucarini, M., Ciero, N., Mamouni, S. El, Silva, A.M.,

2741 Nowak, I., Santini, A., Souto, E.B., 2019. Alpha-Pinene-loaded solid lipid nanoparticles

2742 dispersion analysis. Molecules 24, 2683.

2743