



**HAL**  
open science

## 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 <sup>1,2</sup>, Ouahida Louaer <sup>2</sup>, Abdeslam Hassen Meniai <sup>2</sup>, Hatem Fessi <sup>3</sup>,

Abdelhamid Elaissari <sup>1\*</sup>

<sup>1</sup> Univ Lyon, University Claude Bernard Lyon-1, CNRS, ISA-UMR 5280, 69622 Villeurbanne, France

<sup>2</sup> Environmental Process Engineering Laboratory, University Constantine 3, Salah Boubnider, Constantine, Algeria.

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

\* **Corresponding author** : Abdelhamid Elaissari ; [abdelhamid.elaissari@univ-lyon1.fr](mailto:abdelhamid.elaissari@univ-lyon1.fr)

## Abbreviations

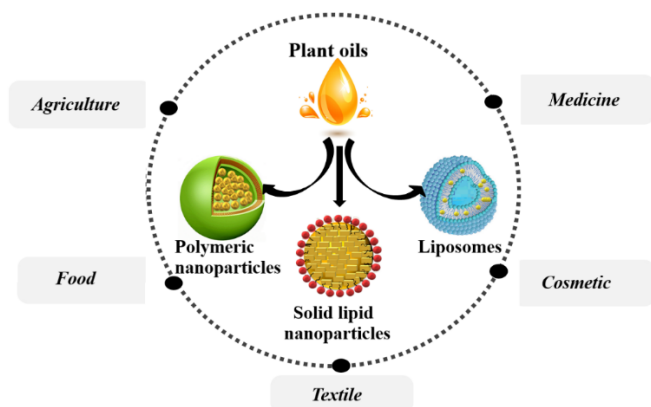
EO: Essential oil; VO: Vegetable oil; pNPs: Polymeric nanoparticles; SLN: Solid lipid nanoparticles; EE%: Encapsulation efficiency; HLB: Hydrophilic lipophilic balance; SUV: Small unilamellar vesicles; LUV: Large unilamellar vesicles; MLV: Multilamellar vesicles; NLC: Nanostructured lipid carriers; MIC: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

25 **Abstract**

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

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

43 **Graphical abstract**



44

## 45 **1. Introduction**

46           The last decade has evidently witnessed a tremendous surge in the use of herbal  
47 medicine as a form of complementary or replacement therapy (Mainardi et al., 2009). The  
48 global acceptance and public concern in the use of herbal medicines, phytonutrients or  
49 nutraceuticals continue to assume exponential increase. It has been estimated that up to 80% of  
50 people worldwide relying on them as a primary source of healthcare (Ekor, 2013). This concern  
51 in drugs of natural origin is related to numerous reasons, namely, the traditional medicine is  
52 more affordable, closer to the patient's ideology and receives greater public access than  
53 chemical synthesized treatment. Furthermore, abusive and/or incorrect use of conventional  
54 medicines results in some cases in harmful side effects (Wachtel-Galor and Benzie, 2011). The  
55 use of aromatic and medicinal plants is incessantly expanding due to increasing consumers  
56 demand and concern in these plants for several applications. In fact, consumers are becoming  
57 more and more aware of the benefits of inherent practice of medicinal and aromatic plants and  
58 their metabolites (Chikezie et al., 2015; Rates, 2001). These plants produce a large variety of  
59 secondary metabolites; among them, essential and vegetable oils deserve particular attention  
60 (Dhifi et al., 2016; Kumar et al., 2016; Pandey et al., 2016; Yara-Varón et al., 2017).

61 Essential oils (EO) comprised volatile and semi-volatile organic compounds determining the  
62 specific aroma, flavor and fragrance of plants. They are volatile and instable at room-  
63 temperature. In the other hand, vegetable oils (VO) consist of esters of glycerol and fatty acids  
64 and are nonvolatile and stable at room temperature (Moghaddam and Mehdizadeh, 2017; Sagiri  
65 et al., 2016). Besides being edible in their refined or virgin form, VO play a crucial role in  
66 therapeutic and prophylactic prevention of diseases such as inflammation, diabetes, cancer and  
67 atherosclerosis (Ganesan et al., 2018; Kochikuzhyil et al., 2010; Saha and Ghosh, 2011; Yu et  
68 al., 2004). Subsequently, EO received significant attention in food, agricultural and  
69 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. Zhavveh 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.

95            Depending on the preparation method, nanocarriers can be mainly classified into two  
96 main groups: polymer-based nanocarriers and lipid-based nanocarriers. Among the several  
97 colloidal systems investigated in drug delivery, polymeric nanoparticles (pNPs), liposomes and  
98 solid lipid nanoparticles (SLN) gained more interest (Allen and Cullis, 2013; El-say and El-  
99 sawy, 2017; Geszke-Moritz and Moritz, 2016; Immordino et al., 2006; Mehnert and Mäder,  
100 2012; Rani et al., 2017). In this context, the present review covers literature data summarizing  
101 the current development of nanocarrier systems for plant oils delivery with a focus on the main  
102 properties and preparation technique of pNPs, liposomes and SLN. In addition, the chemical  
103 composition of both essential and vegetable oils along with the emerging and potential  
104 applications of plant oils loaded nanocarriers in several fields were explored.

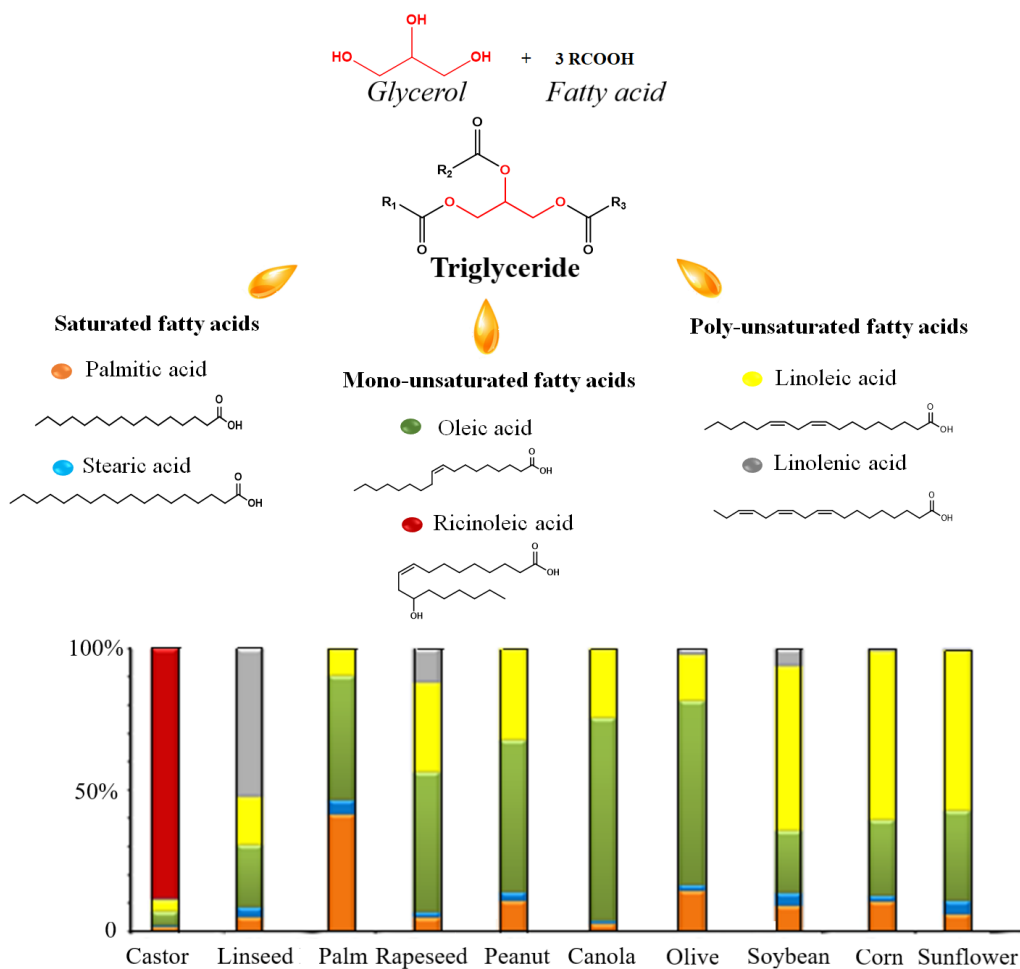
## 105 **2. Chemical composition of vegetable oils**

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

### 111 **2.1. Triglycerides**

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

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



122  
123 **Fig. 1.** Triglycerides composition of different vegetable oils.

124 **2.2. Minor Components**

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

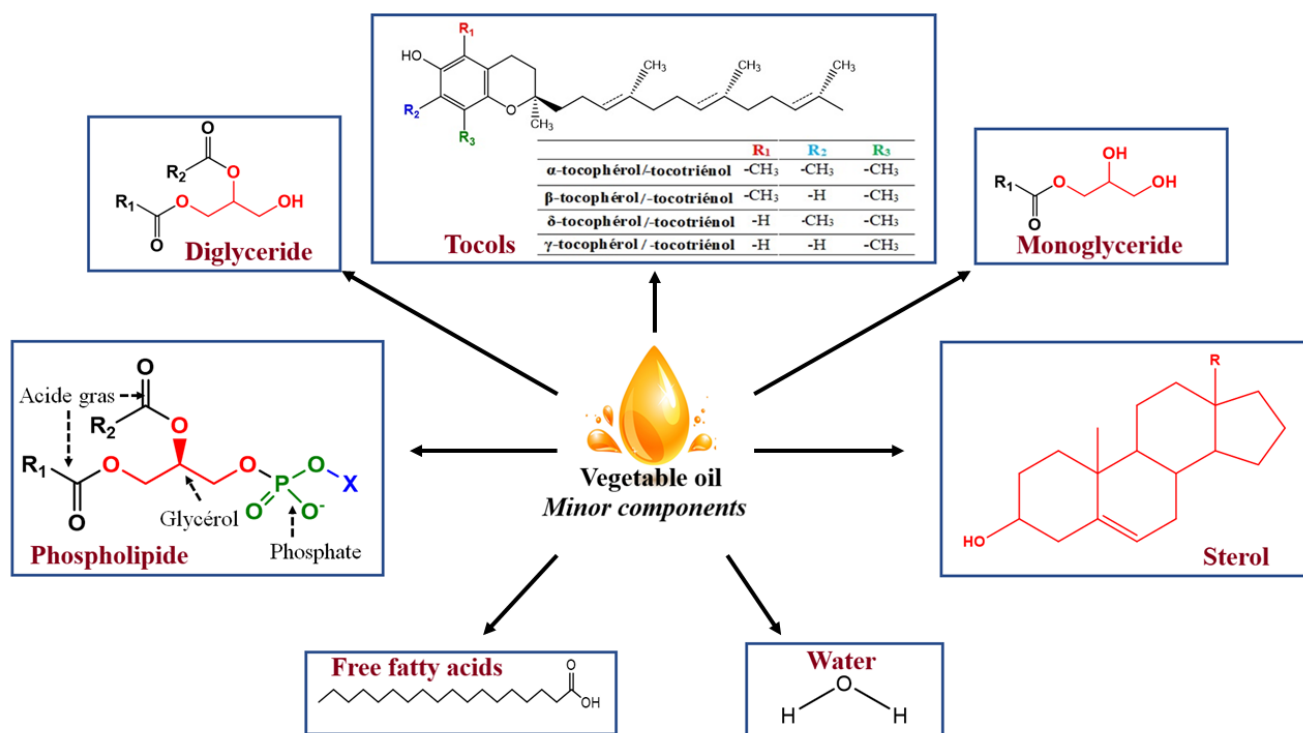


Fig. 2. Minor components of vegetable oils.

### 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).



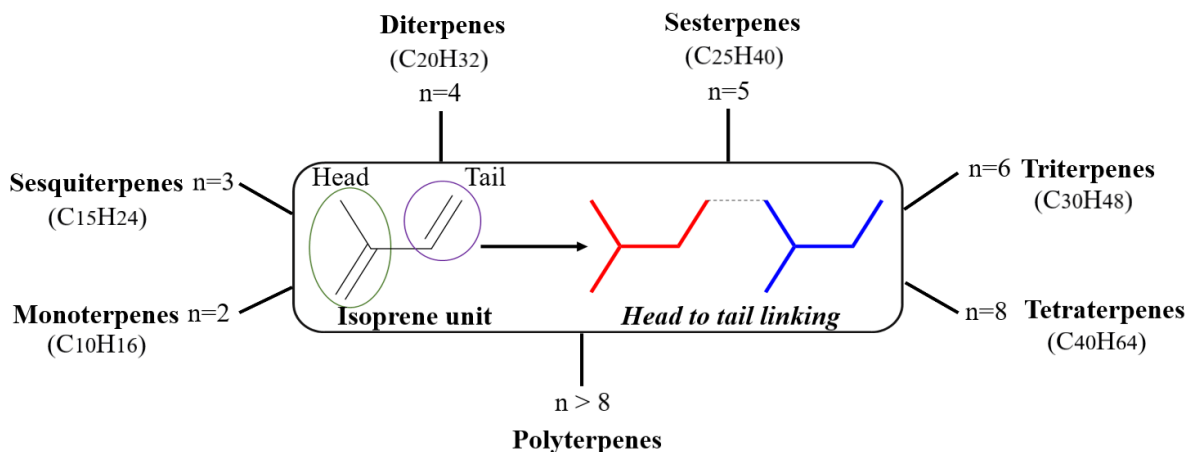
146 Terpene compounds can be divided into two main categories: terpene hydrocarbons and  
147 oxygenated compounds (Moghaddam and Mehdizadeh, 2017).

### 148 **3.1.1. Terpenes hydrocarbon**

149 The essential building block of terpenes is the isoprene unit joined in a head-to-tail  
150 manner. Basing on the number of isoprene units, different terpenes can be found in EO, as  
151 demonstrated in **Fig. 3** (El-Asbahani et al., 2015; Morsy, 2017). Terpenes hydrocarbons are the  
152 first main group of components composed completely of carbon and hydrogen atoms and varied  
153 significantly in size and complexity (Moghaddam and Mehdizadeh, 2017). Monoterpenes and  
154 sesquiterpenes are the dominant terpenes found in plant EO. They are built up by two and three  
155 isoprene units, respectively. These terpenes could present acyclic, cyclic or aromatic structures.  
156 Cyclic terpenes can be classified depending on their ring size into monocyclic, bicyclic or  
157 tricyclic terpenes (**Table 1**). These compounds oxidize rapidly due to their fast reaction to heat  
158 and air sources (George et al., 2015). Diterpenes result by the combination of four isoprene  
159 units in a head-to-tail manner; they are essential constituents of plant resins (Langenheim,  
160 2003). Commonly, diterpenes, triterpenes and tetraterpenes are present in EOs at a very low  
161 concentration. Their content may vary with the extraction method (Morsy, 2017).

### 162 **3.1.2. Terpenoids**

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



169  
170

**Fig. 3.** Composition of terpenes.

### 171 3.2. Phenylpropanoid

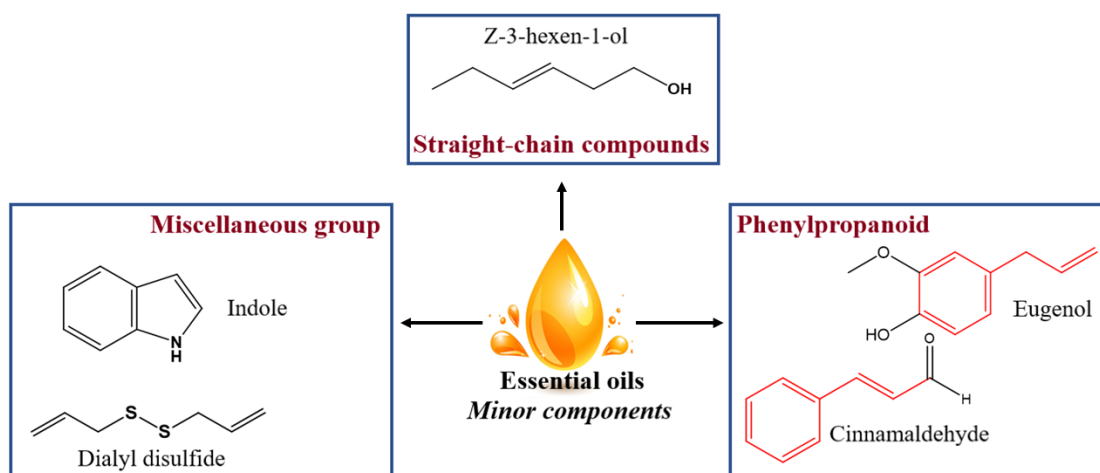
172 This class of compounds, derived from phenylpropene, is synthesized from the amino  
 173 acid phenylalanine and l-tyrosine via the shikimic acid pathway. Their name is derived from  
 174 the aromatic phenyl group and the propene tail. The propyl side chain may contain hydroxyl or  
 175 carboxyl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

### 179 3.3. Straight-chain compounds

180 This group contains only straight-chain compounds, not containing any side branches.  
 181 They range from n-heptane, to compounds with 35 carbon atoms. The leaf alcohol (3(Z)-hexen-  
 182 1-ol) (**Fig. 4**) represents an example of this class; it gives an intense grassy-green odor upon  
 183 cutting green grass and leaves (Morsy, 2017).

### 184 3.4. Miscellaneous group

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



188

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

190

#### 191 **4. Limitation in clinical use of plant oils**

192 Since ancient times, EO have been recommended all over the world for a variety of

193 health problems and diseases (Moghaddam and Mehdizadeh, 2017). Enormous studies have

194 investigated the biological properties of EO, including antimicrobial, antifungal (Ceole et al.,

195 2017; Garcia-Rellán et al., 2016), antiviral (Zeghib et al., 2017), insecticidal (Chen et al., 2016;

196 Jassbi et al., 2017), antioxidant (Hassanen et al., 2015; Limaverde et al., 2017), anticancer

197 (Carneiro et al., 2017; Thakre et al., 2016), antidiabetic (Tahir et al., 2016), anti-inflammatory

198 (Chansang et al., 2018; Nonato et al., 2012), antihypertensive (Cherkaoui-Tangi et al., 2016)

199 and immunomodulatory (Orhan et al., 2016; Ozek et al., 2017). In medical field, EO have been

200 used against nosocomial infections, as a cleaning liquid for disinfection of medical equipment

201 and surfaces (Warnke et al., 2009) or as an aerosol in operating blocks and waiting rooms for

202 air cleaning to limit contaminations (De Billerbeck, 2007). The application of EO has emerged

203 to food and agriculture fields. They are used as antioxidants and preservatives in food

204 (Khosravi, 2013; Pandey et al., 2016), as plant and crop protectants (Abdullah et al., 2018) and

205 incorporated into foodstuff packaging (Ribeiro-Santos et al., 2017).

206 In the other side, VO is a source of everlasting components which are responsible of  
207 pertinent biological properties. Many of the fatty acids and other compounds present in VO  
208 have long been known to benefit our health. Numerous experimental studies approved that a  
209 dietary intake of omega-3 polyunsaturated fatty acids can reduce inflammation and may prevent  
210 the risk of chronic diseases like heart disease, cancer, and arthritis (Gammone et al., 2019;  
211 Hardman and Fakas, 2016; Kris-Etherton et al., 2003). In addition, polyphenols, medium chain  
212 fatty acids and tocopherol present in some VO were the reason of their antioxidant and antistress  
213 activities (Duthie et al., 2016; Yaep et al., 2015). Current animal studies have indicated that  
214 palmitic acid had a potent antiviral property against HIV-1 and HIV-2 (Özçelik et al., 2005).  
215 Linoleic and oleic acids were considered as effective antibacterial agents (Dilika et al., 2000).  
216 Further experimental studies highlighted other biological benefits of VO such as anti-  
217 inflammatory (Hsu and Parthasarathy, 2017), analgesic and antipyretic (Intahphuak et al.,  
218 2010), hypolipidemic (Ali and El-Anany, 2017), antibacterial (Tabassum and Vidyasagar,  
219 2014), antiviral (Orhan et al., 2011), hepatoprotective and gastroprotective properties (Cheng  
220 et al., 2015).

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

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

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

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

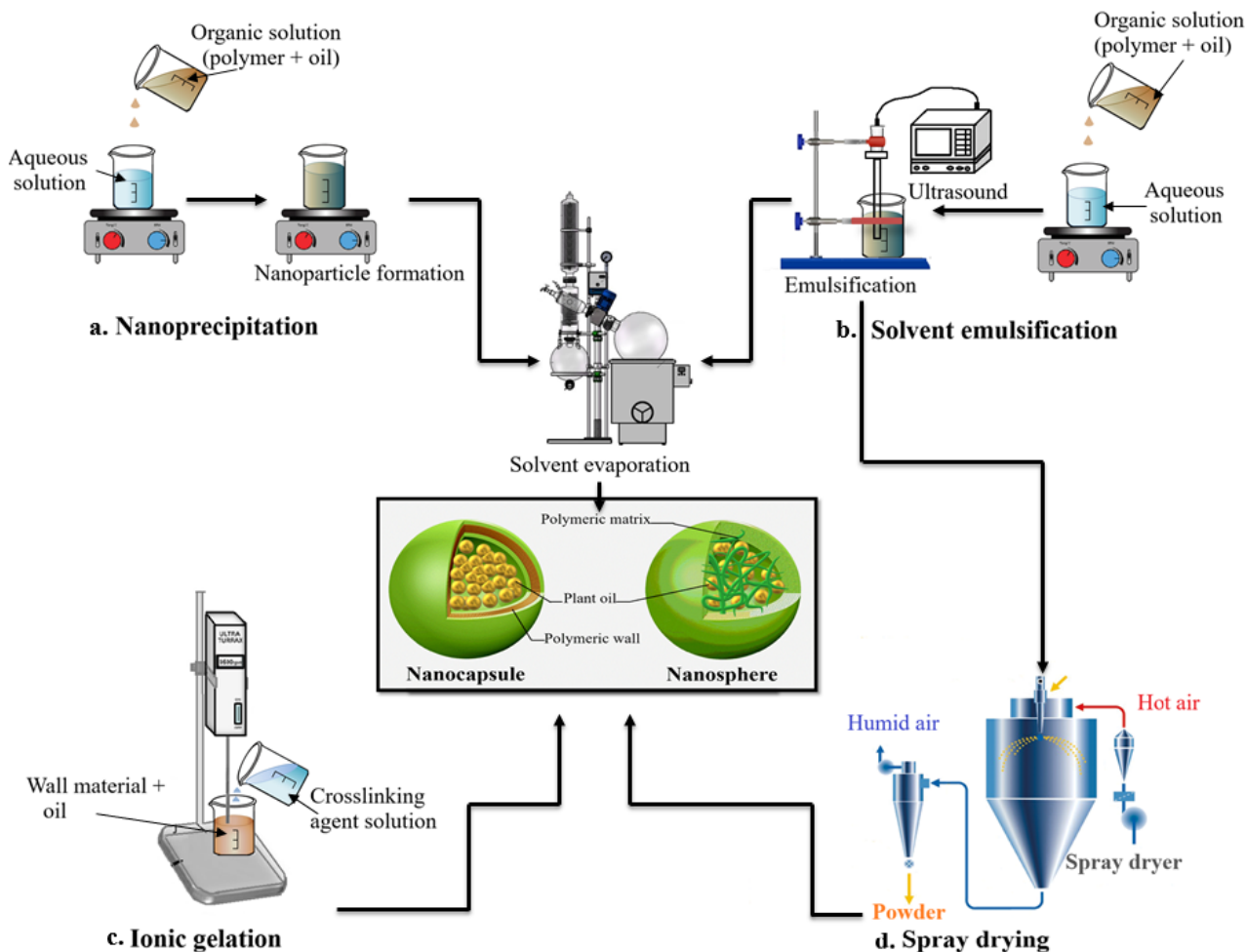
## 252 **5. Plant oils-loaded nanodelivery systems**

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

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

### 261 **5.1. Encapsulation in polymer-based nanocarriers**

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



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

278

279 **5.1.1. Spray drying**

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

288           Regarding the particle size and the encapsulation efficiency (EE%) of the particles  
289 produced by spray drying technique, high average diameter with moderate oil entrapment  
290 amount have been reported by numerous work studies, as depicted in **Table 1**. Hoyos-leyva et  
291 al. (2019) reported that almond oil loaded taro starch particles had an average size ranging from  
292 1.4 to 31.1 $\mu\text{m}$  with an EE% of 37.5%. In addition, De-Oliveira et al. (2014) found that *Lippia*  
293 *sidoides* EO loaded alginate : cashew gum nanoparticles exhibited a spherical shape with size  
294 ranging from 223 to 399 nm, zeta potential values in range of  $-30$  to  $-36$  mV and EE% of about  
295 50 %. In another work, the same EO was encapsulated in chitosan : cashew gum based  
296 nanoparticles owning an EE% of 70% with an average particle sizes in the range 335–558 nm  
297 (Abreu et al., 2012). Furthermore, the mixture maltodextrin : soy protein was used to  
298 encapsulate walnut oil and the resultant particles showed an average diameter of 4 to 10  $\mu\text{m}$   
299 with an EE% equal to 60% (González et al., 2016).

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

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



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

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

326 Several parameters have to be taken into consideration to efficiently entrap plant oils in  
327 polymeric micro- and nanoparticles by spray drying technique. The influence of type and  
328 amount of wall material on plant oils-loaded particles characteristics has been extensively  
329 studied in the literature (Bae and Lee, 2008; Chin et al., 2018; Gallardo et al., 2013;  
330 Laohasongkram et al., 2011; Lozano et al., 2012; Rodea-gonzález et al., 2012; Rubilar et al.,  
331 2012; Shamaei et al., 2017). Carneiro et al. (2013) investigated the microencapsulation of  
332 flaxseed oil by spray drying technique. They studied the potential of maltodextrin mixed with  
333 different wall materials: arabic gum, whey protein concentrate and two types of modified starch  
334 (Hi-Cap 100TM and Capsul TA) on droplets size. Results showed that the highest viscosity  
335 presented by maltodextrin : arabic gum emulsion implies a higher resistance to droplets  
336 movement, thus preventing coalescence and leading to smaller droplets size. Shamaei et al.  
337 (2017) related the differences in the mean droplet size of the emulsions using different wall

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

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

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

363 studied the encapsulation of coffee oil and observed that as the air flow temperature increases  
364 the EE% decreases due to the fact that higher temperature leads to faster drying of the external  
365 phase which creates cracks in the particle wall, resulting in oil loss. Moisture content is an  
366 important variable for the shelf life of powders. It was reported that increasing the inlet  
367 temperature reduced the moisture content (Mohammed et al., 2017). However, higher values  
368 (more than 175 °C) resulted in an increase in moisture content due to the formation of rapid  
369 crust which hampered the water evaporation leading to particles with more moisture content.  
370 The particle size is another parameter which vary when modifying the air inlet temperature. In  
371 2017, Mohammed and coworkers pointed out that an increased inlet air temperature produced  
372 larger-sized *Nigella sativa* EO particles and ascribed this result to the microcapsule structure.  
373 Indeed, high temperature enable the particles to form early which in turn prevents the shrinkage  
374 of particles during drying (Mohammed et al., 2017).

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

### 388 5.1.2. Emulsion evaporation

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

396 The emulsion evaporation technique produces nanoparticles with higher EE% and  
397 smaller average diameter, as compared to the spray drying technique. In this context, Gomes et  
398 al. (2011a) reported a particle size of 179.3 and 173.8 nm with an EE% of 98 and 92% for  
399 eugenol- and trans-cinnamaldehyde loaded poly (lactide-co-glycolide) nanoparticles,  
400 respectively. Similarly, chia seed oil loaded nanoparticles using chia mucilage as wall material  
401 exhibited a small particle size (205 nm) with negative zeta potential (-11.58 mv) and high EE%  
402 (82.8%) (Campo et al., 2017). Moreover, poly (lactide-co-glycolide) nanoparticles were  
403 prepared to encapsulate clove EO, rich in eugenol which has potent antimicrobial activities  
404 (Priyadarshini et al., 2018). The average size of the resultant nanoparticles was about 237 nm  
405 with negative zeta potential of -40 mv and an EE% equal to 93%.

406 The nanoparticles prepared by emulsion evaporation process exhibited *in vitro* release  
407 pattern similar to that of particles produced by spray drying. In 2018, Priyadarshini et al. pointed  
408 out that *in vitro* cumulative clove EO release from poly (lactide-co-glycolide) nanoparticles  
409 followed a biphasic profile with an initial burst release at the first 4h due to the release of clove  
410 EO found near the nanoparticles surface (Priyadarshini et al., 2018). A cumulative amount of  
411 75% was progressively released up to ~15 days. Similar *in vitro* release kinetics were governed  
412 by eugenol and trans-cinnamaldehyde from poly (lactide-co-glycolide) nanoparticles where 64

413 and 87% of the initial load was released in the medium within 72 h, respectively (Gomes et al.,  
414 2011a).

415 The stability of the pNPs formulated by this technique was investigated in the literature.  
416 In 2017, Campo et al. studied the oxidation of chia seed oil by gas chromatography with flame  
417 ionization detector in both emulsions and chia seed mucilage based-nanoparticles at accelerated  
418 conditions ( $40\pm 1^\circ\text{C}$ ) during 28 days of storage (Campo et al., 2017). No significant change was  
419 shown in term of particle size, zeta potential or polydispersity index. However, the fatty acid  
420 methyl esters content reduction in pNPs was smaller than in emulsions; therefore, the chia seed  
421 mucilage provided a high protection against oil oxidation (Campo et al., 2017).

422 With respect to the emulsification evaporation process, several parameters may affect  
423 the nanoparticles properties. Freiburger et al. (2015) investigated the effect of polymer type  
424 (poly(3-hydroxybutyrate-co-3-hydroxyvalerate)/polylactide); dispersion mechanism  
425 (ultrasonication / high shear homogenization) and polymer : oil ratio on the average size and  
426 oil recovery of biocompatible nanoparticles containing coffee oil. The statistical analysis  
427 showed non-significant effect of the experimental factors on the nanoparticle size within the  
428 experimental range. While for the coffee oil recovery, regression analysis produced a significant  
429 model. Less oil was lost by volatilization when sonication was used, because the required  
430 dispersion time (3min) was smaller when compared to the ultraturrax time (10min). Results  
431 showed also that less coffee oil loss was pronounced when using poly(3-hydroxybutyrate-co-  
432 3-hydroxyvalerate) combined to the high shear homogenization as well as using polylactide  
433 combined with sonication. This was explained by the high viscosity of poly(3-  
434 hydroxybutyrate-co-3-hydroxyvalerate)-dichloromethane solution which could avoid oil  
435 volatilization even with high shear homogenization (Freiburger et al., 2015). Regarding the  
436 polymer:oil ratio, an increase in polymer amount lead to increase the viscosity of the solution  
437 resulting in efficient oil protection from the heat generated by the homogenizer.

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

### 443 **5.1.3. Nanoprecipitation**

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

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

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

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

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

488 consists essentially of cinnamaldehyde which reacts with hydroxyl group of cellulose acetate  
489 giving hemiacetal bound and hence combats the nanocapsules. Liakos and his coworkers  
490 assessed also in their study higher zeta-potential upon increasing lemongrass EO concentration,  
491 suggesting that some EO molecules are present onto the outer surface of the particles (Liakos  
492 et al., 2018). Similarly, it was reported that the presence of lime EO decreased the zeta potential  
493 and the values were 61.1 and 57.0 mV for free- and loaded- chitosan nanocapsules, respectively.  
494 They attributed this result to the diminution of free  $\text{NH}_3^+$  groups of chitosan following their  
495 interaction with lime EO (Sotelo-Boyás et al., 2017b). However, in another work study, the  
496 presence of rosemary EO did not affect the zeta potential of poly ( $\epsilon$ -caprolactone) nanoparticles  
497 which confirm its presence in the core of the nanoparticles instead of being adsorbed on their  
498 surface (Khoobdel et al., 2017).

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



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

521        Recently, a novel form of pNPs was developed called lipid-core nanocapsules which is  
522 composed of a mixture of oil and solid lipid surrounded by a polymeric wall (Ourique et al.,  
523 2010). For instance, the oily core of pNP may consist of a liquid lipid, a mixture of liquid lipids,  
524 or a mixture of liquid lipid and solid lipid. The latter concerns a specific form of nanocapsules  
525 called lipid-core nanocapsules (Frank et al., 2015). Several research works have been already  
526 published investigated the feasibility to entrap VO into lipid core NPs (Almeida et al., 2009;  
527 Drozdek and Bazyli, 2016; Friedrich et al., 2008; Marchiori et al., 2017; Rigo et al., 2013;  
528 Weber et al., 2016). In this context, nanoprecipitation technique was efficiently carried out to  
529 develop borage oil : betamethasone co-loaded lipid-core nanocapsules with a mean size around  
530 210 nm, negative zeta potential (-16.6mv), low polydispersity index (<0.05) and high EE% (up  
531 to 100%) (Weber et al., 2016). Furthermore, Rigo et al. (2013) studied the influence of the type  
532 of VO on the release kinetic of clobetasol propionate, selected as model drug, from the lipid  
533 core nanoparticles. Results revealed a biphasic drug release profiles for all the formulations.  
534 After 168 h, the concentration of clobetasol propionate released from the formulation was in  
535 the following order: Sunflower oil-pNPs < Soybean oil-pNPs < Rice bran-pNPs. The authors  
536 related these results to the consistency indices of the mixture oil : sorbitan monostearate, used

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

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

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

555 Overall, the nanoprecipitation or solvent displacement method is widely used to develop  
556 pNPs for plants oils encapsulation. According to the **Table 1**, the polymers commonly used to  
557 design the polymeric matrix are synthetic polyesters like poly (lactide-co-glycolide)  
558 (Esfandyari-Manesh et al., 2013; Iannitelli et al., 2011; Sousa et al., 2013), poly ( $\epsilon$ -  
559 caprolactone) (Badri et al., 2018; Christofoli et al., 2015; Ephrem et al., 2014; Jummes et al.,  
560 2020; Khoobdel et al., 2017), polylactide (Liakos et al., 2016), Eudragit®L100 (Averina and  
561 Allémann, 2013), S100 (Averina and Allémann, 2013), L100-55 (Pina-Barrera et al., 2019) and

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

#### 570 **5.1.4. Ionic gelation**

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

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

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

592         Currently, several research works have been reported to investigate the effect of pNPs  
593 composition and operating conditions on physicochemical properties of particles prepared by  
594 ionic gelation method. The optimization of the type and amount of polymer and crosslinking  
595 agent is crucial to develop pNPs with suitable characteristics. In this approach, *Carum copticum*  
596 EO-loaded chitosan nanoparticles were prepared by ionic gelation method using two types of  
597 crosslinking agents: tripolyphosphate and hexametaphosphate (Esmaeili and Asgari, 2015). The  
598 efficacy of crosslinking agent type and tripolyphosphate concentration on the EE% were  
599 evaluated. The particles prepared using hexametaphosphate (0.5% (w/v)) had significantly  
600 lower loading capacity and EE% than those prepared using tripolyphosphate (0.5% (w/v)). This  
601 was attributed to the ring structure and bigger size of hexametaphosphate which in turn lead to  
602 decrease the crosslinking phenomenon. In the same work, different nanoparticles were prepared  
603 using different tripolyphosphate concentrations (0.25, 0.5, 0.75 and 1% (w/v)) and results  
604 indicated that maximum EE% was obtained with the concentration of 0.5% (w/v). The low  
605 value of EE% obtained with the concentration of 0.25% (w/v) was explained by the shortage of  
606 tripolyphosphate concentration to crosslink the nanoparticles; while the low values shown with  
607 0.75 and 1% (w/v) tripolyphosphate concentrations were related to the particle shrinkage  
608 (Esmaeili and Asgari, 2015).

609         With respect to the polymer effect, the viscosity of chitosan was optimized for  
610 fabrication of vanilla oil loaded microcapsules using the coacervation method (Yang et al.,  
611 2014). Results showed that at low chitosan viscosity, no microcapsules were formed because

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

614         Regarding the EO concentration, Hasheminejad et al. (2019) stated that both particle  
615 size and zeta potential decreased significantly when increasing clove EO concentration. The  
616 reduction in particle size was explained by the great packing of polymer chains, due to the high  
617 number of amino groups in chitosan responsible for the interaction with the oil. Additionally,  
618 the thermogravimetric analysis performed by Hosseini et al. (2013) on oregano EO loaded-  
619 chitosan nanoparticles demonstrated that as the initial EO content increases from 0.1 to 0.8 g/g  
620 chitosan, loading capacity increases too from 3 to 8%, but the EE% decreases from 47 to 21%.  
621 This was explained by the saturation of oregano EO loaded into chitosan nanoparticles. The EO  
622 concentration was found to affect also the *in vitro* release profile. Indeed, Hosseini and his  
623 coworkers reported that low concentration of oregano EO (0.1 g/g chitosan) leads to burst  
624 release (82% of encapsulated EO was released from the nanoparticles within 3 h). While, as  
625 oregano EO amount increased, the burst effect was dramatically alleviated and the cumulative  
626 release was reduced from 82 to 12% after 3h. This phenomenon was attributed to the fact that  
627 chitosan nanoparticles with smaller particle size would have bigger surface-to-volume ratio  
628 which may result in fast release of oregano EO adsorbed on their surfaces (Hosseini et al.,  
629 2013). Another factor affecting the release profile was found to be the composition of the  
630 encapsulated material. In 2014, Dima et al. investigating the release of *Pimenta dioica* EO  
631 found that chitosan microspheres covered with k-carrageenan are more fragile and exhibit  
632 higher swelling degree with zero order release kinetics, as compared to the chitosan : k-  
633 carrageenan microspheres hardened by glutaraldehyde crosslinking which show non-Fickian  
634 release mechanism (Dima et al., 2014).

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

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

644 On the whole, ionic gelation method is broadly used to encapsulate plants oils when  
645 compared to simple emulsion evaporation method. Gelatin (Devi et al., 2012; Dong et al., 2011;  
646 Sutaphanit and Chitprasert, 2014; K. Zhang et al., 2012), arabic gum (Dong et al., 2011; Lv et  
647 al., 2014; X. Yang et al., 2015; K. Zhang et al., 2012), alginate (Devi et al., 2012; Natrajan et  
648 al., 2015) and chitosan (Feyzioglu and Tornuk, 2016; Hosseini et al., 2013; Jamil et al., 2016;  
649 Liu et al., 2017; López-meneses et al., 2018) are the most commonly used wall materials. In  
650 addition, tripolyphosphate (Hasheminejad et al., 2019; Hosseini et al., 2013; Hu et al., 2015;  
651 Liu et al., 2017; Woranuch and Yoksan, 2013) and glutaraldehyde (Devi et al., 2012; Dima et  
652 al., 2014; Natrajan et al., 2015; Sutaphanit and Chitprasert, 2014) are widely used as  
653 crosslinking agents. The main advantages of ionic gelation method are, in particular; the  
654 avoidance of high shear forces and the use of aqueous solvents instead of organic ones.  
655 Moreover, ionic gelation is simple, economic and reproducible. However, moderate EE% and  
656 larger particle size were assessed using this method as compared to the nanoprecipitation  
657 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 (%)			
<b><i>Nanoprecipitation method</i></b>								
Costus	<i>Saussurea lappa</i>	Eudragit RS 100	145	+45	/	Anticholinesterase, anti-inflammatory	Medicine	(Lammari et al., 2021)
Baccharis dracunculifolia	<i>Baccharis dracunculifolia</i> DC	Eudragit RS 100	151.6	+51.7	99.4	Antibacterial	Food	(Timbe et al., 2020)
Oregano	<i>Origanum vulgare</i> L.	PCL	158-300	-13.8 to -28.5		Antibacterial	Food	(Souza et al., 2020)
Palmorasa	<i>Cymbopogon martini</i> 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	<i>Zataria multiflora</i> Boiss.	PCL	192-398	+13.9 to +29.2	75-79	Insecticide	Agriculture	(Ahsaei et al., 2020)
Thyme	<i>Thymus vulgaris</i> L.	Eudragit L 100-55	153.9	-4.11	52.81	Antioxidant	Food	(Pina-Barrera et al., 2019)
	<i>Thymus leptobotrys</i> L.	Eudragit RS 100	144	+80.9	/	Bacteriostatic, fungistatic	Medicine	(El-Asbahani et al., 2015)
	<i>Thymus satureoides</i> L.	Eudragit RS 100	132	81.6	/	Bacteriostatic, fungistatic	Medicine	(El-Asbahani et al., 2015)
	<i>Thymus serpyllum</i> L.	Chitosan	117-226	+27	/	Antimicrobial	Agriculture	(Sotelo-Boyás et al., 2015)
		Chitosan	/	/	68	Antimicrobial	Agriculture	(Sotelo-Boyás et al., 2017a)
Sweet orange	<i>Citrus sinensis</i> L.	Eudragit RS100	57- 208	+39 to +74	56-96	Antimicrobial	Food	(Froiio et al., 2019)
Bergamot	<i>Citrus bergamia</i> Risso.	Eudragit RS100	57- 208	+39 to +74	28-84	Antimicrobial	Food	(Froiio et al., 2019)
Rosemary	<i>Rosmarinus officinalis</i> 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	<i>Lavandula dentate</i> L.	Eudragit EPO	200	/	41	Antioxidant	Cosmetics	(Silva-Flores et al., 2019)
		PEO-b-PLA	10-75	/	70-75	Antimicrobial	Textile	(Popiolski et al., 2016)
Peppermint	<i>Mentha piperita</i> L.	Cellulose acetate	180	-38	/	Antimicrobial	Medicine	(Liakos et al., 2018)
Cinnamon	<i>Cinnamomum cassia</i> persl.	Cellulose acetate	150	-40	/	Antimicrobial	Medicine	(Liakos et al., 2018)
Lemongrass	<i>Cymbopogon citratus</i> 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	<i>Nigella sativa</i> 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 Free fatty acid	<i>Pinus pinea</i> L. /	Eudragit L 100-55 / Eudragit L100 / Eudragit S100	236-296 260-319	/ /	85-91 83-99	Source of PUFA	Medicine	(Averina and Allémann, 2013)
Babassu	<i>Attalea speciosa</i> Mart.	PLGA	209.2	-15.8	/	Treatment of benign prostatic hyperplasia	Medicine	(Sousa et al., 2013)
<b>Emulsion evaporation method</b>								
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- cinnamaldehy de	/	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)
<b>Ionic gelation method</b>								
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- aflatoxicogenic	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. <i>Summer savory</i>	Chitosan	50–100	>+50	>90	Antimicrobial	Medicine	(Jamil et al., 2016)
		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 <sup>3</sup>	/	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)
<b>Spray drying method</b>								
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 <sup>3</sup>	/	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 <sup>3</sup>	/	90.0-95.3	Source of MUFA and PUFA	/	(Chew et al., 2018)
		β-cyclodextrin +sodium caseinate						
Chia seed	<i>Salvia hispanica</i> L.	β-cyclodextrin + gum arabic + sodium caseinate						
		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 <sup>3</sup>	/	10-30	Antioxidant	Cosmetic (Nosari et al., 2015)
		Arabic gum	7880-13.10 <sup>3</sup>	/	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);

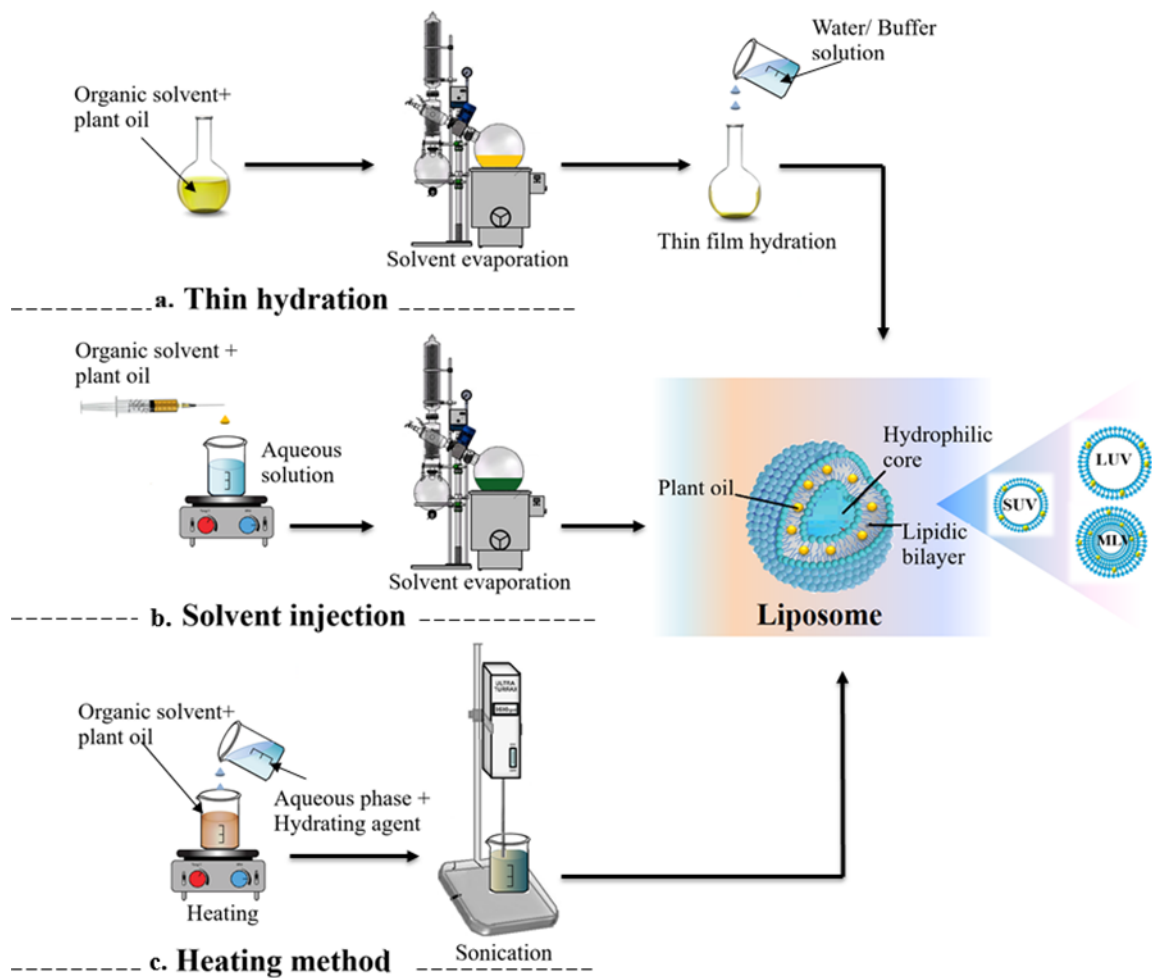
660 HPC: Hydroxypropylcellulose; HPMC: Hydroxypropylmethylcellulose; PVA: Poly vinyl alcohol; PUFA: Poly unsaturated fatty acids; MUFA: Mono unsaturated fatty acids.

661

## 662 **5.2. Encapsulation in lipid based nanocarriers**

### 663 **5.2.1. Liposomes**

664 Liposomes were first developed for drug delivery purposes by Bangham et al. in 1965  
665 (1965). Liposomes are vesicles formed by one or more lipid bilayers defining one or several  
666 aqueous compartments. They can be classified depending on their size and lamellarity to: i)  
667 small unilamellar vesicles (SUV) with a size between 20nm and 100 nm, ii) large unilamellar  
668 vesicles (LUV) with a size greater than 100 nm and iii) multilamellar vesicles (MLV) with a  
669 size greater than 0.5 $\mu$ m, as demonstrated in **Fig. 6** (El-Asbahani et al., 2015). Generally, the  
670 liposome bilayer consists of natural and/or synthetic phospholipids like phosphatidylcholine,  
671 phosphatidylethanolamine, phosphatidylserine, phosphatidylglycerol and phosphatidylinositol.  
672 Cholesterol may also be incorporated to the lipidic bilayer to reduce the permeability of water-  
673 soluble molecules through the membrane and improve its fluidity, and stability (Laouini et al.,  
674 2012). Due to the lipophilic character of the liposome bilayer, plant oils like essential or  
675 vegetable oils are highly entrapped to enhance their bioavailability and hurdle their  
676 physicochemical instability upon exposure to light, oxygen and temperature (El-Asbahani et  
677 al., 2015). Several methods have been used to develop liposomes containing plants oils, while  
678 the thin film hydration, solvent injection and heating methods were widely used in the last  
679 decade.



680

681

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

682

### 5.2.1.1. Thin lipid film hydration

683

684

685

686

687

688

689

690

691

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**.

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

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

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

723         The liposome size was not only affected by the EO concentration. In fact, Nazari et al.,  
724 (2019) developing garlic EO nanophytosomes by thin hydration method, investigated the effect  
725 of the preparation method. For instance, nanophytosomes were a novel lipid based vesicular  
726 delivery systems where stable hydrogen bonds are formed between the phosphatidylcholine  
727 molecules and nutraceuticals leading to the formation of stable complex (Ghanbarzadeh et al.,  
728 2016). In this study, MLVs reduction size was performed using three different types of methods:  
729 sonication, homogenization and the combination of sonication and homogenization. Results  
730 showed that the combination of two methods produced the smallest liposomes (115 nm) with  
731 transparent suspension view. Homogenization produced larger particles than probe sonication  
732 method and the average size was around 161 and 135 nm, respectively. Considering the zeta  
733 potential, all the prepared phytosomes had lower values (-12.36 to -3.86 mV) than the expected  
734 and reported values for soy bean phosphatidylcholine made nanovesicular systems (around -26  
735 mV). This was linked to the interaction between the positively charged allicin (the main  
736 component of garlic EO) and the negatively charged phosphate group of phosphatidylcholine  
737 (Nazari et al., 2019). In another work study, Salari and his colleague (2019) developing  
738 rosemary EO loaded- L- $\alpha$ -phosphatidylethanolamine dioleoyl : cholesteryl hemisuccinate  
739 liposomes found that sonication method produced smaller liposome than filtration method. The  
740 average sizes were 142.5 and 437.2 nm, respectively. Results showed also that increasing the



741 lipid ratio of L- $\alpha$ -phosphatidylethanolamine dioleoyl to cholesteryl hemisuccinate from 3:2 to  
742 7:3 resulted in much larger liposomes with more negative zeta potential.

743 As there are several types of phospholipids, it is reliable to alter the size, charge and  
744 EE%, upon variation of type or addition of new ingredients to the lipid mixture. In this  
745 approach, the effect of lipid composition on the EE% of *Anethum graveolens* EO-loaded  
746 liposomes was investigated by Ortan et. al (2009). Liposomes with different lipids; fresh egg  
747 yolk, dimiristroylphosphatidyl choline, dipalmitoylphosphatidyl choline,  
748 dimiristroylphosphatidyl glycerol and dioleoylphosphatidyl choline, were prepared by thin  
749 hydration method. Results showed that oil entrapment varied in this way:  
750 dimiristroylphosphatidyl glycerol (55.2%) < dimiristroylphosphatidyl choline (58.9%) <  
751 dioleoylphosphatidyl choline (77%) < dipalmitoylphosphatidyl choline (97%) < fresh egg yolk  
752 (98%). Although dipalmitoylphosphatidyl choline showed good entrapment efficiency, its use  
753 was difficult as it required high temperature due to its high transition temperature. The authors  
754 related the low values of EE% of dioleoylphosphatidyl choline, dimiristroylphosphatidyl  
755 glycerol and dimiristroylphosphatidyl choline to their unsaturation.

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

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

768         Regarding the stability of EO loaded in liposomes, Liolios et al. (2009) investigated the  
769 oxidative stability of carvacrol and thymol isolated from *Origanum dictamnus* L. EO and their  
770 mixtures, before and after their encapsulation in egg L- $\alpha$  phosphatidylcholine/cholesterol-based  
771 liposomes by differential scanning calorimetry analysis. Results showed the appearance of  
772 exothermic peaks related to the auto-oxidation process of the samples. The onset temperatures  
773 at which the auto-oxidation process starts were in the following order: Carvacrol  
774 (258°C)<Thymol (273°C)<Carvacrol : Thymol (302°C) <Empty liposomes (362°C) <  
775 Liposomes +Carvacrol : Thymol (392°C). One can conclude that carvacrol and thymol  
776 presented better antioxidant action when encapsulated than when in pure form. The antioxidant  
777 activity of empty liposomes is lower than that of oil loaded- liposome, suggesting that the  
778 liposome membranes were stabilized by the link of the lipophilic compounds with lipid bilayers  
779 (Liolios et al., 2009).

780         Beyond EO, liposomes can potentially enable the encapsulation of VO and their  
781 derivatives, as illustrated in **Table 3**. Recently, numerous studies have been investigated to  
782 encapsulate fatty acids in liposomes. Among the several polyunsaturated fatty acids (PUFAs),  
783 dietary  $\omega$ 3 like eicosapentaenoic and docosahexaenoic acids have been extensively investigated  
784 for their beneficial effects (Hadian, 2016). Alaarg et al. (2016) developed docosahexaenoic  
785 acid- loaded liposomes by thin hydration method. The obtained liposomes exhibited small  
786 average diameter around 100 nm, narrow size distributions, negative zeta potential ( $15.7 \pm$   
787  $2.5\text{mv}$ ) and high EE% of 81.35 %. Moreover, eicosapentaenoic and docosahexaenoic acids  
788 were entrapped in nanoliposomes (i.e. nanoscale lipid vesicles) developed by thin hydration  
789 followed by either extrusion ultrasonic irradiation; bath sonication; probe sonication; or  
790 combined probe and bath sonication (Hadian et al., 2014). Results showed that probe sonication

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

797 In overall, thin hydration method is widely employed to develop plant oils loaded  
798 liposomes due to its simplicity. Several phospholipids are used in the literature including  
799 soybean phosphatidylcholine (Ge & Ge, 2016; Ge & Ge, 2015; Khatibi et al., 2017; Nazari et  
800 al., 2019; Rasti et al., 2012; Q. Wang et al., 2015), dipalmitoyl phosphatidylcholine (Detoni et  
801 al., 2012), egg phosphatidylcholine (Saffari et al., 2016), phospholipon<sup>®</sup>90G (Risaliti et al.,  
802 2019). Cholesterol is the most used fluidifying agent (Alikhani-Koupaei, 2015; H. Cui, Yuan,  
803 et al., 2017; Y. Cui et al., 2010; Y. Ge & Ge, 2016; Ge & Ge, 2015; Khatibi et al., 2017; Lin et  
804 al., 2018; Lin, Chen, et al., 2019; Q. Wang et al., 2015); in other cases, tween 80 (Y. Ge et al.,  
805 2019; Y. Ge & Ge, 2016; Ge & Ge, 2015; Lin, Chen, et al., 2019) and poly vinyl pyrrolidone  
806 (Cui et al., 2017a, 2017b, 2016a, 2016b, 2015; Lin et al., 2019b, 2018) were incorporated as  
807 surfactants.

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

#### 814 **5.2.1.2 Solvent injection**

815 The solvent injection method, firstly described in 1973 (Batzri and Korn, 1973), implies  
816 the dissolution of the lipid into an organic phase such as ethanol or ether, followed by the  
817 injection of the lipid solution into aqueous solution resulting in liposomes dispersion (Laouini  
818 et al., 2012). After that, the organic solvent was evaporated under reduced pressure (**Fig. 6.b**).  
819 This technique is widely used for plant oil encapsulation, as demonstrated in **Table 2**. The  
820 solvent injection' main feature is that narrow size distribution of submicron liposomes (under  
821 100 nm) could be produced without extrusion or sonication (Stano et al., 2004). Moreover,  
822 compared with thin hydration method, the ethanol injection technique was found to be scalable.  
823 In fact, clove EO-liposomes were successfully scaled-up using a membrane contactor (600ml)  
824 and a pilot plant (3L) (Sebaaly et al., 2015a). Furthermore, various eugenol- and clove EO-  
825 liposomes were prepared at laboratory (ethanol injection) and large scale (membrane  
826 contactor): free hydroxypropyl- $\beta$ -cyclodextrin loaded liposomes; drug in hydroxypropyl- $\beta$ -  
827 cyclodextrin in liposomes (DCL) and DCL<sub>2</sub> obtained by double loading technique, where the  
828 drug is added in the organic phase and the inclusion complex in the aqueous phase (Sebaaly et  
829 al., 2016a). Results showed that eugenol and clove EO loaded DCL and DCL<sub>2</sub> developed at  
830 large scale had a mean size similar to those obtained by laboratory scale. Besides, Eugenol and  
831 clove EO loaded DCL and DCL<sub>2</sub> had a mean particle size significantly smaller than that of free  
832 hydroxypropyl- $\beta$ -cyclodextrin liposomes containing either eugenol or clove EO at both  
833 laboratory and large scales. This was explained by the complete incorporation of the aromatic  
834 cycle of eugenol inside the hydrophobic cavity of hydroxypropyl- $\beta$ -cyclodextrin, resulting in  
835 limit interaction between eugenol and lipidic bilayers. Regarding the polydispersity index and  
836 zeta potential, no difference was assessed between all the tested liposomes.

837 Currently, several studies have been reported to investigate the effect of liposome  
838 composition and operating conditions on physicochemical properties of liposomes prepared by  
839 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).

864           Regarding the stability of liposomes prepared by ethanol injection process, Liu et al.  
865 (2016) investigated the stability of galanga EO-loaded liposomes at low temperature (4°C) and  
866 dark conditions and results revealed minor change in mean particle size and polydispersity  
867 index. Furthermore, the photostability of eugenol in aqueous solution and in liposome  
868 formulations (Phospholipon 80H, Phospholipon 90H and Lipoid S100) was investigated under  
869 UV light irradiation for 96hours (Sebaaly et al., 2015b). Results revealed that liposomes  
870 formulations protect eugenol more than aqueous solutions. The percentages of remaining  
871 eugenol were 58, 82, 91 and 95% for aqueous solution, Phospholipon 80H-, 90H- and S100-  
872 liposomes, respectively. The highest value of remaining eugenol for lipoid S100 was related to  
873 the flexibility of the membrane resulting in a deep insertion of eugenol into the lipid bilayer  
874 leading to better protection from any UV light effect (Sebaaly et al., 2015b).

875           Despite using ethanol injection for EO encapsulation in liposomes, a few reports have  
876 been published during the last decade regarding the encapsulation of VO. Recently, Huang et  
877 al. (2020) developed co-loaded linseed oil with quercetin in liposomes with the aim of  
878 enhancing their solubility and stability. The produced liposomes owned a spherical shape with  
879 a small average size (262.2 nm). In 2019, Bai and his coworkers investigated the effect of  
880 different coix seed oil:  $\beta$ -carotene ratios on the physiochemical properties, stability and  
881 antioxidant activity of coix seed oil :  $\beta$ -carotene co-loaded-liposomes (C. Bai et al., 2019).  
882 Results showed that by increasing coix seed oil, the EE% of  $\beta$ -carotene in the liposomes  
883 decreased. The values of EE% for 1:1, 1:5, and 1:10,  $\beta$ -carotene:coix seed oil liposomes were  
884 83.8, 81.3, and 80.8 %, respectively, which were slightly lower than that of liposomes  
885 containing  $\beta$ -carotene alone (86.0%). This was ascribed to the ability of coix seed oil to compete  
886 for the available hydrophobic domains within the phospholipid bilayers.

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

889 reduction. According to the previous work studies, phospholipon<sup>®</sup>90H (Sebaaly et al., 2016a,  
890 2016b), phospholipon<sup>®</sup>80H (Sebaaly et al., 2016b), lipoid<sup>®</sup> S100 (Hammoud et al., 2019;  
891 Sebaaly et al., 2016b) and egg phospholipids (C. Bai et al., 2019; Rushmi et al., 2017) are  
892 widely used as bilayer forming lipids. Ethanol injection method suffers from several drawbacks  
893 including continuous exposure of plant oils to high temperature and organic solvents which  
894 may affect both the safety and stability of the liposomes (Nkanga et al., 2019).

### 895 **5.2.1.3. Heating method**

896 The heating method, called also Mozafari method, was first developed in 2005. It is  
897 known to be the most attractive method for liposomes preparation due to its organic  
898 solvent/detergents free characteristics (Mozafari & Mortazavi, 2005). In this technique, lipids  
899 are hydrated in the presence of hydrating agent (glycerin or propylene glycol) and heated at 40–  
900 120°C (at the temperature which is above the transition temperature of the phospholipids)  
901 depending on the properties of the ingredients, the presence or absence of cholesterol, and the  
902 type of material to be entrapped (**Fig.6.c**) (Mozafari et al., 2008).

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

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

921 Like the methods discussed above, Mozafari method was affected by several operating  
922 conditions. In 2013, Rasti et al. investigated the effect of shear rate, mixing and sonication times  
923 on colloidal properties of polyunsaturated fatty acids (docosahexaenoic acid and  
924 eicosapentaenoic acid) nanoliposomes (Rasti et al., 2013). In their study, response surface  
925 methodology was applied to predict the optimum levels of liposome preparation condition  
926 producing maximum EE% and minimum average size. According to ANOVA analysis, all the  
927 independent variables and their interactions were found significant; while, the main significant  
928 effect on liposome size and EE% was found to be the shear rate. After optimizing the operating  
929 parameters; shear rate (795 rpm), mixing time (60 min) and sonication time (10 min), the  
930 nanoliposome exhibited an average diameter of 81.4nm with an EE% of 100% (Rasti et al.,  
931 2013).

932 Besides using heating method to encapsulate VO in liposomes, no report was found  
933 regarding the encapsulation of EO maybe due to their high sensitivity and volatility upon  
934 exposure at high temperature. Thus, this technique is not suitable for thermosensitive bioactive  
935 agents. In closing, Mozafari method showed to be a fast, simple, scalable, and non-toxic  
936 technique for liposome preparation with high EE%. In addition, the obtained liposomes can be  
937 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 (%)			
<b><i>Thin hydration method</i></b>								
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- $\alpha$ -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 Anti-inflammatory	Medicine	(Risaliti et al., 2019)
		Soybean phospholipid	188.5	-48.38	46.5	Antibacterial	Food	(Cui et al., 2016b)
Rosemary	<i>Rosmarinus officinalis</i> L.	L- $\alpha$ -PEA dioleoyl	79	-2.77	45	Anticancer	Medicine	(Salari and Salari, 2019)
		Phospholipon 90G	≈200	-20 to -35	65	Antioxidant; antibacterial Anti-inflammatory	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)
		Soybean PCH	75	-7.45	96.08	Antimicrobial	/	(Ge and Ge, 2016)
Ajwain	<i>Trachyspermum copticum</i> L.	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- $\alpha$ -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)
Clove	<i>Syzygium aromaticum</i> L.	Phospholipid	125.6	-35.5	35.6	Antimicrobial; antioxidant	Medicine	(Cao et al., 2016)
		Phospholipon 90H	/	/	54.2 - 59.7	Anti-inflammatory	Medicine	(Sebaaly et al., 2016a)
Eugenol	/	Phospholipid	/	/	/	Anti-inflammatory	Medicine	(Sebaaly et al., 2015b)
		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)
Linseed oil + quercetin	<i>Linum usitatissimum</i> L.	Phospholipid	/	/	/	Anti-inflammatory	Medicine	(Sebaaly et al., 2015b)
		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)
<b>Heating method</b>								
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

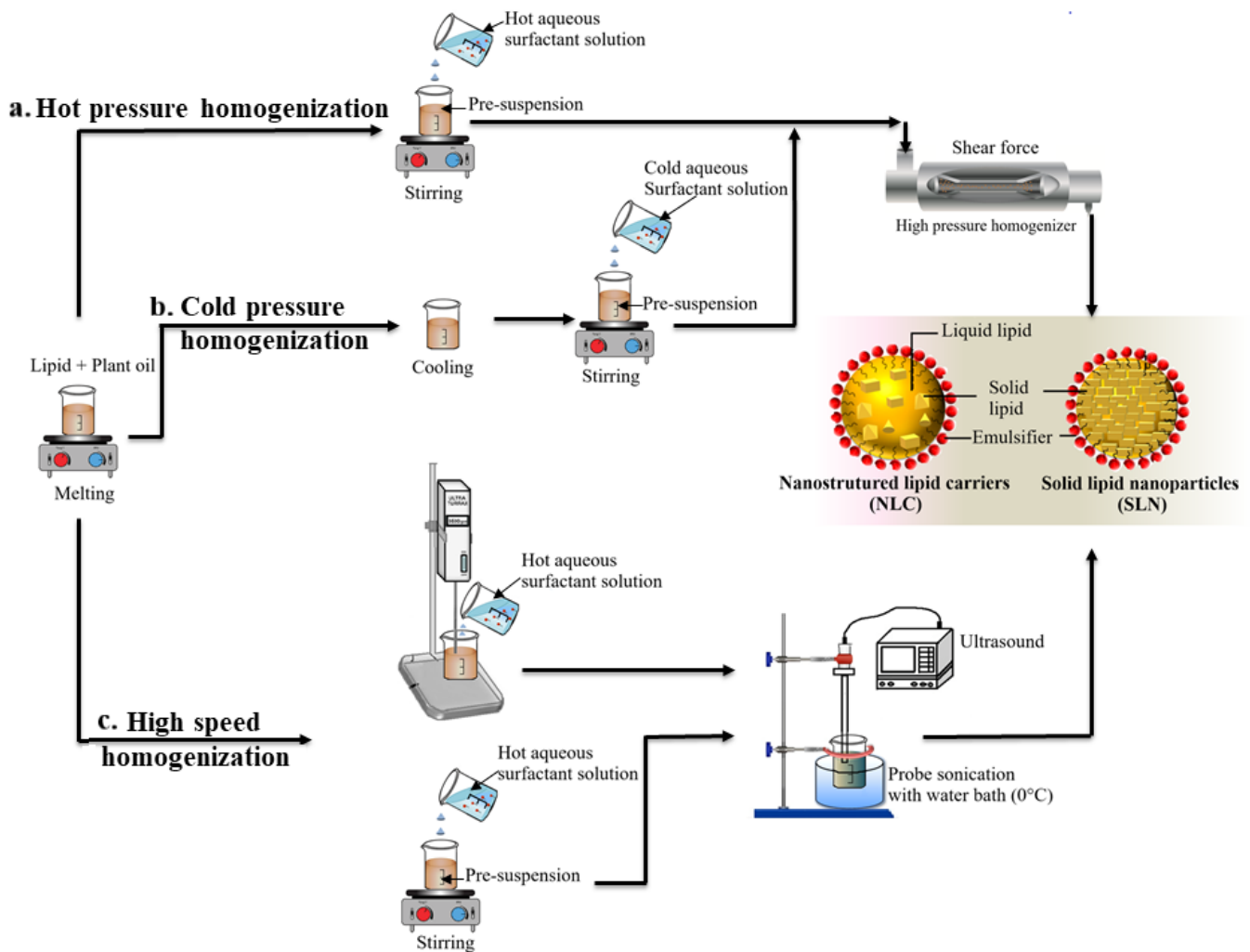
### 943 **5.2.2. Solid lipid nanoparticles and nanostructured lipid carriers**

944 Solid lipid nanoparticles (SLN) are other lipid-based carriers that have emerged as they  
945 combine the benefits of liposomes and polymeric nanoparticles (Sarangi and Padhi, 2016).  
946 Solid lipid nanoparticles, developed since 1990, are suspensions of nanosized solid lipid  
947 particles dispersed in an aqueous media (Patel, 2013). They are composed of surfactants and a  
948 lipid matrix that acquires a solid-state lipid at ambient temperature (Bayón-Cordero et al.,  
949 2019). The commonly used materials to structure the lipid core are fatty acids (stearic acid,  
950 palmitic acid, decanoic acid and benzoic acid), triacylglycerols (trimyristin, trilaurin, tristearin  
951 and tripalmitin) and acyl glycerols (glycerol monostearate, glycerol palmitostearate and  
952 glycerol benzoate). These lipids are characterized by their purity, low price, safety and  
953 biodegradability. In the other hand, phospholipids (phosphatidylcholine, soy and egg lecithins),  
954 poloxamer, pluronic<sup>®</sup>F127, bile salts, tween 80 and polyvinyl alcohol are example of commonly  
955 used surfactants (Kaliampurthi and Selvaraj, 2016).

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

962 Considering the delivery of plant oil, the main reason to use SLN or NLC as nanocarriers is the  
963 improvement of entrapment efficiency. Since the oils are mostly lipophilic, they present a good  
964 miscibility with the lipid matrix, resulting high amount of oil could be entrapped (Falcao et al.,  
965 2015). In addition, these lipid-based carriers protect the labile and sensitive oil components  
966 from chemical, photochemical or oxidative degradation, due to the immobilization by solid  
967 lipids. Different methods are employed to produce SLN, however, high pressure

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



970  
971 **Fig. 7.** Schematic illustration of solid lipid nanoparticles and nanostructured lipid carriers'  
972 preparation methods.

### 973 5.2.2.1. High pressure homogenization

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

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

980 Using the high-pressure homogenization to encapsulate plants oils, the lipid is heated at  
981 5 to 10°C above its melting point, and the oil is dissolved within (**Fig.7.a**). After that two  
982 approaches are involved: hot or cold homogenization. In hot homogenization, hot aqueous  
983 surfactant solution is dispersed with the plant oil-lipid melt under stirring at the same  
984 temperature creating the pre-emulsion. The resultant pre-emulsion was pushed through a  
985 piston-gap homogenizer creating a hot oil-in-water (O/W) nanoemulsion which is cooled after  
986 at room temperature allowing the crystallization of the lipid and the formation of SLN.

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

992 Regarding the size of SLN prepared by this technique, numerous research works  
993 reported a small average diameter with good stability and high EE%. For example, SLN  
994 containing frankincense and myhrr EO in a ratio 1:1 were developed using hot homogenization  
995 process by Wang et al. (Wang, 2012). An average mean size of 113.3 nm, a zeta potential of -  
996 16.8 mV and an EE% of 80.60% were assessed for the obtained SLN. The same process was  
997 used to prepare SLN encapsulating the VO: copaiba oil with and without allantoin which is  
998 widely used in cosmetology for its keratolytic, moisturizing, soothing and wound healing  
999 properties (Svetlichny et al., 2015). The dynamic light scattering analysis revealed an average  
1000 particle size of 126.06 nm and 118.63 nm for the copaiba oil-loaded SLN and copaiba oil:  
1001 allantoin-co-loaded SLN, respectively.

1002           Concerning the stability of SLN, previous works highlighted their efficiency in  
1003 preserving the quality of encapsulated oil during long-term storage as compared to un-  
1004 encapsulated-form (Tian et al., 2018; Zielinska et al., 2019). Tian et al. (2018) reported that  
1005 SLN can enhance the stability of citral in acidic surroundings. Gas-chromatography analysis  
1006 showed that after 12 days storage, 67% of citral remained in the citral loaded-SLN formulations,  
1007 while only 8% remained in the control. In addition, the overall flavour of the degradation  
1008 products generated from citral-SLN were assessed and results demonstrated that the off-  
1009 flavours had little effect on the whole flavour of citral-SLN in the system sample as compared  
1010 with the control (Tian et al., 2018).

1011           Several factors such as the kind of lipid, surfactant and the operating process conditions  
1012 could influence the physicochemical properties of the particles obtained by high-pressure  
1013 homogenization. In this context, Mai et al. (2018) investigated the influence of homogenization  
1014 conditions on gac fruit EO-loaded SLN prepared by hot and cold homogenization. Results  
1015 showed that increasing hot homogenization speed from 5000 to 10000 rpm was accompanied  
1016 with a decrease in particle size from 3297 to 201 nm. However, further increase in speed leads  
1017 to increase the particle size due to the fact that the oil particles are more likely to collide and  
1018 aggregate with others. Concerning hot homogenization time, short time was found not enough  
1019 for active ingredient encapsulation while more homogenization time result in small particles  
1020 which in turn lead to reduce the volume containing active ingredients (Mai et al., 2018).

1021           In another work study, the impact of the surfactant content, the ratio of citral to lipid,  
1022 and their total content on the physicochemical characteristics of citral-loaded SLN has been  
1023 explored (Tian et al., 2018). As the surfactant amount increases the EE% decreases due to the  
1024 fact that the surface of the formed SLN was not large enough to absorb the excess of surfactant  
1025 which in turn form micelles, resulting a partitioning phenomenon of citral between micelles and  
1026 SLN; therefore, a decrease in entrapment efficiency was noticed. Results revealed also an



1027 increase in particle size and a decrease in EE% when increasing the content of the mixture citral  
1028 : glyceryl monostearate, used as lipid matrix, from 1 to 5%. The increase in the content of citral  
1029 : lipid leads to increase the viscosity of the system which in turn reduce the efficiency of the  
1030 high-pressure homogenization process to decrease the particle size. Additionally, too much  
1031 citral and lipid cannot be emulsified when the surfactant content is kept constant this is why the  
1032 EE% decreased. The same behavior of EE% was observed when increasing the ratio of citral to  
1033 glycerol monostearate. In fact, the excess of citral cannot be entrapped when the content of the  
1034 mixture citral : lipid was kept constant (Tian et al., 2018).

1035 In recent years, NLC were introduced to bypass the potential problems associated with  
1036 the use of SLN. They were widely used for plant oils encapsulation, as depicted in **Table 3**.  
1037 The main feature of these nanocarriers is to enhance the drug loading and prevent drug  
1038 expulsion during long term storage (Sailaja et al., 2011) and this was confirmed by several  
1039 research works. In 2019, using the high-pressure homogenization technique, Miranda and his  
1040 colleagues developed *Ridolfia segetum* EO loaded-NLC with a small particle size (148.1 nm),  
1041 a high zeta potential (16.3 mV) with excellent loading capacity (EE%=100%) (Miranda et al.,  
1042 2019). In another research work, NLC containing sucupira EO produced by hot homogenization  
1043 process owning an average diameter of 143 nm with an EE% of 99.98% (Vieira et al., 2020).

1044 Another characteristic intended by using either SLN or NLC as plant oils carrier is  
1045 providing a controlled released pattern. For this context, *in vitro* release profile of sucupira oil  
1046 from NLC was assessed by means of Franz glass diffusion cells and the recorded release profile  
1047 was fitted into four mathematical models i.e., zero order, first order, Higuchi and Korsmeyer-  
1048 Peppas (Vieira et al., 2020). Results showed that the release profile of sucupira oil followed a  
1049 sustained manner over the course of 8 h. About 17.5% was released within the first hour, while  
1050 the cumulative amount reached 30% at the end of the 8 h (Vieira et al., 2020). Results showed  
1051 also that the best model describing the release of sucupira oil from NLC was the first order with

1052 a regression coefficient close to 1. In contrary to SLN, the release profile of plant oils from  
1053 NLC does not follow Higuchi or Korsmeyers–Peppas model. Indeed, the release was governed  
1054 by sucupira oil concentration inside the particles rather than the physicochemical properties of  
1055 the carriers and this was expected as NLC are made of blend of solid and liquid lipids. Higuchi  
1056 and Korsmeyers–Peppas are typically followed in the case of SLN formulations as these have  
1057 a higher degree of crystallinity which controls better the release profile.

1058         With respect to vegetable oils, NLC were employed for co-delivery of VO with another  
1059 bioactive molecule (Badea et al., 2015; Lacatusu et al., 2015; Rahman et al., 2013, 2014;  
1060 Sidding et al., 2013). The benefit of these nanocarriers is that the VO can complement or even  
1061 enhance the biological activity of the synthetic drug (Lacatusu et al., 2015). For this context,  
1062 diethylamino hydroxybenzoyl hexyl benzoate used as UVA filter was co-encapsulated with  
1063 various vegetable oils and their combinations (pomegranate seed oil, wheat germ oil,  
1064 blackcurrant seed oil, sesame seed oil, carrot root oil, raspberry seed oil and rice bran oil) in  
1065 NLC by high pressure homogenization method in order to enhance its antioxidant activity and  
1066 UV protection performance (Badea et al., 2015). All the prepared NLC owned a mean particle  
1067 size in the range of 108 to 145 nm with narrow size distribution, high zeta potential ranging  
1068 from –34.4 to –44.3 mV and an entrapment efficiency between 51 and 70% (Badea et al., 2015).  
1069 In another work study, in the aim of enhancing the anti-inflammatory properties, olive oil was  
1070 co entrapped with thymoquinone in NLC and the resultant particles owned an average diameter  
1071 around 75 nm with negative zeta potential of -31 mV (Sidding et al., 2013). Olive oil was further  
1072 encapsulated in hydrogenated palm oil-NLC for co-delivery with synthetic drug purpose. The  
1073 resultant particles had a mean diameter, polydispersity index, zeta potential, specific surface  
1074 area, and crystallinity index of 61.14 nm, 0.461, -25.4 mV, 49.07 m<sup>2</sup> and 27.12% respectively  
1075 (How et al., 2013).

1076 Besides the synthesized drugs, VO may be co-encapsulated with EO in NLC. For  
1077 instance, Lacatusu et al. (2015) highlighted the possible blend of plant and animal oils – grape  
1078 seed oil or fish oil with laurel leaf EO in NLC. The mean average diameter of obtained NLC  
1079 reduces after increase of grape seed oil or fish oil content. This was ascribed to the role of the  
1080 long fatty chains of these oils which lead to a more confined lipid core.

1081 On the whole the high-pressure homogenization technique is largely employed thanks  
1082 to its benefits including low cost, good scalability and high stability of particles. While, with  
1083 respect to the encapsulation of plant oils hot homogenization is more used as compared to the  
1084 cold homogenization method. Lipids like tristearin (Salminen et al., 2017), n-hexadecyl  
1085 palmitate (Lacatusu et al., 2015), myritol<sup>®</sup>318 (caprylic/capric triglyceride) (Lacatusu et al.,  
1086 2015), compritol<sup>®</sup>888 ATO (Wang, 2012), glyceryl monolinoleate (Shi et al., 2013; Tian et al.,  
1087 2018), oleoyl macroglycerides (Shi et al., 2013), lipoid<sup>®</sup>S100 (Sidding et al., 2013), cetyl  
1088 palmitate (Svetlichny et al., 2015) and glycerol monostearate (Shi et al., 2013) are usually used  
1089 to structure either SLN or NLC. Soybean lecithin (Salminen et al., 2017; Wang, 2012), tween  
1090 80 (Shi et al., 2013; Sidding et al., 2013; Svetlichny et al., 2015; Wang, 2012), tween 20 (Badea  
1091 et al., 2015; Lacatusu et al., 2015), span 80 (Mai et al., 2018; Tian et al., 2018) poloxamer  
1092 (Badea et al., 2015) and sodium taurodeoxycholate hydrate (Salminen et al., 2017) are example  
1093 of used emulsifiers.

1094 The use of high-speed homogenization process is often limited by the need of high  
1095 energy input and the high temperature which cause oil loss.

#### 1096 **5.2.2.2. Ultrasonication / high speed homogenization**

1097 Solid lipid nanoparticles may also be prepared by ultrasonication or high-speed  
1098 homogenization technique. In brief, the heated aqueous phase was added to the melted lipid  
1099 phase and emulsified by high speed stirrer, probe sonication or by adding the aqueous phase  
1100 drop by drop to the lipid phase under magnetic stirring. The obtained pre-emulsion was

1101 ultrasonicated using probe sonicator with water bath (**Fig.7.c**). In order to prevent re-  
1102 crystallization during the process, the production temperature was kept at least 5°C above the  
1103 lipid melting point (Ramteke et al., 2012; Yadav et al., 2013).

1104 With respect to the encapsulation of plant oils, the ultrasonication technique is widely used,  
1105 as described in **Table 3**. *Zataria multiflora* EO-loaded SLN were developed using Precirol<sup>®</sup>  
1106 ATO 5 (Glyceryl monostearate) as lipidic matrix and tween 80 with poloxamer 188 as  
1107 surfactants (Nasseri et al., 2016). The obtained SLN owned a particle size around 255.5 nm  
1108 with zeta potential of -37.8 mV and high EE% of 84 %. The same technique was used to develop  
1109 cardamom EO loaded-NLC using cocoa butter (as solid lipid), olive oil (as liquid lipid) and  
1110 tween 80 (as surfactant); and the resultant particles had round shape, smooth surface with  
1111 particle size less than 100 nm (Nahr et al., 2018). Similarly, NLC were developed using palm  
1112 stearin as solid lipid and lecithin as emulsifier and the resultant particles were physically and  
1113 chemically stable during 70-day storage at room temperature and 4°C (Zhu et al., 2015).  
1114 Furthermore, Noor et al. (2013) successfully loaded coconut VO into SLN by the same process  
1115 and reported high EE% (99.97%).

1116 Like all the colloidal formulations discussed above, both SLN and NLC prepared by  
1117 high-speed homogenization provide a controlled release profile of plant oils (Pivetta et al.,  
1118 2018; Zhao et al., 2017). The release profile of EO from these nanocarriers may be affected by  
1119 several factors such as the particle size and the composition of lipidic matrix. In 2011, Garg and  
1120 his coworkers compared the release profile of eugenol from SLN and NLC formulations made  
1121 from stearic acid and the mixture stearic acid: caprylic triglyceride, respectively (Garg and  
1122 Singh, 2011). Results revealed a biphasic release pattern from both nanocarriers. After initial  
1123 burst release, the cumulative amounts of eugenol released within 12 h were 65 and 78% from  
1124 SLN and NLC, respectively. This was related to the structure of the nanocarrier's matrix. The  
1125 addition of liquid lipid in the case of NLC provides fewer barriers to partitioning of eugenol to

1126 the dissolution media. The authors ascribed also this result to the small particle size of NLC  
1127 (87.7 nm) as compared to that of SLN (332 nm). Indeed, the addition of liquid lipid decreases  
1128 the viscosity of the organic phase (lipid solution) to be dispersed in the aqueous one resulting  
1129 in smaller particles. Moreover, liquid lipid may inhibit the crystallization of solid lipid leading  
1130 to smaller particle size (Garg and Singh, 2011). One may conclude that the incorporation of  
1131 liquid lipid improves the EE% but decreases the barrier provided by lipid matrix for the  
1132 diffusion of bioactive molecule in the dissolution medium.

1133 The particle size and zeta potential of NLC were influenced by several parameters  
1134 including solid lipid composition, oil and surfactant (type and concentration), lipid:surfactant  
1135 ratio, etc. The impact of these factors was extensively studied in the literature (Krasodomska et  
1136 al., 2016; Lacatusu et al., 2013; Soleimanian et al., 2018). It was found that increasing stearic  
1137 acid concentration results in increasing the size of *Eugenia caryophyllata* EO-loaded SLN  
1138 prepared by ultrasonication method (Bazzaz et al., 2018). Moreover, Soleimanian et al. (2018)  
1139 developing pomegranate seed oil-loaded NLC using two types of natural waxes: beeswax and  
1140 propolis wax, investigated the influence of solid lipid composition, surfactant blend  
1141 concentration and oil content on NLC physicochemical properties. Results demonstrated that  
1142 increasing oil amount resulted in a decrease in particle size of beeswax NLC. This was related  
1143 to the reduction of core viscosity and enhancement of fluidity which results in a decrease in  
1144 particle size. The opposite behavior was observed in the case of propolis wax NLC. The particle  
1145 size increases by increasing the oil content. The authors ascribed that to enhanced interfacial  
1146 tension or swelling rate of the core as result of greater oil concentration. Concerning the impact  
1147 of solid lipid type, Soleimanian et al. (2018) reported that small differences in the lipid  
1148 composition (particularly, the melting point) might have considerable impact on size and  
1149 quality of nano lipid carriers. Beeswax consisting of a longer series of carboxylic acid  
1150 homologues, alcohols and hydrocarbons exhibits higher melting point, leading to higher

1151 viscosity of the dispersed phase which in turn results in increasing particle size (203 nm). On  
1152 the other hand, propolis wax having lower proportion of components produced smaller NLC  
1153 (143 nm). Regarding the zeta potential, the same authors reported that increasing the  
1154 concentration of surfactant mixture (Lecithin:Tween 80) results in decreasing the zeta potential  
1155 of NLC. They related this result to the differences in mobility and redistribution of used  
1156 surfactants. In fact, high amounts of surfactant decrease the surface tension and enhance the  
1157 particle partition during homogenization, resulting to a decrease in particle size and thus new  
1158 NLC appear. The time required for the redistribution of surfactant molecules to cover the new  
1159 surfaces differ. Indeed, low molecular weight surfactants such as tween 80 adsorb rapidly at the  
1160 interface, while lecithin, as high molecular weight surfactant, needs more time to be adsorbed.  
1161 Therefore, tween 80, external hydrophilic non-ionic surfactant, will cover the internal lipophilic  
1162 surfactant (i.e. lecithin), and thus the zeta potential decreases (Soleimanian et al., 2018).

1163 In summary, the ultrasonication is chosen by scientists to design both SLN and NLC  
1164 systems to entrap plant oils. The commonly used lipid are glyceryl behenate (Zhao et al., 2017),  
1165 stearic acid (Bazzaz et al., 2018; Garg and Singh, 2013, 2011), carnauba wax (Lacatusu et al.,  
1166 2013), whey protein isolate (Azizi et al., 2019), glycerol stearate (Lacatusu et al., 2013),  
1167 palmitic acid (Azizi et al., 2019), propolis (Soleimanian et al., 2018), palm stearin (Zhu et al.,  
1168 2015), beeswax (Shakeri et al., 2019; Soleimanian et al., 2018), illipe butter (Pivetta et al.,  
1169 2018), cocoa butter (Nahr et al., 2018), Precirol® ATO 5 (glyceryl palmitostearate) (Ghodrati  
1170 et al., 2019), miglyol®812 (caprylic/capric triglycerides) (Ghodrati et al., 2019) and myverol®  
1171 RX GMS 95P (mixture of glycerol palmitic (57,8%) stearic (37.3%) and myristic (1.3%) acid)  
1172 (Krasodomska et al., 2016). Lecithin (Soleimanian et al., 2018; Zhu et al., 2015), poly vinyl  
1173 alcohol (Zhao et al., 2017), tween 80 (Lacatusu et al., 2013; Nahr et al., 2018; Noor et al., 2013),  
1174 poloxamer (Ghodrati et al., 2019; Lacatusu et al., 2013) and pluronic® F68 (Pivetta et al., 2018)  
1175 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 (%)			
<b><i>Solid lipid nanoparticles</i></b>								
<b><i>High pressure homogenization</i></b>								
Carvacrol	/	Cocoa butter	/	/	/	Antioxidant	Medicine	(Carvalho et al., 2020)
Geranial	/	Monoterpene	120.1	0	/	/	/	(Zielińska et al., 2020)
Ziziphora	<i>Ziziphora clinopodioides</i>	Imwitor® 900K Percinol ATO5	241.1	-22.6	93	Insecticide	Agriculture	(Jajarm et al., 2020)
Eugenol	/	Campritol 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)
Thymol	/	Coconut oil Hydrogenated palm oil	166.4-170.5 198.0-202.1	/	/	Antifungal	Food	(McDaniel et al., 2019)
Cinnamaldehyde	/	Coconut oil						
Sclareol	/	Compritol	128	-29.3	/	Treatment of metabolic disorder	Medicine	(Cerri et al., 2019)
Chamomile	<i>Matricaria chamomilla</i> L.	Stearic acid	542	-35.9	/	Wound healing	Cosmetics	(Gad et al., 2019)
α-pinene	/	Imwitor® 900K Monoterpene	136.7 89.7	/ 0	/ /	Antimicrobial, antioxidant	/	(Zielinska et al., 2019) (Zielińska et al., 2020)
Citral	/	Imwitor® 900K Glyceryl monostearate	215.4	/	/	Flavoring agent	Food	(Tian et al., 2018)
		Monoterpene Imwitor® 900K	125.4	0	/	/	/	(Zielińska et al., 2020)
Gac fruit EO	<i>Momordica cochinchinensis</i> L.	Emulgade	200	/	90	Antioxidant; Anti-aging Skin tanning, skin care and skin protection	Cosmetics	(Mai et al., 2018)
Frankincense + Myhrr oil	<i>Commiphora myrrha</i> L.	Compritol888 ATO	113.3	-16.8	80-60	Antitumor	Medicine	(Wang, 2012)
Copaiba oil	<i>Copaifera officinalis</i> 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)
<b>Ultrasonication method</b>								
<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	255.5	-37.8	84	Antifungal	Medicine	(Nasseri et al., 2016)
$\beta$ -elemene	/	Precirol®ATO 5 Glyceryl monostearate	128.4	-3.07	/	Antitumor	Medicine	(He et al., 2019)
		Glyceryl tristearate						
Clove	<i>Syzygium aromaticum</i> L.	Precirol®ATO 5 Stearic acid Glyceryl monostearate	397.2	-20.9	/	Antimicrobial	Medicine	(Bazzaz et al., 2018)
Linalool	/	Myristyl myristate Cetyl esters	90-130	-4	>80	Anticancer	Medicine	(Rodenak-Kladniew et al., 2017)
Eugenol	/	Cetyl palmitate Stearic acid/Compritol	363– 423	/	/	Antifungal	Medicine	(Garg and Singh, 2013)
		Stearic acid Caprylic triglyceride	87.7	-19.2	98.5	Antifungal	Medicine	(Garg and Singh, 2011)
Coconut	<i>Cocos nucifera</i> L.	Stearic acid	608	-47.5	99.9	Moisturizing lotion	Cosmetics	(Noor et al., 2013)
<b>Nanostructured lipid carriers</b>								
<b>High pressure homogenization</b>								
Cinnamon	<i>Cinnamomum cassia</i> persl.	Cocoa butter Almond oil	100-120	-14.9 to -17.5	>82.1	Antimicrobial, antioxidant	Food	(Bashiri et al., 2020b)
Sucupira	<i>Pterodon emarginatus</i> L.	Imwitor® 900 K Tripalmitin	148.1	/	99.9	Antidiabetic	Medicine	(Vieira et al., 2020)
Squaw mint	<i>Mentha pulegium</i> L.	Precirol®ATO 5 Miglyol®812	40-250	-10 to -15	/	Wound healing	Cosmetics	(Khezri et al., 2020)

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)

Glycerol  
monostearate  
Myritol®318

**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	(Ghodrati 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>							
Plum	Duchesne. <i>Prunus domestica</i> L.							

## 1180 **6. Application**

### 1181 **6.1. Agriculture field**

1182           The indiscriminate use of chemicals in field as well as during postharvest poses serious  
1183 problems for the environment and the human health. The excessive application of synthetic  
1184 fungicides can also have other negative side effects. The appearance of resistance in the  
1185 pathogen populations has been notified for many fungi (Saharan et al., 2013). In addition, over  
1186 the last few years increasing consumers concern regarding contamination of crops with  
1187 fungicidal residues has been reported (Shukla, 2018). Therefore, low toxicity and more  
1188 environmentally friendly compounds as an alternative to chemical fungicides was brought to  
1189 the forefront. Among them, GRAS (generally regarded as safe) antifungal compounds such as  
1190 EO have been reported (Shukla, 2018; Sotelo-Boyás et al., 2015). Due to their broad spectrum  
1191 of activity against plant pathogenic fungi and insects-pests, EO have been used as antifungal,  
1192 insecticidal, repellent, antifeedant and oviposition deterrent (De Souza et al., 2005; Shukla,  
1193 2018). However, the replacement of synthetic compounds is not easy due to the poor stability  
1194 shown by EOs during the processing steps. Therefore, nanoencapsulation has been proposed  
1195 for this purpose (Maryam et al., 2015). According to the literature, pNPs are widely used for  
1196 EO encapsulation in agriculture industry.

1197           Recently, Khoobdel et al. (2017) investigated the insecticidal activity of *Rosmarinus*  
1198 *officinalis* EO-loaded pNPs against the red flour beetle, *Tribolium castaneum*. Fumigant and  
1199 contact toxicity assays revealed that the developed particles had significant increase in fumigant  
1200 and contact toxicity as compared to the pure EO. At the 72 h exposure for fumigant toxicity,  
1201 the mortality of *Tribolium castaneum* adults was 83.3 % for free EO at a concentration of 27.76  
1202  $\mu\text{L/L}$  air and 100 % for EO-loaded nanoparticles at concentration of 19.12  $\mu\text{L/L}$  air (Khoobdel  
1203 et al., 2017). Moreover, Zhavah et al. (2015) related the superior performance of *Cuminum*  
1204 *cuminum EO* nanogels against *Aspergillus flavus* as compared to the free oil to the encapsulation

1205 in chitosan : caffeic acid nanoparticles. Similar results were already reported when investigating  
1206 insecticidal activity against *Bemisia tabaci* for *Zanthoxylum rhoifolium* EO-loaded  
1207 nanoparticles as compared to the free oil (Christofoli et al., 2015). Therefore, the  
1208 nanoencapsulation can enhance the insecticidal potential of EO due to the controlled and slow  
1209 release of EO and increased surface area of the nanoparticles.

1210 Sotelo-Boyas and his coworkers (2015) combined the bacterial efficiency of chitosan  
1211 with those of lime and thyme EO in pNPs to eradicate *Pectobacterium carotovorum*, plant  
1212 phytopathogenic bacteria, involved in the decay of fresh vegetables and fruits like radishes,  
1213 onions, potatoes, cucumbers, carrots, eggplant, squash, peppers, tomato and cabbage. For  
1214 instance, chitosan was highly used for its potential effect in the control of phytopathogenic  
1215 fungi Gram-negative and Gram positive bacteria (Benhabiles et al., 2012; Kaur et al., 2012;  
1216 Zhu et al., 2016). The antibacterial study demonstrated that thyme based-nanoparticles showed  
1217 the highest inhibitory effect on the growth of *Pectobacterium carotovorum* than free chitosan  
1218 nanoparticles and lime based- nanoparticles. The inhibition halo diameters were found 15, 13  
1219 and 24 mm for chitosan free nanoparticles, lime-chitosan nanoparticles and Thyme-chitosan  
1220 nanoparticles, respectively. Moreover, the number of colonies forming units (CFU) could not  
1221 be determined (countless colonies) for chitosan free nanoparticles. While for lime- and thyme-  
1222 chitosan nanoparticles, CFU were found 450 and 240, respectively (Sotelo-Boyás et al., 2015).  
1223 Furthermore, the results of antifungal assay carried out on chitosan:pepper tree EO  
1224 nanoparticles revealed that higher activity was assessed for the nanoparticles on the viability of  
1225 *Aspergillus parasiticus* spores as compared to that of chitosan and pepper tree oil present  
1226 individually. One may conclude that the antifungal effect of chitosan nanoparticles was  
1227 attributed to two reasons: 1) the small size of nanoparticles will increase the contact area with  
1228 fungus; 2) The cationic nature of chitosan allows electrostatic interaction with proteins and

1229 phospholipids of the plasmatic membrane of the microorganism which in turn cause membrane  
1230 destabilization and death.

1231           With respect to the use of lipid based-nanocarriers in agriculture industry, few reports  
1232 have been investigated in the last decade. Liposomes were used for the first time for rosemary  
1233 EO encapsulation to inhibit the seed germination of invasive alien species (*Acacia saligna*)  
1234 (Maccioni et al., 2019). The incorporation of rosemary EO in liposomes limited the loss of EO  
1235 volatile components and delivering them into the seed resulting in enhancing EO efficacy.  
1236 Similarly, Adel et al. (2015) pointed out that *Pelargonium graveolens* EO loaded-SLN were  
1237 stable under field conditions and exhibit higher larvicidal activity against *Phthorimaea*  
1238 *operaculella* as compared to the free oil.

## 1239 **6.2. Food field**

1240           In recent years, consumer demands in eating healthy and less processed foods have  
1241 boosted remarkably. Functional foods play a pivotal role in promoting health and preventing  
1242 degenerative diseases such as heart disease, cancer and diabetes, which account for almost two  
1243 thirds of deaths in the world (Conto et al., 2012; Rubilar et al., 2012). Foods enriched with long  
1244 chain omega-3 polyunsaturated fatty acids are classified as functional foods by acting on human  
1245 health. The ingestion of omega-3 fatty acids is accompanied with a prevention of cardiovascular  
1246 diseases, a decreased risk of cancer, autoimmune and inflammatory diseases (Azizi et al., 2019;  
1247 Conto et al., 2012; Gallardo et al., 2013). However, polyunsaturated fatty acids are very  
1248 susceptible to oxidation during processing and storage resulting in decreased nutritional value  
1249 and sensory quality. Thus, micro and nanoencapsulation of lipids have been used in this concern  
1250 (Gökmen et al., 2011).

1251           Currently, several nanocarriers have been designed in the literature to encapsulate  
1252 several healthful oils like chia seed oil (Campo et al., 2017), walnut oil (Shamaei et al., 2017),

1253 flaxseed oil (Carneiro et al., 2013; Gallardo et al., 2013; Pu et al., 2010), pomegranate oil  
1254 (Soleimanian et al., 2018), roasted coffee oil (Freiberger et al., 2015) and fruit seed oil  
1255 (blackcurrant, blackberry, raspberry, strawberry and plum) (Krasodomska et al., 2016). In 2012,  
1256 Rubilar et al. developed a soup fortified with linseed oil microcapsules and depicted that  
1257 microencapsulation protected linseed oil from oxidation with respect to free oil (Rubilar et al.,  
1258 2012). Similarly, Gökmen et al. (2011) demonstrated the feasibility to include flaxseed oil  
1259 nanoparticles in bread without affecting the sensorial properties.

1260         At the same time, foods are paramount carriers of many damaging agents like virus,  
1261 bacteria, parasites, and toxins which can cause food-borne diseases (Dussault et al., 2014).  
1262 Every year, around 30% of people suffer from foodborne diseases in developed countries (Lee  
1263 et al., 2014). Meanwhile, due to the increased consumer awareness to the use of synthetic food  
1264 preservatives or aromatic agents, the tendency toward natural ones is gaining more and more  
1265 attention (Alikhani-Koupaei, 2015). In light of that, using EO with antioxidant, antibacterial  
1266 and antifungal properties and applying nanoparticulate systems are effective approaches in this  
1267 regard (Bazzaz et al., 2018; Khatibi et al., 2017). In 2017, Cui and his coworkers developed  
1268 thyme EO-loaded liposomes to treat salmonellosis, an important food-borne disease, usually  
1269 associated with direct consumption or cross contamination of animal origin foods, especially  
1270 poultry, and poultry related products (Cui et al., 2017b). They investigated in their study the  
1271 time-kill analysis of liposome-encapsulated thyme oil on fresh chicken contaminated with  
1272 *Salmonella enteritidis*. Results demonstrated that *Salmonella enteritidis* colonies reduced by  
1273 71.16, 90.45, 83.02, 89.53 and 97.71% after exposure to 300 mg/mL liposomes for 3, 4, 5, 6,  
1274 and 7 days, respectively (Cui et al., 2017b). In another work study, the antimicrobial activity of  
1275 curry plant EO loaded-liposomes against *Bacillus cereus* in rice flour was investigated (Cui et  
1276 al., 2017a). Results showed that the antibacterial activity and active time of curry plant EO  
1277 loaded-liposomes were significantly boosted when compared to the free EO. For instance, the

1278 population of *Bacillus cereus* in rice flour was almost unchanged or even increased after EO  
1279 treatment. However, it reduced significantly after 4 days liposomes treatment (Cui et al.,  
1280 2017a). Gomes et al. (2011b) related the boosting in trans cinnamaldehyde or –eugenol against  
1281 both *Salmonella* and *Listeria Spp* activity to three reasons: the improved hydrophilicity, the  
1282 sustained release, and the small size of pNPs. In 2018, Lin et al. investigated the antimicrobial  
1283 activity of thyme EO-loaded liposomes against *Escherichia coli* O157:H7 in four vegetable  
1284 juices: tomato, carrot, cucumber and lettuce juices (Lin et al., 2018). Indeed,  
1285 Enterohaemorrhagic *Escherichia coli* serotype O157:H7 as a main human pathogen may cause  
1286 food borne outbreaks, bloody diarrhea, hemorrhagic colitis and hemolytic uremic syndrome  
1287 and even death (Khatibi et al., 2017). Results showed that solid liposomes exhibited significant  
1288 reduction in *Escherichia coli* O157:H7 when compared to group control. For instance, no  
1289 bacterial growth was observed on nutrient agar plate in the case of cucumber juice and lettuce  
1290 juice treated with 5 mg/mL liposomes. While, treating tomato juice and carrot juice with the  
1291 same concentration of liposomes lead to 99.99 and 99.80% reduction of *Escherichia coli*  
1292 O157:H7 (Lin et al., 2018). Moreover, Khatibi et al. (2017) found that the relative  
1293 transcriptional level of Stx2A gene of *Escherichia coli* O157:H7 was decreased from 0.721 to  
1294 0.646 when using 75% minimum inhibitory concentration (MIC) of *Zataria multiflora* EO  
1295 loaded-nanoliposomes.

1296 The antibacterial mechanism of EOs loaded-nanocarriers has been investigated. In 2015,  
1297 Cui et al. investigated the antibacterial mechanism of liposomes containing clove EO against  
1298 *Staphylococcus aureus* in Tofu (Cui et al., 2015). A selective antimicrobial activity for  
1299 *Staphylococcus aureus* by means of pore-forming toxins to activate clove oil release from  
1300 liposomes was noticed. In fact, the liposomes did not fuse with biological membranes but  
1301 release clove oil after toxins secretion by the bacteria. About 99.87% reduction in population  
1302 was observed in *Staphylococcus aureus* after 24 h of liposome treatment. However, no



1303 reduction was observed in *Escherichia coli* population after liposome treatment due to the fact  
1304 that these bacteria did not secrete toxins and therefore clove oil could not reach them (Cui et  
1305 al., 2015).

1306 The antioxidant and antimicrobial activities of EO-loaded nanocarriers were found to  
1307 be conserved for long period. In this context, the physicochemical qualities of fresh-cut bananas  
1308 in contact with free rosemary EO, rosemary oil plus mucilage and rosemary oil liposomes were  
1309 evaluated during 9 days storage at 5°C (Alikhani-Koupaei, 2015). Sensory analysis revealed  
1310 that liposomal formulations was more efficient in enhancing the quality of fresh-cut bananas  
1311 and extending their shelf life (Alikhani-Koupaei, 2015). Likewise, the conversion of cardamom  
1312 EO to NLC (Nahr et al., 2018) and nanoliposomes (Nahr et al., 2019) greatly conserves its  
1313 antioxidant and antimicrobial activities for long period. The NLC showed MIC values around  
1314 1100 µg/ml for both bacteria after 30 days compared to that of cardamom oil emulsion. The  
1315 MIC values were around 4400 and 2200 µg/ml for *Staphylococcus aureus* and *Escherichia coli*,  
1316 respectively (Nahr et al., 2018).

1317 The biological activity of nanocarriers encapsulated plant oils was affected by operating  
1318 parameters and particles ingredients. In 2017, Mohammed and his coworkers depicted that a  
1319 high antioxidant efficiency of *Nigella sativa* EO-loaded microparticles prepared by spray  
1320 drying process was associated with high ratio of wall material (30%), medium of oil  
1321 concentration (10%) and low inlet temperature (160°C) (Mohammed et al., 2017).  
1322 Furthermore, Bazzaz et al. (2018) investigated the antimicrobial activity of SLN encapsulated  
1323 *Eugenia caryophyllata* EO against *Salmonella typhi*, *Pseudomonas aeruginosa*,  
1324 *Staphylococcus aureus* and *Candida albicans* using time-kill methods. Results demonstrated  
1325 that the SLN formulations were effective in Gram negative bacteria and fungi killing, especially  
1326 those containing stearic acid compared to glycerol monostearate (Bazzaz et al., 2018).

1327 In recent years, the use of EO has emerged to the food packaging industry as reported  
1328 by several work studies (Cui et al., 2016a, 2016b; Engel et al., 2017; Liu et al., 2017). Cinnamon  
1329 EO, known for its antimicrobial properties, has been formulated in chitosan/poly lactic acid  
1330 fibers for food packaging application as an alternative for synthetic chemicals due to consumer  
1331 concerns over food safety (Liu et al., 2017). Results showed high long-term inactivation rates  
1332 against *Escherichia coli* and *Staphylococcus aureus* (Liu et al., 2017). Cinnamon EO was  
1333 further formulated in liposomes and tested for its Methicillin-resistant *Staphylococcus aureus*  
1334 antibiofilm properties on the surfaces of different materials like stainless steel, gauze, nylon  
1335 membrane, and non-woven fabrics (Cui et al., 2016a). Results revealed a significant  
1336 enhancement of the anti-biofilm activities and active time for liposome-encapsulated cinnamon  
1337 EO when compared to the free oil. For instance, the counts of viable *Staphylococcus aureus* in  
1338 biofilms formed were reduced by 2.08 and 2.82 logs on gauze and 4.55 and 5.42 logs on non-  
1339 woven fabrics after five days treatment with free cinnamon oil and liposome containing  
1340 cinnamon oil, respectively (Cui et al., 2016a). Additionally, the antibacterial effect of salvia EO  
1341 nanoliposomes against *Staphylococcus aureus* biofilms attached on milk container was  
1342 explored by scanning electron microscopy and confocal laser scanning microscopy and results  
1343 revealed that salvia EO nanoliposomes have high anti-biofilm activity against *Staphylococcus*  
1344 *aureus* biofilms on milk container (Cui et al., 2016b). Furthermore, Engel et al. (2017) noticed  
1345 the antimicrobial potential of liposome-encapsulated thymol and carvacrol against pools of  
1346 *Staphylococcus aureus* and *Salmonella* adhered to stainless steel.

### 1347 **6.3. Medicinal field**

#### 1348 **6.3.1. Antimicrobial activity**

1349 The management of bacterial infection is raising serious concern across the globe. The  
1350 emergence of multi-drug-resistant bacterial pathogens and the ability of microorganisms to  
1351 form biofilms result high tolerance to high amounts of antibiotics and to all host defense

1352 mechanisms (Mandal et al., 2014). Faced with this challenge, the scientists throughout the  
1353 world search for new antimicrobial agents, such as plant oils based formulations which are  
1354 economic and ecologic antimicrobial agents; and combine them with nanotechnology (Liakos  
1355 et al., 2018). In this context, Iannitelli et al. (2011) investigated the effects of carvacrol-loaded  
1356 poly (lactide-co-glycolide)-nanocapsules on the viscoelastic features of *Staphylococcus*  
1357 *epidermidis* biofilms by rheological measurements. Results revealed the ability of carvacrol  
1358 loaded nanoparticles to reduce the elasticity and mechanical stability of preformed biofilms  
1359 which in turn enable the penetration of antimicrobial agents into the deep core of biofilms  
1360 (Iannitelli et al., 2011). Liakos et al. (2016) tested the antibiofilm activity of poly lactide  
1361 nanoparticles encapsulating lemongrass EO against *Candida albicans*, *Escherichia coli*,  
1362 *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Results showed higher anti-biofilm  
1363 effect for *Candida albicans* and *Escherichia coli* tested strains. The cytotoxicity of the prepared  
1364 nanoparticles was further analyzed and results revealed a high cell viability and good growth  
1365 of human cells (Liakos et al., 2016). Subsequently, in 2018, the same research team tested the  
1366 antibiofilm activity of cellulose acetate pNPs containing either lemongrass, peppermint or  
1367 cinnamon EO and the results showed high antibiofilm activity against *Candida albicans* and  
1368 *Staphylococcus aureus* (Liakos et al., 2018). Manconi et al. (2018) proposed the use of  
1369 liposomes containing *Thymus capitatus* EO as antibacterial-antioxidant mouthwash for the  
1370 treatment of oral cavity diseases. The liposomes were biocompatible, able to prevent oxidative  
1371 stress and favor wound repair in keratinocytes. Their antibacterial activity was evidenced  
1372 against commensal *Streptococcus sanguinis* and cariogenic *Streptococcus mutans* and  
1373 *Lactobacillus acidophilus* (Manconi et al., 2018). Similarly, Priyadarshini et al. (2018)  
1374 proposed the use of poly (lactide-co-glycolide)-nanoparticles containing clove EO as  
1375 antibacterial systems for dental purposes by removing bacterial plaque and reducing dental  
1376 diseases. Confocal microscopy demonstrated successful delivery and position of clove oil

1377 loaded-nanoparticles inside dentinal tubules. In another work study, the antiviral activity of  
1378 *Santolina insularis* EO loaded-liposomes against Herpes simplex virus-type 1 was investigated  
1379 (Valenti et al., 2001). Although the *in vitro* activity of free oil was higher than liposomal oil,  
1380 the high stability of liposomes make them an interesting delivery system for antiviral treatment;  
1381 they could be administered in drops for ocular herpetic infection, parenterally for diffused  
1382 systemic infections or topically on lips and mucosae from gel or cream formulations (Valenti  
1383 et al., 2001). Furthermore, Zhao et al. (2017) highlighted the use of SLN as a carrier for the  
1384 encapsulation and sustained inhalation delivery of yuxingcago EO for the treatment of  
1385 respiratory infectious diseases. Besides prolonging pulmonary retention up to 24h after  
1386 intratracheal administration to rats, yuxingcago EO loaded-SLN enhance the area under the  
1387 curve (AUC ) values by 4.5-7.7 folds compared to the intratracheally dosed EO solution and by  
1388 257–438 folds to the intravenously dosed EO solution (Zhao et al., 2017).

### 1389 **6.3.2. Antifungal activity**

1390 Considering the antifungal properties of *Zataria multiflora* EO, Nasser et al. developed  
1391 *Zataria multiflora* EO loaded-SLN to enhance its activity against *Aspergillus ochraceus*,  
1392 *Aspergillus niger*, *Aspergillus flavus*, *Alternaria solani*, *Rhizoctonia solani*, and *Rhizopus*  
1393 *stolonifera* (Nasser et al., 2016). Results showed that the encapsulated oil was more efficient  
1394 than the free one. For instance, the MIC for the encapsulated oil on the fungal pathogens of  
1395 *Aspergillus ochraceus*, *Aspergillus niger*, *Aspergillus flavus*, *Alternaria solani*, *Rhizoctonia*  
1396 *solani*, and *Rhizopus stolonifer* was 200, 200, 200, 100, 50 and 50 ppm, respectively; while for  
1397 un-encapsulated oil, it was 300, 200, 300, 200, 200 and 200 ppm (Nasser et al., 2016).  
1398 Furthermore, the nanoencapsulation enhanced the antifungal properties of copaiba oil against  
1399 *Candida krusei*, *Microsporum canis*, *Candida parapsilosis* and *Trichophyton rubrum* with  
1400 MIC<sub>90</sub> values of 250, 1.95, 7.8 and 1.95µg/mL, respectively. In another work study,  
1401 microparticles encapsulating *Lippia sidoides* EO were found more efficient than ketaconazole,

1402 used as positive control, in eradicating *Candida albicans*, *Candida glabrata*, *Candida krusei*  
1403 and *Candida parapsilosis* (Fernandes et al., 2008).

1404 Recently, many studies related the occurrence of some diseases like teratogenesis,  
1405 mutation and hepatocellular carcinoma to the high exposure to aflatoxin which is secondary  
1406 metabolites synthesized by toxigenic fungi: *Aspergillus flavus*, *Aspergillus parasiticus* and  
1407 *Aspergillus nomius*. López-meneses et al. (2018) investigated the antifungal and  
1408 antiaflatoxic activities against *Aspergillus parasiticus* of *Shinus molle* EO-loaded chitosan  
1409 nanoparticles. Results showed that the prepared nanoparticles affected the spore's germination  
1410 and viability, delayed mycelial growth and reduced aflatoxin production.

### 1411 **6.3.3. Larvicidal activity**

1412 Currently, several reports has demonstrated the larvicidal activity of *Lippia sidoides* EO  
1413 against larvae of *Aedes (Stegomyia aegypti)*, the dengue vector which is responsible for many  
1414 diseases, and even deaths, in tropical countries like Brazil (Carvalho et al., 2003). In order to  
1415 boost its larvicidal effect, Paula et al. (2010) developed angico gum : chitosan nanoparticles  
1416 containing *Lippia Sidoides* EO and investigated the *in vivo* activity on 20 third instar *Stegomyia*  
1417 *aegypti* larvae. Results demonstrated that the larval mortality was proportional to the oil  
1418 loading. For instance, the sample oil: angico gum-chitosan 1:20 showed the lowest loading  
1419 (3.3%) and consequently the lowest mortality, with 52 % after 24 h and 60 % after 48 h. Sample  
1420 oil: angico gum-chitosan 1:10 showed 85 and 92 % mortality after 24 and 48 h, respectively  
1421 (Paula et al., 2010). Similar results were found by Abreu et al. when studying the larvicidal  
1422 activity of *Lippia Sidoides* EO loaded-cashew gum : chitosan nanoparticles (Abreu et al., 2012).

### 1423 **6.3.4. Antitumor activity**

1424 The antitumor activity of frankincense and myrrh oil loaded-SLN was assessed on H22  
1425 tumor-bearing mice and results revealed an enhancement in antitumor efficiency of SLN when  
1426 compared to that of suspension and cyclodextrine inclusion (Wang, 2012). The inhibition rates

1427 were 31.23, 34.81 and 43.66% for oil suspension, oil- $\beta$ -cyclodextrin and oil-SLN, respectively.  
1428 Similarly, Celia et al. (2013) found that liposomal formulations encapsulating bergamot EO  
1429 showed a greater reduction in human SH-SY5Y neuroblastoma cells viability and a greater  
1430 increase in cell mortality at various concentrations and time points as compared to their free  
1431 drug counterparts. Same results were also reported by Detoni et al. (2012) where MLVs and  
1432 SUVs containing *Zanthoxylum tingoassuiba* EO were more efficient in reducing the viability  
1433 of glioma cells than free EO. In another work study, docosahexaenoic acid was encapsulated in  
1434 liposomes and investigated for its anticancer activity and results showed a strong inhibition of  
1435 FaDu head, neck squamous carcinoma and 4T1 breast cancer cells in *in vitro* cultures (Alaarg  
1436 et al., 2016). In 2013, Shi and his coworkers developed NLC containing  $\beta$ -elemene and  
1437 investigated their pharmacokinetics, anti-tumor effects, and venous irritation (Shi et al., 2013).  
1438 In this study,  $\beta$ -elemene-NLC suspensions were injected in an ear vein test, and compared with  
1439 elemene injection and saline solution used as positive and negative controls, respectively.  
1440 Results demonstrated no obvious discoloration or damage at the injection site in either  $\beta$ -  
1441 elemene-NLC groups or saline solution group, two days after the injection. However, un-  
1442 encapsulated  $\beta$ -elemene caused macroscopic edema and erythema at the injection site.  
1443 Additionally, the pharmacokinetic study revealed that the availability of the  $\beta$ -elemene was  
1444 increased by formulation into NLC since they showed higher AUC and slower clearance as  
1445 compared to elemene injection. Furthermore, the anti-tumor efficacy of  $\beta$ -elemene-NLC was  
1446 significantly higher than that of elemene injections with inhibition rates of 34.36 and 24.11%,  
1447 respectively (Shi et al., 2013).

#### 1448 **6.4. Cosmetic field**

1449 Wound healing is one of the most complicated physiological processes. Indeed, tissue  
1450 regeneration enhancement and infection prevention are key factors to reduce pain, discomfort,  
1451 and scar formation (Jahromi et al., 2018). Several chemical products have been proposed for

1452 wound repair; however, their uses are limited due to the complications and side effects (Purohit  
1453 et al., 2012). Recently, researchers have paid great attention to the effectiveness of plant oils  
1454 thanks to their antioxidant, antimicrobial, and anti-inflammatory properties (Raut and  
1455 Karuppayil, 2014). In this context, Ghodrati et al. (2019) investigated the therapeutic effect of  
1456 NLC containing peppermint EO on infected wound. For *in vivo* study, two full-thickness  
1457 wounds with the size of 5mm were created in each mouse and inoculated with *Pseudomonas*  
1458 *aeruginosa* and *Staphylococcus aureus*. Results showed that peppermint EO-NLC could  
1459 accelerate wound healing in the infected wound model by reducing the total bacterial count,  
1460 and increasing neovascularization, fibroblast infiltration, collagen deposition, re-epithelization,  
1461 and levels of FGF-2 and EGF mRNA expressions when compared to control group. Similarly,  
1462 Zhang et al. reported a decrease in TGF- $\beta$ 1, MMP-1, collagen I and collagen III levels and an  
1463 increase in apoptosis cells, caspase -3 and -9 levels after application of *Ligusticum chuanxiong*  
1464 EO-loaded liposomes on formed hypertrophic scars in the rabbit ear model (H. Zhang et al.,  
1465 2012). Furthermore, NLC based on olive oil and loaded with eucalyptus oil promote wound  
1466 healing in rat burn model by cell proliferation enhancement, good bioadhesion, cell  
1467 biocompatibility and antimicrobial properties (Saporito et al., 2018). In 2018, Pivetta et al.  
1468 prepared carbopol-gels containing thymol loaded-NLC as promising approach for treating skin  
1469 inflammatory disorders (Pivetta et al., 2018). In their study, they investigated the anti-  
1470 inflammatory effects of thymol-NLC gel on two mouse models: the cutaneous acute  
1471 inflammation model induced by croton oil and ear edema model induced by anthralin. Results  
1472 showed that thymol encapsulated in NLC provided better anti-inflammatory effect than free  
1473 thymol (Pivetta et al., 2018).

1474           Chronic skin infections in immunocompromised patients has become an important  
1475 public health issue because they can become serious, resulting in invasive infections  
1476 (Svetlichny et al., 2015). In this context, Ortan et al. (2013) developed hydrogels containing

1477 *Anethum graveolens* oil entrapped in liposomes to treat fungal infections in skin. The *in vitro*  
1478 release kinetics study using Franz diffusion cell showed that the designed hydrogels follow a  
1479 zero order kinetic model after a period of three hours from the beginning of the experiment  
1480 (Ortan et al., 2013). Moreover, hydrogel containing eugenol entrapped in either stearic acid- or  
1481 Compritol-SLN were designed for epidermal targeting to treat fungal infections in skin (Garg  
1482 and Singh, 2013). *Ex vivo* permeation and retention studies for almond oil solution of eugenol  
1483 and three types of hydrogels containing: eugenol-stearic acid-SLN, eugenol-compritol-SLN or  
1484 eugenol-hydroxypropyl- $\beta$ -cyclodextrin complex; were established with full thickness human  
1485 cadaver skin using Franz diffusion cell. Results revealed higher accumulation of eugenol in the  
1486 epidermis (62.65 and 52.86  $\mu\text{g}/\text{cm}^2$  for eugenol-stearic acid-SLN and eugenol-compritol-SLN,  
1487 respectively) when compared to that of almond oil solution of eugenol (3.45  $\mu\text{g}/\text{cm}^2$ ) and  
1488 eugenol-hydroxypropyl-  $\beta$ -cyclodextrine complex (9.77  $\mu\text{g}/\text{cm}^2$ ) (Garg and Singh, 2013).

1489 Currently, VO exhibit a great concern as raw materials in the development of natural  
1490 and eco-friendly cosmetics due to their benefits including antioxidant, moisturizers and  
1491 emollients properties. In addition, they provide skin protection against reactive oxygen species  
1492 and prevent oxidative stress (Dhavamani et al., 2014; Saraf et al., 2010). In order to obtain  
1493 efficient formulations with UV protection performance and antioxidant activity, Badea et al.  
1494 (2015) formulated creams containing NLC entrapping various VO and their combinations  
1495 (pomegranate seed oil, wheat germ oil, blackcurrant seed oil, sesame seed oil, carrot root oil,  
1496 raspberry seed oil and rice bran oil) with a synthetic UVA filter (diethylamino hydroxy benzoyl  
1497 hexyl benzoate). The UV protection factors were evaluated on the individual VO and on cream  
1498 formulations based on NLC and results showed that the best UV protection was assured by  
1499 pomegranate seed oil combined with wheat germ-loaded NLC based cream resulting in a SPF  
1500 of 5.1 and an UVAPF of 9.5 (Badea et al., 2015).

## 1501 **6.5. Textiles**



1502            Nowadays, functional textiles fascinated consumers interest due to their crucial benefits  
1503 as they enhance the native properties and promote new functions in the textile products like  
1504 flame retardency, UV resistance, photo-catalytic, antimicrobial, antibiotic and wrinkle recovery  
1505 to the fabrics (Javid et al., 2014). In medical field, textile consumers are becoming more aware  
1506 and conscious of the deleterious effect that microorganisms may have upon textile materials  
1507 like drapes, bed sheets, pillow cases, gowns and masks which are frequently used in hospitals  
1508 (Thelagavath and Kannaian, 2008). In this context, Li et al. (2013) grafted moxa oil  
1509 microcapsules made with gelatin and arabic gum on cotton fabric and investigated their  
1510 antibacterial activity against *Staphylococcus aureus* and the results showed strong antibacterial  
1511 effect. Similarly, ozonated red pepper seed oil antimicrobial microcapsules were applied on  
1512 100% polypropylene non-woven fabric and showed good antimicrobial activity against  
1513 *Staphylococcus aureus*, *Escherichia coli* and *Candida albicans* (Ozyıldız et al., 2012).  
1514 Furthermore, Rajendran et al. (2013) reported that *Ocimum sanctum* oil loaded alginate-  
1515 nanoparticles possessed remarkable antibacterial activities with excellent wash durability. After  
1516 20 washes, the inhibition percentage was 100% for *Bacillus cereus*, *Pseudomonas aeruginosa*  
1517 and *Staphylococcus aureus* except for *Escherichia coli* (90%). After 30 washes, the bacterial  
1518 inhibition was reduced to 95, 87, 98 and 98% for *Bacillus cereus*, *Escherichia coli*,  
1519 *Pseudomonas aeruginosa* and *Staphylococcus aureus*, respectively (Rajendran et al., 2013). In  
1520 2013, Javid et al. reported that antibacterial activity of cotton fabric grafted with chitosan  
1521 capsules containing eucalyptus and sandal wood oils increased with the increase in chitosan  
1522 and EO concentrations (Javid et al., 2014).

1523            Recent developments in textile industry were conducted to perfumed textiles in jackets,  
1524 sweaters, T-shirts and undershirts to meet consumers' needs for comfort and wellbeing. During  
1525 wearing, the mechanical forces on the capsules result in opening of the capsules and releasing  
1526 of the designed aroma and deodorant (Ghayempour and Montazer, 2016). In this context, Liu

1527 et al. (2015) treated methyl methacrylate–styrene nanoparticles containing cologne EO on the  
1528 cotton fabric through immersion and the release study revealed that 6.8% cologne EO remained  
1529 in fabrics after being washed 15 times. In another work, Wang et al. reported that ethyl cellulose  
1530 microcapsule can retain 50% of the lavender oil after 2 months, while almost no EO persisted  
1531 on the direct sprayed fabric after 7 days (Wang et al., 2009). Additionally, Li et al. (2013) found  
1532 that orange oil retention of microcapsules on the cotton and polyester fabrics was 8 days longer  
1533 than free oil.

## 1534 **7. Conclusion and perspectives**

1535 In the last two decades, the growing demand for natural bioactive products especially  
1536 essential and vegetable oils with the same efficiency or even more than chemical synthesized  
1537 drugs has urged researchers to focalize most of their efforts on developing new approaches of  
1538 extending the shelf life of these bioactive agents. In fact, plant oils are very sensitive to external  
1539 factors when used as such. The encapsulation of these bioactive agents represents a relevant  
1540 alternative to extend their physical stabilities, protecting them from oxidation and other  
1541 deleterious environmental factors like light, heat, oxygen and humidity, besides improving their  
1542 efficacy mainly owing to their nanometer size range. In this bibliographic paper, we emphasize  
1543 recent advances of both polymer and lipid based-nanocarriers including polymeric  
1544 nanoparticles, liposomes and solid lipid nanoparticles in the emergence of new concepts for the  
1545 effective use of plant oils. A number of benefits and drawbacks are linked to each carrier. For  
1546 instance, both solid lipid nanoparticles and polymeric nanoparticles have more oil stability and  
1547 prolonged release than liposomes; while liposomes offer wide application spectrum especially  
1548 to the skin delivery thanks to their chemical nature which is very close to that of the skin layers.  
1549 Although solid lipid nanoparticles are safer than polymeric nanoparticles since the avoidance  
1550 of organic solvents, they were less used to encapsulate both essential and vegetable oils,  
1551 according to the investigations discussed above. This may be related to the high

1552 temperature requirements which in turn cause oil loss and thus decrease the encapsulation  
1553 efficiency. Several preparation methods have been reported for each nanocarrier; they are  
1554 differentiated by the complexity of their execution and the characteristic of their final product;  
1555 nonetheless, the right selection of the suitable carrier with the appropriate preparation method  
1556 is the crucial key to determine the carrier features responsible for the best attainment of the final  
1557 goal. The discussed nanostructured systems provide pertinent perspectives for applications in  
1558 several fields like medicinal, cosmetic, culinary, agriculture and textiles. Nowadays, the  
1559 association of plants oils and active molecules is attracting special attention. Lipid core  
1560 nanocapsules and nanostructured lipid carriers represent promising carriers to entrap both plant  
1561 oil and synthetic drugs. The appropriate selection of plant oil is very important for achieving  
1562 the high loading capacity and physical stability of the hydrophobic drugs. In addition, the oil  
1563 may complement or even enhance the biological activities of these drugs. Hence, the research  
1564 in the field of plants oils encapsulation can make an important contribution to the development  
1565 of new methodologies in the treatment and diagnosis of major chronic diseases.

1566         Experimental advances are necessary in engineering plant oils loaded nanocarriers with  
1567 broader applications and functionalities. Some techniques discussed in this review provide poor  
1568 control over the final structure and stability of the obtained colloidal systems. Others lack from  
1569 scalability and reproducibility; therefore, new techniques with improved control and  
1570 reproducibility are crucial to design nanocarriers with predictable properties.

1571         Even if several advances have been already reported in the literature regarding the  
1572 application of plants oils nanocarriers for pharmaceutical and cosmetics purposes, more *in vivo*  
1573 studies are required to provide reliable results. Additionally, plant oils mechanism of action,  
1574 toxic effects, pharmacokinetic parameters, biodistribution in biological systems and removal  
1575 mechanisms must be investigated. Moreover, with the aim of improving the biodistribution of  
1576 colloidal systems, scientists throughout the world are currently focalizing their efforts on the

1577 functionalization of the particle surface with special ligands to target specific organs and tissues.  
1578 However, to our knowledge, there are no reports in the literature that deal with targeting  
1579 delivery of plant oils loaded nanocarriers. Such demonstrations would provide a blueprint for  
1580 the development of new concepts and products in large-scale for broader application.

#### 1581 **CRedit authorship contribution statement**

1582 **Narimane Lammari:** Conceptualization, Writing - original draft, Investigation, Visualization.

1583 **Ouahida Louaer:** Supervision, Writing - review & editing. **Abdeslam Hassen Meniai:**  
1584 Writing - review & editing. **Hatem Fessi:** Conceptualization. **Abdelhamid Elaissari:**  
1585 Supervision, Writing - review & editing, Conceptualization.

#### 1586 **Declaration of Competing Interest**

1587 The authors declare that they have no known competing financial interests or personal  
1588 relationships that could have appeared to influence the work reported in this paper.

#### 1589 **Funding**

1590 This research did not receive any specific grant from funding agencies in the public,  
1591 commercial, or not-for-profit sectors.

#### 1592 **References**

1593 Abdullah, S.W., Ahmed, K.S.D., Khidher, K.Q., 2018. Plant essential oils as grain protectants  
1594 against *Rhizopertha dominica* (Coleoptera:Bostrichidae) during storage. Tikrit J. Pure Sci.  
1595 23, 41–44.

1596 Abreu, F.O.M.S., Oliveira, E.F., Paula, H.C.B., Paula, R.C.M., 2012. Chitosan/cashew gum  
1597 nanogels for essential oil encapsulation. Carbohydr. Polym. 89, 1277–1282.  
1598 <https://doi.org/10.1016/j.carbpol.2012.04.048>

1599 Adel, M., Atwa, W., Hassan, M., Salem, N., Farghaly, D.S., Ibrahim, S., 2015. Biological  
1600 activity and field persistence of *Pelargonium graveolens* (Geraniales : Geraniaceae)  
1601 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 ( $\epsilon$ -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  $\beta$  -  
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-



1702 refinery of orange peels waste: A new concept based on integrated green and solvent free  
1703 extraction processes using ultrasound and microwave techniques to obtain essential oil,  
1704 polyphenols and pectin. *Ultrason. Sonochem.* 24, 72–79.

1705 Calo, J.R., Crandall, P.G., O'Bryan, C.A., Ricke, S.C., 2015. Essential oils as antimicrobials in  
1706 food systems – A review. *Food Control* 54, 111–119.

1707 Calvo, P., Remunan Lopez, J.L., Vila-Jato, Alonso, M.J., 1997. Novel hydrophilic chitosan –  
1708 polyethylene oxide nanoparticles as protein carriers. *J. Appl. Polym. Sci.* 63, 125–132.

1709 Campo, C. De, Pereira, P., Maria, T., Costa, H., Guterres, S.S., Rios, A.D.O., Flôres, H., 2017.  
1710 Nanoencapsulation of chia seed oil with chia mucilage (*Salvia hispanica* L.) as wall  
1711 material: characterization and stability evaluation. *Food Chem.* 234, 1–9.  
1712 <https://doi.org/10.1016/j.foodchem.2017.04.153>

1713 Cao, Y., Zhou, W., Li, J., Huang, X., Yuan, Y., Lin, L., 2016. Preparation and stability  
1714 evaluation of pectin coated galanga essential oil liposomes, in: 2nd International  
1715 Conference on Architectural, Civil and Hydraulics Engineering (ICACHE 2016)  
1716 Preparation. pp. 285–290.

1717 Carneiro, H.C.F., Tonon, R. V, Grosso, C.R.F., Hubinger, M.D., 2013. Encapsulation efficiency  
1718 and oxidative stability of flaxseed oil microencapsulated by spray drying using different  
1719 combinations of wall materials. *J. Food Eng.* 115, 443–451.  
1720 <https://doi.org/10.1016/j.jfoodeng.2012.03.033>

1721 Carneiro, N.S., Alves, C.C., Alves, J.M., Egea, M.B., Martins, C.H., Silva, T.S., Bretanha,  
1722 L.C., Balleste, M.P., Mücke, G.A., Silveira, E. V, Miranda, M.L., 2017. Chemical  
1723 composition, antioxidant and antibacterial activities of essential oils from leaves and  
1724 flowers of *Eugenia klotzschiana* Berg (Myrtaceae). *An. Acad. Bras. Cienc.* 89.

1725 Carvalho, A., Melo, V., Craveiro, A., Machado, M., Bantim, M., Rabelo, E., 2003. Larvicidal  
1726 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. Schmiedebergs. 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 triazolinedione- 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  $\alpha$  -  
1866 tocopherol and d  $\gamma$  -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 Esmacili, 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., Masoumpour, F., 2020. Formulation and characterization of  
2026 nanoemulsion from *Alhagi maurorum* essential oil and study of its antimicrobial,

2027 antibiofilm, and plasmid curing activity against antibiotic-resistant pathogenic bacteria. J.  
2028 Environ. Heal. Sci. Eng. 18, 1015–1027.

2029 He, H., Yao, J., Zhang, Y., Chen, Y., Wang, K., Lee, R.J., Yu, B., Zhang, X., 2019. Solid lipid  
2030 nanoparticles as a drug delivery system to across the blood-brain barrier. Biochem.  
2031 Biophys. Res. Commun. 519, 385–390. <https://doi.org/10.1016/j.bbrc.2019.09.017>

2032 Herculano, E.D., Paula, H.C.B. De, Dias, F.G.B., Pereira, V.D.A., 2015. Physicochemical and  
2033 antimicrobial properties of nanoencapsulated *Eucalyptus staigeriana* essential oil. LWT -  
2034 Food Sci. Technol. 61, 484–491. <https://doi.org/10.1016/j.lwt.2014.12.001>

2035 Hosseini, S.F., Zandi, M., Rezaei, M., Farahmandghavi, F., 2013. Two-step method for  
2036 encapsulation of oregano essential oil in chitosan nanoparticles: Preparation ,  
2037 characterization and *in vitro* release study. Carbohydr. Polym. 95, 50–56.  
2038 <https://doi.org/10.1016/j.carbpol.2013.02.031>

2039 How, C.W., Rasedee, A., Abbasalipourkabir, R., 2013. Characterization and cytotoxicity of  
2040 nanostructured lipid carriers formulated with olive oil, hydrogenated palm oil, and  
2041 polysorbate 80. IEEE Trans. Nanobioscience 12, 72–78.

2042 Hoyos-leyva, J.D., Bello-perez, L.A., Agama-acevedo, J.E., Alvarez-ramirez, J., Jaramillo-  
2043 Echeverry, L.M., 2019. Characterization of spray drying microencapsulation of almond  
2044 oil into taro starch spherical aggregates. LWT - Food Sci. Technol. 101, 526–533.  
2045 <https://doi.org/10.1016/j.lwt.2018.11.079>

2046 Hsu, E., Parthasarathy, S., 2017. Anti-inflammatory and antioxidant effects of sesame oil on  
2047 atherosclerosis: A descriptive literature review. Cureus 9, 1438.

2048 Hu, J., Wang, X., Xiao, Z., Bi, W., 2015. Effect of chitosan nanoparticles loaded with cinnamon  
2049 essential oil on the quality of chilled pork. LWT - Food Sci. Technol. 63, 519–526.  
2050 <https://doi.org/10.1016/j.lwt.2015.03.049>

2051 Huang, J., Wang, Q., Chu, L., Xia, Q., 2020. Liposome-chitosan hydrogel bead delivery system

2052 for the encapsulation of linseed oil and quercetin: Preparation and *in vitro* characterization  
2053 studies. LWT - Food Sci. Technol. 117, 108615.

2054 Iannitelli, A., Grande, R., di Stefano, A., di Giulio, M., Sozio, P., Bessa, L.J., Laserra, S.,  
2055 Paolini, C., Protasi, F., Cellini, L., 2011. Potential antibacterial activity of carvacrol-loaded  
2056 poly(DL-lactide-co-glycolide) (PLGA) nanoparticles against microbial biofilm. Int. J.  
2057 Mol. Sci. 12, 5039–5051. <https://doi.org/10.3390/ijms12085039>

2058 Immordino, M.L., Dosio, F., Cattel, L., 2006. Stealth liposomes: Review of the basic science,  
2059 rationale, and clinical applications, existing and potential. Int. J. Nanomedicine 1, 297–  
2060 315.

2061 Intahphuak, S., Khonsung, P., Panthong, A., 2010. Anti-inflammatory, analgesic, and  
2062 antipyretic activities of virgin coconut oil. Pharm. Biol. 48, 151–157.

2063 Jahromi, M.M., Zangabad, P.S., Basri, S.M., Zangabad, M.S., Ghamarypour, A., Aref, A.,  
2064 Karimi, M., Hamblin, M., 2018. Nanomedicine and advanced technologies for burns:  
2065 preventing infection and facilitating wound healing. Adv. Drug Deliv. Rev. 123, 33–64.

2066 Jajarm, F.H., Moravvej, G., Awal, M.M., Golmohammadzadeh, S., 2020. Insecticidal activity  
2067 of solid lipid nanoparticle loaded by *Ziziphora clinopodioides* Lam. against *Tribolium*  
2068 *castaneum* (Herbst, 1797) (Coleoptera: Tenebrionidae). Int. J. Pest Manag.  
2069 <https://doi.org/10.1080/09670874.2020.1713420>.

2070 Jamil, B., Abbasi, R., Abbasi, S., Imran, M., Khan, S.U., Ihsan, A., Javed, S., Bokhari, H.,  
2071 Imran, M., 2016. Encapsulation of cardamom essential oil in chitosan nano-composites :  
2072 In-vitro efficacy on antibiotic-resistant bacterial pathogens and cytotoxicity studies. Front.  
2073 Microbiol. 7, 1–10. <https://doi.org/10.3389/fmicb.2016.01580>

2074 Jassbi, A.R., Zare, M., Jamebozorgi, F.H., 2017. Chemical composition and biological activity  
2075 of the essential oil and solvent extracts of Scaligeria nodosa. Open Bioact. Compd. J. 5,  
2076 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- $\epsilon$ -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  $\alpha$ -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  $\beta$  - 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-quiros, 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., Escribano, E., Milia, E., Pinna, R., Palmieri, A.,  
2221 Firoznejhad, 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

2402 cells. Int. J. Biol. Macromol. 164, 4010–4021.

2403 Rajkumar, V., Gunasekaran, C., Dharmaraj, J., Chinnaraj, P., Paul, C.A., Kanithachristy, I.,  
2404 2020. Structural characterization of chitosan nanoparticle loaded with *Piper nigrum*  
2405 essential oil for biological efficacy against the stored grain pest control. Pestic. Biochem.  
2406 Physiol. 166, 104566.

2407 Ramteke, K.H., Joshi, S.A., Dhole, S.N., 2012. Solid lipid nanoparticle : A review. IOSR J.  
2408 Pharm. 2, 34–44.

2409 Rani, S., Sharma, A.K., Khan, I., Gothwal, A., 2017. Polymeric nanoparticles in targeting and  
2410 delivery of drugs, in Nanotechnology-Based Approaches for Targeting and delivery of  
2411 Drugs and Genes. Elsevier Science Publishing Co Inc.: New York, USA.  
2412 <https://doi.org/10.1016/B978-0-12-809717-5.00008-7>

2413 Rao, J.P., Geckeler, K.E., 2011. Polymer nanoparticles : Preparation techniques and size-  
2414 control parameters. Prog. Polym. Sci. 36, 887–913.  
2415 <https://doi.org/10.1016/j.progpolymsci.2011.01.001>

2416 Rasti, B., Jinap, S., Mozafari, M.R., 2013. Optimization on preparation condition of  
2417 polyunsaturated fatty acids nanoliposome prepared by Mozafari method. J. Liposome Res.  
2418 2104, 1–7. <https://doi.org/10.3109/08982104.2013.839702>

2419 Rasti, B., Jinap, S., Mozafari, M.R., Yazid, A.M., 2012. Comparative study of the oxidative  
2420 and physical stability of liposomal and nanoliposomal polyunsaturated fatty acids prepared  
2421 with conventional and Mozafari methods. Food Chem. 135, 2761–2770.  
2422 <https://doi.org/10.1016/j.foodchem.2012.07.016>

2423 Rates, S.M.K., 2001. Plants as source of drugs. Toxicon 39, 603–613.

2424 Raut, J.S., Karuppayil, S.M., 2014. Experimental evaluation of *Aloe vera* leaves pulp as topical  
2425 medicament on wound healing. Ind. Crop. Prod. 62, 250–264.

2426 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., Vignani, 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



2502 herbal moisturizers. *Pharmacognosy Res.* 2, 146–151.

2503 Sarangi, M.K., Padhi, S., 2016. Solid lipid nanoparticles- A review. *J. critica Rev.* 3, 5–12.

2504 <https://doi.org/10.5958/0975-4377.2016.00030.6>

2505 Sebaaly, C., Charcosset, C., Stainmesse, S., Fessi, H., Greige-gerges, H., 2016a. Clove essential

2506 oil-in-cyclodextrin-in-liposomes in the aqueous and lyophilized states : From laboratory

2507 to large scale using a membrane contactor. *Carbohydr. Polym.* 138, 75–85.

2508 Sebaaly, C., Greige-Gerges, H., Agusti, G., Fessi, H., Charcosset, C., 2015a. Large-scale

2509 preparation of clove essential oil and eugenol-loaded liposomes using a membrane

2510 contactor and a pilot plant. *J. Liposome Res.* 26, 126-38.

2511 <https://doi.org/10.3109/08982104.2015.1057849>

2512 Sebaaly, C., Greige-gerges, H., Stainmesse, S., Fessi, H., Charcosset, C., 2016b. Effect of

2513 composition , hydrogenation of phospholipids and lyophilization on the characteristics of

2514 eugenol-loaded liposomes prepared by ethanol injection method. *Food Biosci.* 15, 1–10.

2515 <https://doi.org/10.1016/j.fbio.2016.04.005>

2516 Sebaaly, C., Jraij, A., Fessi, H., Charcosset, C., Greige-gerges, H., 2015b. Preparation and

2517 characterization of clove essential oil-loaded liposomes. *Food Chem.* 178, 52–62.

2518 <https://doi.org/10.1016/j.foodchem.2015.01.067>

2519 Shakeri, F., Shakeri, S., Hojjatoleslami, M., 2014. Preparation and characterization of carvacrol

2520 loaded polyhydroxybutyrate nanoparticles by nanoprecipitation and dialysis methods. *J.*

2521 *Food Sci.* 79, 697–705. <https://doi.org/10.1111/1750-3841.12406>

2522 Shakeri, M., Hadi, S., Shakeri, S., 2019. Carvacrol and astaxanthin co-entrapment in beeswax

2523 solid lipid nanoparticles as an efficient nano-system with dual antioxidant and anti-biofilm

2524 activities. *LWT - Food Sci. Technol.* 107, 280–290.

2525 <https://doi.org/10.1016/j.lwt.2019.03.031>

2526 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  $\beta$ -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( $\epsilon$ -  
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/10.1111/1750-3841.12929>
- 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

2652 liposomes at high ionic strength. *Food Hydrocoll.* 93, 10–18.

2653 Wang, Z., 2012. Preparation and characterization of solid lipid nanoparticles loaded with  
2654 frankincense and myrrh oil. *Int. J. Nanomedicine* 7, 2033–2043.  
2655 <https://doi.org/10.2147/IJN.S30085>

2656 Warnke, P., Becker, S., Podschun, R., Sivananthan, S., Springer, I., Russo, P., Wiltfang, J.,  
2657 Fickenscher, H., Sherry, E., 2009. The battle against multi-resistant strains: Renaissance  
2658 of antimicrobial essential oils as a promising force to fight hospital-acquired infections. *J.*  
2659 *Craniomaxillofac. Surg.* 37, 392–7.

2660 Warshaw, E.M., Maibach, H.I., Taylor, J.S., Sasseville, D., DeKoven, F., Zirwas, M.,  
2661 Fransway, A., Mathias, C., Zug, K., DeLeo, V., Fowler, J., Marks, J., Pratt, M., Storrs, F.,  
2662 Belsito, D., 2015. North American contact dermatitis group patch test results: 2011-2012.  
2663 *Dermatitis* 26, 49–59.

2664 Weber, J., Funk, N.L., Motta, M.H., Guedes, A.M., Visintainer, A.P.C., Tedesco, S.B., Silva,  
2665 C.D.B., Chalmers, H., 2016. Association of borage oil and betamethasone dipropionate in  
2666 lipid-core nanocapsules: characterization, photostability and *in vitro* irritation test. *J.*  
2667 *Nanosci. Nanotechnol.* 16, 1354–1362. <https://doi.org/10.1166/jnn.2016.11674>

2668 Woranuch, S., Yoksan, R., 2013. Eugenol-loaded chitosan nanoparticles : I . Thermal stability  
2669 improvement of eugenol through encapsulation. *Carbohydr. Polym.* 96, 578–585.  
2670 <https://doi.org/10.1016/j.carbpol.2012.08.117>

2671 Wu, Z., Zhou, W., Pang, C., Deng, W., Xu, C., Wang, X., 2020. Multifunctional chitosan-based  
2672 coating with liposomes containing laurel essential oils and nanosilver for pork  
2673 preservation. *Food Chem.* 295, 16–25.

2674 Xenakis, A., Papadimitriou, V., Sotiroudis, T.G., 2010. Colloidal structures in natural oils. *Curr.*  
2675 *Opin. Colloid Interface Sci.* 15, 55–60. <https://doi.org/10.1016/j.cocis.2009.11.007>

2676 Yadav, N., Khatak, S., Sara, U.V.S., 2013. Solid lipid nanoparticles- A review. *Int. J. Appl.*

2677 Pharm. 5, 8–18.

2678 Yaep, S., Beh, B., Ali, N., Yusof, H., 2015. Antistress and antioxidant effects of virgin coconut  
2679 oil *in vivo*. *Exp. Ther. Med.* 9, 39–42.

2680 Yang, J., Han, S., Zheng, H., Dong, H., Liu, J., 2015. Preparation and application of  
2681 micro/nanoparticles based on natural polysaccharides. *Carbohydr. Polym.* 123, 53–66.

2682 Yang, X., Gao, N., Hu, L., Li, J., Sun, Y., 2015. Development and evaluation of novel  
2683 microcapsules containing poppy-seed oil using complex coacervation. *J. Food Eng.* 161,  
2684 87–93. <https://doi.org/10.1016/j.jfoodeng.2015.03.027>

2685 Yang, Z., Peng, Z., Li, J., Li, S., Kong, L., Li, P., Wang, Q., 2014. Development and evaluation  
2686 of novel flavour microcapsules containing vanilla oil using complex coacervation  
2687 approach. *Food Chem.* 145, 272–277. <https://doi.org/10.1016/j.foodchem.2013.08.074>

2688 Yara-Varón, E., Li, Y., Balcells, M., Canela-Garayoa, R., Fabiano-Tixier, A.-S., Chemat, F.,  
2689 2017. Vegetable oils as alternative solvents for green oleo-extraction, purification and  
2690 formulation of food and natural products. *Molecules* 22, 1474.  
2691 <https://doi.org/10.3390/molecules22091474>

2692 Yoshida, P.A., Yokota, D., Foglio, M.A., Rodrigues, R.A.F., Pinho, S.C., 2010. Liposomes  
2693 incorporating essential oil of Brazilian cherry (*Eugenia uniflora* L.): Characterization of  
2694 aqueous dispersions and lyophilized formulations. *J. Microencapsul.* 27, 416–425.  
2695 <https://doi.org/10.3109/02652040903367327>

2696 Yu, F.L., Greenlaw, R., Fang, Q., Bender, W., Yamaguchi, K., Xue, B.H., Yu, C.C., 2004.  
2697 Studies on the chemopreventive potentials of vegetable oils and unsaturated fatty acids  
2698 against breast cancer carcinogenesis at initiation. *Eur. J. Cancer Prev.* 13, 239–248.

2699 Zabihi, A., Basti, A.A., Amoabediny, G., Khanjari, A., Bazzaz, J.T., Mohammadkhan, F.,  
2700 Bargh, A.H., Vanaki, E., 2017. Physicochemical characteristics of nanoliposome garlic (  
2701 *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 CO<sub>2</sub> 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 Zhaveh, 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