
Encapsulation of Essential Oils by Cyclodextrins: Characterization and Evaluation

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Abstract

The essential oils normally had low physicochemical stability and low solubility in water. These facts limit their industrial applications in general and in food formulations particularly. This chapter characterizes the physicochemical properties and the antioxidant and antimicrobial activities of three encapsulated essential oils – guava leaf, yarrow and black pepper essential oils – in hydroxypropyl- β -cyclodextrin (HP β CD).

Keywords: essential oils, cyclodextrins, food technology applications, pharmacological applications, antioxidant activity, antimicrobial activity

1. CDs in food science and food technology

There is much interest in manipulating the complex-forming ability of cyclodextrins (CDs) with a view to developing applications [1–10]. In the last years, several reviews describing the use of CDs in food and flavor applications have been published [5, 6, 11–16]). CDs have been recommended for applications in food processing and as food additives with a variety of aims: (i) to protect lipophilic food components that are sensitive to oxygen and light- or heat-induced degradation; (ii) to solubilize food colorings and vitamins; (iii) to stabilize fragrances, flavors, vitamins, and essential oils against unwanted changes; (iv) to suppress unpleasant odors or tastes and (v) to achieve a controlled release of certain food constituents.

Indeed, CDs form inclusion complexes with a variety of molecules including fats, flavors and colors. For instance, they are used for the removal and masking of undesirable components and

controlled release of desired food constituents [17]. Moreover, CDs are used in food formulations for flavor protection or flavor delivery [18]. Most natural and artificial flavors are volatile oils or liquids, and complexation with CDs provides a promising alternative to the conventional encapsulation technologies for flavor protection. CDs act as molecular encapsulants, protecting the flavor throughout many rigorous food-processing methods such as freezing, thawing and microwaving. β -CD as a molecular encapsulant allows the flavor quality and quantity to be preserved to a greater extent and longer period compared to other encapsulants and provides longevity to the food item [19]. In Japan, CDs have been approved as “modified starch” for food applications for more than two decades, serving to mask odors in fresh food and to stabilize fish oils. One or two European countries—for example, Hungary—have approved γ -CD for use in certain applications because of its low toxicity. It was proved that CDs may alter the sensory profile of a food and the flavor release depends of the CD type [20], the temperature [21] and may depend the solvent nature that is, water, water/alcohol mixtures, etc. [22]. Their beneficial effects essentially derive from the ability to form stable inclusion complexes with sensitive lipophilic nutrients and constituents of flavor and taste, making easy to prepare powdered flavor materials [23–25] and even to release such flavors during cooking [26]. Toxicological data are examined and an assessment of CDs from the standpoint of safety for human consumption is made [27]. Regulations are covered, showing a general trend toward a wider acceptance of CDs as food additives. The growing health consciousness of consumers and expanding market for functional foods and nutraceutical products are opening up to CDs a promising future in food industry [11].

The complexation of CDs with sweetening agents such as aspartame stabilizes and improves the taste. It also eliminates the bitter aftertaste of other sweeteners such as stevioside, glycyrrhizin and rubusoside. CD itself is a promising new sweetener. Enhancement of flavor by CDs has been also claimed for alcoholic beverages such as whisky and beer [28]. The bitterness of citrus fruit juices is a major problem in the industry caused by the presence of limonoids (mainly limonin) and flavonoids (mainly naringin). Cross-linked CD polymers are useful to remove these bitter components by inclusion complexation [29]. CDs are also used to control bitterness in tannins, plant and fungal extracts; skim milk hydrolyses and overcooked tea and coffee [30]. They can also be used to keep the profile of oil volatiles in paste samples that were vacuum- or spray-dried [31, 32], due to their high encapsulation efficiency. The most prevalent use of CD in process aids is the removal of cholesterol from animal products such as eggs or dairy products, like cheese [33]. CD-treated material shows 80% removal of cholesterol. Free fatty acids can also be removed from fats using CDs, thus improving the frying property of fat (e.g., reduced smoke formation, less foaming, less browning and deposition of oil residues on surfaces) [30]. Fruits and vegetable juices are also treated with CD to remove phenolic compounds, which cause enzymatic browning. In juices, polyphenol oxidase converts the colorless polyphenols to colored compounds and addition of CDs removes polyphenoloxidase from juices by complexation. Sojo et al. [34] studied the effect of CDs on the oxidation of *o*-diphenol by banana polyphenoloxidase and found that CDs act as activator as well as inhibitor. By combining 1–4% CD with chopped ginger root, Sung [35] established that it could be stored in vacuum at cold temperature for 4 weeks or longer without browning or rotting.

Other studies describes the development of a gas chromatography-mass spectrometry (GC-MS) library to identify optically active compounds in the flavor and fragrance field using enantioselective GC with CD derivatives (CDs) as chiral selectors in combination with MS

[36, 37], but also olfactometry can be used for detection to have extra information about flavors [38]. The ability to separate and quantitate enantiomers at low levels should be useful for detecting adulterated products, for evaluating fermentation processes and for the accurate characterization of enantiomeric flavor components, growth regulators, pesticides, and herbicides as well as their chiral environmental degradation products and metabolites [39].

Flavonoids and terpenoids are good for human health because of their antioxidative and antimicrobial properties but they cannot be utilized as foodstuff owing to their very low aqueous solubility and bitter taste. Sumiyoshi [40] discussed the improvement of the properties of these plant components (flavonoids and terpenoids) with CD complexation. CDs are used in preparation of foodstuffs in different ways. For example, highly branched CDs are used in flour-based items like noodles, pie dough, pizza sheets and rice cakes to impart elasticity and flexibility to dough [41]. They are also used in the preparation of antimicrobial food preservatives containing trans-2-hexanal in apple juice preparation [42] and in the processing of medicinal mushrooms for the preparation of crude drugs and health foods. CDs are used in the preparation of controlled release powdered flavors and confectionery items and are also used in chewing gum to retain its flavor for longer duration, a property highly valued by customers [43]. CDs are also used in the detection of aflatoxin in food samples [44].

A large variety of commercial encapsulation practices are currently followed, however, those involving the formation of flavor/CD molecular-inclusion complexes offer great potential for protection of volatile and labile flavoring materials present in a multicomponent food system throughout many rigorous food-processing methods (cooking, pasteurization, etc.) [14, 45–47]. In the same way, CDs can eliminate some taste. In fact, a bitter taste is the main reason for the rejection of various food products although exceptions to this rule are rooted in many cultures: in some foods and beverages, such as coffee, beer, and wine, a certain degree of bitterness is expected [2, 48–51]. Bitterness, however, has proved a major limitation in the acceptance of commercial citrus juices. A commercial process is needed that removes bitter components without adding anything to the juice, while still maintaining the expected flavor and nutritional value of the product. CDs can be used for the removal or masking of undesirable components. Some foods have a peculiar smell, but, when CDs are added in their manufacture, these components form CD-inclusion complexes deodorizing the result product. For instance, this process is used for deodorizing soybean milk and soy protein, and also for removing the peculiar fish odors, seafood and meat products [52–54]. On the other hand, the formation of inclusion complexes with CDs can protect some lipophilic food components that are sensitive to oxygen and heat- or light-induced degradation [55]. In addition, CDs protected phenolic compounds from enzymatic oxidation by forming inclusion complexes [56–59].

2. Essential oils

Both *in vitro* and *in vivo* studies have demonstrated the important applications of essential oils, such an antioxidant or antibacterial activity, even antitumor or anti-inflammatory, with important technological applications in food science and pharmacology [60–64]. Indeed the presence of eugenol, carvacrol or thymol as main component of these oils guarantee their properties both antioxidants and antibiotics (**Figure 1**).

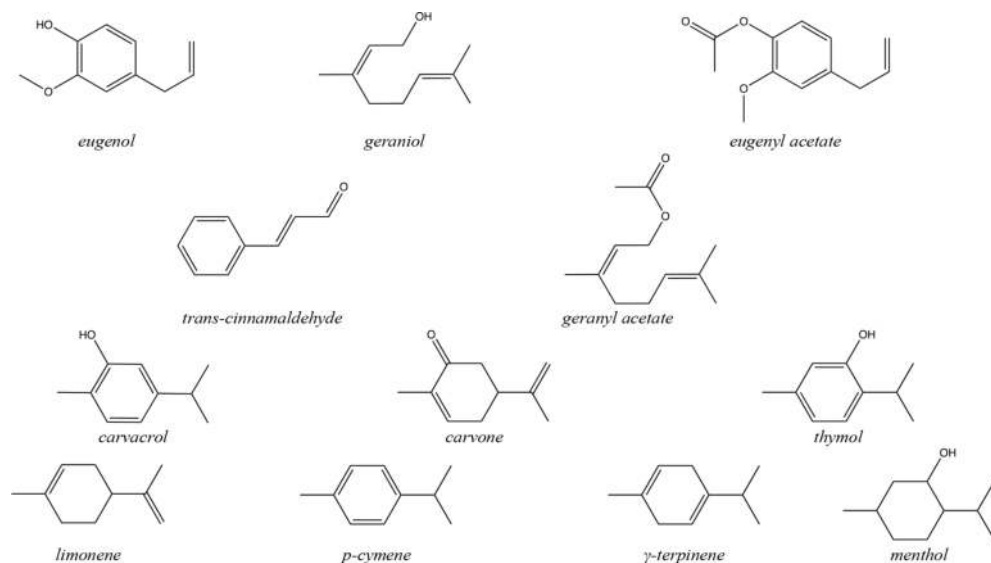


Figure 1. Main components of essential oils [60].

As example, in the present chapter we have selected some essential oils to characterize their inclusion complex in (hydroxypropyl- β -CD) (Figure 2). They were black pepper essential oil, guava essential oil and yarrow essential oil.

Black pepper (*Piper nigrum* L.) is considered the king of spices because of its pungent of piperine [65]. It can be used for different purposes such as medicine, human dietaries, preservatives and bio control agents [65–67]. It has been already reported that essential oil from black pepper possess antioxidant [68] and antimicrobial activities [69]. Black pepper oil is basically composed of terpenes, which have been found to be β -caryophyllene, limonene, δ -3-carene and pinene (Figure 3) [68, 70]. The major composition of black pepper oil was found to be β -caryophyllene [68, 70]. Nevertheless, some active compounds in essential oils are sensitive toward the chemical modification under effect of some external factors such as temperature, light, oxygen, etc. [71]. Besides, to apply in foods, an extremely low flavor threshold of essential oils can drastically change the sensory properties of foods, and highly water insoluble may have limited contact with pathogens [72].

Guava (*Psidium guajava* L.) has been used as a traditional medicine because of its biological properties [73–75]. Essential oil from guava leaves contains several bioactive compounds, which are responsible for anti-proliferation, antioxidant and antimicrobial activities [76, 77]. Limonene, β -caryophyllene, 1,8-cineole and α -pinene are the major constituents (Figure 4) [78, 79]. However, essential oils have some limitations for food applications. Their low solubility in water limits contact with food pathogens in aqueous matrices [72]. Besides, some active compounds in essential oils are sensitive to chemical modifications under the effect of external factors such as temperature, light or oxygen [71].

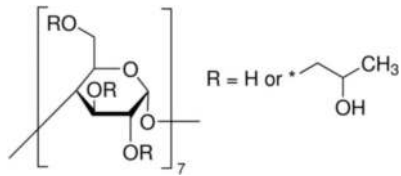


Figure 2. (2-Hydroxypropyl)- β -CD.

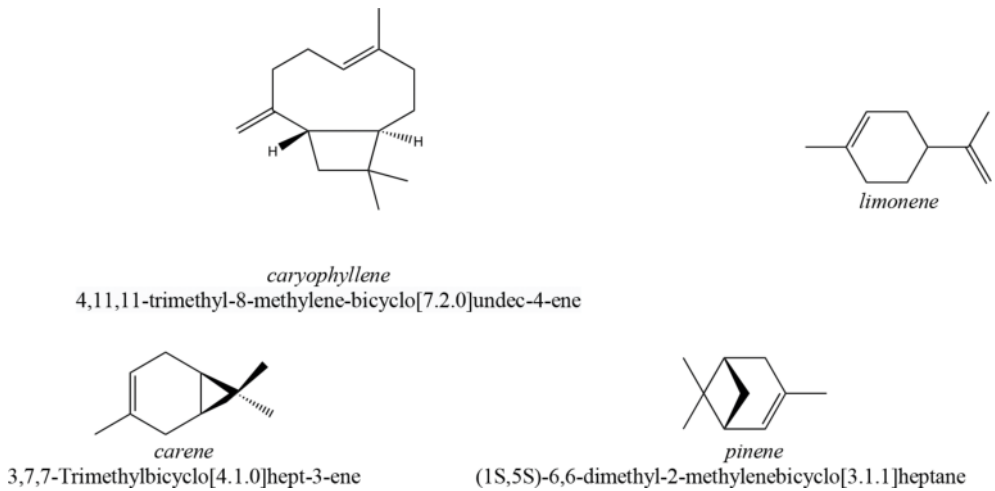


Figure 3. Main components of black pepper [68, 70].

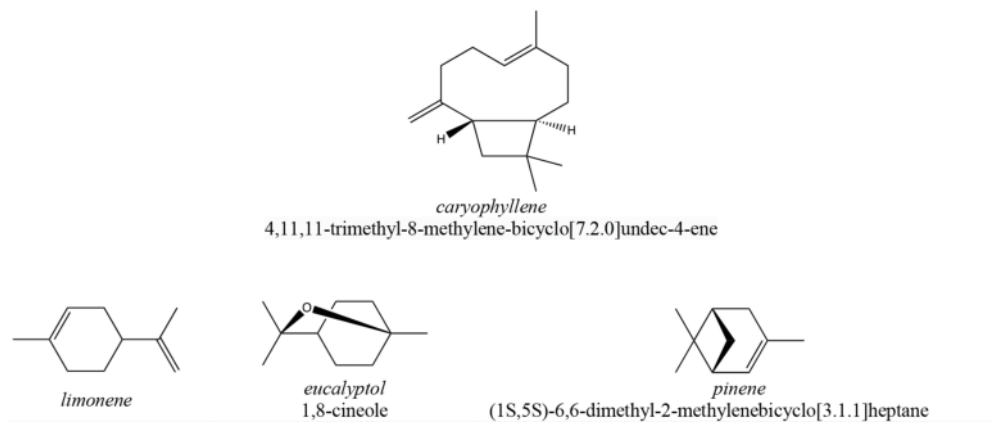


Figure 4. Main components of guava [78, 79].

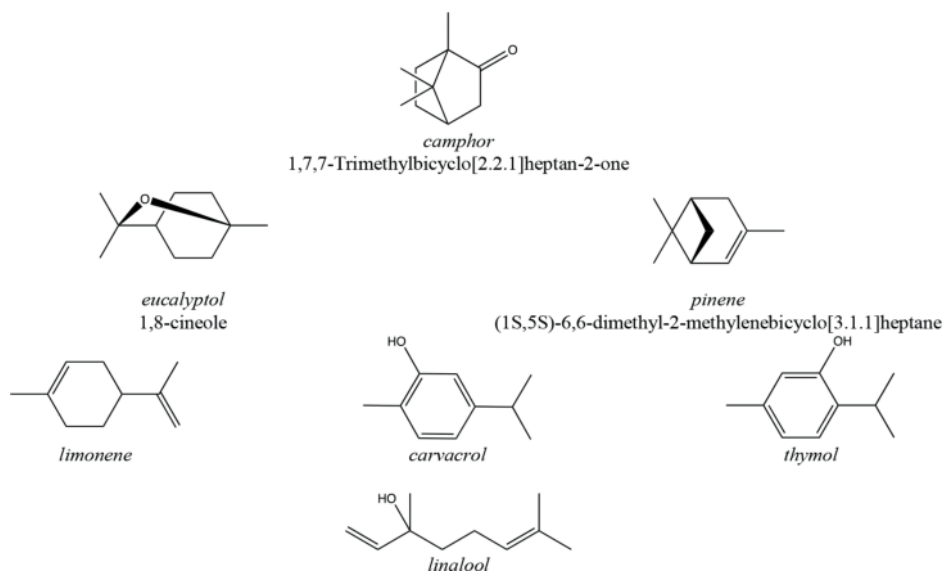


Figure 5. Main components of yarrow [87].

Yarrow (*Achillea millefolium* L. s. l.) has a broad spectrum of pharmacological activities. It is widely used in folk medicine [80]. In Europe, it has been used as a remedy to treat digestive problems, diabetes, hepatic-biliary diseases, amenorrhea, and consumed for its antitumor and anti-inflammatory properties [81–83]. In addition, antimicrobial and antioxidant properties of yarrow have also been reported [84–86]. Chemical components of yarrow essential oil have been found to be carvacrol, linalool, 1,8-cineole, camphor and thymol was mostly found as a major component (Figure 5) [87]. However, some active chemical components of yarrow oil (such as carvacrol and thymol) are sensitive to environmental factors such as, light, oxygen and temperature. Encapsulation of yarrow essential oil could offer possible solutions for the limitation.

3. CDs and essential oils

The use of CDs for the essential oils encapsulation can protect the active compounds of essential oils from environmental conditions [13, 14] and improve the aqueous solubility of essential oils for increasing their capacity to functionalize the products in which it is used as additive [88]. As quote above, CDs are cyclic oligosaccharides consisting of glucopyranosyl units linked by α -(1,4) bonds [89]. The widely used natural CDs are α -, β - and γ -CD consisting of 6, 7 and 8 glucopyranose units, respectively [90, 91]. These molecules have a unique structure with a hydrophobic cavity and a hydrophilic surface, which can form inclusion complex with a wide variety of guests. They can be used to enhance the solubility of insoluble compounds,

stabilize labile guests against oxidation, control volatility and sublimation, modify taste by masking off flavors, entrap odors and control the releasing of drugs and flavors [92]. Among those CDs, β -CD is the most widely applicable kind because of its suitable cavity size for common guests with molecular weights between 200 and 800 g/mol and its availability and reasonable price [93]. Although β -CD can be used with many guests, its solubility in water is low (1.8 g in 100 mL water at 25°C). In some cases, there is a need to enhance water solubility of β -CD by adding the hydroxyl-alkyl groups on the β -CD surface. A hydroxyl-alkylated or hydroxypropyl- β -CD derivative (HP β CD) is relatively high aqueous solubility (above 60 g in 100 mL water at 25°C) with low toxicity and satisfactory inclusion ability [94].

On the other hand, encapsulation of essential oils or their chemical components with CDs or CD derivatives for improvement of biological properties have been observed [5, 95–98] or their antimicrobial activity [99].

Indeed, a large amount of contributions about technologic applications of CD-inclusion complex of essential oils and their main components has been published in the last 10 years, some of them are included in **Table 1**.

Essential oil	Guest	References	Essential oil component	Guest	References
Black pepper essential oil	Hydroxypropyl- β -CD	[100]	Allyl isothiocyanate	α -CD	[101]
Cinnamon essential oil	β -CD	[99, 102, 103]	Allyl isothiocyanate	β -CD	[101, 104]
Citronella oil	β -CD	[105]	Barbigerone	Hydroxypropyl- β -CD	[106]
Clove bod oil	β -CD	[99, 107]	Carvacrol	β -CD	[108, 109]
Coriander essential oil	β -CD	[71]	Carvacrol	Hydroxypropyl- β -CD	[110]
Garlic oil	β -CD	[102, 111]	Cinnamaldehyde	β -CD	[99, 103]
Guava leaf oil	Hydroxypropyl- β -CD	[112]	Citronellal	β -CD	[105]
Lemon oil	β -CD	[113]	Citronellol	β -CD	[105]
Olive leaf oil	β -CD	[114]	Eugenol	β -CD	[99, 115–118]
Oregano essential oil	β -CD	[107, 119]	Limonene	β -CD	[120]
Thyme essential oil	β -CD	[121, 122]	2-Nonanone	β -CD	[123]
Sweet basil essential oils	β -CD	[124]	Thymol	β -CD	[103, 109, 121]
Yarrow essential oil	Hydroxypropyl- β -CD	[125]	Vanillin	β -CD	[126, 127]

Table 1. Contributions about host-guest complex formation between CDs and CDs derivatives and essential oils.

3.1. Encapsulation efficiency

As quoted above, we present the encapsulation efficiency of three essential oils (guava oil, yarrow oil and black pepper oil) in hydroxypropyl- β -CD (HP β CD).

In the case of yarrow oil and carvacrol (yarrow oil major component), their efficiency were 45.05 and 86.59%, respectively [125] see **Table 2**. Black pepper [100] exhibit similar behavior with efficiency of 50.55 and 85.30, respectively, for essential oil and its main component (β -caryophyllene). Finally, guava leaf oil encapsulation efficiency was 52.5%, while it reached 91.8% for limonene, the major pure compound of guava leaf oil [112].

This difference in encapsulation efficiency of the pure compound and the essential oil results from the presence of other minority components. In the case of yarrow oil and carvacrol [125], the other components like 1,8 cineole, thymol, camphor and linalool have also high affinities for CD [6, 121, 128–132] that compete for inclusion complex formations. Kamimura et al. [110] reported that the encapsulation efficiency values of pure carvacrol in HP β CD prepared by kneading and freeze-drying methods were around 78 and 84%, respectively.

Similar explanation would justify the differences in encapsulation efficiency of the pure compound and the black pepper oil [100] because the presence of other components in the black pepper oil such as limonene, δ -3-carene and pinene [68] that also have high affinities for HP β CD. In the case of guava leaf oil [112], the large values found are due to minority components, such as β -caryophyllene, 1,8-cineole and α -pinene, exhibit low affinity for the β -CD that are not easily encapsulated and the competition between the other host for the guest is not so important.

Similar observation has been reported for other authors in the literature [99] showing that encapsulation efficiencies of cinnamon oil and clove oil were 41.72 and 77.74%, respectively. The encapsulation efficiencies of major components including trans-cinnamaldehyde in cinnamon oil and eugenol in clove oil were also examined and showed higher encapsulation efficiency of 84.70 and 90.15%, respectively. In addition, comparable values of encapsulation efficiency were found in other carriers such as alginate-chitosan system. In this case, the yarrow oil components exhibited 82.4% efficiency of polyphenol encapsulation [133, 134].

Compound	Encapsulation efficiency (%)	Compound	Encapsulation efficiency (%)
Black pepper oil	50.55	β -caryophyllene	85.30
Yarrow oil	45.05	Carvacrol	86.59
Guava leaf oil	52.50	Limonene	91.80
Cinnamon oil	41.72	Cinnamaldehyde	84.70
Clove oil	77.74	Eugenol	90.15

Table 2. Encapsulation efficiency value in HP β CD.

3.2. Characterization of host-guest complex

3.2.1. Morphological examinations

It is well known that the inclusion complex formation would change the morphology of CDs [135]. **Figure 6** presents the morphology of the encapsulated oils studied by SEM.

The particle shape and morphology of the encapsulated oil were similar to those of free HP β CD in the cases evaluated – guava, yarrow and black pepper – see **Figure 7**. It indicates the hydrogen bonding of the free HP β CD molecules interact with each other in solution producing the cluster of HP β CD [136, 137]. This case not occurs in inclusion complex because inclusion complex formation also induces the conformation change of CD and obstructs the agglomeration among them. Similar observations have been previously reported that the distribution of inclusion complex of carvacrol and β -CD, and the gathering of free β -CD were also found [135].

By contrast, the free HP β CD particle sizes are much larger than those of the encapsulated products. These results are in agreement with Guimaraes et al. [135], who analyze carvacrol encapsulation with β -CD. Considering that HP β CD form clusters in solution through intermolecular hydrogen bonds [136, 137], it seems that the incorporation of different essential oils interferes in these interactions and reduces particle size.

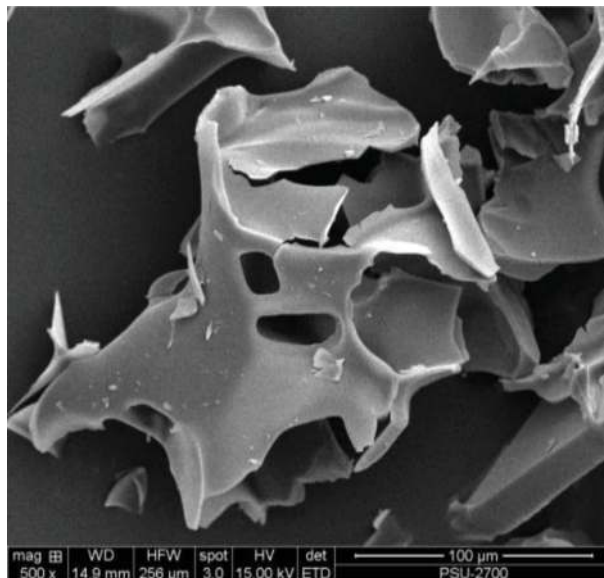


Figure 6. SEM micrographs of free HP β CD at 500 times magnification.

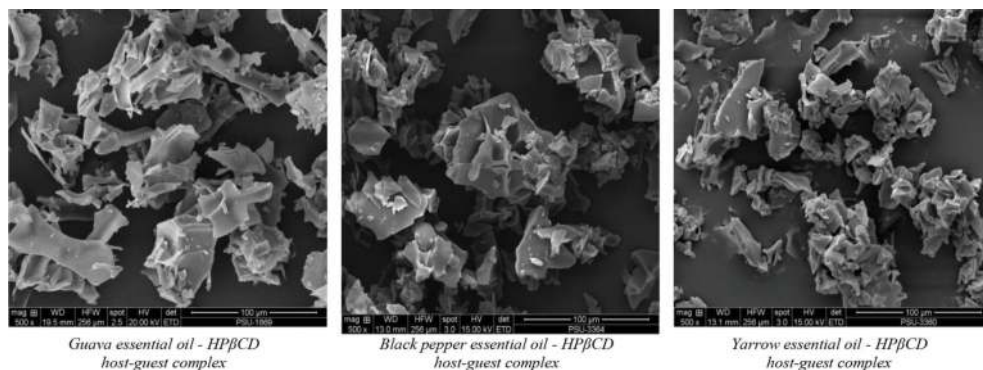


Figure 7. SEM micrographs of encapsulated essential oils at 500 times magnification.

3.2.2. Fourier-transform infrared spectroscopy (FT-IR)

FT-IR technique can be used to investigate the variation of shape, intensity and position of peaks [138].

FT-IR spectrum of black pepper oil consisted of the prominent absorption bands at 2954, 2923 and 2865 cm^{-1} for C–H stretching vibration of methylene group, 1638 cm^{-1} for H–O–H bending, 1447 cm^{-1} for C–H scissoring vibration, 1369 cm^{-1} for symmetrical deformation vibration of CH_3 , 886 cm^{-1} for C–H deformation vibration and 789 cm^{-1} for S–C absorption. However, FT-IR spectrum of the encapsulated black pepper oil showed that no character similar to the free black pepper oil. All bands of black pepper oil spectrum were totally obscured by HP β CD bands it was possible that black pepper oil entered the cavity of HP β CD and inclusion complex was formed.

In the case of yarrow oil, its FT-IR spectrum of yarrow oil shows prominent absorption bands at 2956 cm^{-1} for $=\text{CH}_2$ symmetrical stretching vibration, 2926 cm^{-1} for C–H stretching vibration of methylene group, 2869 cm^{-1} for –CH stretching, 1652 cm^{-1} for H–O–H bending, 1626 cm^{-1} for C=C stretching vibration of the allyl group, 1446 cm^{-1} for C–H scissoring vibration, 1380 cm^{-1} for symmetrical deformation vibration of $-\text{CH}_3$, 1366 cm^{-1} for symmetrical deformation vibration of $-\text{CH}_3$, 1240 cm^{-1} and 1103 cm^{-1} for P–O and P=O, 1022 cm^{-1} for C–O–C stretching vibration, 916 cm^{-1} for C–S–C stretching vibration, 875 cm^{-1} and 865 cm^{-1} for C–H bending of aromatic ring. The spectrum of HP β CD shows prominent absorption bands at 3406 cm^{-1} for O–H stretching vibration, 2970 cm^{-1} for $=\text{CH}_2$ symmetrical stretching vibration, 2930 cm^{-1} for C–H stretching vibration, 1646 cm^{-1} for H–O–H bending vibration, 1157 cm^{-1} for C–O–C asymmetrical stretching vibration, 1083 cm^{-1} and 1033 cm^{-1} for symmetric C–O–C stretching vibration [139]. FT-IR spectrum of inclusion complex was identical to HP β CD and no feature similar to yarrow oil. The results indicated that HP β CD covered all the absorption bands of yarrow oil in the spectrum of inclusion complex indicating the entering to the cavity of HP β CD and the formation of inclusion complex.

Finally, FT-IR spectrum of guava leaf oil showed prominent absorption bands at 2921 cm^{-1} for C–H stretching vibration of methylene group, 1642 cm^{-1} for H–O–H bending, 1447 cm^{-1} for C–H scissoring vibration, 1376 cm^{-1} for symmetrical deformation vibration of CH₃, 886 cm^{-1} for C–H deformation vibration and 789 cm^{-1} for S–C absorption. FT-IR spectrum of encapsulated guava leaf oil shows no feature similar to the free guava oil. The bands of guava leaf oil spectrum were almost completely concealed by very intense and broad bands of HP β CD. However, the absorption band at 608 cm^{-1} of HP β CD disappeared in encapsulated guava leaf oil. This change may be related to the interaction between guava leaf oil and HP β CD in the inclusion complex.

The inclusion complex formation of β -CD was also investigated by Liu et al. [140] using FT-IR analysis. The absorption bands of β -caryophyllene were not detected in the spectrum of inclusion complex. The changes were related to the inclusion complex formation of β -CD and the guests which whole of guest could be contained in the CD cavity. Wang et al. [139] have reported similar results. In their study, the inclusion complex formation of soybean lecithin and β -CD was determined by FT-IR. All the absorption bands of soybean lecithin encapsulated in β -CD were obscured by β -CD spectrum showing that inclusion complex of β -CD and soybean lecithin was formed. However, Gomes et al. [141] reported that the absorption band at 1738 cm^{-1} of the red bell pepper pigments was observed after encapsulation in β -CD indicating that some region of the encapsulated molecules was not contained in the cavity of β -CD.

3.2.3. Ultraviolet-visible spectrophotometry (UV-Vis)

Essential oils contain various bioactive chemicals, which adsorb ultraviolet (UV) or visible light (Vis) at different wavelengths. CD host-guest complex formation would alter UV-Vis absorption spectra [142]. Otherwise, the spectra of the guests appear in line of CD [140]. Therefore, UV-Vis spectrophotometry, evaluated the inclusion complex formation of HP β CD and the three essential oils. The UV absorption spectra of guava leaf oil, limonene and their inclusion complexes were compared. Indeed, maximum absorption value of guava leaf oil was at 214.5 nm , which was mainly attributed to limonene. The absorption peak at 205 nm corresponds to β -caryophyllene and/or pinene. The peak at 275 nm of guava leaf oil was ascribed to 1,8-cineole.

The spectra of the physical mixture of HP β CD with guava leaf oil and with limonene before complexation were consistent with that of guava leaf oil or pure compound. The absorption spectra of the physical mixture of HP β CD with guava leaf oil and with limonene were in accordance to with the spectra of guava leaf oil and pure limonene, respectively. When the active compounds in essential oil or the pure compound were encapsulated into the cavity of HP β CD, the absorption peaks of each compound disappeared in the spectra of the inclusion complexes. To recover active compounds encapsulated in the HP β CD cavity, the active compounds were extracted from HP β CD by dissolving the inclusion complexes in 95% acetonitrile. The encapsulated compounds were released from the cavity of HP β CD and HP β CD was separated from guava leaf essential oil or limonene in solution by centrifugation. The solution was diluted 100 times with acetonitrile and the absorbance was measured by UV spectrophotometer.

After extraction from the inclusion complexes, the absorption peaks of encapsulated compounds in guava leaf oil could be observed. In this line, besides limonene, the absorption peaks at 205 and 275 nm suggested the presence of β -caryophyllene and 1,8-cineole, respectively. The results indicated that the active compounds in guava leaf oil had formed inclusion complex with HP β CD. Therefore, the chemical components of guava leaf oil were successfully encapsulated in the HP β CD.

UV spectrum of yarrow oil shows peaks at 270–275 nm indicated the presence of carvacrol, 1,8-cineole, thymol and camphor. A minor peak at 243 nm attributed to linalool. The spectra of the physical mixture of HP β CD with yarrow oil and with pure compound (carvacrol) conformed to UV spectra of yarrow oil and pure carvacrol, respectively. When the active compounds in yarrow oil or carvacrol were entrapped with HP β CD, the absorption peaks of each compound also disappeared in the spectrum of the inclusion complexes.

After extraction from the inclusion complex, the absorption peaks of entrapped compounds in yarrow oil appeared at 270–275 nm implying carvacrol and also are 1,8-cineole, thymol, camphor and linalool. In this study, the chemical components of yarrow oil were successfully entrapped in the HP β CD, as in the previous case. However, the encapsulation efficiency of yarrow oil was much lower than those of its pure compound. This was likely because the competition of major active compound among other components in essential oil has occurred during inclusion complex formation.

Finally, the absorption spectrum of black pepper oil was recorded with absorption peaks at 200, 205 and 214.5 nm for δ -3-carene, β -caryophyllene and limonene, respectively [140]. The maximum absorption peak at 205 nm was ascribed to β -caryophyllene. The spectra of the physical mixture of HP β CD with black pepper oil and with β -caryophyllene accorded with UV spectra of black pepper oil and pure β -caryophyllene, respectively. When the active compounds in black pepper oil or the pure compound (β -caryophyllene) were entrapped into the cavity of HP β CD, the absorption peaks of the compounds also disappeared in the spectrum of the inclusion complex.

After extraction from the complex, the observable peaks of entrapped compounds in black pepper oil could be seen. The spectrum of encapsulated compounds from black pepper oil show absorption peaks at 205 and 214.5 nm indicating β -caryophyllene and limonene, respectively. The UV spectrum indicated that the chemical components of black pepper oil were successfully entrapped in the HP β CD. As in the previous cases, the encapsulation efficiency of active compounds of black pepper oil was much lower than those of its pure compound. This was likely because the competition of major active compound among other components in black pepper oil has occurred during inclusion complex formation.

3.2.4. Phase solubility

Phase solubility study is generally performed to evaluate the stability and to classify the inclusion complex when they are in the solution. The phase solubility profiles can be obtained from the interaction between the guests (encapsulated compounds) and the hosts (CDs or derivatives) in the solution. In solution, a fundamental parameter such as stability constant (K_s) of inclusion complex formation can be used to evaluate the stability of the inclusion complex [143] – see **Table 3**.

Inclusion complex	T/°C	K_s/M^{-1}	Inclusion complex	T/°C	K_s/M^{-1}
Black pepper oil-HP β CD	25	104.5	β -caryophyllene-HP β CD	25	132.8
Black pepper oil-HP β CD	35	100.0	β -caryophyllene-HP β CD	35	114.0
Guava leaf oil-HP β CD	25	25.0	Limonene-HP β CD	25	628.0
Guava leaf oil-HP β CD	35	33.8	Limonene-HP β CD	35	605.9
Yarrow oil-HP β CD	25	106.6	Carvacrol-HP β CD	25	360.9
Yarrow oil-HP β CD	35	92.0	Carvacrol-HP β CD	35	309.7

Table 3. Phase solubility parameters and stability constants (K_s) of encapsulated essential oil and their main component.

In the case of black pepper, A linear relationship between the amount of dissolved essential oil or β -caryophyllene and the concentrations of HP β CD in this study with slope <1 was classified as a typical A_L -type (type A reveals an inclusion complex formation where the amount of encapsulated compounds increase as the HP β CD concentration increases, subscript L indicates a 1:1 molecular ratio formation of soluble complexes) [144]. As the majority of encapsulated compounds are mono- and sesquiterpenoids and phenylpropane derivatives of an average molecular weight of 120–160 g/mol, a 1:1 complex formation is observed [16]. The molar ratio of host to guest molecules is usually 1:1 for inclusion complexes formed in solution, except for complexes with long-chain or bifunctional guest molecules (e.g. guest molecules having two aromatic rings on opposite sides of a small central molecule segment). In aqueous system, black pepper oil and β -caryophyllene show difference in stability of complex form with the K_s of 104.5 and 132.8 L/mol at 25°C, respectively. This might be because of the other components in black pepper oil might compete to HP β CD form complex with β -caryophyllene. The decreases in K_s values with increasing temperatures were expected for exothermic processes [99].

Equivalent results were observed for yarrow oil host-guest complex, as we can observe in **Table 3**. In agreement with the results reported in **Table 3** – for black pepper essential oil and yarrow essential oil – similar Hill et al. [99] and Kamimura et al. [110] have reported observations. The water solubility of trans-cinnamaldehyde, eugenol, cinnamon bark extracts and clove bud extract samples increased with increasing temperatures while the K_s value of the samples decreased with increasing temperature [99]. Kamimura et al. [110] reported that water solubility of the pure carvacrol increased and the K_s value decreased with increasing temperatures.

Regarding to guava leaf essential oil – see **Table 3**, low K_s value were obtained for guava leaf oil than for limonene. They were in the order of those for β -CD complexes according to Connors [145]. This might be due to the competence of the other components in guava leaf oil with limonene to form HP β CD complexes. In addition, the decrease in K_s values with increasing temperature reflects that complex formation is an exothermic process [99]. However, these results reflect that the aqueous solubility of guava leaf oil can be increased with increasing HP β CD concentration. Considering that very labile complexes ($K_s < 100$ L/mol) result in premature release of the guests because of the weak interaction between hosts and guests [92], the very labile encapsulated guava leaf oil could be useful for fast release systems such as pharmaceutical applications.

3.3. Evaluation of antioxidant activity of host-guest complex

Antioxidant activity was evaluated in terms of DPPH scavenging capacity (%) of free and encapsulated guava leaf oil compared to a synthetic chemical antioxidant (BHT) at concentrations ranged from 5 to 50 $\mu\text{g/mL}$.

It was established that the components responsible for the antioxidant activity of guava leaf oil are limonene, α -pinene and β -caryophyllene [146]. While limonene has a moderate antioxidant activity [147], β -caryophyllene and α -pinene show weak and moderate DPPH scavenging activity, respectively [146, 147]. Unfortunately, the encapsulated guava leaf oil gave slightly lower DPPH scavenging activity than that of the free guava leaf oil. This could be because HP β CD blocks the functional groups of the active compounds that react with DPPH radicals [110].

In the case of yarrow oil carvacrol as a major component shows strong antioxidant activity (72% DPPH scavenging at 50 $\mu\text{g/mL}$). The most effective antioxidants usually contain aromatic or phenolic rings, which interrupt the free radical chain reaction by donating $\text{H}\bullet$ to the free radicals [148]. The encapsulated yarrow oil gave slightly lower antioxidant activity than the activity of the free yarrow oil. It was a result of the HP β CD was blocking the functional groups of active compounds during reacting with DPPH radicals [110]. However, the encapsulation has been reported to increase the stability of the essential oils [13, 14].

Black pepper oil shows antioxidant activity with 54% DPPH scavenging (50 $\mu\text{g/mL}$ black pepper oil) (**Figure 5**). It was established that the components responsible for the antioxidant activity are β -caryophyllene, limonene and α -pinene [146]. β -caryophyllene, a major component of black pepper oil, was found to give a weak DPPH scavenging activity [146]. Limonene, a minor composition, has been reported to give a moderate antioxidant activity and another component, α -pinene, also possesses a moderate antioxidant property [147]. It should be noted that free HP β CD did not show antioxidant activity.

However, the inclusion complexes have been reported to increase the stability of the essential oils [13, 14]. After exposure to sunlight, the DPPH scavenging of free guava leaf oil drastically decreased around 43–54% at all tested concentrations (5–50 $\mu\text{g/mL}$), which was likely due to limonene and pinene sensitive to sunlight [149]. Then, the inclusion complexation of guava leaf oil with HP β CD could protect the active components against the effect of light. In effect, after sunlight exposure, the DPPH radical scavenging capacity of the encapsulated guava leaf oil was more stable than the free guava leaf oil by 26–38%.

Similar results were found for yarrow essential oil, where DPPH radical scavenging (with concentration range from 5 to 35 $\mu\text{g/mL}$ of essential oil) decreased around 41–51% after exposure to sunlight for 12 h. The yarrow oil with higher concentration range (40–50 $\mu\text{g/mL}$) exhibited lower loss of DPPH radical scavenging (36–37%). Obviously, as in the previous case, the encapsulation of yarrow oil in HP β CD could protect the active components against the effect of sunlight. The complexation with HP β CD improved the stability of yarrow oil by 27–30% in a similar range that guava leaf oil (26–38% -*vide supra*).

The DPPH radical scavenging capacity of black pepper oil drastically decreased after 12 h exposure to sunlight (**Figure 4**). At the sample concentration range of 5–25 $\mu\text{g/mL}$, the DPPH

scavenging capacity decreased around 42–48%, while the decreasing of 30–39% was found at higher concentration range (30–50 µg/mL). The stability of encapsulated black pepper oil was improved from the free black pepper oil by 18–24%. This effect is lower that observed for guava and yarrow essential oils (26–38 and 27–30%, respectively).

3.4. Evaluation of antibacterial activity of host-guest complex

Table 4 shows minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values of essential oil for *Staphylococcus aureus* and *Escherichia coli*.

Guava leaf oil displayed antibacterial activity against both bacteria with MIC value of 500 µg/mL, that could be attributed to guava leaf oil monoterpenes (such as limonene) which have been found to play efficient role in antimicrobial activity via membrane structures increasing membrane fluidity and permeability [150]. Pure limonene was reported to give antimicrobial activity against *S. aureus* and *E. coli* with MIC values of 8.0 and 10.0 µg/mL, respectively [151].

The antibacterial activity of guava leaf oil was improved after encapsulation in HPβCD by 4 and 2 times against *S. aureus* and *E. coli*, respectively. It has been reported that inclusion complexes with HPβCD could increase aqueous solubility of the encapsulated guests, thus improving the antimicrobial efficiency of essential oils at lower concentrations [99] due to a better accessibility of the active compounds to cells [111].

Yarrow oil exhibited antibacterial activity against *S. aureus* and *E. coli* with the MIC values of 250 µg/mL and 500 µg/mL, respectively. The antimicrobial activity of yarrow essential oil might be because its oxygenated phenolic compounds, such as carvacrol and thymol, have been reported to give strong antimicrobial activity. These compounds were found to increase membrane permeability and membrane disruption of microbial cells (*Pseudomonas aeruginosa* and *S. aureus*) [152]. Antimicrobial potential of oxygenated phenolic compounds, were also reported in the literature [153–157]. In addition, *S. aureus*, a representative for Gram-positive bacteria, was more sensitive to tested samples than *E. coli*. This was because the external surface of outer membrane of *E. coli* that composes of lipopolysaccharides and proteins is more

Antimicrobial compound	<i>S. aureus</i>		<i>E. coli</i>	
	MIC (µg/mL)	MBC (µg/mL)	MIC (µg/mL)	MBC (µg/mL)
Free guava leaf oil	500	1000	500	1000
Encapsulated guava leaf oil [*]	125	250	250	500
Yarrow oil	250	500	500	1000
Encapsulated yarrow oil [*]	62.5	125	62.5	125
Black pepper oil	1000	2000	2000	>2000
Black pepper oil-HPβCD complex [*]	250	500	500	1000

^{*}Values were based on the actual concentrations of essential oil encapsulated in the HPβCD (calculated from encapsulation efficiency).

Table 4. Minimum inhibitory and bactericidal concentration (MIC, MBC) against *Staphylococcus aureus* and *Escherichia coli* for both free and encapsulated essential oil.

tolerate to the tested samples, and the O-side chains of the lipopolysaccharides of *E. coli* has a hydrophilic surface protecting the hydrophobic molecules to enter the bilayer [146].

The antibacterial efficacy of yarrow oil was much improved after encapsulated in HP β CD by 4 and 8 times against *S. aureus* and *E. coli*, respectively, while antibacterial activity of black pepper oil was improved by 4 times against both *S. aureus* and *E. coli*. As quote above, inclusion complex formation with HP β CD could increase aqueous solubility and improve antimicrobial efficacy at lower concentrations of encapsulated compounds [99]. As the primitive sites for antimicrobial action were found at the cell membrane and inside the cytoplasm, HP β CD may enhance the accession of essential oils to these regions by improving water solubility of essential oils [111].

4. Conclusions

Microencapsulation of essential oils in HP β CD was achieved proving that the host-guest complex formation implies different physicochemical characteristics from free essential oil. As advantage, the DPPH radical scavenging capacity of the encapsulated oil was more stable than for the free oil indicating that the inclusion complex with HP β CD could protect the active components of oil against the effect of sunlight. As well, encapsulation also increased the antibacterial activity of essential oils against both *S. aureus* and *E. coli* the observed behavior implies an important increase.

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