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Review

Essential oils: From extraction to encapsulation

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ABSTRACT

Essential oils are natural products which have many interesting applications. Extraction of essential oils from plants is performed by classical and innovative methods. Numerous encapsulation processes have been developed and reported in the literature in order to encapsulate biomolecules, active molecules, nanocrystals, oils and also essential oils for various applications such as in vitro diagnosis, therapy, cosmetic, textile, food etc. Essential oils encapsulation led to numerous new formulations with new applications. This insures the protection of the fragile oil and controlled release. The most commonly prepared carriers are polymer particles, liposomes and solid lipid nanoparticles.

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Contents

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1. Introduction

Essential oils (EOs) have gained a renewed interest in several areas. As natural products, they have interesting physicochemical characteristics with high added values respecting the environment. EOs also have diverse and relevant biological activities. For instance, they are used in the medical field thanks to their biocidal activities (bactericidal, virucidal and fungicidal) and medicinal properties. Numerous studies have highlighted EOs antimicrobial effects even against multi-resistant bacteria (Mayaud et al., 2008; Burt, 2004). Furthermore, EOs have been used against nosocomial infections, as a cleaning liquid for disinfection of medical equipment and surfaces (Warnke et al., 2009) or as an aerosol in operating blocks and waiting rooms for air cleaning to limit contaminations (Billerbeck, 2007). They could also provide a pleasant feeling of psychic comfort for patients thanks to their pleasant odor. Use of EOs as food preservatives has also been described (Burt, 2004; Tiwari et al., 2009). Because of their complex chemical composition, often composed of more than 100 different terpenic compounds, EOs have a broad biological and antimicrobial activity spectrum (antibacterial, antifungal, antimoulds, antiviral, pest control, insect repellents). In the pharmaceutical field, EOs are included in the composition of many dosage forms (capsules, ointments, creams, syrups, suppositories, aerosols and sprays). Preparations' number is constantly growing. They are intended mainly of local applications as mixtures with vegetable oils or inhalation.

Food industry also presents a growing demand for EOs because of their important applications as food preservatives (Burt, 2004), innovation in food packaging and the fight against pathogens generating dangerous food poisoning (*Listeria monocytogenes*, *Salmonella typhimurium*, *Clostridium perfringens*, *Pseudomonas putida* and *staphylococcus aureus*). Numerous studies have demonstrated the efficiency of EOs in low doses in the fight against bacterial pathogens encountered in food industry and meat product (Oussalah et al., 2006, 2007). Likely, there was an increased public concern about the use of antibiotics in livestock feed because the emergence of antibiotic resistant bacteria and their possible transmission from livestock's to humans. In fact, in the European Union, use of synthetic antibiotics, health and growth promoters as additives in livestock feed has been prohibited since 2006 (Castanon, 2007). In this context, EOs were shown to be an interesting alternative because of their well known and well documented antimicrobial activity. EOs contain components with biocide and antiviral properties that can be used as substitutes of synthetic drugs in livestock (Varona et al., 2013). The Food and Drug Administration recognized EOs as safe substances according to Code of Federal Regulations and some contain compounds can be used as antibacterial additives (CFR, 2015; Ait-Ouazzou et al., 2011; Cox et al., 2001; Deans and Ritchie, 1987; Nerio et al., 2010; Muyima et al., 2002).

Other applications include medical and technical textiles. In this case, encapsulation is the technique of choice in industries process as a means of imparting finishes and properties on textiles that were not possible or cost-effective using other technologies. In textiles, the major application of encapsulation is durable fragrances and skin softeners. Other applications include insect repellents, dyes, vitamins, antimicrobial agents, phase-change materials and medical applications, such as antibiotics, hormones and other drugs.

EOs are unstable and fragile volatile compounds. Consequently, they could be degraded easily (by oxidation, volatilization, heating, light) if they are not protected from external factors. Such protection could increase their action duration and provide a controlled release. EOs stability could be increased by encapsulation (Hong and Park, 1999). Encapsulation was also shown to improve the antibacterial activity of several antibiotics (Drulis-Kawa and Dorotkiewicz-Jach, 2010). The aim of this review is to report the EOs properties, the ways of their extraction, their encapsulation processes and applications.

2. What is an essential oil?

According to the European Pharmacopoeia 7th edition, EOs are defined as: "Odorant product, generally of a complex composition, obtained from a botanically defined plant raw material, either by driving by steam of water, either by dry distillation or by a suitable mechanical method without heating. An essential oil is usually separated from the aqueous phase by a physical method that does not lead to significant change in its chemical composition". EOs could be then subjected to an appropriate further treatment. They are commercially called as deterpenated, desesquiterpenated, rectified or private from "x" according to 7th edition of the European Pharmacopoeia.

EOs are oily aromatic liquids extracted from aromatic plant materials. They could be biosynthesized in different plant organs as secondary metabolites such as, flowers (jasmine, rose, violet and

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lavender), herbs, buds (clove), leaves (*Thym, Eucalyptus, Salvia*), fruits (anis, star anise), twigs, bark (cinnamon), zest (citrus), seeds (cardamom), wood (sandal), rhizome and roots (ginger). They could be extracted by different methods. Due to their hydrophobic nature and their density often lower than that of water, they are generally lipophilic, soluble in organic solvents, immiscible with water. They could be separated from the aqueous phase by decantation. However, their extraction yields vary depending on species and organs. They remain, however, very low (about 1%), which makes them highly valuable rare substances. Among the plant species, only 10% contain EOs and are called aromatic plants (over 17,000 plant species, distributed all over the world (Svoboda and Greenaway, 2003)). The genres in which they could be found are sorted in a small number of families: Lamiaceae, Lauraceae, Asteraceae, Rutaceae, Myrtaceae, Poaceae, Cupressaceae and Piperaceae (Bruneton, 1999).

3. Essential oil secretion

EOs are biosynthesized, accumulated and stored in specialized histological structures, the secretory glandules (Bouwmeester et al., 1995; Bruneton, 1987). Svoboda and Greenaway (2003) confirmed that there are two types of secretory glandules: those located on the plant surfaces with exogenous secretion and those located inside the plant in internal organs with endogenous secretion. They are also localized in the cytoplasm of some secretory cells in one or more plant organs. We can distinguish different types (see Table 1).

3.1. External secretion tissue

Such tissue is located outside of the plant

- The epidermal papillae: they are conical epidermal cells which secrete essences that are generally encountered in flower petals (i.e. *Rosa* sp.).
- The glandular trichomes (secretory glandules or bristles): they develop from epidermal cells. They are biosynthesis and accumulation site of EOs and are characteristic of the Lamiaceae family (Turner et al., 2000). The synthesized essential oil is accumulated in a pocket between secretory cells and a common cuticle (Fig. 1a–d). There are many types of glandular trichomes (Rezakhanlo and Talebi, 2010): sessile (Fig. 1a) and stalked trichomes. The latter are of three types: peltate (Fig. 1b), capitate and digitiform trichomes (Fig. 1e) (Rezakhanlo and Talebi, 2010; Baran et al., 2010; Ascensão and Pais, 1998).
-

The non glandular trichomes: they are bristles having similar structure to glandular trichomes found also in some Labiatae (Fig. 1f) (Kremer et al., 2014; Rezakhanlo and Talebi, 2010). Q7

3.2. Internal secretion tissue

This tissue is located inside of the plant. We distinguish

- The secretory canals: they are small canals (Fig. 1g) which sometimes extend over the entire length of the plant and the walls of which are formed of seated secreting cells (Apiaceae).
- The schizogenous pockets (or secretory pockets): it is an intercellular space, often spherical, which is filled by EOs droplets synthesized by the cells which border it.
- Cells with intracellular secretion: they are isolated cells specialized in the accumulation and secretion of EOs inside their vacuoles. When the EOs concentration attains high levels, these cells die (e.g. cells of cinnamon, laurel leaves, rhizome of calamus).

For some authors, it is necessary to distinguish between plant essence and essential oil. The first term corresponds to the natural secretions produced in the plant by specialized secretory cells. The second refer to the extract obtained by steam or hydro-distillation, which means that EOs are the distilled plant essence. For instance, the extract obtained from the zest of citrus fruit by cold expression is the essence but that obtained by steam distillation is the essential oil. The different tissues specialized in the storage and accumulation of EOs offer an ideal protection for these fragile products against external factors to which they are vulnerable (light, heat, moisture and oxidation). They release their contents by tearing after a humidity variation, or by mechanical action. It is the case when extracting EOs of which we will discuss the main approaches in the following paragraphs. Biological roles of EOs in plants remain hypothetical but it seems that they play a role in plant–plant interactions (inhibition of germination and growth of other plants) and plant–animal interactions (attractors of pollinators and pest repellents). They also provide a defensive role against fungi and pathogenic microorganisms and against herbivores (inappetent) and insects (Erman, 1985). The specialists consider EOs as source of chemical signals that allow the plant to control and regulate their environment (Bruneton, 2009). The EOs extracts could vary in quality, quantity and in composition according to climate, soil composition, plant organ, age and vegetative cycle stage (Masotti et al., 2003; Angioni et al., 2006).

Table 1
Secretory structures specialized in accumulation and stockage of essential oils. Q22

Secretory structures	Description	Organ plant	Example	Botanic family
External secretory tissus				
Epidermic papillae	Conical epidermal secretory cells	Flower Petals	*Rosa damascena* *Convallaria majalis*	Rosaceae Asparagaceae
Secretory bristles or glandular trichomes	Terminal cells of trichomes secreting EOs	Stem Leaves	*Pelargonium* sp. *Salvia* sp., *Mentha* sp.	Geraniaceae Lamiaceae
Internal secretory tissus				
The schizogenous or secretory pockets	Intercellular space filled with the cells secretions	Epicarp of fruit	*Citrus* sp.	Rutaceae Myrtaceae
Secretory canals	Small canals formed of aggregated secreting cells throughout the plant	Stem	*Petroselinum* sp. *Pimpinella* sp. *Daucus* sp.	Apiaceae
Intracellular secretory cells	Cells specialized in the EOs accumulation inside their vacuoles	Stem Leaves Rhizome	*Cinnamomum ceylanicum* *Laurus nobilis* *Acorus calamus*	Lauraceae

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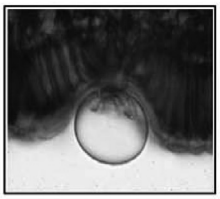


Fig. 1a. Sessile secretory Glandule on the upper leaf surface of *origanum heracleoticum* leave showing subcuticular space filled with essential oil and a fully-extended cuticle (magn. x 420) (Svoboda and Greenaway, 2003)

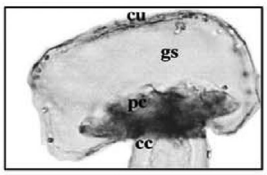


Fig. 1b. Peltate trichomes (cu: cuticle, gs:glandular space filled with EO, pc: periphery cells, cc: central cells) (Baran et al., 2010)

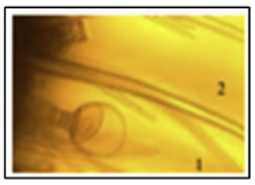


Fig. 1c. Digitiform trichome of *Stachys lavandulifolia* vahl (Light micrograph). (Rezakhanlo and Talebi, 2010)

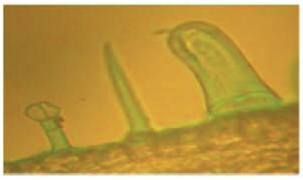


Fig.1d. Different types of secretory trichomes in *salvia officinalis* (Franchomme and Pénoël, 2001) (C.S. Secretory cell; C.B. Basal cell; P.E. Essential oil Pocket)

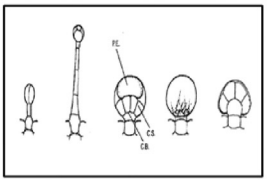


Fig. 1e. Light micrograph of protective and secretory bristles of *P. graveolens* leaf (Gx 400) – (Boukhatem et al., 2010)

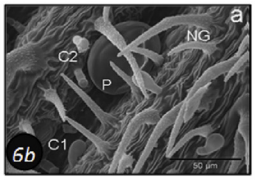


Fig. 1f. SEM micrographs of *Micromeria kerneri* showing non-glandular trichomes (NG) (Kremer et al., 2014)

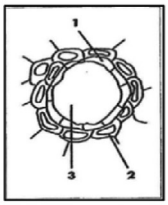


Fig 1g. Cross section of a channel schizogenous glandular leaf of Pinus pinaster (Franchomme and Pénoël, 2001) (1.Secretory cells; 2. Protective sheath formed of adjacent lignified cells; 3. Channel).

Fig. 1. Plant parts that allow essential oil biosynthesis and secretion.

4. Chemical composition of the essential oils

EOs are complex mixtures of volatile compounds extracted from a large number of plants. In general they represent a small fraction of plant composition (less than 5% of the vegetal dry matter) and comprise mainly hydrocarbon terpenes (isoprenes) and terpenoids. The first compounds are monoterpenes (they have 10 carbon atoms and represent more than 80% of EOs composition) and sesquiterpenes (they have 15 carbon atoms). They could present hydrocarbon acyclic structures, so as mono-, bi- or tricyclic structures. The second ones, also called isoprenoids. They are oxygenated derivatives of hydrocarbon terpenes such as, alcohols, aldehydes, ketones, acids, phenols, ethers and esters (Bakkali et al., 2008; Templeton, 1969). They comprise both oxygenated mono- and sesquiterpenes (sesquiterpenoids). Some EOs contains another class of oxygenated molecules which are phenylpropanoids and their derivatives. They are found in special cases (*Sassafras*, Cinnamon bark, vetiver, clove) (Barceloux, 2008) (see Table 2). Terpenes represent a very large class of most abundant natural hydrocarbons. They have various functions (Gershenzon and Dudareva, 2007). Some terpenes are potent drugs against diseases such as cancer (Ebada et al., 2010), malaria (Parshikov and Netrusov, 2012) and heart disease (Liebgott et al., 2000). Others show insecticidal properties (Rossi et al., 2012). The fundamental building block of terpenes is the isoprene unit (2-methyl-1,3-butadiene) linked in a head-to-tail fashion. It is represented by general structural formula $(C_5H_8)_n$ where n is the number of linked isoprene units. The isoprene rule, developed by Ruzicka in

Table 2
A few components of essential oils with some physicochemical properties and biological activities.

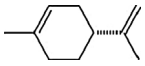
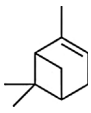
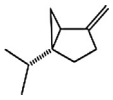
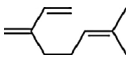
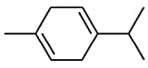
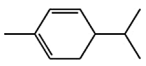
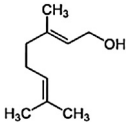
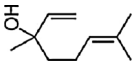
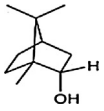
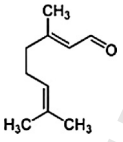
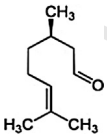
EO components	CAS number	Molecular structure	Chemical formula	Molecular weight	Boiling point °C	Refractive index (20 °C)	Relative density g/mL (20 °C)	Plant source	Some biological activities	References
Monoterpenes										
D-Limonène	5989-27-5		$C_{10}H_{16}$	136.23	175.4	1.473	0.842	*Citrus limon*	Antifungal, antioxydant	(Singh et al., 2010)
α-Pinène	7785-70-8		$C_{10}H_{16}$	136.23	157.9	1.465	0.858	*Pinus pinaster*	Anti-inflammatory, anti-oxydant	(Bae et al., 2012; Marija and Lesjak, 2014)
Sabinene	3387-41-5		$C_{10}H_{16}$	136.23	164	1.467–1.473	0.844	*Quercus ilex, Oenanthe crocata*	Antifungal, antioxidant, anti-inflammatory	(Valente and Zuzarte, 2013)
Myrcène	123-35-3		$C_{10}H_{16}$	136.23	167	1.469	0.791	*Citrus aurantium*	Gastroprotective antioxydant	(Flavia Bonamin, 2014)
γ-Terpinène	99-85-4		$C_{10}H_{16}$	136.23	183	1.474	0.85	*Origanum vulgare*	Antioxydant	(Ruben Olmedo, 2014)
para-Cymène	99-87-6		$C_{10}H_{16}$	136.23	176–178	1.49	0.86	*Cuminum cyminum*	Antifungal, antiaflatoxigenic, antioxydant	(Akash Kedia, 2013; Chen et al., 2014)
Terpenic alcools										
Geraniol	106-24-1		$C_{10}H_{18}O$	154.25	229.5	1.474	0.879	*Pelargonium graveolens*	Insecticide, antimicrobial, anticancer, anti-oxidant	(Chen and Viljoen, 2010)
Linalool	78-70-6		$C_{10}H_{18}O$	154.25	197.5	1.462	0.87	*Lavandula officinalis*	Insect-repellent, anti-tumor, anti-inflammatory, antimicrobial	(Changmann Yoon, 2011; Miyashita and Sadzuka, 2013; Huo et al., 2013; Park et al., 2012)
Borneol	464-43-7		$C_{10}H_{18}O$	154.25	213	–	1.011	*Thymus satureioides*	Broad-spectrum, antimicrobial, antioxydant, antitumor	(Abdelrhafour Tantaoui-Elaraki, 1993; Jaafari et al., 2007)
Aldehyde terpenes										
Citral	5392-40-5		$C_{10}H_{16}O$	152.23	229	1.488	0.888	*Aloysia citrodora*	Antifungal, antibacterial, painkiller	(Fan et al., 2014; Nengguo Tao, 2014; Clara Miracle Belda-Galbis, 2013; Nishijima et al., 2014)
Citronellal	5949-05-3		$C_{10}H_{18}O$	154.25	201–207	1.446	0.851	*Cymbopogon citratus*	Insecticide, antifungal, antimicrobial, antioxydant	(Sadaka et al., 2013; Singh et al., 2012)
Ketones alcohols										
Camphor	76-22-2		$C_{10}H_{16}O$	152.23	204	–	0.999	*Lavendula stoechas*	Antispasmodic, sedative, diuretic antirheumatic, anti-	(Braden et al., 2009)

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Table 2 (*Continued*)

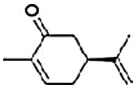
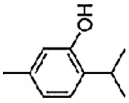
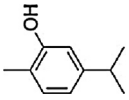
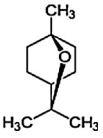
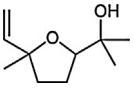
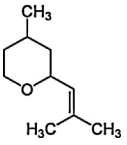
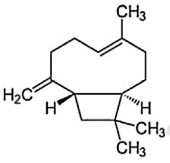
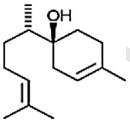
EO components	CAS number	Molecular structure	Chemical formula	Molecular weight	Boiling point °C	Refractive index (20 °C)	Relative density g/mL (20 °C)	Plant source	Some biological activities	References
									inflammatory, anti-anxiety	
Carvone	6485-40-1		$C_{10}H_{14}O$	150.22	231	1.497	0.959	*Mentha spicata*	Antispasmodic, antimicrobial, antihyperglycemic	(Souza et al., 2013; Esfandyari-Manesh et al., 2013; Udaiyar Muruganathan, 2013)
Phenolic terpenes										
Thymol	89-83-8		$C_{10}H_{14}O$	150.22	233	–	0.965	*Thymus vulgaris*	Strong antimicrobial, antiseptic, antitussive, anti-inflammatory, cicatrizing	(Wattanasatcha et al., 2012; Gavliakova and Biringerova, 2013; Riella et al., 2012)
Carvacrol	499-75-2		$C_{10}H_{14}O$	150.22	237.7	1.522	0.977	*Thymus maroccanus*	Strong antimicrobial, anti-inflammatory	(Lima et al., 2013)
Terpenic oxides										
1,8-Cineole	470-82-6		$C_{10}H_{18}O$	154.25	176	1.457	0.921	*Eucalyptus polybractea*	Anti-inflammatory activity (asthma)	(Juergens et al., 2003)
Linalool oxide ($C_{10}H_{18}O_2$)	60047-17-8		$C_{10}H_{18}O_2$	170.25	198.5	–	0.945	*Pelargonium graveolens*	Anxiolytic-like effects	(Flávia Negromonte Souto-Maior, 2011)
Terpenic oxides										
Cis-Rose oxide	3033-23-6		$C_{10}H_{18}O$	154.25	70–71	1.454	0.871	*Rosa damascena*	Anti-inflammatory, relaxant	(Nonato et al., 2012; Boskabady et al., 2006)
Sesquiterpenes										
β-Caryophyllene	87-44-5		$C_{15}H_{24}$	204.36	268.4	1.498–1.504	0.905	*Rosmarinus oficinalis*	Anti-inflammatory, antispasmodic, anticolitique	–
Oxygenated sesquiterpenes										
α-Bisabolol	23089-26-1		$C_{15}H_{26}O$	222.37	153	1.496	0.92	*Matricaria recutita*	Anti-irritant, anti inflammatory, antimicrobial	–
Caryophyllen oxid	1139-30-6		$C_{15}H_{24}O$	220.35	279.68	1.495	0.985	*Chenopodium ambrosioides, Psidium guajava*	Induced apoptosis in human cancer cells (prostat & breast cells), Analgesic and anti-inflammatory	(Park et al., 2011; Chavan et al., 2010)

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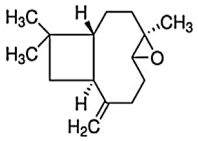
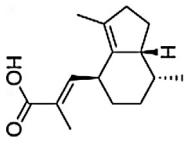
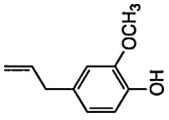
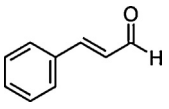
Table 2 (*Continued*)

EO components	CAS number	Molecular structure	Chemical formula	Molecular weight	Boiling point °C	Refractive index (20 °C)	Relative density g/mL (20 °C)	Plant source	Some biological activities	References
										
Valerenic acid	3569-10-6		$C_{15}H_{22}O_2$	234.33	374.5		1.06	*Valeriana officinalis*	Sedatif, anti-anxiolytic	(Houghton, 1999; Stevinson and Ernst, 2000)
Phenylpropanoids										
Eugenol	97-53-0		$C_{10}H_{12}O_2$	164.20	254	1.544	1.067	*Eugenia, Caryophyllata*	Antifungal, antibacterial-dental care	(Abbaszadeh et al., 2014; Ghosh et al., 2014)
Cinnamaldehyde	104-55-2		C_9H_8O	132.16	248–250	1.621	1.05	*Cinnamomum, Zeylanicum*	Bactericide, fungicide, insecticide	(Ye et al., 2013)

1921 played key role in structure determination (Ruzicka, 1953). Classification of terpenes is based on the number of isoprene units. Monoterpenes consist of two isoprene units ($2 \times C_5$) and has molecular formula ($C_{10}H_{16}$) while sesquiterpenes contains three isoprene units ($3 \times C_5$) and has molecular formula ($C_{15}H_{24}$). Table 2 contains compositions of some EOs along with their physicochemical properties and biological activities.

5. Essential oils extraction methods

EOs are obtained from plant raw material by several extraction methods (Wang and Weller, 2006) (Dick and Starmans, 1996). Such methods could be classified into two categories: conventional/classical methods and advanced/innovative methods. Investigation in new technologies (ultrasound, microwave) in the last decades has led to the emergence of new innovative and more efficient extraction processes (reduction of extraction time and energy consumption, increase of extraction yield, improvement of EOs quality).

5.1. Conventional and classical methods

These are conventional methods based on water distillation by heating to recover EOs from plant matrix.

5.1.1. Hydrodistillation

This method is the most simple and old that is used for the extraction of EOs (Meyer-Warnod, 1984). Historically, Avicenna, (980–1037), was the first to develop extraction through the alembic. He has extracted the first pure essential oil that of the rose. The plant material is immersed directly in the water inside the alembic and the whole is brought to boiling. The extraction device includes a source of heating surmounted by a vessel (alembic) in which we could put plant material and water. The set up comprises also a condenser and a decanter to collect the condensate and to separate EOs from water, respectively (see Fig. 2). The principle of extraction is based on the azeotropic distillation. In fact, at atmospheric pressure and during extraction process (heating), water and EOs molecules form a heterogeneous mixture which attained its boiling temperature at a lower point close to 100 °C while for EOs components this point is very high (see Table 2). The mixture EOs/water is then distilled simultaneously as if they were a single compound. This is referred as co-distillation in the presence of vapors of water as solvent drive.

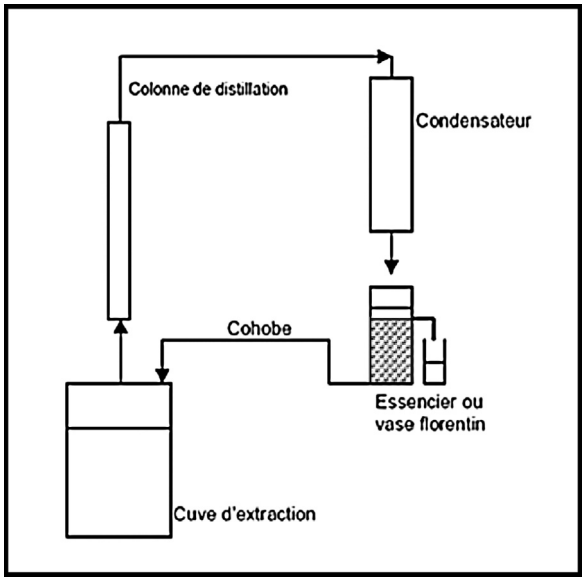


Fig. 2. Hydrodistillation apparatus (Richard, 1999).

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The advantage of water is that it is immiscible with the majority of the terpenic molecules of EOs and thus, after condensation, EOs could be easily separated from water by simple decantation. The hydrodistillation by Clevenger system is recommended by the third edition of the European Pharmacopoeia for the determination of EOs yields. It allows the recycling of the condensates through a cohobage system. This method is suitable for the extraction of petals and flower (i.e. petals of rose) as it avoids compacting and clumping of plant material during extraction. The hydrodistillation has, however, several drawbacks: (i) long extraction time (3–6 h; 24 h for the rose petals), (ii) artifacts and chemical alterations of terpenic molecules by prolonged contact with boiling water (hydrolysis, cyclization . . .) and (iii) overheating and loss of some polar molecules in the water extraction (Bohra et al., 1994). An optimized variant of this technique, the turbodistillation (Seiller and Martini, 1999) allows to obtain high yields by recycling the aromatic water. It reduces distillation time thanks to the presence of turbines (allow fragmentation and agitation). In addition, it enables almost complete recovery of EOs present in the vapor through the plate column. In industrial scale, this method is still used for several reasons: (i) simplicity of installations (does not require expensive equipment), (ii) easiness of method implementing and (iii) its selectivity.

5.1.2. Entrainment by water steam

It is one of the official methods for the obtaining of EOs. It is a widely used method for EOs extraction (Masango, 2005). It is based on the same principle as hydrodistillation with the difference that there is no direct contact between plant and water. Extraction duration is shortened thus reducing chemical alterations. There are other variants:

5.1.2.1. Vapor-hydrodistillation. Extraction is done within the alembic except that there is a system of perforated plate or grid that maintains the plant suspended above the base of the still containing water which avoids their direct contact. The extraction is done by injection of water vapors which cross plant matter from the bottom up and carries the volatile materials. Artifacts are minimized. The extraction time is reduced as well as the loss of polar molecules (see Fig. 3a).

5.1.2.2. Vapor-distillation (steam distillation). This method has the same principles and advantages as the vapor-hydrodistillation, but the generation of vapors occurs outside of the distillation alembic (Masango, 2005). The steam can then be saturated or superheated; at slightly above atmospheric pressure, the steam is introduced into the lower part of the extractor and therefore passes through the raw material charge. This technique avoids some artifacts compared to hydrodistillation (see Fig. 3b) (Masango, 2006).

5.1.2.3. Hydrodiffusion. This is a particular case of vapor-distillation where vapors' flow occurs downward. It is also called down hydrodiffusion or hydrodiffusion and gravity.

5.1.3. Organic solvent extraction

The plant material is macerated in an organic solvent; the extract is concentrated by removing the solvent under reduced pressure. This technique avoids alterations and chemical artifacts by cold extraction compared to hydrodistillation. Indeed, during hydrodistillation, the immersion of plant material in the bowling water causes water solubilisation of some fragrance constituents and reduces medium pH to 4–7 (sometimes less than 4 for some fruits). The constituents of the original plant species are subjected to the combined effects of heat and acid, and are subject to chemical modifications (hydrolysis, deprotonations, hydrations and cyclizations). Obtained EOs differ significantly from the original essence, especially, if boiling is long, and pH is low. In another hand, extracts obtained by organic solvent contain residues that pollutes the foods and fragrances to which they are added (Faborode and Favier, 1996). This compromises the safety of products extracted by this technique. Thus, it is impossible to use them for food or pharmaceutical applications. These disadvantages could be avoided by using a combination technology of organic solvent with low boiling point (e.g. *n*-pentane) and steam distillation process (OS-SD) (Li and Tian, 2009).

5.1.4. Cold pressing

Cold pressing is the traditional method to extract EOs from citrus fruit zest. During extraction, oil sacs break and release volatile oils which are localized in the external part of the mesocarpe (sacs oils or oil glands). This oil is removed mechanically by cold pressing yielding a watery emulsion. Oil is recovered subsequently by centrifugation (Ferhat et al., 2007). In this case we obtain the vegetable essence of citrus zest which is used in food and pharmaceutical industries and as flavoring ingredients or additives (food industry, cosmetics and some home care products).

5.2. Innovative techniques of essential oils extraction

One of the disadvantages of conventional techniques is related with the thermolability of EOs components which undergo chemical alterations (hydrolyse, isomerization, oxidation) due to the high applied temperatures. The quality of extracted EOs is

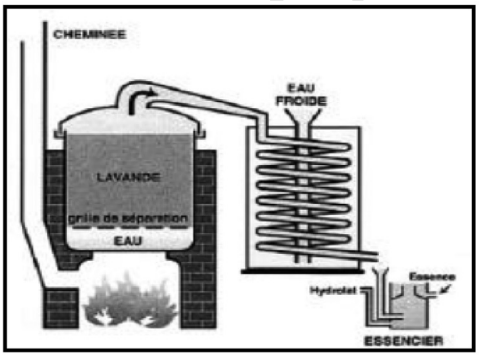

Fig.3a Schematic presentation of Vapohydrodistillation

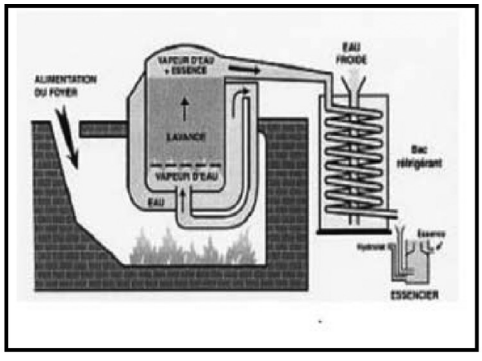

Fig.3b Schematic presentation of vapor-distillation

Fig. 3. Vaporhydrodistillsation and vapor-distillation.

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therefore extremely damaged particularly if the extraction time is long. It is important that extraction methods could maintain EOs chemical composition and natural proportion at its original state. New extraction techniques must also reduce extraction times, energy consumption, solvent use and CO_2 emissions.

5.2.1. Supercritical fluid extraction (SCFE)

For fluids, the supercritical state is reached at well defined conditions: critical pressure (Pc) and temperature (Tc). Fluids could then exhibit very interesting properties: (i) low viscosity, (ii) high diffusivity, (iii) density close to that of liquids. Carbon dioxide is generally the most widely used solvent for EOs extraction because of its numerous advantages: (i) critical point is easily reached (low critical pressure, Pc: 72.9 atm, and temperature, Tc: 31.2 °C), (ii) unaggressive for thermolabile molecules of the plant essence (Table 3) (Herrero et al., 2006); (iii) it is chemically inert and non-toxic, (iv) non flammable, (v) available in high purity at relatively low cost, (vi) easy elimination of its traces from the obtained extract by simple depression (Pourmortazavi and Hajimirsadeghi, 2007) and (vii) its polarity similar to pentane which makes it suitable for extraction of lipophilic compounds. SCFE was used for the extraction of several EOs (Mara and Braga, 2005; Carvalho et al., 2005; Lucinewton and Moura, 2013; Khajeh et al., 2004; Aghel et al., 2004). The principle is based on the use and recycling of fluid in repeated steps of compression/depression. By highly compressing and heating, CO_2 reaches the supercritical state. It passes through the raw plant material and loaded volatile matter and plant extracts. This is followed by a depression step: the extract is routed to one or more separators, where the CO_2 is gradually decompressed (thus losing its solvent power) to separate the obtained extract from the fluid. The latter could be turned into a released gas and then could be recycled (see Fig. 4) (Fornari et al., 2012). The use of this technique for EOs extraction has increased in the last two decades. The only one obstacle to its development is the high cost of the equipments, their installations and their maintenance operations. Indeed, several plants have been subjected to SFE to produce EOs (Fornari et al., 2012; Gomes et al., 2007; Cao et al., 2007; Geng et al., 2007; Guan et al., 2007; Petra Kotnik, 2007). Supercritical extracts proved to be of superior quality, with better functional and biological activities (Capuzzo et al., 2013) in comparison with extracts produced by hydro-distillation or with liquid solvents (Vági et al., 2005; Glišić et al., 2007). Furthermore, some studies showed better antibacterial and antifungal properties for the supercritical product. An example of improved biological activity exhibited by supercritical extracts was reported by Glišić et al., (2007), demonstrating that supercritical carrot essential oil was more effective against *Bacillus cereus* than that obtained by hydrodistillation.

5.2.2. Subcritical extraction liquids ($H_2$and CO_2)

Some research works illustrated the use of water in its subcritical state for EOs extraction (Özel et al., 2006). Subcritical state is reached when the pressure is higher than the critical pressure (Pc) but the temperature is lower than the critical

Table. 3
Comparison between supercritical CO_2 extraction and SWE extraction.

Aspect	SC-CO_2 extraction	SWE
Drying stage	Yes (−)	No (+)
Co-extraction of cuticular waxes	Yes (−)	No (+)
Acquisition coast	High (−)	Medium (+)
Maintenance coast	High (−)	Low (+)
Extraction conditions	Mild (+)	Medium (−)
Pre-concentration effect	Yes (+)	No (−)
Environmentally clean character	Yes (+)	Yes (+)

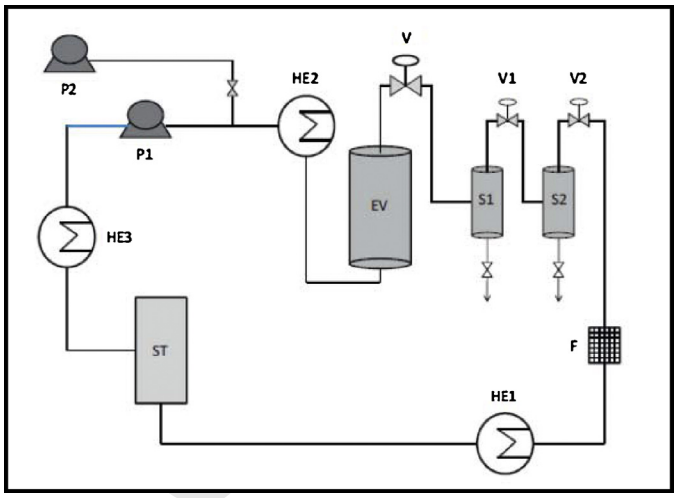

Fig. 4. Typical SFE scheme for the extraction of plant matrix (Fornari et al., 2012) P1: CO_2 pump; P2: cosolvent pump; HE1, HE2, HE3: heat exchangers; EV: extraction vessel; S1, S2: separator cells; V, V1, V2: back pressure regulator valves; ST: CO_2 storage tank; F: filter.

temperature (Tc), or conversely. At this state, water and CO_2 are the most widely used fluids for EOs extraction. Obtained fluids have very interesting properties: low viscosity, density close to that of the liquids and diffusivity between that of the gas and liquids. Soto Ayala and Luque de Castro, (2001) and Rovio et al., (1999) have reported that subcritical water extraction (SWE) of EOs is a powerful alternative, because it enables a rapid extraction and the use of low working temperatures. This avoids loss and degradation of volatile and thermolabile compounds. Additional positive aspects of the use of SWE are its simplicity, low cost, and favorable environmental impact. The most important advantages of this technique over traditional extraction techniques are shorter extraction time, higher quality of the extract, lower costs of the extracting agent, an environmentally compatible technique (Herrero et al., 2006) and low solvent consumption (see Fig. 5). Little residues are generated with great EOs efficiency and quality. A comparison study between supercritical CO_2 and SWE was established (Luque de Castro et al., 1999). Authors concluded that that, although SWE is less expensive than supercritical CO2 extraction, it is still quite expensive to implement because installation requires specific equipment. SWE extraction conditions are also softer. (see Table 5)(Mohammad and Eikani, 2007).

5.2.3. Extraction with subcritical CO_2

CO_2 subcritical state is obtained when the temperature is between 31 °C and 55 °C and pressure between 0.5 MPa and 7.4 MPa. Under these conditions, the CO_2 behaves as a non-polar solvent (Moyler, 1993). This method avoids the degradations observed in the steam distillation or entrainment by vapor due to the high temperatures and the presence of water. According to Chen et al., (1986), extracts obtained by this technique present flavors very similar to those of fresh vegetable raw materials. Moreover, the quality of the extracts obtained by subcritical CO_2 is much better than those obtained by subcritical water. Table 5 shows a comparison between supercritical CO_2 extraction and SWE extraction.

5.2.4. Ultrasound assisted extraction of EOs (UAE)

This technique was developed in 1950 at laboratory-scale size equipment (Vinatoru, 2001). Ultrasound allows intensification and selective of EOs extraction by accelerating their release from plant material when used in combination with other techniques (hydrodistillation and solvent extraction). The vegetable raw

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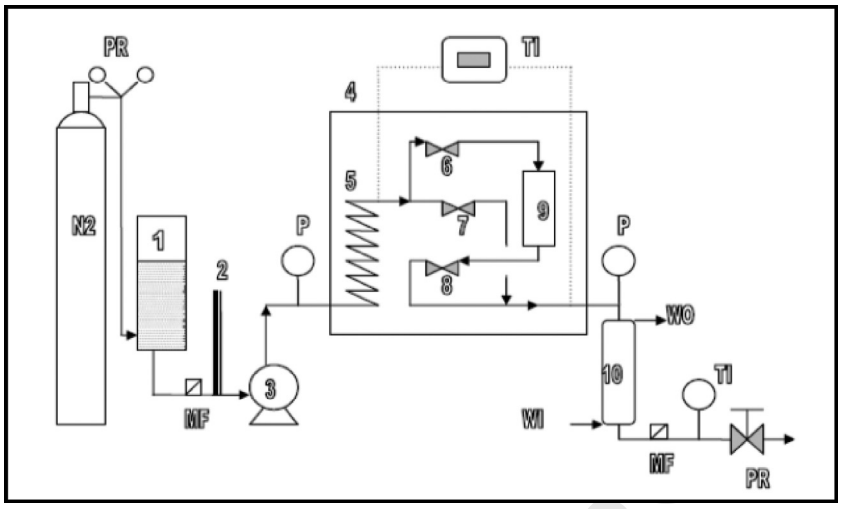

Fig. 5. Schematic diagram of subcritical water extraction system (Mohammad and Eikani, 2007) 1, water reservoir; 2, burette; 3, pump; 4, oven; 5, preheater; 6, inlet water; 7, bypass stream; 8, outlet water; 9, extraction cell; 10, heat exchanger; MF, micro filter; P, pressure indicator; PR, pressure regulator; TI, temperature indicator; WI, cooling water in; WO, cooling water out.

material is immersed in water or solvent and at the same time it is subjected to the action of ultrasound. This technique has been used for the extraction of many EOs particularly from seeds (Karim Assami, 2012; Sereshti et al., 2012). However, it has been developed especially for the extraction of certain molecules of therapeutic interest (Chemat and Lucchesi, 2006; Sališová et al., 1997; Hromádková et al., 1999). The used ultrasonic waves have a frequency of 20 kHz–1 MH. This induces mechanical vibration of the walls and membranes of plant extract inducing a rapid release of EOs droplets. The extraction mechanism involves two types of phenomena: diffusion trough the cell walls and washing out the cell content once the walls are broken (Vinatoru, 2001). In fact, EOs are stored in the plant in specific internal or external structures in the form of glands filled with EOs droplets. Their skins are very thin that can be easily destroyed by sonication (in the case of external structures). For internal ones, the milling degree of plant material plays an important role in the obtained yield as shown in Table 4. It is obvious that reducing the size of plant material will increase the number of cells exposed to ultrasonically induced cavitations.

Compared with traditional extraction methods, UAE improves extraction efficiency and rate, reduces extraction temperature, and increases the selection ranges of the solvents (Romanik et al., 2007). The equipments are relatively simple and inexpensive compared to other techniques such SCFE or microwave assisted extraction (MAE). Moreover, UAE is beneficial to botanical materials which are sensitive to temperature. The other advantages of ultrasound are mass transfer intensification, cell disruption, improvement of solvent penetration and capillary effect.

5.2.5. Microwave assisted extraction (MAE)

Microwaves are electromagnetic based waves with frequency between 300 MHz and 30 GHz and a wavelength between 1 cm and 1 m. The commonly used frequency is 2450 MHz which corresponds to a wavelength of 12.2 cm. The use of MAE evolved with the development of the green extraction concept and the need for new energy saving extraction methods. More attention has been paid to the application of microwave dielectric heating for EOs extraction. Starting from compressed air microwave distillation (CAMD) (Craveiro, 1989) and vacuum microwave hydrodistillation (VMHD) (Mengal and Mompon, 1994), innovation in the microwave assisted extraction (MAE) led to the development of a large number of variants such as microwave assisted hydrodistillation (Stashenko et al., 2004; Golmakani and Rezaei, 2008), solvent free microwave extraction (SFME) (Lucchesi et al., 2004a,b), microwave-accelerated steam distillation (MASD) (Chemat and Lucchesi, 2006), microwave steam distillation (Sahraoui et al., 2008), microwave hydrodiffusion and gravity (MHG) (Vian et al., 2008) and portable microwave assisted extraction (PMAE). The MAE, largely developed by Chemat and co-workers, became rapidly one of the most potent EOs extraction methods and one of the upcoming and promising techniques. It offers high reproducibility in shorter times, simplified manipulation, reduced solvent consumption and lower energy input. We distinguish:

5.2.6. Solvent free microwave extraction (SFME)

This method was developed by Chemat and co-workers (Lucchesi et al., 2004a,b). Based on the combination of microwave heating energy and dry distillation, it consists on the microwave dry-distillation at atmospheric pressure of a fresh plant without adding water or any organic solvent (Filly et al., 2014) (Fig. 6). The selective heating of the in situ water content of plant material causes tissues to swell and makes the glands and oleiferous receptacles burst. This process thus frees EOs, which are spontaneously evaporated by azeotropic distillation with the water present in the plant material (Li et al., 2013). A pilot scale was proposed and prove to be feasible to industrial application (Filly et al., 2014) compared to a SFME Lab scale. Many EOs were extracted at a laboratory scale by this technique (Filly et al., 2014).

Table 4
Influence of milling degree on the extraction of clove flowers.

Extraction time (min)	Extraction technique	Milling degree	Eugenol extracted (g/100 g)
30	Silent	Not milled	4.10
30	Silent	0.1–0.5 mm	25.20
30	US	Not milled	4.22
30	US	0.1–0.5 mm	32.66

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Table 5
Applications of particles loaded with essential oils and their advantages.

Pharmaceutical form	Encapsulated essential oil	Application	Size	Zeta potential (mV)	Polymers	Method	Advantages	References
Nanoparticles	*Lippia sidoides* essential oil	Larvicide	335–558 nm	4–49.6	Chitosan and cashew gum	Complex coacervation	Sustained release, enhanced larvicide activity	(Abreu et al., 2012)
Microparticles	*Origanum vulgare* essential oil	Food preservative	<10 μm	–	Starch	Supercritical fluid technology	–	(Almeida et al., 2013)
Microparticles	*Origanum vulgare* essential oil	–	3–4.5 μm	–	Inulin	Spray drying	Different releasing, profiles patterns	(Beirão-da-Costa et al., 2013)
Nanoparticles	*Mentha piperita* essential oils	Antimicrobial	<100 nm	–	Chitosan and cinnamic acid	Ionic gelation	Enhancement of antimicrobial activity and stability	(Beyki et al., 2014)
Microparticles	Rosemary essential oil	–	12.1–13.5 μm	–	Gum Arabic, maltodextrin and modified starch	Spray drying	–	(Fernandes et al., 2014)
Nanoparticles	*Lippia sidoides* essential oil	Antimicrobial	223–399 nm	−36 to (−30)	Alginate/cashew gum	Spray drying	Extended release	(De Oliveira et al., 2014)
Microparticles	*Pimenta dioica* essential oil	–	1172–1224 μm	–	Chitosan and k-carrageenan	Complex coacervation	Enhancement of antimicrobial activity	(Dima et al., 2014)
Microparticles	*Satureja hortensis* essential oil	–	47–117 μm	–	Alginate	Ionic gelation	Enhanced antibacterial activity, extended release	(Hosseini et al., 2013a, b)
Microparticles	*Schinus molle Rev* L. essential oil	Insecticidal	0.2–40 μm	–	Maltodextrin and gum Arabic	Spray drying	Prolonged effect	(López et al., 2014)
Nanoparticles	Jasmine essential oil	–	74–384 nm	−8.67 to (−1.92)	Gelatin and gum Arabic	Complex coacervation	Enhanced stability	(Lv et al., 2014)
Microparticles	*Salvia hispanica* L. essential oil	–	13.17–28.20 μm	–	Whey protein concentrate and gum Arabic or whey protein concentrate and mesquite gum	Spray drying	–	(Rodea-González et al., 2012)
Microparticles	*Lavandula hybrida* essential oil	Biocide in ecological agriculture	30–100 μm	–	PEG	Particles from gas saturated solutions	–	(Varona et al., 2010)
Microparticles	*Zanthoxylum limonella* essential oil	Mosquito repellent	209.41–223.17 μm	–	Alginate et gelatin	Emulsion solvent evaporation	–	(Banerjee et al., 2013)
Microparticles	*Origanum vulgare* essential oil	Antibacterial	–	–	Starch, inulin and gelatin/sucrose	Spray drying	Higher, antioxidant and antimicrobial activity, higher stability	(Beirão da Costa et al., 2012)
Liposomes	*Atractylodes macrocephala Koidz* essential oils	Digestive diseases	173 nm	–	Phosphatidylcholine and cholesterol	RESS	–	(Wen et al., 2010)
Microparticles	*Cymbopogom citratus* essential oil	Antimicrobial	10–250 μm	–	Polyvinylalcohol	Simple coacervation	Extended release	(Leimann et al., 2009)
Nanoparticles	*Origanum vulgare* L. essential oil	Food conservative	40–80 nm	–	Chitosan	Ionic gelation	Extended release	(Hosseini et al., 2013a, b)
Nanoparticles	Carvone and anethole	Antimicrobial	112–472 nm	–	Poly(lactide-co-glycolide)	Emulsion solvent evaporation, nanoprecipitation	Extended release	(Esfandyari-Manesh et al., 2013)
Nanoparticles	Eugenol	Antioxidant for thermal processing	80–100 nm	16.2–33.5	Chitosan	Ionic gelation	Thermal stability improvement	(Woranuch and Yoksan, 2013)
Microparticles	*Ocimum sanctum* Linn essential oil	–	392.30 μm	–	Gelatin	Simple coacervation	Stability improvement	(Sutaphanit and Chitprasert, 2014)
Liposomes	Carvacrol and thymol	–	–	–	Egg L-a-phosphatidylcholine and cholesterol	Film hydration	Enhancement of antimicrobial activity	(Liolios et al., 2009)
Nanoparticles	Benzyl benzoate	Pesticide	0.125	30	Polylactide acide (PLD)	Nanoprecipitation	–	(Audrey Ladj-Minost, 2012)
Nanoparticles	Carvacrol	Anti-microbial biofilm	0.209	−18.99	PLGA	Nanoprecipitation		(Iannitelli et al., 2011)

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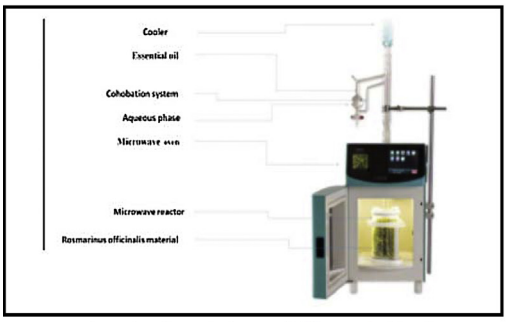

Fig. 6 a. A Lab scale SFME (Filly et al., 2014)

Fig. 6 b. Pilot scale SFME (Filly et al., 2014)

Fig. 6. Solvent free microwave extraction (SFME).

This technique allows the isolation and concentration of volatile compounds in only 30 min while it requires 2 h for conventional hydro-distillation.

5.2.7. Microwave hydrodiffusion and gravity (MHG)

MHG was designed and developed for the first time by Chemat and co-workers. Vian et al. (2008) developed a combination of microwave heating of a reversed alembic and earth gravity at atmospheric pressure (Fig. 7a). Plant material is placed in a reversed microwave reactor without any added solvent or water. The internal heating of water plant material distends the plant cells and leads to the rupture of glands and oleiferous receptacles (by a heating microwave action) and thus frees EOs and plant water outside of the plant material. Under gravity, extracts are driven from top to bottom out of the microwave reactor to the cooling system (Fig. 7). Microwave hydrodiffusion and gravity (MHG) have been reported by Chemat and Lucchesi (2006) as an efficient, economical and environmental friendly approach. It was conceived for the extraction of volatile compounds from fresh plant materials with a minimum 60% of initial moisture. The performances of this technique are: a reduction of extraction time (only 20 min whereas it takes 90 min in the case of hydro-distillation) and power saving and reducing of environmental impact (Vian et al., 2008). A similar technique was developed by Farhat et al. (2010): the microwave dry-diffusion and gravity process (MDG) for essential oil extraction of dried caraway seed (Fig. 7b). It has the same principle as for MHG except that the extraction is done on a dry plant material without adding any solvent or water. Compared to hydrodiffusion, this technique allows a rapid extraction of EOs (45 min versus 300 min for HD). It enables also energy saving, cleanliness, fast and efficient extraction. It reduces waste and avoids water and solvent consumption.

5.2.8. The microwave steam distillation (MSD) and microwave steam diffusion (MSDf)

The MSD (Fig. 8a) have been investigated by Sahraoui et al. (2008) and Naima Sahraoui (2011) for the extraction of respectively, orange peel EOs and dry Lavender flower. Compared to conventional steam distillation, this innovative method prove to be more effective offering important advantages like very shorter extraction time (the same yield is obtained within 6 min for MSD at optimized power 500 W, versus 2 h for SD) and cleaner features. It also provides EOs with better sensory properties (better reproduction of natural fresh fruit aroma of the citrus essential oil) without causing considerable changes in the volatile oil composition. Due to its performances, MSD could be exploited at large industrial scale using existing large-scale extractors with addition of microwave coaxial antenna which is suitable for the extraction of 100 kg of fresh plant material (Fig. 8b) (Guido Flamini, 2007). The microwave steam diffusion (MSDf) (Fig. 8c) was investigated

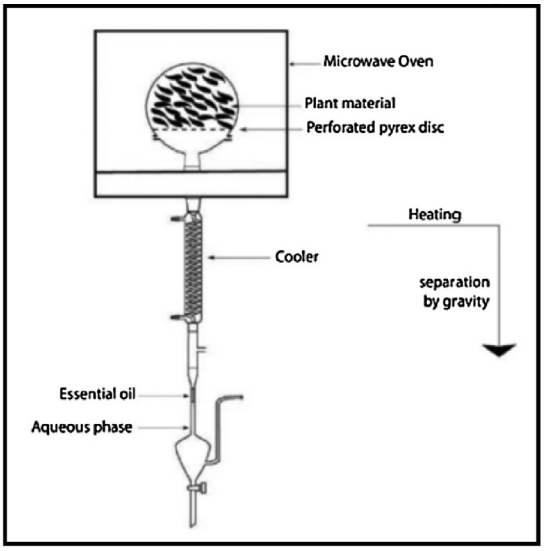

Fig. 7a. Microwave hydrodiffusion and gravity (Vian et al., 2008) (Farhat et al., 2010)

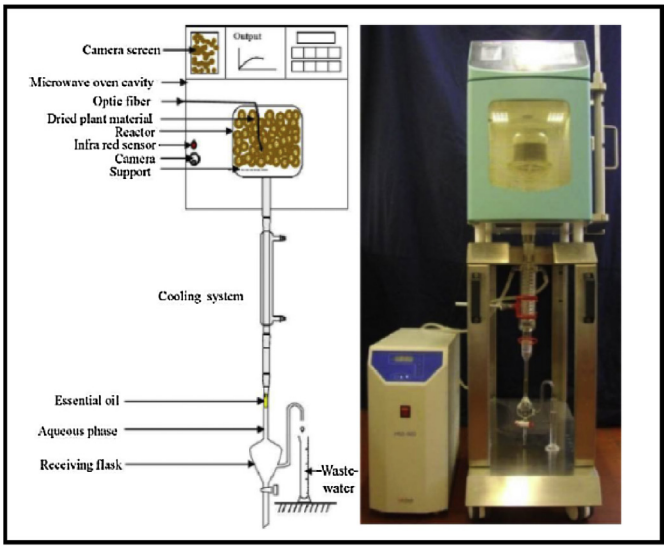

Fig. 7b. Microwave dry-diffusion and gravity process

Fig. 7. Microwave hydrodiffusion and gravity.

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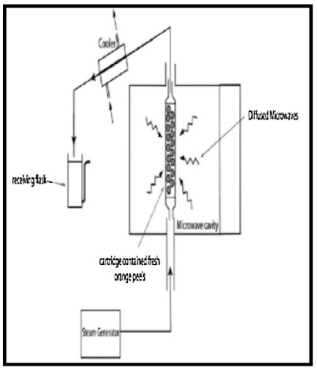

Fig. 8a. Microwave steam distillation Apparatus (Naima Sahraoui, 2011)

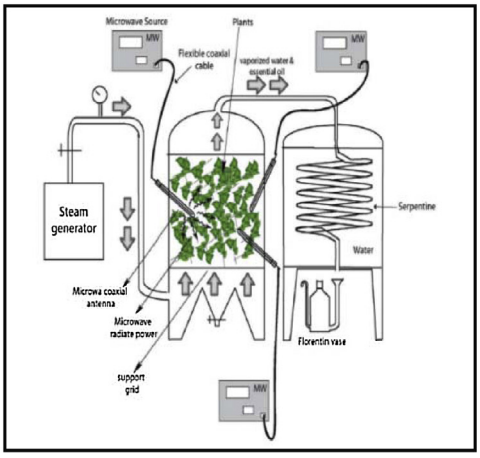

Fig. 8b. Microwase steam diffusion apparatus (Naima Sahraoui, 2011)

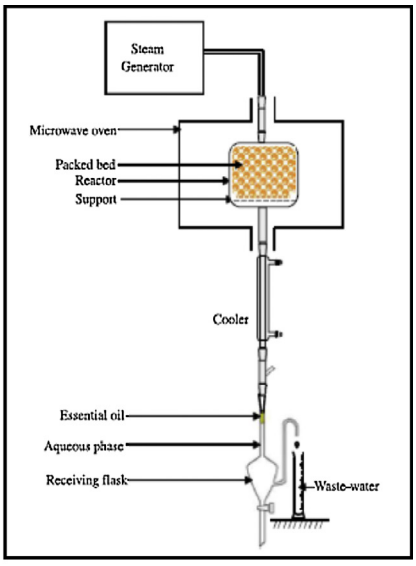

Fig. 8c. Potential scaling-up of MSD (Guido Flamini, 2007)

Fig. 8. Microwave steam distillation and microwave steam diffusion.

for the extraction of the EOs of several plants such as, Lavender (Farhat et al., 2009); orange peel (Asma Farhat, 2011). It is based on the same principle as for the MSD except that vapors flow through the plant material down. By comparison to other extraction methods of Lavendin EO (Périno-Issartier et al., 2013). This method proved to be more efficient in terms of kinetic of extraction (3 mn versus 6 mn for MSD and 20 mn for conventional steam diffusion), energy saving and cleanliness, quality of the extracts and waste water reduction. Highest extraction efficiency was obtained under optimal conditions: steam flow rate Gv = 25 g min^{-1} and microwave power Pw = 2000 W. Microwave steam diffusion is a green, cleaner, environmentally friendly and an economic procedure.

5.2.9. The instant controlled pressure drop

This method was particularly investigated by K. Allaf and co-workers for EOs extraction (Kristiawan et al., 2008; Berka-Zougali et al., 2010) and both EOs and antioxidant from vegetables matrices (Tamara Allaf, 2012). This was tested on a laboratory apparatus as well as on a pilot plant. Compared to conventional hydrodistillation, DIC give, for Lavendin essential oil, an improvement of extraction yield (4.25 versus 2.30 g/100 g of raw material), a reduction of extraction time (480 s against 4 h for HD) and consequently a great decreasing of energy and water consumption (662 kWh/t and 42 kg water/t of raw material). DIC is characterized mainly by a sharp decline of pressure to the vacuum, following treatment type HTST (high temperature/high pressure – short term). The phenomena of abrupt autovaporisation allow the evaporation of a greater amount of volatile molecules (compared with progressive autovaporisation) and to reach also very quickly a lower level of temperature. DIC treatment generally consists of four steps: (1) putting under initial vacuum; (2) applying a steam bath, under determined pressure and temperature; (3) instant detente to the void and (4) the cell processing is returned to atmospheric pressure. The reactor (a 7 L processing vessel with a heating jacket) undergoes thermal treatment using saturated steam with pressure varying from 5 kPa up to 1 MPa (see Fig. 9). A pneumatic valve ensures an "instant" connection between the vacuum tank (maintained at 5 kPa) and the processing vessel. EOs are recovered as stable oils in water emulsion. Afterward, the plant raw material could be recovered and dried at room temperature in order to be stored for other extractions (Tamara Allaf, 2012).

6. Encapsulation in polymeric particles

Encapsulation of EOs in polymeric particles has been investigated. However, major limitation is EOs loss especially in techniques that include a heating or an evaporation step. On the other hand, encapsulation could provide many advantages such as protection of EOs from degradation. In fact, high temperatures, UV light and oxidation could compromise the biological activity of fragile EOs through volatilization or degradation of active ingredients. Formulation of EOs as microcapsules or microspheres could also be used for controlling release of encapsulated EOs. Table 5 contains examples of particles loaded with EOs along with the advantages that was obtained following encapsulation.

6.1. Nanoprecipitation

Nanoprecipitation or solvent displacement technique was first developed by Fessi et al. (1989). It is a simple and reproducible technique that allows the obtaining of monodisperse nanoparticles. It also has the advantages of being fast and economic. Nanoprecipitaion allows the obtaining of reproducible submicronic particle size with narrow distribution using low external energy source (Chorny et al., 2002; Legrand et al., 2007). This technique is suitable for encapsulating hydrophobic materials such as EOs. In nanoprecipitation, two miscible phases are needed: an organic phase and an aqueous phase. Organic phase contains a polymer solution in an organic solvent and the essential oil. Aqueous phase comprises a non-solvent or a mixture of non-solvents for polymer which could be supplemented with one or more naturally occurring or synthetic surfactants (Khoee and Yaghoobian, 2009). This method has attracted considerable attention for encapsulation of hydrophobic materials (Rosset et al., 2012; Tang et al., 2011). Polymers could be synthetic or natural. Poly-e-caprolactone (PCL), poly(lactide) (PLA) and poly (lactide-co-glycolide) (PLGA) biodegradable polymers are the frequently used polymers (Khoee and Yaghoobian, 2009). The

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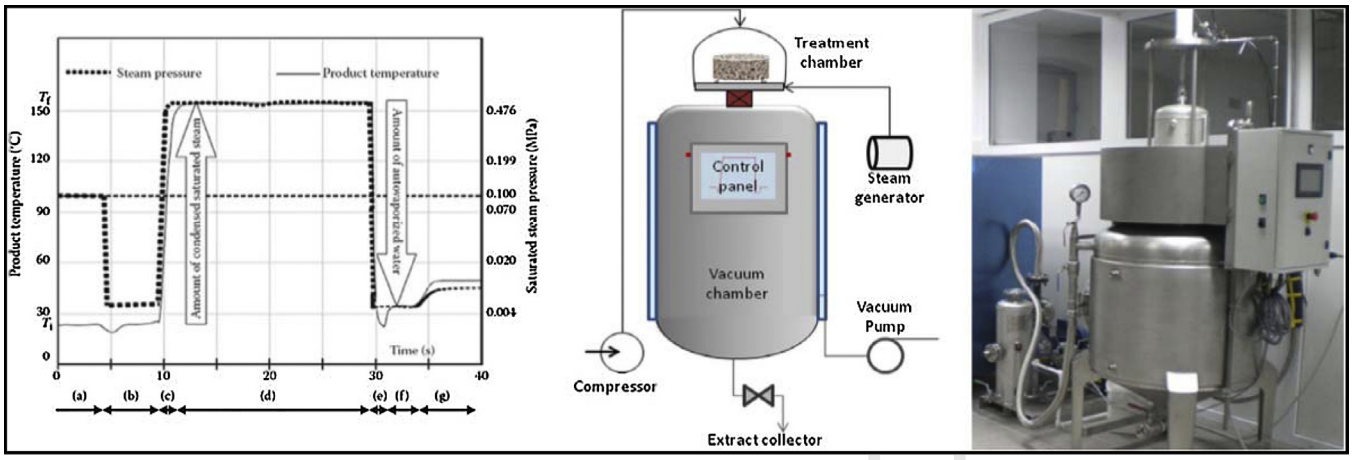

Fig. 9. Instant controlled pressure drop (DIC) lab-scale apparatus (from the company ABCAR-DIC Process (La Rochelle, France)) and a DIC cycle temperature and pressure of a DIC processing cycle (which can be divided into seven steps) (Tamara Allaf, 2012) (Ti is the initial temperature and Tf the highest temperature of the product: (a) sample at atmospheric pressure; (b) initial vacuum; (c) saturated steam injection to reach the selected pressure; (d) constant temperature corresponding to saturated steam pressure; (e) abrupt pressure drop toward a vacuum; (f) vacuum; (g) release to atmospheric pressure).

hydrophobic characteristics of EOs make them a good candidate for encapsulation in nanoparticular systems via nanoprecipitation. Ladj-Minost (2012) compared encapsulation of indomethacin (hydrophobic active) and doxorubicin (hydrophilic active) by nanoprecipitation using polylactide polymer. It was concluded that hydrophobicity decreased the size of nanoparticles and increased the active molecule entrapment efficiency (Ladj-Minost, 2012).

6.2. Coacervation

Coacervation technique could either be simple or complex if one or two polymers are used, respectively. Coacervation is generally defined as the separation of two liquid phases in a colloidal solution. One phase is rich in polymer and called coacervate phase and the other doses not contain polymer and is called equilibrium solution. In case of simple coacervation there is only one polymer whereas complex coacervation involves the interaction of two oppositely charged colloids (Kaushik et al., 2014).

6.2.1. Simple coacervation

In 1949, Bungenberg de Jong classified coacervation into simple and complex types (Bungenberg de Jong et al., 1949). Simple coacervation is based on the addition of a poor solvent to a hydrophilic colloidal solution which results in the formation of two phases: one is rich in colloid molecules (coacervate), and the other is almost coacervate free. For example, when sodium sulfate solution, acetone, or alcohol is gradually added to a gelatin solution under stirring, a coacervate forms (Shimokawa et al., 2013).

6.2.2. Complex coacervation

Complex coacervation is a spontaneous phenomenon that occurs between two oppositely charged polymers. The neutralization of these charges induces a phase separation (polymer rich phase versus aqueous phase). This technique has been applied widely in microencapsulation (Piacentini et al., 2013). Typical steps in microencapsulation of hydrophobic material by complex coacervation process were mentioned by Piacentini et al. (2013). They include: (1) emulsification of hydrophobic material in an aqueous solution containing two different polymers, usually at a temperature above the gelling point of protein and pH that is above the isoelectric point of protein; (2) separation into two liquid phases (an insoluble polymer rich phase and an aqueous phase that is depleted in both polymers) as a result of attractive electrostatic interactions between oppositely charged polymers; (3) wall formation due to deposition of the polymer rich phase around the droplets of the hydrophobic material-induced by controlled cooling below the gelling temperature; and (4) wall hardening by addition of a crosslinking agent in order to obtain hard microcapsules. Gelatin and Arabic gum are the common used wall materials for complex coacervation (Lemetter et al., 2009).

6.3. Spray drying

Spray drying is a popular method of forming microparticles because it is easy to perform in an industrial level and allows continuous production (Wu et al., 2014). It consists of liquid atomization into small droplets, a drying step is carried out using a warmed gas and collection of the solid particles (De Souza et al., 2013). Arabic gum is one of the most common wall materials used in microencapsulation by spray drying. In fact, it presents many advantages such as, high solubility, low viscosity and good emulsifying properties. However, the oscillation in supply, as well as the increasing prices, is leading researches to look for other alternatives (Charve and Reineccius, 2009). For example, maltodextrin is commonly used as alternative. However, because of its low emulsifying capacity, it is generally used in combination with other surface active biopolymers, such as Arabic gum, modified starches and proteins in order to obtain an effective microencapsulation (Carneiro et al., 2013).

6.4. Rapid expansion of supercritical solutions (RESS)

Conventional methods have some disadvantages such as, the use of large amounts of organic solvents, broad particle size distributions, and solvent residues. To overcome these disadvantages, supercritical fluids based processes have been used. The latter process has become an attractive alternative to encapsulate natural substances due to the use of environmentally friendly solvents (Santos et al., 2013). Among the spectrum of supercritical fluids, supercritical CO_2 is widely used in both the process for designing particles of organic and pharmaceutical compounds due to its environmentally benign nature and low cost (Yim et al., 2013). Supercritical CO_2 is often used thanks to its low critical temperature (31.1 °C) which is very useful thermally sensitive materials precipitation (Yim et al., 2013). In the RESS, the solutes are dissolved in supercritical CO_2 at high pressures (up to 250 bar) and temperatures (up to 80 °C), and then the solutions are

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expanded. The solubility of the solutes reduces at lower pressures and as a result they precipitate. For encapsulation, both the solutes and the used active molecule should be soluble in supercritical CO_2 (Vinjamur et al., 2013).

7. Encapsulation in liposomes

Liposomes are systems formed by one or several phospholipids bilayers defining one or several aqueous compartments. Phospholipids are amphiphilic molecules that are able to self-organize spontaneously in aqueous media. Liposomes could be classified depending on their size and lamellarity to: (1) multilamellar vesicles (MLV) with a size greater than 0.5 μm, (2) small unilamellar vesicles (SUV) with a size between 20 nm and 100 nm and (3) large unilamellar vesicles (LUV) with a size greater than 100 nm (Sherry et al., 2013). They are widely used as carriers of both hydrophilic molecules in aqueous compartments and lipophilic ones in the bilayers, but also amphiphilic molecules (Yoshida et al., 2010). In addition, the use of liposomes for encapsulation of EOs is an attractive approach to overcome their physicochemical stability concerns (sensibility to oxygen, light, temperature, and volatility) and their reduced bioavailability which is due to low solubility in water (Detoni et al., 2012). Different methods have been used to encapsulate EOs, from most conventional Bangham method (Bangham, 1978) to those employing supercritical fluids.

7.1. Thin film hydration method

Thin film method, known as the Bangham classical method (Bangham et al., 1967), is used to form multilamellar vesicles (MLV) with a size up to few micometers. Phospholipids and essential oils are dissolved in an organic phase. A thin phospholipid film of stacked bilayers is obtained at the bottom of the flask after rotative evaporation of the organic solvent under pressure. This dry film is hydrated with an aqueous phase under agitation which allows spontaneous formation of MLV. However, this method gives large vesicles with heterogeneous size distribution and lamellarity (Patil and Jadhav, 2014). Different approaches are used to obtain liposomes suspension with homogenous and reduced size. The basic principle is the conversion of MLVs into SUVs (small unilamellar vesicles) or LUVs (large unilamellar vesicles). Sonication and extrusion are the most common methods (see Fig. 10) (Patil and Jadhav, 2014). However, sonication was the most frequently used final step to encapsulate EOs in liposomes by thin film hydration method (Sinico et al., 2005; Valenti et al., 2001; Detoni et al., 2012). Ultrasonic wave application provides enough energy to disrupt MLVs. Although this technique is simple to implement, several disadvantages has been raised. Phospholipids and other materials may be degraded. The resulting liposomes exhibits also low encapsulation efficiency (Patil and Jadhav, 2014). The thin film hydration method has been also used by Varona et al. (2011) to encapsulate lavandin essential oil. They modified the classical method by trying three different procedures. In the first one, the thin film was heated above the lipid transition temperature (60 °C for soybean lecithin) during 20 min and placed in an ultrasound bath for sonication for 30 min. It has been proved that this condition transforms lipids in gel state, which favors continuous closed bilayered structures formation (Mozafari, 2005). In the second one, the lipid film hydrated in the aqueous phase was agitated in a vortex mixer at 1700 rpm for 15 min, and then hydration of lipid film was carried out during 2 h in the dark at room temperature. In the last procedure, the lipid film was heated at 60 °C during 20 min, and then, shaken in a vortex mixer at 1700 rpm for 15 min. The results showed that liposome size ranged from 0.42 μm to 1.29 μm, and was greater when the lavandin

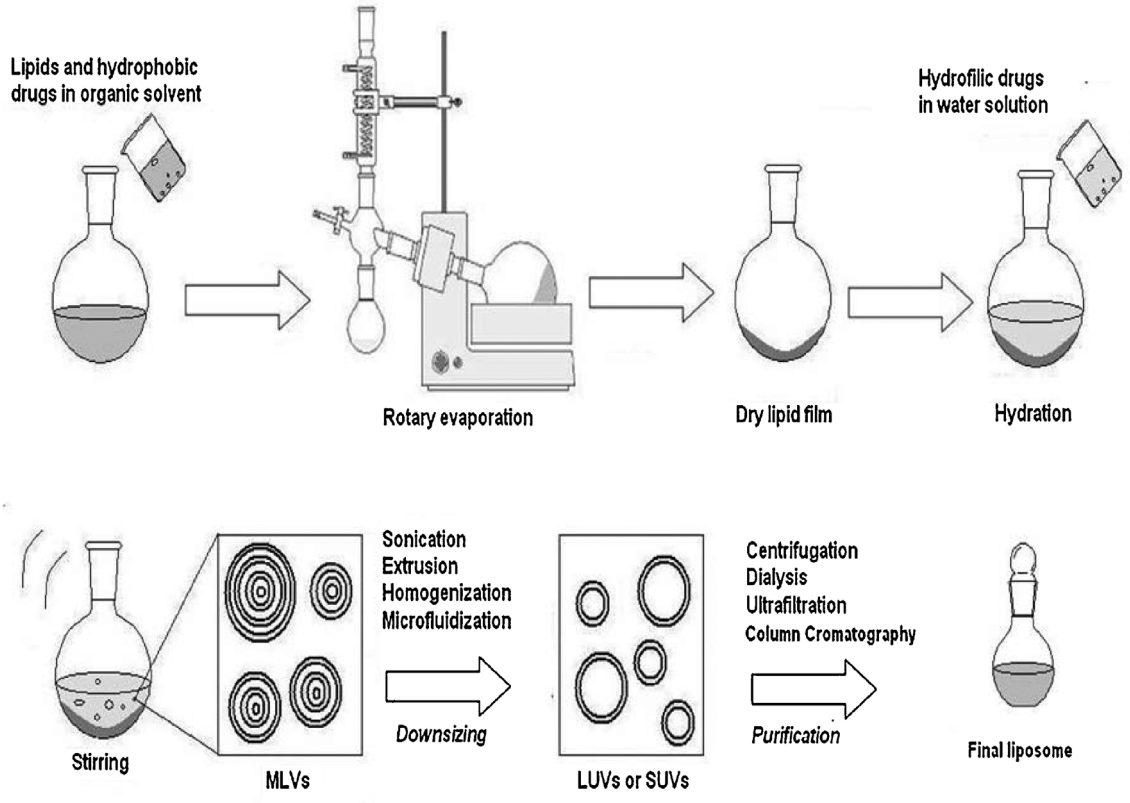

Fig. 10. Thin film hydration method and methods of size reduction (Araújo Lopes et al., 2013).

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oil/lipid ratio increased. Generally, cholesterol is added in the liposome preparation to improve stability and enhance membrane permeability (Chan et al., 2004). Varona et al. (2009, 2011) observed an impact on the liposome size: a decrease of the amount of cholesterol reduced the liposome size. Vortex mixing gave smaller vesicles than sonication. The incorporation efficiency was better with the second procedure until about 60% with a lavandin/lipid ratio of 3:5. But the better stability after 50 days is obtained with the third method.

7.1.1. Extrusion

Extrusion is a common method which is used to reduce size and lamellarity of MLVs produced by thin film hydration. The passage through a track-etched polycarbonate membrane with pores of different diameters is performed several times. The size of membrane pore is the most important parameter to take into account since it affects the final liposome size and size distribution depends mainly of it. However, the pressure applied on the membrane has also an impact (Patil and Jadhav, 2014). Celia et al. have encapsulated bergamot essential oil with this method. Their results showed the formation of small liposomes (less than 200 nm) with an encapsulation efficiency of 75%. However, it has been reported that the presence of the essential oil in the formulation leads to polydispersity (Celia et al., 2013).

7.1.2. Freeze-thaw

Freeze-thaw technique is another mean to homogenize and reduce liposome size formed by thin film hydration method, generally MLVs. It was reported that this technique would permit to obtain LUVs from MLVs. The main advantage is the higher encapsulation efficiency because of the increase interactions between the lipid film and the EO to incorporate during freeze-thaw cycles (Colletier et al., 2002). It was used by Moghimipour et al. (2012) to prepare liposomes entrapping essential oil of *Eucalyptus camaldulensis* Leaf. Phospholipids and cholesterol were dissolved in a cosolvent (chloroform/methanol) which was then removed by rotatory evaporation under vacuum. The lipid film was hydrated with a phosphate buffer saline (pH 7.4) containing the essential oil and vortexed during 5 min. Then, 3 freeze-thaw cycles were performed. The freeze step was carried out in ice-ethanol or acetone during 5–10 min and the thaw step was made at room temperature. Moghimipour et al. (2012) succeeded to have stable liposomes during 3 months with an encapsulation efficiency of 95%. They highlighted that to form small liposomes, short freezing time with a good homogenization were essential.

7.2. Reverse phase evaporation method

The reverse phase evaporation is a conventional method capable to form LUV (large unilamellar vesicles). It consists of the preparation of an oil-in-water emulsion by mixing a phospholipids organic phase, containing generally the lipophilic active substances, in an aqueous phase. Then the organic solvent is evaporated, giving LUVs (Deamer and Bangham, 1976; Szoka and Papahadjopoulos, 1978). However, Gruner et al. (1985) also reported formation of MLV. Pidgeon et al. (1987) showed that MLV proportion may be reduced with lower concentrations of phospholipids. It is interesting to notice that only few works have been dedicated to EOs encapsulation in liposomes using this this method. Van Vuuren et al. (2010) incorporated into liposomes three different EOs distilled from *Artemisia afra*, *Eucalyptus globulus* and *Melaleuca alternifolia*. The method of preparation employed was the conventional one except that sonication with a probe was applied to reach nanosize dispersions. After the removal of the organic phase, a 3–5 freeze-thaw cycles last step was performed to transform the eventual MLV to unilamellar vesicles. The size of liposomes ranged from 8 μm to 10 μm. These large vesicles gave good encapsulation efficiency, respectively 69.2% for *E. globulus* and 47.1% for *M. alternifolia* but results showed a fail with encapsulation of *A. afra* with an encapsulation efficiency of 18.7%. Therefore, it may be considered that all EOs are not adapted for entrapment in liposomes. Some of them could exhibit destructive effects on phospholipid bilayers.

Low et al. (2013) used a modified reverse phase evaporation method to capture in liposomes tea tree oil (TTO), an EO from *M. alternifolia*. Indeed, the TTO was directly dispersed into the aqueous phase resulting in an emulsion on which is applied sonication. This emulsion is stabilized by polvinylalcohol (PVA). The phospholipids organic phase was added slowly into this previous phase. Then, the organic solvent was removed as previously described. Nevertheless, authors did not mention the different characteristics of prepared liposomes such as size, size distribution, zeta potential and encapsulation efficiency.

7.3. Supercritical fluid technology

Conventional supercritical fluid based methods are not all directly applied for liposome preparation and may require some modifications. For encapsulation of EOs or their components, two methods have been used: rapid expansion of supercritical solutions (RESS) and particles from gas saturated solutions (PGSS)-drying of emulsion.

7.3.1. Modified rapid expansion of supercritical solution technique (RESS)

In the conventional RESS process, solutes must be dissolved in the supercritical solvent and the solution is rapidly expanded into atmosphere to precipitate the solutes as microparticles (see Fig. 11). However, phospholipids are dissolved hardly in the pure supercritical CO_2. Furthermore, phospholipids can only assemble themselves into liposomes in an aqueous medium. As a result, conventional RESS process is not applicable for liposomes formation. Wen et al. (2010) adapted conventional method for liposome formation to encapsulate EOs or their components. For self-assembly of phospholipids in liposomes, an aqueous phase is needed. The modified RESS technique consists to predissolve phospholipids, cholesterol and the essential oil in ethanol and not directly in supercritical CO_2 because of their poor solubility. Ethanol is then used as a cosolvent to enhance phospholipids solubility. This organic phase is sealed into a reactor. Supercritical CO_2, which is obtained from liquefaction of CO_2 gas in a refrigerating system, is introduced via syringe pump into the reactor. After 1 h of equilibrium at desired temperature and pressure, all components are dissolved in the supercritical carbon dioxide (SC-CO_2)/ethanol mixture. Then, this phase is dispersed in an aqueous phase and sprayed into a collector allowing rapid elimination of CO_2. Finally, liposomal suspension is freeze-dried (Wen et al., 2010). Preparation of liposomes entrapping essential oil from *Atractylodes macrocephala* Koidz by modified RESS technique. Authors reported, however, that this technique is not effective for micronizing soy lecithin. Wen et al. (2010, 2011b) have revisited his modified RESS technique for liposomal encapsulation of other EOs components (atractylone and hinesol, rose oil) (Wen et al., 2010, 2011b). This method is newly termed rapid expansion from supercritical to surfactant solution (RESSS). In fact, EOs components and other liposomal materials were dissolved in a SC-CO_2/ethanol phase, as previously described, and then the mixture was sprayed into a surfactant solution. Here, 2 h of equilibration is required. When the dissolved phospholipids and EOs components reach desired pre-expansion pressure and temperature, they precipitate simultaneously. The latter phase is, then, sprayed into a collector by releasing CO_2 rapidly via a nozzle. This collector

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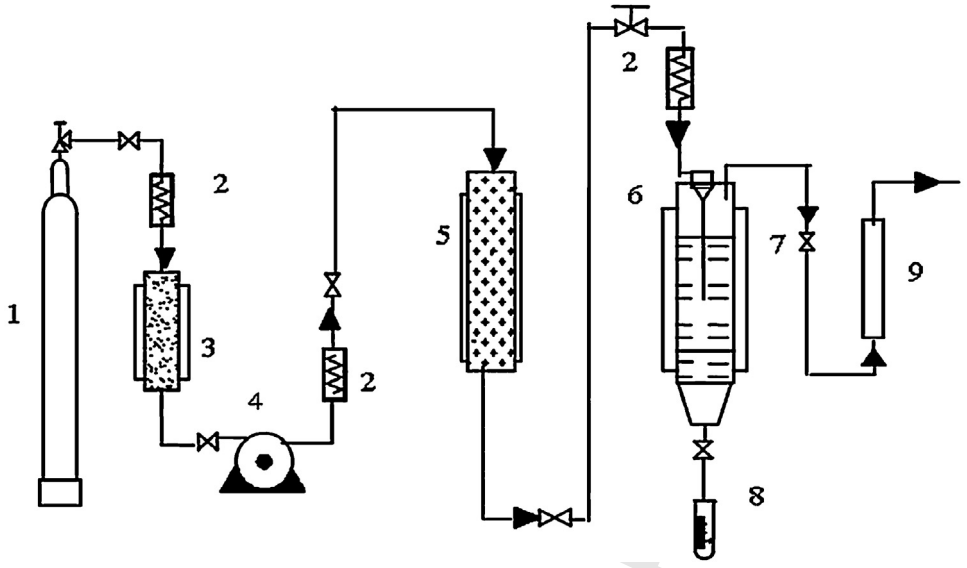

Fig. 11. Schematic diagram of the RESS (Wen et al., 2011b). (1, Cylinder; 2, heat exchanger; 3, refrigerating machine; 4, syringe pump; 5, reactor; 6, nozzle; 7, collector, 8, volumetric cylinder; 9, rotameter).

contains a surfactant solution where EOs components/phospholipid co-precipitates are hydrated. This leads to the self-assembly of phospholipids in liposomes with incorporation of EOs components. The SC-CO_2 flow is maintained for 1 h to eliminate residual ethanol in the liposomal suspension before its expansion in the atmosphere. Here, the role of the surfactant is to provide a better stability of the prepared liposomes, by limiting particle growth and reducing agglomeration. Excessive bubble formation, related to SC-CO_2 depressurization and phase conversion into a gas, is also prevented. It has been demonstrated that poloxamer 188 was the better surfactant. It offers a steric stabilization, a narrow size distribution and high entrapment efficiency.

7.3.2. Particles from gas saturated solution (PGSS)-drying process

The PGSS-drying process is another supercritical fluid precipitation method which could be used for encapsulation of EOs components (see Fig. 12). It has permitted to incorporate EOs in different polymeric particles (PEG, starches) for agricultural applications (Varona et al., 2009). Only Varona et al. (2011) worked on the liposomes encapsulation of EOs by PGSS-drying of

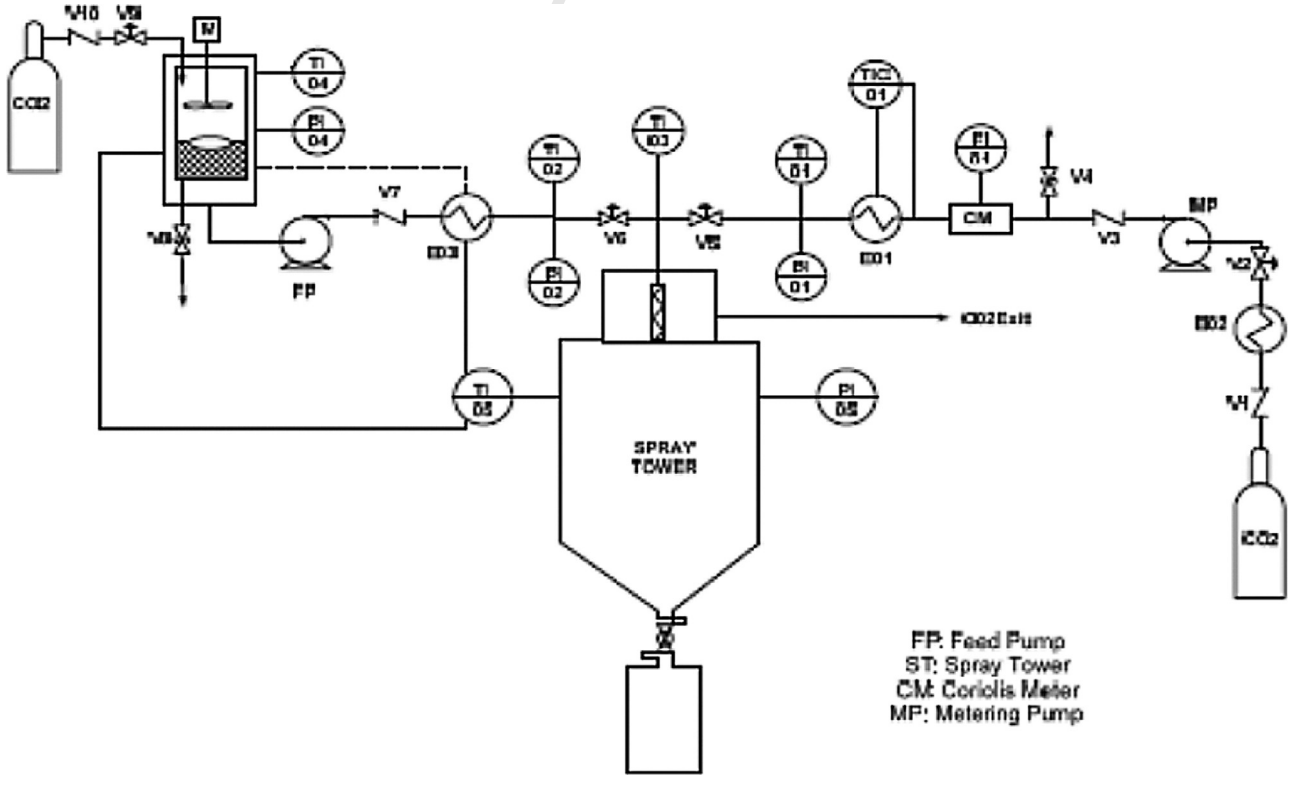

Fig. 12. Schematic diagram of the PGSS-drying system (Varona et al., 2011).

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Table 6
Applications of liposomes loaded with essential oils and their advantages.

Method	EOs or components	Average size (nm)	Entrapment efficiency (%)	Applications	Advantages	References
Modified RESS	*Atractylodes macrocephala* Koidz	173	82.18	Treating various digestive diseases and tumors	–	(Wen et al., 2010)
RESSS	Rose	94	89.46	Antibacterial activity, antioxidant and antimutagenic effects, regulating internal secretion, relieving tension and skin activation	–	(Wen et al., 2011a)
	Hinesol	124	88.26	Stomach antiulcer action	–	(Zhen and You, 2010)
	Atractylone	124	87.25	Inhibition of tumour revascularization and tumour cell proliferation with a particular interest for hepatic diseases	–	(Wen et al., 2011b)
PGSS drying	Lavandin	1390–24,840	6–14.5	Antimicrobial and antiviral agent in livestock	–	(Varona et al., 2011)
Reverse phase evaporation method	*Artemisia afra*	8269	18.7	Antibacterial activity	Enhancement of antimicrobial activity, extended release	(Van Vuuren et al., 2010)
	Eucalyptus globulus	9914	69.2			
	Melaleuca alternifolia	9280	41.7			
	Tea tree oil	ND	–	Antibacterial activity	Enhancement of antimicrobial efficacy	(Low et al., 2013)
Ethanol				injection + extrusion	Terpenes mixture (cineol, citral, D-limonene)	105.4–169.3
–	Penetration enhancer	Skin	penetration	enhancement	(Dragicevic-Curic et al., 2009)	
Thin film hydration + freeze-thaw	*Eucalyptus camaldulensis* Leaf	157.66	95	Antifungal therapy for dermatophyte infections	–	(Moghimipour et al., 2012)
Thin film				hydration + extrusion	*Citrus bergamia* Risso et Poiteau	188.25
	75			Antiproliferative activity against neuroblastoma cells	Enhance water solubility of the phytocomponents, increase anticancer activity	(Celia et al., 2013)
	Linalyl acetate	–	–	Antimicrobial activity	–	(Trombetta et al., 2005)
Menthol	–	–		Antimicrobial activity	–	
Thin film				hydration + sonication	*Anethum graveolens*	70–150
	until 91.5		–	(Ortan et al., 2009)		
	Artemisia arborescens L.	78–123	until 66	Antiviral activity against Herpes viruses	Enhancement of vitro antiherpetic activity	(Sinico et al., 2005)
	Santolina insularis	63	80	Antiviral activity against Herpes viruses	Stability improvement, less toxicity	(Valenti et al., 2001)
Zanthoxylum tingoassuiba	210	68.5		Antimicrobial activity, antiglioma activity	Stability improvement, enhanced apoptotic-inducing activity for glioma cells	(Detoni et al., 2012)
Thin film hydration	*Anethum graveolens*	230–457	until 95.5		–	(Ortan et al., 2009)
	Artemisia arborescens L.	232–304	until 74	Antiviral activity against Herpes viruses	Enhancement of vitro antiherpetic activity	(Sinico et al., 2005)
	Rose	702	81.76		–	(Wen et al., 2011a)
	Santolina insularis	467	78.5	Antiviral activity against Herpes viruses	Stability improvement, less toxicity	(Valenti et al., 2001)
	Zanthoxylum tingoassuiba	3630	79.25	Antimicrobial activity, antiglioma activity	Stability improvement, enhanced apoptotic-inducing activity for glioma cells	(Detoni et al., 2012)
	Carvacrol	–	4.16	Anti-inflammatory properties, antimicrobial activity	Solubility enhancement, stability improvement	(Coimbra et al., 2011)
	p-Cymene	–	–	Antimicrobial activity	–	(Cristani et al., 2007)
	Geraniol	–	–	Antimicrobial activity	–	(Bard et al., 1988)
	g-Terpinene	–	–	Antimicrobial activity	–	(Cristani et al., 2007)
	Thymol	–	6	Anti-inflammatory properties, antimicrobial activity	Solubility enhancement, stability improvement	(Coimbra et al., 2011)

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Table 6 (*Continued*)

Method	EOs or components	Average size (nm)	Entrapment efficiency (%)	Applications	Advantages	References
	Hinesol	704	80.9	Stomach antiulcer action	–	(Zhen and You, 2010)
	Atractylone	702	80.9	Inhibition of tumour revascularization and tumour cell proliferation whith a particular interest for hepatic diseases	–	(Wen et al., 2011b)
Modified thin film hydration	Lavandin	420–1290	upto 50	Antimicrobial and antiviral agent in livestock	–	(Varona et al., 2011)

emulsion, especially with lavandula oil. This method requires in prior the preparation of an essential oil-in-water emulsion. Lecithins are dispersed in deionized water at 50 °C under magnetic stirring. Then, EOs is gradually incorporated in the suspension while keeping agitation. The obtained coarse emulsion is passed under a rotor-stator machine to refine the droplets. After this, the emulsion is saturated with CO_2 at a convenient pressure and temperature in order to lower the viscosity. Thus, this saturated-CO_2 emulsion is easily pumped into supercritical CO_2 at high pressure and temperature. Only a few second contact is required to achieve an intimate mixing. Then, the vaporisation and expansion of CO_2 is triggered by a return to atmospheric pressure via a nozzle. Accordingly, a very fine and dried powder is formed. The liposome encapsulating the lavandula oil appears only after hydration of the previously dried powder (Varona et al., 2011). But during the spray step, it is essential to work at temperature conditions above the dew line of the temperature-composition phase equilibrium diagram of CO_2 and water in order to generate dry powder. The obtained liposome size ranged from 1.39 μm to 24.84 μm. The encapsulation efficiency reached 14.5%. The effectiveness of this method depends on several parameters. Indeed, the liposomes become smaller when the gas to product ratio (GPR) is higher or when the pre-expansion temperature and pressure decrease. This is explained by an increased CO_2 concentration in the emulsion, which implies a better atomization. Conversely, particle size increased when phospholipids concentration increased because it makes the emulsion more viscous which generates an opposition to atomization. The encapsulation efficiency is also affected by the GPR. When GPR increased, essential oil evaporates, which decreases entrapment efficiency. When pre-expansion temperature and pressure increased, the encapsulation efficiency also increased (Varona et al., 2011). Table 6 shows different examples of essential oils entrapped in liposomes for different applications, mainly antimicrobial agents. EOs or their components are also used as penetration enhancers for skin drug delivery.

8. Encapsulation in solid lipid nanoparticles (SLN)

In the 1990s, three working groups, Müller and co-workers (Schwarz et al., 1994; Freitas, 1994), Gasco and co-workers (Morel et al., 1996; Cavalli et al., 1997) and Westesen and co-workers (Bunjes et al., 1996), developed the first generation of lipid nanoparticles, called solid lipid nanoparticles (SLN) (Weber et al., 2014). SLN are nanocarriers which contain lipids which are solids in room temperature. The lipid component could include lipid and lipid-like molecules such as triacylglycerols or waxes (Mehnert and Mäder, 2012; Weiss et al., 2008; Bilia et al., 2014). SLN provide many advantages: physical stability, protection of encapsulated material from degradation, and controlled release (Wissing et al., 2004). In addition, lipid matrix is made from physiological lipids which decreases toxicity (ALHaj, 2010). Common components of SLNs include solid lipids, emulsifiers and water. The term lipid is used here in a broader sense and includes triglycerides (e.g. tristearin), partial glycerides (e.g. Imwitor), fatty acids (e.g. stearic acid), steroids (e.g. cholesterol) and waxes (e.g. cetyl palmitate) (Mehnert and Mäder, 2012). Several techniques have been used to prepare SLNs such as, high shear homogenization and ultrasound, high pressure homogenization, and microemulsion based preparation techniques. We will focus on high pressure technique as it has many advantages compared to the other methods, e.g. easy scale up, avoidance of organic solvents and short production time. High pressure homogenizers push a liquid with high pressure (100–2000 bar) through a narrow gap (in the range of a few microns). The fluid accelerates on a very short distance to very high velocity (over 1000 km/h). Very high shear stress and cavitation forces disrupt the particles down to the submicron range. Two general approaches of the homogenization step, the hot and the cold homogenization techniques, can be used for the production of SLN (Fig. 13) (Zur Mühlen et al., 1998). In both cases, a preparatory step involves the drug incorporation into the bulk lipid by dissolving or dispersing the drug in the lipid melt (Mehnert and Mäder, 2012). Table 7 contains some examples of SLN that were developed to encapsulate EOs.

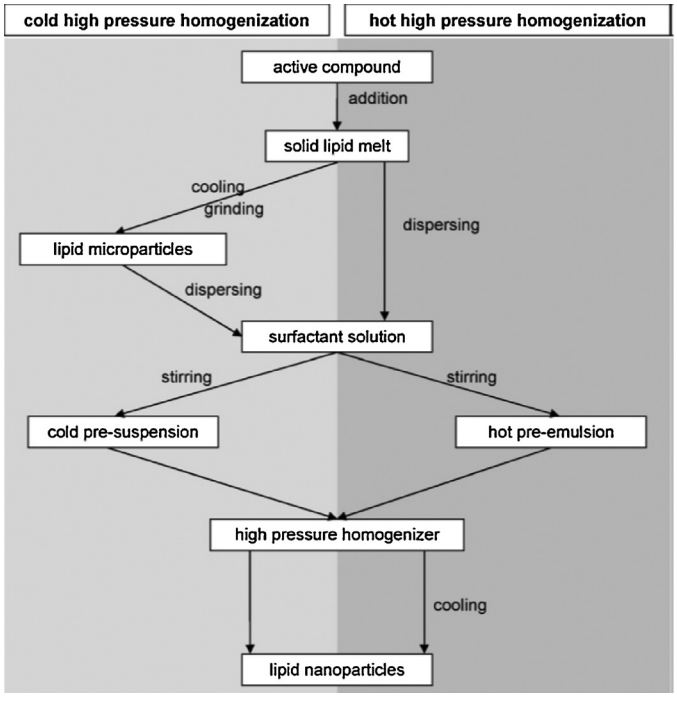

Fig. 13. Production process of lipid nanoparticles using cold (light gray background) and hot (dark gray background) high pressure homogenization technique (Pardeike et al., 2009).

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Table 7
Applications of solid lipid nanoparticles loaded with essential oils and their advantages.

Methods	EOs or components	Average size (nm)	Entrapment efficiency (%)	Applications	Advantages	References
Precipitation technique and hot homogenization method	*Zataria multiflora*	650	38.66	–	Extrended release	(Moghimipour et al., 2013)
Hot-pressure homogenization	*Artemisia arborescens*	219 and 223	87 and 92	Antiherpetic	Higher skin permeation	(Lai et al., 2007)
High-pressure homogenization	*Nigella sativa* L.	66.27–142.7	–	–	–	(ALHaj, 2010)
High-pressure homogenization	Frankincense and myrrh essential oils	113.3	80.60	Antitumor	Decrease of evaporation loss of active components, better antitumor efficacy	(Shi et al., 2012)

9. Conclusion

Essential oils are natural products which consist of complex blends of many volatile molecules. They have been used for several applications in pharmaceutical, cosmetic, agricultural, and food industries. Extraction could be carried out by various techniques. Innovative methods avoid shortcomings of conventional techniques like chemical alteration risk, long extraction time and high energy input. Despite their numerous applications, essential oils are very sensitive to environmental factors when used as such. Encapsulation has emerged is a relevant alternative that could enhance essential oils stability. Various techniques have been successfully used to attain this purpose with interesting results. Many other advantages were obtained after loading essential oils in particles or liposomes such as, enhanced efficacy and sustained release. Nowadays the combination of essential oils and active molecules is attracting special attention in order to obtain colloidal particles mainly for dermatology, local skin therapy and now cosmeto-textile as new application.

Uncited references

ACTIFS (2015), Franchomme and Pénoël (2001), and Procede, 2015.

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References

Abbaszadeh, S., Sharifzadeh, A., Shokri, H., Khosravi, A.R., Abbaszadeh, A., 2014. Antifungal efficacy of thymol carvacrol, eugenol and menthol as alternative agents to control the growth of food-relevant fungi. J. Med. Mycol. 24, 51–56.
Abdelrhafour Tantaoui-Elaraki, N.L., 1993. Composition and antimicrobial activity of the essential oils of *Thymus broussonettii*, *T. zygis* and *T. satureioides*. J. Essent. Oil Res. 5, 45–53.
Abreu, F.O.M.S., Oliveira, E.F., Paula, H.C.B., de Paula, R.C.M., 2012. Chitosan/cashew gum nanogels for essential oil encapsulation. Carbohydr. Polym. 89, 1277–1282.
ACTIFS ET. ADDITIFS EN COSMETOLOGIE, 2015. 2ème édition – Monique Seiller, Collectif,Marie-Claude Martini, n.d.
Aghel, N., Yamini, Y., Hadjiakhoondi, A., Pourmortazavi, S.M., 2004. Supercritical carbon dioxide extraction of *Mentha pulegium* L. essential oil. Talanta 62, 407–411.
Ait-Ouazzou, A., Cherrat, L., Espina, L., Lorán, S., Rota, C., Pagán, R., 2011. The antimicrobial activity of hydrophobic essential oil constituents acting alone or in combined processes of food preservation. Innov. Food Sci. Emerg. Technol. 12, 320–329.
Akash Kedia, B.P., 2013. Antifungal and antiaflatoxigenic properties of *Cuminum cyminum* (L.) seed essential oil and its efficacy as a preservative in stored commodities. Int. J. Food Microbiol. 1–7.
ALHaj, 2010. Characterization of *Nigella sativa* L. essential oil-loaded solid lipid nanoparticles. J. Pharmacol. 5, 52–57.
Almeida, A.P., Rodríguez-Rojo, S., Serra, A.T., Vila-Real, H., Simplicio, A.L., Delgadilho, I., Beirão da Costa, S., Beirão da Costa, L., Nogueira, I.D., Duarte, C.M.M., 2013. Microencapsulation of oregano essential oil in starch-based materials using supercritical fluid technology. Innov. Food Sci. Emerg. Technol. 20, 140–145.
Angioni, A., Barra, A., Coroneo, V., Dessi, S., Cabras, P., 2006. Chemical composition seasonal variability, and antifungal activity of *Lavandula stoechas* L. ssp. stoechas essential oils from stem/leaves and flowers. J. Agric. Food Chem. 54, 4364–4370.
Ascensão, L., Pais, M.S., 1998. The leaf capitate trichomes of *Leonotis leonurus*: histochemistry, ultrastructure and secretion. Ann. Bot. 81, 263–271. doi:http://dx.doi.org/10.1006/anbo.1997.0550.
Asma Farhat, A.-S.F.-T., 2011. Microwave steam diffusion for extraction of essential oil from orange peel: kinetic data: extract's global yield and mechanism. Food Chem. 125, 255–261.
Bae, G.-S., Park, K.-C., Choi, S.B., Jo, I.-J., Choi, M.-O., Hong, S.-H., Song, K., Song, H.-J., Park, S.-J., 2012. Protective effects of alpha-pinene in mice with cerulein-induced acute pancreatitis. Life Sci. 91, 866–871.
Bakkali, F., Averbeck, S., Averbeck, D., Idaomar, M., 2008. Biological effects of essential oils – a review. Food Chem. Toxicol. 46, 446–475.
Banerjee, S., Chattopadhyay, P., Ghosh, A., Goyary, D., Karmakar, S., Veer, V., 2013. Influence of process variables on essential oil microcapsule properties by carbohydrate polymer-protein blends. Carbohydr. Polym. 93, 691–697.
Bangham, A.D., 1978. Properties and uses of lipid vesicles: an overview. Ann. N. Y. Acad. Sci. 308, 2–7.
Bangham, A.D., De Gier, J., Greville, G.D., 1967. Osmotic properties and water permeability of phospholipid liquid crystals. Chem. Phys. Lipids 1, 225–246.
Baran, P., Aktaş, K., Özdemir, C., 2010. Structural investigation of the glandular trichomes of endemic *Salvia smyrnea* L. South Afr. J. Bot. 76, 572–578.
Barceloux, D.G., 2008. Frontmatter. Medical Toxicology of Natural Substances. John Wiley & Sons, Inc., pp. i–xxi.
Bard, M., Albrecht, M.R., Gupta, N., Guynn, C.J., Stillwell, W., 1988. Geraniol interferes with membrane functions in strains of *Candida* and *Saccharomyces*. Lipids 23, 534–538.
Beirão da Costa, S., Duarte, C., Bourbon, A.I., Pinheiro, A.C., Serra, A.T., Moldão Martins, M., Nunes Januário, M.I., Vicente, A.A., Delgadillo, I., Duarte, C., Beirão da Costa, M.L., 2012. Effect of the matrix system in the delivery and in vitro bioactivity of microencapsulated Oregano essential oil. J. Food Eng. Int. Conf. Food Innov. – FoodInnova 110, 190–199.
Beirão-da-Costa, S., Duarte, C., Bourbon, A.I., Pinheiro, A.C., Januário, M.I.N., Vicente, A.A., Beirão-da-Costa, M.L., Delgadillo, I., 2013. Inulin potential for encapsulation and controlled delivery of oregano essential oil. Food Hydrocoll. 33, 199–206.
Berka-Zougali, B., Hassani, A., Besombes, C., Allaf, K., 2010. Extraction of essential oils from Algerian myrtle leaves using instant controlled pressure drop technology. J. Chromatogr. A 1217, 6134–6142.
Beyki, M., Zhaveh, S., Khalili, S.T., Rahmani-Cherati, T., Abollahi, A., Bayat, M., Tabatabaei, M., Mohsenifar, A., 2014. Encapsulation of *Mentha piperita* essential oils in chitosan–cinnamic acid nanogel with enhanced antimicrobial activity against *Aspergillus flavus*. Ind. Crops Prod. 54, 310–319.
Bilia, A.R., Guccione, C., Isacchi, B., Righeschi, C., Firenzuoli, F., Bergonzi, M.C., 2014. Essential oils loaded in nanosystems: a developing strategy for a successful therapeutic approach. Evid. Based Complement. Altern. Med. 2014, e651593.
de. Billerbeck, V.-G., 2007. Huiles essentielles et bactéries résistantes aux antibiotiques. Phytothérapie 5, 249–253. doi:http://dx.doi.org/10.1007/s10298-007-0265-z.
Bohra, P.M., Vaze, A.S., Pangarkar, V.G., Taskar, A., 1994. Adsorptive recovery of water soluble essential oil components. J. Chem. Technol. Biotechnol. 60, 97–102.
Boskabady, M.H., Kiani, S., Rakhshandah, H., 2006. Relaxant effects of *Rosa damascena* on guinea pig tracheal chains and its possible mechanism(s). J. Ethnopharmacol. 106, 377–382.
Bouwmeester, H.J., Davies, J.A.R., Toxopeus, H., 1995. Enantiomeric composition of carvone, limonene, and carveols in seeds of dill and annual and biennial caraway varieties. J. Agric. Food Chem. 43, 3057–3064.
Braden, R., Reichow, S., Halm, M.A., 2009. The use of the essential oil lavandin to reduce preoperative anxiety in surgical patients. J. Perianesth. Nurs. 24, 348–355.
Bruneton, J., 1987. Eléments de Phytochimie et de Pharmacognosie. Technique et Documentation Lavoisier.
Bruneton, J., 1999. Pharmacognosy: Phytochemistry, Medicinal Plants. Intercept Limited.
Bruneton, J., 2009. Pharmacognosie: Phytochimie, Plantes médicinales. Tec & Doc Lavoisier.

UNCORRECTED PROOF

Bunjes, H., Westesen, K., Koch, M.H.J., 1996. Crystallization tendency and polymorphic transitions in triglyceride nanoparticles. Int. J. Pharm. 129, 159–173.
Burt, S., 2004. Essential oils: their antibacterial properties and potential applications in foods—a review. Int. J. Food Microbiol. 94, 223–253.
Cao, H., Xiao, J.B., Xu, M., 2007. Comparison of volatile components of *Marchantia convoluta* obtained by supercritical carbon dioxide extraction and petrol ether extraction. J. Food Compos. Anal. 20, 45–51.
Capuzzo, A., Maffei, M.E., Occhipinti, A., 2013. Supercritical fluid extraction of plant flavors and fragrances. Molecules 18, 7194–7238.
Carneiro, H.C.F., Tonon, R.V., Grosso, C.R.F., Hubinger, M.D., 2013. Encapsulation efficiency and oxidative stability of flaxseed oil microencapsulated by spray drying using different combinations of wall materials. J. Food Eng. 2nd ISEKI_Food Conf. 115, 443–451.
Carvalho, R.N., Moura, L.S., Rosa, P.T.V., Meireles, M.A.A., 2005. Supercritical fluid extraction from rosemary (*Rosmarinus officinalis*): kinetic data, extract's global yield, composition, and antioxidant activity. J. Supercrit. Fluids 35, 197–204.
Castanon, J.I.R., 2007. History of the use of antibiotic as growth promoters in European poultry feeds. Poult. Sci. 86, 2466–2471. doi:http://dx.doi.org/10.3382/ps.2007-00249.
Cavalli, R., Caputo, O., Carlotti, M.E., Trotta, M., Scarnecchia, C., Gasco, M.R., 1997. Sterilization and freeze-drying of drug-free and drug-loaded solid lipid nanoparticles. Int. J. Pharm. 148, 47–54.
Celia, C., Trapasso, E., Locatelli, M., Navarra, M., Ventura, C.A., Wolfram, J., Carafa, M., Morittu, V.M., Britti, D., Di Marzio, L., Paolino, D., 2013. Anticancer activity of liposomal bergamot essential oil (BEO) on human neuroblastoma cells. Colloids Surf. B Biointerfaces 112, 548–553.
CFR – Code of Federal Regulations Title 21 [WWW Document], 2015 n.d. URL http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=182.20 (accessed 09.12.14).
Changmann Yoon, S.-R.M., 2011. Repellency of lavender oil and linalool against spot clothing wax cicada, *Lycorma delicatula* (Hemiptera: Fulgoridae) and their electrophysiological responses. J. Asia-Pac. Entomol. 14, 411–416. doi:http://dx.doi.org/10.1016/j.aspen.2011.06.003.
Chan, Y.-H., Chen, B.-H., Chiu, C.P., Lu, Y.-F., 2004. The influence of phytosterols on the encapsulation efficiency of cholesterol liposomes. Int. J. Food Sci. Technol. 39, 985–995.
Charve, J., Reineccius, G.A., 2009. Encapsulation performance of proteins and traditional materials for spray dried flavors. J. Agric. Food Chem. 57, 2486–2492.
Chavan, M.J., Wakte, P.S., Shinde, D.B., 2010. Analgesic and anti-inflammatory activity of Caryophyllene oxide from *Annona squamosa* L. bark. Phytomed. Int. J. Phytother. Phytopharm. 17, 149–151.
Chen, W., Viljoen, A.M., 2010. Geraniol – a review of a commercially important fragrance material. S. Afr. J. Bot. 76, 643–651.
Chen, C.C., Kuo, M.C., Wu, C.M., Ho, C.T., 1986. Pungent compounds of ginger (*Zingiber officinale* Roscoe) extracted by liquid carbon dioxide. J. Agric. Food Chem. 34, 477–480.
Chen, Q., Gan, Z., Zhao, J., Wang, Y., Zhang, S., Li, J., Ni, Y., 2014. In vitro comparison of antioxidant capacity of cumin (*Cuminum cyminum* L.) oils and their main components. LWT – Food Sci. Technol. 55, 632–637.
Chemat, F., Lucchesi, M.E., 2006. Microwave accelerated steam distillation of essential oil from lavender: a rapid, clean and environmentally friendly approach. Anal. Chim. Acta 157–160.
Chorny, M., Fishbein, I., Danenberg, H.D., Golomb, G., 2002. Lipophilic drug loaded nanospheres prepared by nanoprecipitation: effect of formulation variables on size, drug recovery and release kinetics. J. Control. Release: Off. J. Control. Release Soc. 83, 389–400.
Clara Miracle Belda-Galbis, M.C.P.-P., 2013. Impact assessment of carvacrol and citral effect on *Escherichia coli* K12 and *Listeria innocua* growth. Food Control 33, 536–544.
Coimbra, M., Isacchi, B., van Bloois, L., Torano, J.S., Ket, A., Wu, X., Broere, F., Metselaar, J.M., Rijcken, C.J.F., Storm, G., Bilia, R., Schiffelers, R.M., 2011. Improving solubility and chemical stability of natural compounds for medicinal use by incorporation into liposomes. Int. J. Pharm. 416, 433–442.
Colletier, J.-P., Chaize, B., Winterhalter, M., Fournier, D., 2002. Protein encapsulation in liposomes: efficiency depends on interactions between protein and phospholipid bilayer. BMC Biotechnol. 2, 9.
Cox, S.D., Mann, C.M., Markham, J.L., Gustafson, J.E., Warmington, J.R., Wyllie, S.G., 2001. Determining the antimicrobial actions of tea tree oil. Molecules 6, 87–91.
Cristani, M., D'Arrigo, M., Mandalari, G., Castelli, F., Sarpietro, M.G., Micieli, D., Venuti, V., Bisignano, G., Saija, A., Trombetta, D., 2007. Interaction of four monoterpenes contained in essential oils with model membranes: implications for their antibacterial activity. J. Agric. Food Chem. 55, 6300–6308.
Deamer, D., Bangham, A.D., 1976. Large volume liposomes by an ether vaporization method. Biochim. Biophys. Acta BBA – Biomembr. 443, 629–634.
Deans, S.G., Ritchie, G., 1987. Antibacterial properties of plant essential oils. Int. J. Food Microbiol. 5, 165–180.
De Oliveira, E.F., Paula, H.C.B., Paula, R.C.M., 2014. Alginate/cashew gum nanoparticles for essential oil encapsulation. Colloids Surf. B Biointerfaces 113, 146–151.
De Souza, J.R.R., Feitosa, J.P.A., Ricardo, N.M.P.S., Trevisan, M.T.S., de Paula, H.C.B., Ulrich, C.M., Owen, R.W., 2013. Spray-drying encapsulation of mangiferin using natural polymers. Food Hydrocoll. 33, 10–18.
Detoni, C.B., de Oliveira, D.M., Santo, I.E., Pedro, A.S., El-Bacha, R., da Silva Velozo, E., Ferreira, D., Sarmento, B., de Magalhães Cabral-Albuquerque, E.C., 2012. Evaluation of thermal-oxidative stability and antiglioma activity of *Zanthoxylum tingoassuiba* essential oil entrapped into multi- and unilamellar liposomes. J. Liposome Res. 22, 1–7.
Dick, A.J., Starmans, H.H.N., 1996. Extraction of secondary metabolites from plant material: a review. Trends Food Sci. Technol. 191–197.
Dima, C., Cotârlet, M., Alexe, P., Dima, S., 2014. Microencapsulation of essential oil of pimento [*Pimenta dioica* (L) Merr.] by chitosan/k-carrageenan complex coacervation method. Innov. Food Sci. Emerg. Technol. 22, 203–211.
Dragicevic-Curic, N., Scheglmann, D., Albrecht, V., Fahr, A., 2009. Development of different temoporfin-loaded invasomes—novel nanocarriers of temoporfin: characterization, stability and in vitro skin penetration studies. Colloids Surf. B Biointerfaces 70, 198–206.
Drulis-Kawa, Z., Dorotkiewicz-Jach, A., 2010. Liposomes as delivery systems for antibiotics. Int. J. Pharm. 387, 187–198. doi:http://dx.doi.org/10.1016/j.ijpharm.2009.11.033.
Ebada, S.S., Lin, W., Proksch, P., 2010. Bioactive sesterterpenes and triterpenes from marine sponges: occurrence and pharmacological significance. Mar. Drugs 8, 313–346.
Erman, W.F., 1985. Chemistry of the Monoterpenes: An Encyclopedic Handbook. M. Dekker.
Esfandyari-Manesh, M., Ghaedi, Z., Asemi, M., Khanavi, M., Manayi, A., Jamalifar, H., Atyabi, F., Dinarvand, R., 2013. Study of antimicrobial activity of anethole and carvone loaded PLGA nanoparticles. J. Pharm. Res. 7, 290–295.
Faborode, M.O., Favier, J.F., 1996. Identification and significance of the oil-point in seed-oil expression. J. Agric. Eng. Res. 65, 335–345.
Fan, F., Tao, N., Jia, L., He, X., 2014. Use of citral incorporated in postharvest wax of citrus fruit as a botanical fungicide against *Penicillium digitatum*. Postharvest Biol. Technol. 90, 52–55.
Farhat, A., Fabiano-Tixier, A.-S., Visinoni, F., Romdhane, M., Chemat, F., 2010. A surprising method for green extraction of essential oil from dry spices: microwave dry-diffusion and gravity. J. Chromatogr. A 1217, 7345–7350.
Farhat, A., Ginies, C., Romdhane, M., Chemat, F., 2009. Eco-friendly and cleaner process for isolation of essential oil using microwave energy: experimental and theoretical study. J. Chromatogr. A 1216, 5077–5085.
Ferhat, M.A., Meklati, B.Y., Chemat, F., 2007. Comparison of different isolation methods of essential oil from citrus fruits: cold pressing: hydrodistillation and microwave dry distillation. Flavour Fragr. J. 22, 494–504.
Fernandes, R.V., Borges, S.V., Botrel, D.A., 2014. Gum arabic/starch/maltodextrin/inulin as wall materials on the microencapsulation of rosemary essential oil. Carbohydr. Polym. 101, 524–532.
Fessi, H., Puisieux, F., Devissaguet, J.P., Ammoury, N., Benita, S., 1989. Nanocapsule formation by interfacial polymer deposition following solvent displacement. Int. J. Pharm. 55, R1–R4.
Filly, A., Fernandez, X., Minuti, M., Visinoni, F., Cravotto, G., Chemat, F., 2014. Solvent-free microwave extraction of essential oil from aromatic herbs: from laboratory to pilot and industrial scale. Food Chem. 150, 193–198.
Flavia Bonamin, T.M.M., 2014. The effect of a minor constituent of essential oil from *Citrus aurantium*: the role of β-myrcene in preventing peptic ulcer disease. Chem. Biol. Interact..
Flávia Negromonte Souto-Maior, F.L. de C., 2011. Anxiolytic-like effects of inhaled linalool oxide in experimental mouse anxiety models. Pharmacol. Biochem. Behav. 100, 259–263.
Fornari, T., Vicente, G., Vázquez, E., García-Risco, M.R., Reglero, G., 2012. Isolation of essential oil from different plants and herbs by supercritical fluid extraction. J. Chromatogr. A 1250, 34–48.
Franchomme, P., Pénoël, D., 2001. L'aromathérapie exactement. Roger Jollois, Limoges (France).
Freitas, C., 1994. P238 effect of storage conditions on long-term stability of solid lipid nanoparticles (SLN) in aqueous dispersion. Eur. J. Pharm. Sci. 2.
Gavliakova, S., Biringerova, Z., 2013. Antitussive effects of nasal thymol challenges in healthy volunteers. Respir. Physiol. Neurobiol..
Geng, Y., Liu, J., Lv, R., Yuan, J., Lin, Y., Wang, X., 2007. An efficient method for extraction: separation and purification of eugenol from *Eugenia caryophyllata* by supercritical fluid extraction and high-speed counter-current chromatography. Sep. Purif. Technol. 57, 237–241.
Gershenzon, J., Dudareva, N., 2007. The function of terpene natural products in the natural world. Nat. Chem. Biol. 3, 408–414.
Ghosh, V., Mukherjee, A., Chandrasekaran, N., 2014. Eugenol-loaded antimicrobial nanoemulsion preserves fruit juice against, microbial spoilage. Colloids Surf. B Biointerfaces 114, 392–397.
Glišić, S.B., Mišić, D.R., Stamenić, M.D., Zizovic, I.T., Ašanin, R.M., Skala, D.U., 2007. Supercritical carbon dioxide extraction of carrot fruit essential oil: chemical composition and antimicrobial activity. Food Chem. 105, 346–352.
Golmakani, M.-T., Rezaei, K., 2008. Comparison of microwave-assisted hydrodistillation withthe traditional hydrodistillation method in the extraction of essential oils from *Thymus vulgaris* L. Food Chem. 109, 925–930.
Gomes, P.B., Mata, V.G., Rodrigues, A.E., 2007. Production of rose geranium oil using supercritical fluid extraction. J. Supercrit. Fluids 41, 50–60.
Gruner, S.M., Lenk, R.P., Janoff, A.S., Ostro, M.J., 1985. Novel multilayered lipid vesicles: comparison of physical characteristics of multilamellar liposomes and stable plurilamellar vesicles. Biochemistry (Moscow) 24, 2833–2842.
Guan, W., Li, S., Yan, R., Tang, S., Quan, C., 2007. Comparison of essential oils of clove buds extracted with supercritical carbon dioxide and other three traditional extraction methods. Food Chem. 101, 1558–1564.
Guido Flamini, M.T., 2007. Comparison between the conventional method of extraction of essential oil of *Laurus nobilis* L. and a novel method which uses

UNCORRECTED PROOF

microwaves applied in situ without resorting to an oven. J. Chromatogr. A 1143, 36–40.
Herrero, M., Cifuentes, A., Ibañez, E., 2006. Sub- and supercritical fluid extraction of functional ingredients from different natural sources: plants, food-by-products, algae and microalgae: a review. Food Chem. 98, 136–148.
Hong, K., Park, S., 1999. Melamine resin microcapsules containing fragrant oil: synthesis and characterization. Mater. Chem. Phys. 58, 128–131.
Hosseini, S.F., Zandi, M., Rezaei, M., Farahmandghavi, F., 2013a. Two-step method for encapsulation of oregano essential oil in chitosan nanoparticles: preparation, characterization and in vitro release study. Carbohydr. Polym. 95, 50–56.
Hosseini, S.M., Hosseini, H., Mohammadifar, M.A., Mortazavian, A.M., Mohammadi, A., Khosravi-Darani, K., Shojaee-Aliabadi, S., Dehghan, S., Khaksar, R., 2013b. Incorporation of essential oil in alginate microparticles by multiple emulsion/ionic gelation process. Int. J. Biol. Macromol. 62, 582–588.
Houghton, P.J., 1999. The scientific basis for the reputed activity of Valerian. J. Pharm. Pharmacol. 51, 505–512.
Hromádková, Z., Ebringerová, A., Valachovič, P., 1999. Comparison of classical and ultrasound-assisted extraction of polysaccharides from *Salvia officinalis* L. Ultrason. Sonochem. 5, 163–168.
Huo, M., Cui, X., Xue, J., Chi, G., Gao, R., Deng, X., Guan, S., Wei, J., Soromou, L.W., Feng, H., Wang, D., 2013. Anti-inflammatory effects of linalool in RAW 264.7 macrophages and lipopolysaccharide-induced lung injury model. J. Surg. Res. 180, e47–54.
Iannitelli, A., Grande, R., Di Stefano, A., Di Giulio, M., Sozio, P., Bessa, L.J., Laserra, S., Paolini, C., Protasi, F., Cellini, L., 2011. Potential antibacterial activity of carvacrol-loaded poly(DL-lactide-co-glycolide) (PLGA) nanoparticles against microbial biofilm. Int. J. Mol. Sci. 12, 5039–5051.
Jaafari, A., Mouse, H.A., Rakib, E.M., M'barek, L.A., Tilaoui, M., Benbakhta, C., Boulli, A., Abbad, A., Zyad, A., 2007. Chemical composition and antitumor activity of different wild varieties of Moroccan thyme. Rev. Bras. Farmacogn. 17, 477–491.
Juergens, U.R., Dethlefsen, U., Steinkamp, G., Gillissen, A., Repges, R., Vetter, H., 2003. Anti-inflammatory activity of 1:8-cineol (eucalyptol) in bronchial asthma: a double-blind placebo-controlled trial. Respir. Med. 97, 250–256.
Karim Assami, D.P., 2012. Ultrasound induced intensification and selective extraction of essential oil from *Carum carvi* L. seeds. Chem. Eng. Process. Process Intensif. 62, 99–105.
Kaushik, P., Dowling, K., Barrow, C.J., Adhikari, B., 2014. Microencapsulation of omega-3 fatty acids: a review of microencapsulation and characterization methods. J. Funct. Foods .
Khajeh, M., Yamini, Y., Sefidkon, F., Bahramifar, N., 2004. Comparison of essential oil composition of *Carum copticum* obtained by supercritical carbon dioxide extraction and hydrodistillation methods. Food Chem. 86, 587–591.
Khoee, S., Yaghoobian, M., 2009. An investigation into the role of surfactants in controlling particle size of polymeric nanocapsules containing penicillin-G in double emulsion. Eur. J. Med. Chem. 44, 2392–2399.
Kremer, D., Dunkić, V., Ruščić, M., Matevski, V., Ballian, D., Bogunić, F., Eleftheriadou, E., Stešević, D., Kosalec, I., Bezić, N., Stabentheiner, E., 2014. Micromorphological traits and essential oil contents of *Micromeria kerneri* Murb. and *M. juliana* (L.) Benth. (Lamiaceae). Phytochemistry 98, 128–136.
Kristiawan, M., Sobolik, V., Allaf, K., 2008. Isolation of Indonesian cananga oil using multi-cycle pressure drop process. J. Chromatogr. A 30, 306–318. doi:http://dx.doi.org/10.1016/j.chroma.2008.03.068.
Ladj-Minost, A., 2012. Répulsifs d'arthropodes à durée d'action prolongée: étude pharmacotechnique, devenir in situ et efficacité. PhD Thesis. Université Claude Bernard, Lyon I.
Lai, F., Sinico, C., De Logu, A., Zaru, M., Muller, R.H., Fadda, A.M., 2007. SLN as a topical delivery system for *Artemisia arborescens* essential oil: in vitro antiviral activity and skin permeation study. Int. J. Nanomed. 2, 419–425.
Legrand, P., Lesieur, S., Bochot, A., Gref, R., Raatjes, W., Barratt, G., Vauthier, C., 2007. Influence of polymer behaviour in organic solution on the production of polylactide nanoparticles by nanoprecipitation. Int. J. Pharm. 344, 33–43.
Leimann, F.V., Gonçalves, O.H., Machado, R.A.F., Bolzan, A., 2009. Antimicrobial activity of microencapsulated lemongrass essential oil and the effect of experimental parameters on microcapsules size and morphology. Mater. Sci. Eng. C 29, 430–436.
Lemetter, C.Y.G., Meeuse, F.M., Zuidam, N.J., 2009. Control of the morphology and the size of complex coacervate microcapsules during scale-up. AIChE J. 55, 1487–1496.
Q18 Li, X.-M., Tian, S.-L., 2009. Extraction of *Cuminum cyminum* essential oil by combination technology of organic solvent with low boiling point and steam distillation. Food Chem. 115, 1114–1119.
Liebgott, T., Miollan, M., Berchadsky, Y., Drieu, K., Culcasi, M., Pietri, S., 2000. Complementary cardioprotective effects of flavonoid metabolites and terpenoid constituents of *Ginkgo biloba* extract (EGb 761) during ischemia and reperfusion. Basic Res. Cardiol. 95, 368–377.
Q19 Lima, M., daSilva, L.J., Quintans-Júnior, Santana, W.A., de, C.M., Kaneto, Soares, M.B. P., Villarreal, C.F., 2013. Anti-inflammatory effects of carvacrol: evidence for a key role of interleukin-10. Eur. J. Pharm. 699, 112–117.
Liolios, C.C., Gortzi, O., Lalas, S., Tsaknis, J., Chinou, I., 2009. Liposomal incorporation of carvacrol and thymol isolated from the essential oil of *Origanum dictamnus* L. and in vitro antimicrobial activity. Food Chem. 112, 77–83.
Li, Y., Fabiano-Tixier, A.S., Vian, M.A., Chemat, F., 2013. Solvent-free microwave extraction of bioactive compounds provides a tool for green analytical chemistry. TrAC Trends Anal. Chem. 47, 1–11.
López, A., Castro, S., Andina, M.J., Ures, X., Munguía, B., Llabot, J.M., Elder, H., Dellacassa, E., Palma, S., Domínguez, L., 2014. Insecticidal activity of microencapsulated *Schinus molle* essential oil. Ind. Crops Prod. 53, 209–216.
Low, W.L., Martin, C., Hill, D.J., Kenward, M.A., 2013. Antimicrobial efficacy of liposome-encapsulated silver ions and tea tree oil against *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Candida albicans*. Lett. Appl. Microbiol. 57, 33–39. doi:http://dx.doi.org/10.1111/lam.12082.
Lucchesi, M.E., Chemat, F., Smadja, J., 2004a. Solvent-free microwave extraction of essential oil from aromatic herbs: comparison with conventional hydro-distillation. J. Chromatogr. A 1043, 323–327.
Lucchesi, M.E., Chemat, F., Smadja, J., 2004b. An original solvent free microwave extraction of essential oils from spices. Flavour Fragr. J. 19, 134–138.
Lucinewton, S., Moura, R.N.C.J., 2013. Supercritical fluid extraction from fennel (*Foeniculum vulgare*): global yield, composition and kinetic data. J. Supercrit. Fluids 212–219.
Luque de Castro, M.D., Jiménez-Carmona, M.M., Fernández-Pérez, V., 1999. Towards more rational techniques for the isolation of valuable essential oils from plants. TrAC Trends Anal. Chem. 18, 708–716.
Lv, Y., Yang, F., Li, X., Zhang, X., Abbas, S., 2014. Formation of heat-resistant nanocapsules of jasmine essential oil via gelatin/gum arabic based complex coacervation. Food Hydrocoll. 35, 305–314.
Mara, E.M., Braga, P.A.D.E., 2005. Supercritical fluid extraction from *Lippia alba*: global yields, kinetic data, and extract chemical composition. J. Supercrit. Fluids 149–156.
Marija, M., Lesjak, I.N.B., 2014. Phytochemical composition and antioxidant, anti-inflammatory and antimicrobial activities of *Juniperus macrocarpa* Sibth. et Sm. J. Funct. Foods . Q20
Masango, P., 2005. Cleaner production of essential oils by steam distillation. J. Clean. Prod. 13, 833–839.
Masotti, V., Juteau, F., Bessière, J.M., Viano, J., 2003. Seasonal and phenological variations of the essential oil from the narrow endemic species *Artemisia molinieri* and its biological activities. J. Agric. Food Chem. 51, 7115–7121.
Mayaud, L., Carricajo, A., Zhiri, A., Aubert, G., 2008. Comparison of bacteriostatic and bactericidal activity of 13 essential oils against strains with varying sensitivity to antibiotics. Lett. Appl. Microbiol. 47, 167–173.
Mehnert, W., Mäder, K., 2012. Solid lipid nanoparticles. Adv. Drug Deliv. Rev. 64, 83–101.
Meyer-Warnod, B., 1984. Natural essential oils: extraction processes and application to some major oils. Perfum. Flavorist 9, 93–104.
Miyashita, M., Sadzuka, Y., 2013. Effect of linalool as a component of *Humulus lupulus* on doxorubicin-induced antitumor activity. Food Chem. Toxicol. 53, 174–179.
Moghimipour, E., Aghel, N., Mahmoudabadi, A.Z., Ramezani, Z., Handali, S., 2012. Preparation and characterization of liposomes containing essential oil of *Eucalyptus camaldulensis* leaf. Jundishapur J. Nat. Pharm. Prod. 7, 117–122.
Moghimipour, E., Ramezani, Z., Handali, S., 2013. Solid lipid nanoparticles as a delivery system for *Zataria multiflora* essential oil: formulation and characterization. Curr. Drug Deliv. 10, 151–157.
Mohammad, H., Eikani, F.G., 2007. Subcritical water extraction of essential oils from coriander seeds (*Coriandrum sativum* L.). J. Food Eng. 80, 735–740. doi:http://dx.doi.org/10.1016/j.jfoodeng.2006.05.015.
Morel, S., Ugazio, E., Cavalli, R., Gasco, M.R., 1996. Thymopentin in solid lipid nanoparticles. Int. J. Pharm. 132, 259–261.
Moyler, D.A., 1993. Extraction of essential oils with carbon dioxide. Flavour Fragr. J. 8, 235–247.
Mozafari, M.R., 2005. Liposomes: an overview of manufacturing techniques. Cell. Mol. Biol. Lett. 10, 711–719.
Muyima, N.Y.O., Zulu, G., Bhengu, T., Popplewell, D., 2002. The potential application of some novel essential oils as natural cosmetic preservatives in an aqueous cream formulation. Flavour Fragr. J. 17, 258–266.
Naima Sahraoui, M.A.V., 2011. Valorization of citrus by-products using microwave steam distillation (MSD). Innov. Food Sci. Emerg. Technol. 12, 163–170.
Nengguo Tao, Q.O., 2014. Citral inhibits mycelial growth of *Penicillium italicum* by a membrane damage mechanism. Food Control 41, 116–121.
Nerio, L.S., Olivero-Verbel, J., Stashenko, E., 2010. Repellent activity of essential oils: a review. Bioresour. Technol. 101, 372–378.
Nishijima, C.M., Ganev, E.G., Mazzardo-Martins, L., Martins, D.F., Rocha, L.R.M., Santos, A.R.S., Hiruma-Lima, C.A., 2014. Citral: a monoterpene with prophylactic and therapeutic anti-nociceptive effects in experimental models of acute and chronic pain. Eur. J. Pharmacol. 736, 16–25.
Nonato, F.R., Santana, D.G., de Melo, F.M., dos Santos, G.G.L., Brustolim, D., Camargo, E.A., de Sousa, D.P., Soares, M.B.P., Villarreal, C.F., 2012. Anti-inflammatory properties of rose oxide. Int. Immunopharmacol. 14, 779–784.
Oussalah, M., Caillet, S., Saucier, L., Lacroix, M., 2006. Antimicrobial effects of selected plant essential oils on the growth of a *Pseudomonas putida* strain isolated from meat. Meat Sci. 73, 236–244.
Oussalah, M., Caillet, S., Saucier, L., Lacroix, M., 2007. Inhibitory effects of selected plant essential oils on the growth of four pathogenic bacteria: *E. coli* O157:H7, *Salmonella typhimurium*, *Staphylococcus aureus* and *Listeria monocytogenes*. Food Control 18, 414–420.
Özel, M.Z., Göğüş, F., Lewis, A.C., 2006. Comparison of direct thermal desorption with water distillation and superheated water extraction for the analysis of volatile components of *Rosa damascena* Mill. using GCxGC-TOF/MS. Anal. Chim. Acta 566, 172–177.
Pardeike, J., Hommoss, A., Müller, R.H., 2009. Lipid nanoparticles (SLN:NLC) in cosmetic and pharmaceutical dermal products. Int. J. Pharm. 366, 170–184.

UNCORRECTED PROOF

Park, K.-R., Nam, D., Yun, H.-M., Lee, S.-G., Jang, H.-J., Sethi, G., Cho, S.K., Ahn, K.S., 2011. β-Caryophyllene oxide inhibits growth and induces apoptosis through the suppression of PI3K/AKT/mTOR/S6K1 pathways and ROS-mediated MAPKs activation. Cancer Lett. 312, 178–188.
Park, S.-N., Lim, Y.K., Freire, M.O., Cho, E., Jin, D., Kook, J.-K., 2012. Antimicrobial effect of linalool and α-terpineol against periodontopathic and cariogenic bacteria. Anaerobe 18, 369–372.
Parshikov, I.A., Netrusov, A.I., 2012. Microbial transformation of antimalarial terpenoids. Biotechnol. Adv. 30, 1516–1523.
Patil, Y.P., Jadhav, S., 2014. Novel methods for liposome preparation. Chem. Phys. Lipids 177, 8–18.
Périno-Issartier, S., Ginies, C., Cravotto, G., Chemat, F., 2013. A comparison of essential oils obtained from lavandin via different extraction processes: ultrasound, microwave, turbohydrodistillation, steam and hydrodistillation. J. Chromatogr. A 1305, 41–47.
Petra Kotnik, M.Š., 2007. Supercritical fluid extraction of chamomile flower heads: comparison with conventional extraction, kinetics and scale-up. J. Supercrit. Fluids 43, 192–198.
Piacentini, E., Giorno, L., Dragosavac, M.M., Vladisavljević, G.T., Holdich, R.G., 2013. Microencapsulation of oil droplets using cold water fish gelatine/gum arabic complex coacervation by membrane emulsification. Food Res. Int. 53, 362–372.
Pidgeon, C., McNeely, S., Schmidt, T., Johnson, J.E., 1987. Multilayered vesicles prepared by reverse-phase evaporation: liposome structure and optimum solute entrapment. Biochemistry (Moscow) 26, 17–29.
Pourmortazavi, S.M., Hajimirsadeghi, S.S., 2007. Supercritical fluid extraction in plant essential and volatile oil analysis. J. Chromatogr. A 2, 24. doi:http://dx.doi.org/10.1016/j.chroma.2007.06.021.
Procede et installation d'extraction sans solvant de produits naturels par micro-ondes, 2015, n.d.
Rezakhanlo, A., Talebi, S.M., 2010. Trichomes morphology of *Stachys lavandulifolia* Vahl. (Labiatae) of Iran. Procedia – Soc. Behav. Sci. Innov. Creat. Educ. 2, 3755–3763.
Richard, H., 1999. Epices et aromates. TEC Publications, Paris, Apria.
Riella, K.R., Marinho, R.R., Santos, J.S., Pereira-Filho, R.N., Cardoso, J.C., Albuquerque-Junior, R.L.C., Thomazzi, S.M., 2012. Anti-inflammatory and cicatrizing activities of thymol, a monoterpene of the essential oil from *Lippia gracilis*, in rodents. J. Ethnopharmacol. 143, 656–663.
Rodea-González, D.A., Cruz-Olivares, J., Román-Guerrero, A., Rodríguez-Huezo, M.E., Vernon-Carter, E.J., Pérez-Alonso, C., 2012. Spray-dried encapsulation of chia essential oil (*Salvia hispanica* L.) in whey protein concentrate-polysaccharide matrices. J. Food Eng. 111, 102–109.
Romanik, G., Gilgenast, E., Przyjazny, A., Kamiński, M., 2007. Techniques of preparing plant material for chromatographic separation and analysis. J. Biochem. Biophys. Methods 70, 253–261.
Rosset, V., Ahmed, N., Zaanoun, I., Stella, B., Fessi, H., Elaissari, A., 2012. Elaboration of Argan oil nanocapsules containing naproxen for cosmetic and transdermal local application. J. Colloid Sci. Biotechnol. 1, 218–224.
Rossi, Y.E., Canavoso, L., Palacios, S.M., 2012. Molecular response of *Musca domestica* L. to *Mintostachys verticillata* essential oil: (4R)(+)-pulegone and menthone. Fitoterapia 83, 336–342.
Rovio, S., Hartonen, K., Holm, Y., Hiltunen, R., Riekkola, M.-L., 1999. Extraction of clove using pressurized hot water. Flavour Fragr. J. 14, 399–404.
Ruben Olmedo, V.N., 2014. Antioxidant activity of fractions from oregano essential oils obtained by molecular distillation. Food Chem. 156, 212–219. doi:http://dx.doi.org/10.1016/j.foodchem.2014.01.087.
Ruzicka, L., 1953. The isoprene rule and the biogenesis of terpenic compounds. Experientia 9, 357–367.
Sadaka, F., Nguimjeu, C., Brachais, C.-H., Vroman, I., Tighzert, L., Couvercelle, J.-P., 2013. WITHDRAWN: review on antimicrobial packaging containing essential oils and their active biomolecules. Innov. Food Sci. Emerg. Technol. 20, 350. doi:http://dx.doi.org/10.1016/j.ifset.2013.01.004.
Sahraoui, N., Vian, M.A., Bornard, I., Boutekedjiret, C., Chemat, F., 2008. Improved microwave steam distillation apparatus for isolation of essential oils: comparison with conventional steam distillation. J. Chromatogr. A 1210, 229–233.
Sališová, M., Toma, š., Mason, T.J., 1997. Comparison of conventional and ultrasonically assisted extractions of pharmaceutically active compounds from *Salvia officinalis*. Ultrason. Sonochem. 4, 131–134.
Santos, D.T., Albarelli, J.Q., Beppu, M.M., Meireles, M.A.A., 2013. Stabilization of anthocyanin extract from jabuticaba skins by encapsulation using supercritical CO_2 as solvent. Food Res. Int. Stab. Phytochem. Process. 50, 617–624.
Schwarz, C., Mehnert, W., Lucks, J.S., Müller, R.H., 1994. Solid lipid nanoparticles (SLN) for controlled drug delivery. I. Production: characterization and sterilization. J. Control. Release 30, 83–96.
Sereshti, H., Rohanifar, A., Bakhtiari, S., Samadi, S., 2012. Bifunctional ultrasound assisted extraction and determination of *Elettaria cardamomum* Maton essential oil. J. Chromatogr. A 1238, 46–53. doi:http://dx.doi.org/10.1016/j.chroma.2012.03.061.
Sherry, M., Charcosset, C., Fessi, H., Greige-Gerges, H., 2013. Essential oils encapsulated in liposomes: a review. J. Liposome Res. 232, 268–275. doi:http://dx.doi.org/10.3109/08982104.2013.819888.
Shi, F., Zhao, J.-H., Liu, Y., Wang, Z., Zhang, Y.-T., Feng, N.-P., 2012. Preparation and characterization of solid lipid nanoparticles loaded with frankincense and myrrh oil. Int. J. Nanomed. 7, 2033–2043.
Shimokawa, K., Saegusa, K., Wada, Y., Ishii, F., 2013. Physicochemical properties and controlled drug release of microcapsules prepared by simple coacervation. Colloids Surf. B Biointerfaces 104, 1–4.
Singh, H.P., Kaur, S., Negi, K., Kumari, S., Saini, V., Batish, D.R., Kohli, R.K., 2012. Assessment of in vitro antioxidant activity of essential oil of *Eucalyptus citriodora* (lemon-scented Eucalypt; Myrtaceae) and its major constituents. LWT – Food Sci. Technol. 48, 237–241.
Singh, P., Shukla, R., Prakash, B., Kumar, A., Singh, S., Mishra, P.K., Dubey, N.K., 2010. Chemical profile, antifungal, antiaflatoxigenic and antioxidant activity of *Citrus maxima* Burm. and *Citrus sinensis* (L.) Osbeck essential oils and their cyclic monoterpene, DL-limonene. Food Chem. Toxicol. Int. J. Publ. Br. Ind. Biol. Res. Assoc. 48, 1734–1740.
Sinico, C., De Logu, A., Lai, F., Valenti, D., Manconi, M., Loy, G., Bonsignore, L., Fadda, A. M., 2005. Liposomal incorporation of *Artemisia arborescens* L. essential oil and in vitro antiviral activity. Eur. J. Pharm. Biopharm. Off. J. Arbeitsgemeinschaft Für Pharm. Verfahrenstechnik E.V. 59, 161–168.
Soto Ayala, R., Luque de Castro, M.D., 2001. Continuous subcritical water extraction as a useful tool for isolation of edible essential oils. Food Chem. 75, 109–113.
Souza, F.V.M., da Rocha, M.B., de Souza, D.P., Marçal, R.M., 2013. (−)-Carvone: antispasmodic effect and mode of action. Fitoterapia 85, 20–24.
Stashenko, E.E., Jaramillo, B.E., Martínez, J.R., 2004. Comparison of different extraction methods for the analysis of volatile secondary metabolites of *Lippia alba* (Mill.) N.E. Brown grown in Colombia, and evaluation of its in vitro antioxidant activity. J. Chromatogr. A 1025, 93–103.
Stevinson, C., Ernst, E., 2000. Valerian for insomnia: a systematic review of randomized clinical trials. Sleep Med . 1, 91–99.
Sutaphanit, P., Chitprasert, P., 2014. Optimisation of microencapsulation of holy basil essential oil in gelatin by response surface methodology. Food Chem. 150, 313–320.
Svoboda, K.P., Greenaway, R.I., 2003. Investigation of volatile oil glands of *Satureja hortensis* L. (summer savory) and phytochemical comparison of different varieties. Int. J. Aromather. 13, 196–202.
Szoka, F., Papahadjopoulos, D., 1978. Procedure for preparation of liposomes with large internal aqueous space and high capture by reverse-phase evaporation. Proc. Natl. Acad. Sci. U. S. A 75, 4194–4198.
Tamara Allaf, V.T., 2012. Instant controlled pressure drop technology and ultrasound assisted extraction for sequential extraction of essential oil and antioxidants. Ultrason. Sonochem. 20, 239–246.
Tang, J., Xu, N., Ji, H., Liu, H., Wang, Z., Wu, L., 2011. Eudragit nanoparticles containing genistein: formulation, development, and bioavailability assessment. Int. J. Nanomed. 6, 2429–2435.
Templeton, W., 1969. An Introduction to the Chemistry of Terpenoids and Steroids. Butterworth.
Tiwari, B.K., Valdramidis, V.P., O'Donnell, C.P., Muthukumarappan, K., Bourke, P., Cullen, P.J., 2009. Application of natural antimicrobials for food preservation. J. Agric. Food Chem. 57, 5987–6000.
Trombetta, D., Castelli, F., Sarpietro, M.G., Venuti, V., Cristani, M., Daniele, C., Saija, A., Mazzanti, G., Bisignano, G., 2005. Mechanisms of antibacterial action of three monoterpenes. Antimicrob. Agents Chemother. 49, 2474–2478.
Turner, G.W., Gershenzon, J., Croteau, R.B., 2000. Distribution of peltate glandular trichomes on developing leaves of peppermint. Plant Physiol. 124, 655–664.
Udaiyar Muruganathan, S.S., 2013. Antihyperglycemic effect of carvone: effect on the levels of glycoprotein components in streptozotocin-induced diabetic rats. J. Acute Dis. 2, 310–315.
Vági, E., Simándi, B., Suhajda, Á., Héthelyi, É., 2005. Essential oil composition and antimicrobial activity of *Origanum majorana* L. extracts obtained with ethyl alcohol and supercritical carbon dioxide. Food Res. Int. 38, 51–57.
Valente, J., Zuzarte, M., 2013. Antifungal, antioxidant and anti-inflammatory activities of *Oenanthe crocata* L. essential oil. Food Chem. Toxicol. Int. J. Publ. Br. Ind. Biol. Res. Assoc..
Valenti, D., De Logu, A., Loy, G., Sinico, C., Bonsignore, L., Cottiglia, F., Garau, D., Fadda, A.M., 2001. Liposome-incorporated santolina insularis essential oil: preparation, characterization and in vitro antiviral activity. J. Liposome Res. 11, 73–90.
Van Vuuren, S.F., du Toit, L.C., Parry, A., Pillay, V., Choonara, Y.E., 2010. Encapsulation of essential oils within a polymeric liposomal formulation for enhancement of antimicrobial efficacy. Nat. Prod. Commun. 5, 1401–1408.
Varona, S., Kareth, S., Martín, Á., Cocero, M.J., 2010. Formulation of lavandin essential oil with biopolymers by PGSS for application as biocide in ecological agriculture. J. Supercrit. Fluids Special Issue – Supercrit. Fluid Process. Biopolym. Biomater. 54, 369–377.
Varona, S., Martín, Á., Cocero, M.J., 2009. Formulation of a natural biocide based on lavandin essential oil by emulsification using modified starches. Chem. Eng. Process. Process Intensif. 48, 1121–1128.
Varona, S., Marti'n, A., Cocero, M.J., 2011. Liposomal incorporation of lavandin essential oil by a thin-film hydration method and by particles from gas-saturated solutions. Ind. Eng. Chem. Res. 50, 2088–2097.
Vian, M.A., Fernandez, X., Visinoni, F., Chemat, F., 2008. Microwave hydrodiffusion and gravity, a new technique for extraction of essential oils. J. Chromatogr. A 1190, 14–17.
Vinatoru, M., 2001. An overview of the ultrasonically assisted extraction of bioactive principles from herbs. Ultrason. Sonochem. 8, 303–313.
Vinjamur, M., Javed, M., Mukhopadhyay, M., 2013. Encapsulation of nanoparticles using CO_2-expanded liquids. J. Supercrit. Fluids Special Issue–10th Int. Symp. Supercrit. Fluids 79, 216–226.

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Wang, L., Weller, C.L., 2006. Recent advances in extraction of nutraceuticals from plants. Trends Food Sci. Technol. 17, 300–312.
Warnke, P.H., Becker, S.T., Podschun, R., Sivananthan, S., Springer, I.N., Russo, P.A.J., Wiltfang, J., Fickenscher, H., Sherry, E., 2009. The battle against multi-resistant strains: renaissance of antimicrobial essential oils as a promising force to fight hospital-acquired infections. J. Cranio-Maxillo-fac. Surg. Off. Publ. Eur. Assoc. Cranio-Maxillo-fac. Surg. 37, 392–397.
Wattanasatcha, A., Rengpipat, S., Wanichwecharungruang, S., 2012. Thymol nanospheres as an effective anti-bacterial agent. Int. J. Pharm. 434, 360–365. doi:http://dx.doi.org/10.1016/j.ijpharm.2012.06.017.
Weber, S., Zimmer, A., Pardeike, J., 2014. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) for pulmonary application: a review of the state of the art. Eur. J. Pharm. Biopharm. Off. J. Arbeitsgemeinschaft Für Pharm. Verfahrenstechnik E.V. 86, 7–22.
Weiss, J., Decker, E.A., McClements, D.J., Kristbergsson, K., Helgason, T., Awad, T., 2008. Solid lipid nanoparticles as delivery systems for bioactive food components. Food Biophys. 3, 146–154.
Wen, Z., Liu, B., Zheng, Z., You, X., Pu, Y., Li, Q., 2010. Preparation of liposomes entrapping essential oil from *Atractylodes macrocephala* Koidz by modified RESS technique. Chem. Eng. Res. Des. 88, 1102–1107.
Wen, Z., You, X., Jiang, L., Liu, B., Zheng, Z., Pu, Y., Cheng, B., 2011a. Liposomal incorporation of rose essential oil by a supercritical process. Flavour Fragr. J. 26, 27–33. doi:http://dx.doi.org/10.1002/ffj.2012.
Wen, Z., You, X., Liu, B., Zheng, Z., Pu, Y., Jiang, L., Li, Q., 2011b. Formation of atractylone liposomes by rapid expansion from supercritical to surfactant solution. Asia-Pac. J. Chem. Eng. 6, 624–630.
Wissing, S.A., Kayser, O., Müller, R.H., 2004. Solid lipid nanoparticles for parenteral drug delivery. Adv. Drug Deliv. Rev. 56, 1257–1272.
Woranuch, S., Yoksan, R., 2013. Eugenol-loaded chitosan nanoparticles. I. Thermal stability improvement of eugenol through encapsulation. Carbohydr. Polym. 96, 578–585.
Wu, Y., Zou, L., Mao, J., Huang, J., Liu, S., 2014. Stability and encapsulation efficiency of sulforaphane microencapsulated by spray drying. Carbohydr. Polym. 102, 497–503.
Ye, H., Shen, S., Xu, J., Lin, S., Yuan, Y., Jones, G.S., 2013. Synergistic interactions of cinnamaldehyde in combination with carvacrol against food-borne bacteria. Food Control 34, 619–623.
Yim, J.-H., Kim, W.-S., Lim, J.S., 2013. Recrystallization of adefovir dipivoxil particles using the rapid expansion of supercritical solutions (RESS) process. J. Supercrit. Fluids 82, 168–176.
Yoshida, P.A., Yokota, D., Foglio, M.A., Rodrigues, R.A.F., Pinho, S.C., 2010. Liposomes incorporating essential oil of Brazilian cherry (*Eugenia uniflora* L.): characterization of aqueous dispersions and lyophilized formulations. J. Microencapsul. 27, 416–425.
Zhen, W., You, X.-K., 2010. Self-assembly of liposomes loading hinesol by rapid expansion from supercritical to surfactant solution 26, 617–621.
Zur Mühlen, A., Schwarz, C., Mehnert, W., 1998. Solid lipid nanoparticles (SLN) for controlled drug delivery–drug release and release mechanism. Eur. J. Pharm. Biopharm. Off. J. Arbeitsgemeinschaft Für Pharm. Verfahrenstechnik E.V. 45, 149–155.

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