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Preface

Cyclodextrins (CDs), the cyclic oligosaccharides composed of α-(1,4) linked glucopyranose subunits, are typically produced by intramolecular transglycosylation reaction from degradation of starches by glucanotransferase enzymes. The most common types of native CDs are composed of 6, 7, and 8 glucopyranose units, known as α-, β-, and γ-CDs, respectively. To improve the functionality, for example, the solubility, native CDs are modified, and CD derivatives are synthesized. The cyclic molecular structure of CDs has truncated molecular shape with hydrophobic cavity at the centers which can interact (host) with external hydrophobic compounds (guest molecules) and hydrophilic surface. CDs have also been known as generally recognized as safe (GRAS) in the United States, natural products in Japan, and as novel food in Australia, New Zealand, and European countries. Therefore, CDs are being widely used in food production for many purposes, especially to encapsulate hydrophobic compounds including solid, liquid, and gas molecules aiming to solubilize, stabilize, or control release rate of these compounds. There are a large number of studies dedicating to the encapsulation of CDs for various food applications over the last few decades. This book will provide the comprehensive review on the functionality of CDs in the encapsulation for food applications.

The book includes a total of 16 chapters in which Chap. 1 gives general introduction to CD properties and its applications in food processing, and Chaps. 2–16 are about applications of CDs in the encapsulation for many guest compounds. These compounds include gases, flavors, colors, pigments, polyphenols (plant bioactive compounds), essential oils, lipids (cholesterol and polyunsaturated fatty acids), vitamins, and antifungal and antimicrobial compounds. Functionalities of CDs applied to packaging, masking off-flavor and off-taste, and dietary fiber are also described. The book is suitable for both newcomers to encapsulation technology and for those with experiences in the field including academics, undergraduate and postgraduate students, and food industry professionals.

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Chapter 1
Properties of Cyclodextrins and Their Applications in Food Processing

Yoshiyuki Ishida and Thao M. Ho

1.1 Type and Structure of Cyclodextrins

Cyclodextrins (CDs) are non-reducing, chiral cyclic oligosaccharides in which D-(+)-glucopyranose units are linked α-(1,4)-glycosidically into a ring. Depending on the number of D-(+)-glucopyranose units and thus the size of the ring, a distinction is made between α-CD, β-CD, and γ-CD. α-CD consists of six glucose units, β-CD of seven, and γ-CD of eight. Larger CDs consists of more than nine glucose units can be produced, but the utilization of the CDs is limited due to their structures and properties which are different from α-, β-, and γ-CD (Hedges 2009).

CDs are natural conversion compounds of starch, which is a polymer of glucose. In nature, starch is enzymatically decomposed by specific microorganisms into CDs and saccharide chains. Highly active bacteria that can selectively produce oligosaccharide rings have been selected by combining modern and refined techniques (Schmid et al. 1988). The enzyme for producing oligosaccharide rings is called cyclodextrin glucosyl transferase (CGTase). Researchers succeeded in crystallizing the enzyme in 1991 and reported the crystal structure of CGTase (Klein and Schulz 1991).

CDs have a toroid molecular structure with a cavity height of 0.8 nm. The diameter depends on the number of glucopyranose units. The cavity of CDs is hydrophobic due to hydroxyl-group arrangement, and the outer rims are hydrophilic (Fig. 1.1). The primary hydroxyl groups, which are located at the smaller rim, are rotatable in

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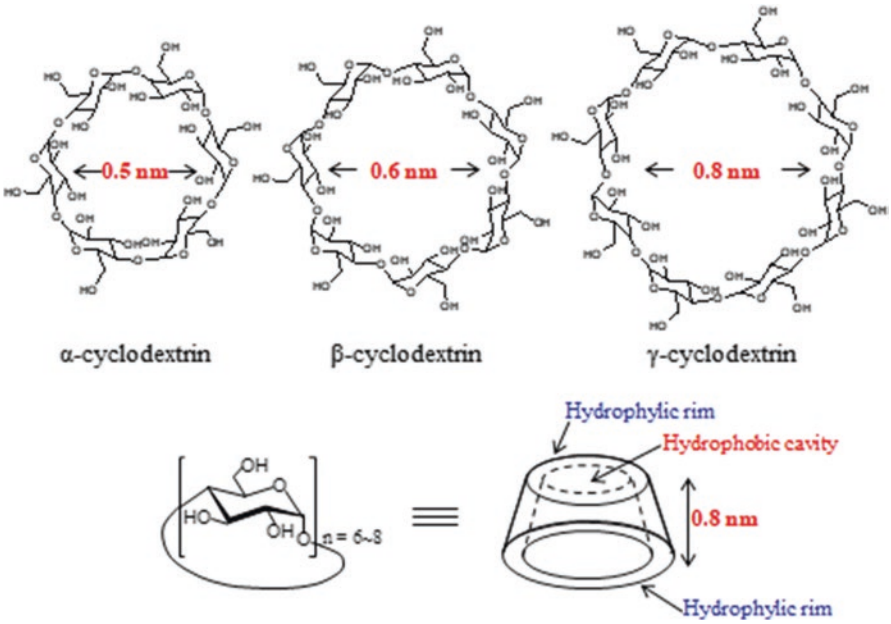

Fig. 1.1 Structures of native α-, β-, and γ-cyclodextrin and their geometric dimensions

such a manner that they can change the size of the rim. Secondary hydroxyl groups are located at the larger rim of the toroid. Intramolecular hydrogen bonding between the secondary hydroxyl groups of each glucopyranose unit plays a major role in the structural flexibility and aqueous solubility of CDs. β-CD has the most rigid structure among all CDs due to the formation of an intramolecular hydrogen bond belt. α-CD is more flexible than β-CD because of truncated formation of the intramolecular hydrogen bond belt due to less glucopyranose units. γ-CD is structurally most flexible and therefore the most soluble of the three CDs (Shieh and Hedges 1996; Davis and Brewster 2004).

A characteristic feature of CD molecules is their ability to enclose lipophilic substances reversibly in their hydrophobic cavity, provided that the guest molecule size and geometric shape fit the cavity. These CD inclusion compounds, which are known as host–guest complexes, are largely held together by van der Waals forces.

Chemically modified CDs, such as hydroxypropylated CD, randomly methylated CD, and sulfobutylated CD, are frequently used for pharmaceutical formulations due to their higher solubilizing power compared to native CDs (Szejtli 1983). In contrast, chemically modified CDs cannot be utilized for food applications from a viewpoint of safety and bioadaptability. Chemically modified CDs generally have a membrane-perturbing effect, resulting in haemolysis and local irritation at higher doses (Szejtli 1984). Therefore, native CDs are the only legally approved CDs to be used for food applications.

1.2 Physical and Chemical Properties of Cyclodextrins

1.2.1 Water Solubility of Cyclodextrins

The water solubility of CDs is lower than that of glucose due to the formation of intramolecular hydrogen bonds between secondary hydroxyl groups on the larger rim of CDs. CDs cannot hydrate enough due to the hydrogen bond belt. The orientation and degree of the hydrogen bonds between the secondary hydroxyl groups of adjacent glucopyranose units are different in each of the CDs. β-CD has the lowest water solubility (1.85 g/100 mL at 25 °C) of the three CDs with the strongest hydrogen bond belt. On the other hand, γ-CD has the highest water solubility (23.2 g/100 mL at 25 °C) of the three CDs due to its weakest hydrogen bond belt. The water solubility of α-CD is the middle of the three CDs (14.5 g/100 mL at 25 °C). The water solubility of CDs increases along with the increase in temperature (Astray et al. 2009).

The acidity of the secondary hydroxyl group of CDs is comparably high. The pK_a of the hydroxyl group is about 12 (Szejtli 1998). Accordingly, CDs are ionized at high pH (pH > 12) and the water solubility of CDs also increases. For example, the water solubility of β-CD reaches 75.0 g/100 mL at pH 12.5 (Hedges 2009).

1.2.2 Thermal Stability of Cyclodextrins

Solid states of α-, β-, and γ-CD are basically stable up to 300 °C. At that temperature, melting of the crystals and thermal decomposition of CDs are observed. The melting of the crystals and decomposition of the structure occur simultaneously and cannot be separated from each other. Therefore, in most cases of food processing, CDs can be applied without any problem (Shieh and Hedges 1996).

1.2.3 Stability of Cyclodextrins in Acids and Bases

The α-1,4 glycosidic bonds of CDs are more resistant to acid hydrolysis than that of starch, because their cyclic structures stabilize them. However, at low pH (pH < 2) and in the presence of strong acids, such as hydrochloric acid or sulfuric acid, α-1,4 glycosidic bonds of CDs are cleaved via hydrolysis yielding a mixture of oligosaccharides and glucose. The rate of hydrolysis increases at lower pH and high temperature (Szejtli and Budai 1976; Szejtli 1988). The α-1,4 glycosidic bonds of CDs are quite stable and not hydrolysed by bases, even at elevated temperatures.

1.2.4 Digestibility of Cyclodextrins in Gut

CDs are digested after oral administration. α-CD and β-CD are not digested by salivary or pancreatic enzymes and are hardly absorbed in small intestines. Approximately, 99% of administered α-CD and β-CD reach the large intestine and they are fermented by the intestinal microflora (Kurkov and Loftsson 2013). The microbial degradation of α-CD results in the generation of short-chain fatty acids (acetate, propionate, butyrate) that provide many health benefits (Nihei et al. 2018; Sakurai et al. 2017). On the other hand, γ-CD differs from α-CD and β-CD in that it is almost completely degraded by salivary and pancreatic α-amylase, similar to digestion of starch and linear dextrins, and therefore γ-CD can be regarded as a slow energy release carbohydrate (Saokham and Loftsson 2017).

1.2.5 Formation of Inclusion Complexes

While CDs are oligosaccharides, their cavities provide a lipophilic environment in aqueous solutions. Various hydrophobic substances can be selectively enclosed in their CDs cavities and form non-covalent reversible inclusion complexes. The formation of inclusion complexes between guest molecules and CDs depends on the polarity and size of guest molecules via driving forces, such as van der Waals forces, hydrophobic interactions, and hydrogen bonds. α-CD forms inclusion complexes with relatively smaller-sized molecules, such as carbon dioxide gas (Neoh et al. 2006) and hydrocarbon chain. β-CD forms inclusion complexes with medium-sized molecules, like monoterpenes, which are typical components of flavor and fragrance (Pollyana et al. 2016), and polyphenols such as hesperidin, which is abundantly found in citrus fruits, and also acts as an antioxidant that contributes to blood-vessel integrity and reduces LDL cholesterol and blood pressure (Monforte et al. 1995; Ohtsuki et al. 2003). γ-CD forms inclusion complexes with larger molecules, such as macrocyclic compounds and lipophilic vitamins, curcumin, coenzyme Q10 (CoQ10), which are used as nutraceutical ingredients in supplements and health foods with various human health benefits (Uekaji and Terao 2019).

1.3 Toxicological Considerations

As for the toxicity of CDs, The FAO/WHO Joint Expert Committee on Food Additives (JECFA) states that they are highly safe because they are natural products of starch.

1.3.1 Toxicity Evaluation of α-CD

Results of acute toxicity studies in rats and mice administered intraperitoneally or intravenously with α-CD have been reported in the range of 500–1000 mg/kg bw as LD_{50}.

In short-term toxicity studies, no significant toxicity was observed in groups of male mice administered orally with α-CD at doses equivalent to 0 or 60 mg/kg bw/day for 15 days. In addition, groups of five Wistar rats of each sex were fed diets equivalent to 0–7500 mg/kg bw/day of α-CD for 4 weeks with no deaths and no significant toxicity observed. Similar results were reported when a group of 20 Wistar rats were fed α-CD at 0–10,000 mg/kg bw/day for 13 weeks, with no deaths and no significant toxicity observed. In addition, groups of four beagle dogs of both sexes were fed diets equivalent to 0–5000 mg/kg bw of α-CD per day for 13 weeks, resulting in no deaths and diarrhoea, but no other toxic effects. There have been some reports of human studies that lack toxicity, but consumption of more than 20 g of α-CD in a single meal may cause gastrointestinal effects.

1.3.2 Toxicity Evaluation of β-CD

In a short-term toxicity study of β-CD, 20 rats of both sexes, aged 6 weeks, were treated with diets containing 0–5% β-CD for 52 weeks. Four deaths were recorded during the study period: three males in the control group, and a female fed a diet containing 1.25% β-CD. None of these deaths were due to β-CD and no other unusual clinical signs were observed. In addition, a group of four beagle dogs of both sexes were treated with diets containing 0–5% β-CD for 52 weeks with no deaths, but elevated urinary protein and potassium levels were observed.

1.3.3 Toxicity Evaluation of γ-CD

In a long-term toxicity study of γ-CD, groups of 20 rats of both sexes were treated with diets containing 0–20% of γ-CD for 12 months, and four deaths were recorded during the study period. No clear toxicity was shown. In a human study, a double-blind crossover study was conducted in two groups of six men and six women to examine gastrointestinal responses to 100 g of plain yogurt containing 0 or 8 g of maltodextrin or γ-CD as a snack within 15 min. There was no statistically significant difference in the incidence of individual symptoms between the maltodextrin group and the γ-CD group, and no toxicity of γ-CD was demonstrated.

Based on the results of the toxicity study of CDs, JECFA evaluates α- and γ-CDs as food additives with no tolerable intake level (Kroes et al. 2006; Abbott 2000), and

Table 1.1 Regulatory status of α-, β-, and γ-CD

Type of CD	Average daily intake (JECFA)	Food approval			
		US	EU	Japan	Australia and New Zealand
α-CD	Not specified	GRAS	Novel food	Available	Novel food
β-CD	5 mg/kg bw/day	GRAS	Food additive	Available	–
γ-CD	Not specified	GRAS	Novel food	Available	Novel food

the acceptable daily intake (ADI) of β-CDs is 5 mg/kg-body-weigh/day based on the data in beagle dogs (Pollit 1996). In the EU, the regulation on the use of CDs is approved as 'Novel Food' for α- and γ-CDs, and as 'Food Additive' for β-CDs. In the USA, CDs are approved by Generally Recognized as Safe (GRAS), and β-CDs are approved to be used as 'Flavor Protectant'. In Japan, α-, β-, and γ-CDs are unconditionally approved for food use. In Australia and New Zealand, α- and γ-CD are approved as Novel Foods (Table 1.1).

1.4 Crystalline and Amorphous Cyclodextrins

CD powders can exist as either crystalline or amorphous structure depending on the arrangement order of molecules in the powders. The commercial CD powders have crystalline form in which molecules are tightly packed in a certain order. In amorphous form, CD molecules are randomly arranged with a loose structure. Theoretically, amorphization of powders can be achieved by quenching of a melt, spray drying, freeze drying, and milling (Einfalt et al. 2013). However, it was found that quenching of a melt and annealing at high temperature (110–150 °C) were not appropriate techniques to produce amorphous CD powders (Kaminski et al. 2012). In the quenching of a melt, CD powders experience extensive chemical degradation (e.g., caramelization) during heating while the annealing approach enables only a small part of the CD structure to undergo phase transformation. Completely amorphous CD powders have been successfully produced by freeze drying (Li et al. 2002), ball milling (Kaminski et al. 2012; Tabary et al. 2011), and spray drying (Ho et al. 2015a, 2017a; Ho 2017; Shrestha et al. 2017; Frieler et al. 2019). During the milling of CD powders, the generation of localized heating effects followed by quenching, or an increase in static disorder adding to the intrinsic dynamic disorder inherent within the lattice up to critical value where structural collapse occurs, results in the amorphous structure of the powder. The degree of amorphization (e.g., partially or completely amorphous) is largely determined by the milling temperature, which must be lower than the glass transition temperature of the powder to induce the amorphization. There is possibly microcrystalline structure remaining in milled CD powders as the mechanical method is unable to completely disrupt all the crystalline structure. Meanwhile, amorphization of CD powders in freeze drying is

attributed to rapid sublimation of water vapour from the solid state at reduced pressure and spray drying is attributed to rapid water evaporation, both of which prevent molecules from reorganizing into a crystalline structure.

Like other amorphous solids, amorphous CD powders are in a thermodynamically non-equilibrium state, and thus they are likely to transform to crystalline structure with a thermodynamically stable state during production and storage. The rate of phase transformation from amorphous to crystalline depends on the mobility of molecules in the powders, which is controlled by the moisture content of powders, relative humidity that the materials are exposed to, and powder temperature. The boundary between low (glassy) and high (rubbery) molecular mobility of amorphous materials is defined as the glass transition temperature. Thus, the determination of glass transition temperature and critical moisture content (e.g., moisture content at which phase transformation is initiated) for amorphous CD powders is very important to prevent or initiate the state transformation for a particular application (Ho et al. 2015a). For amorphous α-, β-, and γ-CD powders produced by ball milling, the glass transition temperatures were unable to be determined via conventional DSC scanning, and they were therefore estimated above thermal degradation points, such as ~270 °C (Kaminski et al. 2012; Tabary et al. 2011). In a study by Ho et al. (2015a) on amorphous α-CD powder produced by spray drying, however, the glass transition temperature determined by DSC scanning was about 84 °C. The differences between crystalline α-, β-, and γ-CDs, and amorphous counterparts produced by spray drying under various analytical techniques are illustrated in Table 1.2, and Figs. 1.2 and 1.3 (Ho et al. 2015a; Frieler et al. 2019; Bhandari and Ho 2020). Methods to characterize quantitatively and qualitatively the amorphous and crystalline food powders including CD powders have been well described in a review by Ho et al. (2017a).

Table 1.2 Differences between crystalline and spray-dried amorphous α-CD powders observed under various analytical techniques

Analytical techniques	Amorphous α-CD	Crystalline α-CD
SEM	Spherical-shape particles with a smooth surface and possessing dents and small vacuoles	Irregular shapes with different sizes Many small particles and clefts on their surface Sharp edges of particles
Polarized light microscope	Homogenously dark background	Colored bright crystal granules with different contrast and shape
X-ray	Only two broad peaks	Many sharp and high intensity peaks
FTIR	Low intensity in FTIR peaks	High intensity in FTIR peaks
^{13}C NMR	Broader spectral peaks	Sharp and split spectral peaks
DSC	A big endothermic hump A signal of glass transition	Multiple endothermic peaks

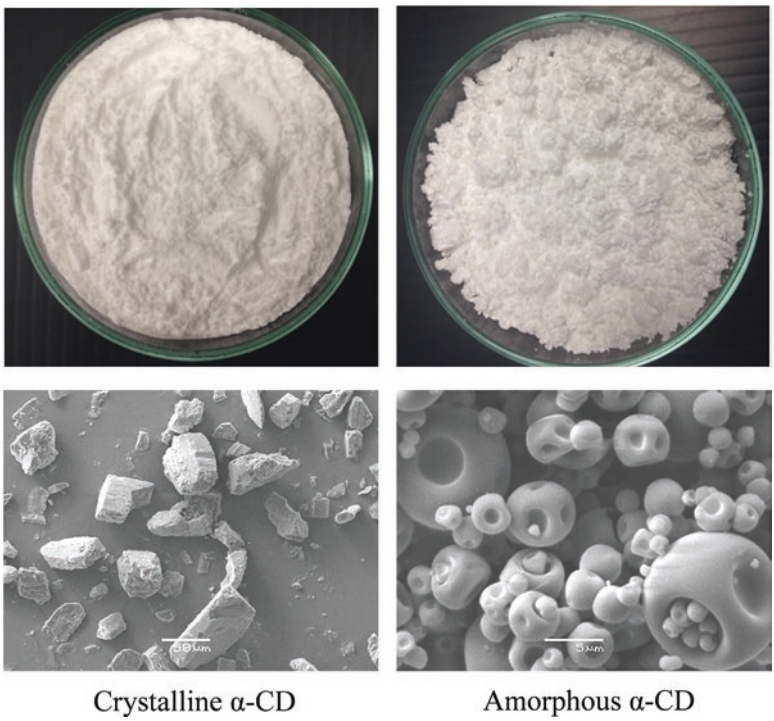

Fig. 1.2 Appearance and SEM images of α-CD powders in crystalline and amorphous structures. (Adapted with permission from Ho et al. 2016b)

When equilibrated at various relative humidities, amorphous α-CD powders crystallized at relative humidities above 65% and absorbed much more water and faster than crystalline α-CD. At equilibrium, the moisture content of amorphous α-CD powder kept at 65% relative humidity was 13.70–14.97 g of moisture per 100 g of dry solids. This relative humidity and moisture content are considered to be critical for the spray-dried amorphous α-CD powder. As shown in Fig. 1.4, a few sharp peaks were observed on the X-ray spectrum of amorphous α-CD powders equilibrated at 65.29% relative humidity, while many sharp peaks were seen on that of amorphous α-CD powders kept at 75.32%, 84.32%, and 97.30% relative humidity (Fig. 1.4a). Some particles of amorphous α-CD powder started to aggregate due to water adsorption when stored at 65.29% relative humidity (Fig. 1.4b), and this phenomenon became clear at 84.32% and 97.30% relative humidity (e.g., powder agglomeration and crystallization).

Recent studies about encapsulation of ethylene and carbon dioxide gases have been performed by directly compressing gases into amorphous solid state α-CD powders, aiming to produce gas complex powders to apply in agriculture and food production (Ho and Bhandari 2016; Ho et al. 2015b). The results demonstrate that the gas encapsulation capacity of crystalline α-CD powder was significantly lower

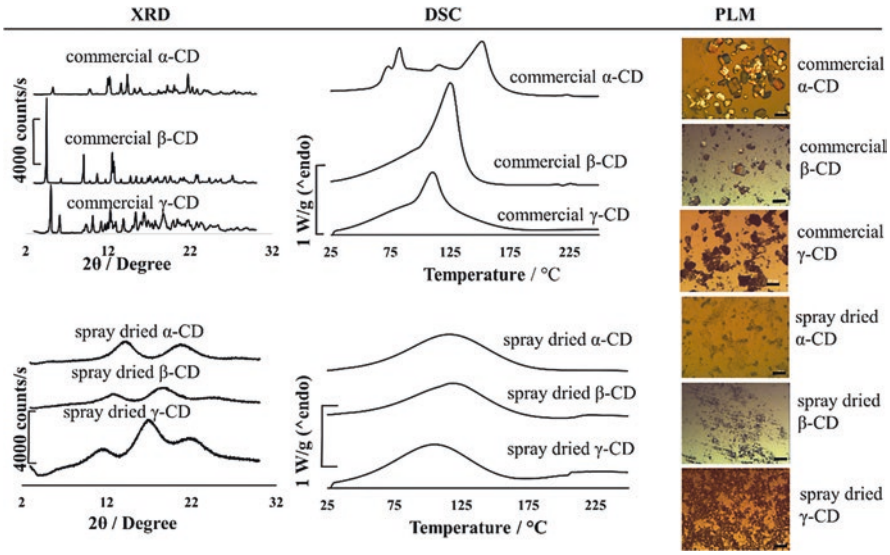

Fig. 1.3 XRD patterns, DSC thermograms, and polarized light microscopy (PLM) of commercial crystalline and spray-dried amorphous α-, β- and γ-CD powders. For images, scale bar = 200μm. (Adapted with permission from Frieler et al. 2019)

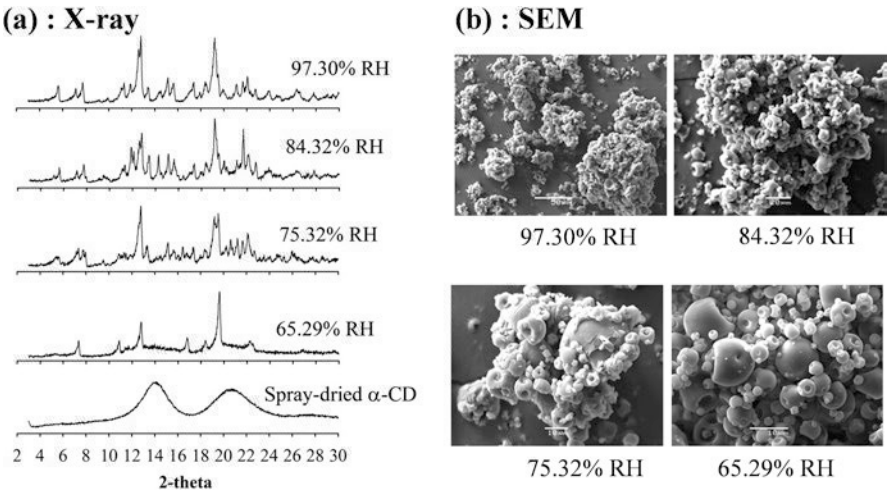

Fig. 1.4 X-ray (**a**) and SEM (**b**) analyses of spray-dried amorphous α-CD powders equilibrated at various relative humidities (RH). (Adapted with permission from Ho et al. 2015a)

than that of amorphous α-CD powder at low pressure and short time (e.g., 0.4–0.8 MPa and 4–24 h). However, due to no long-range order and loose structure of the gas complex powder prepared from amorphous α-CD powder, major part of the encapsulated gas was released upon depressurization. The stability of amorphous gas-α-CD powder can be increased by adding water to a higher than critical value of amorphous α-CD powders (15–17%, w/w) to induce the crystallization of the complex powder during encapsulation (Ho et al. 2016a, b, c). Regarding encapsulation, the advantages of amorphous over crystalline CD powders have been illustrated in studies by Shrestha et al. (2017) and Frieler et al. (2019) for tea tree oil with β-CD powders, and for fish oil with α-, β-, and γ-CD powders, respectively.

1.5 Food Applications of Cyclodextrins

Many reviews describing the applications of CDs have been published (Matencio et al. 2020; Braga 2019; Jansook et al. 2018; Fenyvesi et al. 2016). Indeed, CDs have been frequently applied in the food industry as flavor carriers, protectants of food ingredients, undesired taste masking, and food packaging materials (Szente and Szejtli 2004; Hedges 1998) (Fig. 1.5).

1.5.1 Enhancement Stability of Included Compounds

CD inclusion can stabilize substances that are labile to light (ultraviolet) and heat, as well as unstable guest ingredients that are easily oxidized or hydrolyzed. This effect is applied to prevent flavor volatility, color changing/fading of pigments, and rancidification. CD inclusion can cause changes in color, odor, and taste of fats and oils, and can improve the quality and storage stability of food products (Fenyvesi et al. 2016; Szente and Szejtli 2004; Loftsson 1995). For instance, while allyl

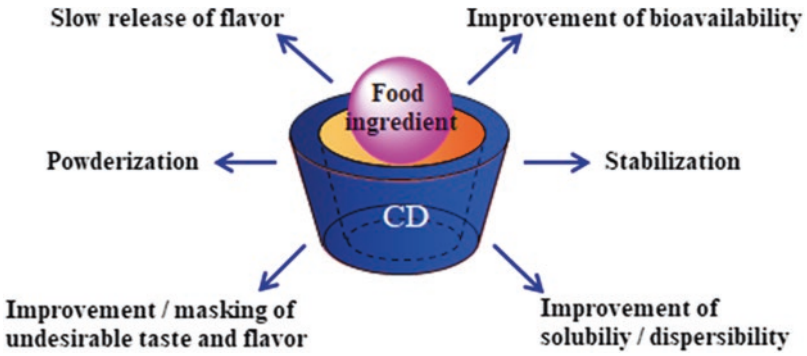

Fig. 1.5 Food applications of CDs by the formation of inclusion complex

isothiocyanate, a pungent ingredient of wasabi and mustard oil, is volatile and easily reacts with some nucleophiles such as water, carotenoids and Vitamin A are readily oxidized and its color fades with light and air. Vitamin D3 is labile under high temperature, and unsaturated fatty acid such as in fish oil is degraded by rancidification due to heat and oxygen. CD can protect from these problems via formation of stable inclusion complexes (Ohta et al. 2000; Sauvant et al. 2012; Szejtli et al. 1980; Yoshii et al. 1997). The inclusion complexes between CD and polyphenols can prevent the color modification of beverages via inhibition of enzymatic browning by polyphenoloxidase (Astray et al. 2009). Stabilization of nutraceutical ingredients by CD inclusion can also improve the absorption of the ingredients into the body after oral administration. R-alpha lipoic acid is a coenzyme in mitochondria and is well known as nutraceutical ingredient. R-alpha lipoic acid is labile in gut and shows poor bioavailability, but CD inclusion can provide sufficient stability to R-alpha lipoic acid and improve its bioavailability (Ikuta et al. 2016).

CD inclusion keeps moisture from entering hygroscopic substances in solid state. Non-solid substances, such as gases and oils, can also be converted into stable powders by encapsulating them with CDs, which makes for easier handling. This effect has been applied to powdered flavor and honey powder, for example. Powdered flavor with CD can easily control the volatile nature of flavor with temperature and moisture (Nguyen and Yoshii 2018), and can be prepared by conventional processes such as by mixing of flavor and CD via kneading and then spray drying or freeze drying (Dziezack 1988; Gibbs et al. 1999; Shahidi and Han 1993). This technique holds great potential for meal flavor enhancement, or for masking of undesirable food flavors.

1.5.2 Enhancement of Solubility of Included Compounds

Water insoluble ingredients cause clouding and sedimentation and may be undesirable in the quality in food products, especially beverages. The formation of inclusion complex by CD can inhibit the aggregation of water-insoluble ingredients, which can improve their water solubility and dispersibility. The solubility enhancement of an ingredient by CD inclusion can be shown in an A-type curve in typical phase-solubility diagram (Higuchi and Connors 1965). As such, CDs are used in processed citrus products, tea drinks, soups, for instance. CDs can also form stable emulsions or whips with oils and some kinds of proteins, and this effect has been used in bakery and confectionery products and milkshakes (Astray et al. 2020). It can also be used in egg-free mayonnaise-like dressings. On the other hand, β-CD has been used as a cholesterol-removing agent from egg yolk and daily products via formation of a water-insoluble complex with cholesterol (Fenyvesi et al. 2016).

CD-inclusion enhancement of water solubility of guest ingredients can improve the absorption of those ingredients into the body after oral administration. It is well known that absorbability of the ingredient is important in the nutraceutical and pharmaceutical fields. It has recently been shown that γ-CD inclusion can uniquely

increase the efficiency of micelle formation by bile acids secreted in the intestine and greatly improve the absorption of the guest ingredient into the body with improved water solubility, especially in the case of highly fat-soluble guest ingredients (Uekaji et al. 2013). The above technique has been used as a γ-CD inclusion body to enhance the absorption of supplement ingredients, such as coenzyme Q10 and curcumin, a component of turmeric (Terao et al. 2006; Purpura et al. 2018).

1.5.3 Improvement of Taste and Flavor

The sense of taste and flavor of food is one of the principal factors to determine the quality and consumer acceptability, as well as shelf-life of food. CDs are useful to control taste and flavor in food industry because of the specific or selective nature of inclusion between CD and the taste and flavor components. Since the inclusion phenomenon of CD reduces the volatile nature of flavor and inhibits the interaction between taste components and their receptors on taste buds, many researchers have reported controlling, reducing, or masking the sensation of taste and flavor by CD (Szejtli and Szente 2005). α-CD has been used to reduce the bitter taste of amino acid and soy protein hydrolysate (Linde et al. 2009). β-CD has been used to reduce undesirable flavors, such as beany flavor from soy protein and soy milk (Lee et al. 2020; Arora and Damodaran 2010), unsaturated aldehyde from watermelon (Yang et al. 2020), and the goaty flavor of several branched chain fatty acids from goat milk (Wang et al. 2018). β-CD has also been used to reduce the bitter tastes of limonin and naringin of citrus juice (Hedges 1998). γ-CD has been applied to reduce the bitter tastes of relatively larger compounds, such as triterpenoid saponin of red ginseng (Tamamoto et al. 2010).

1.6 Conclusion and Future Perspectives

This chapter introduced the basic properties, safety, and inclusion effects of CDs in the food industry. CDs are a very attractive material that has a unique structure and the simple function of inclusion shows a variety of effects. CDs have long been used for foods. CDs are very useful, not only to improve and stabilize the quality of food, including physical properties and flavor, but also to improve the bioavailability of guest ingredients. In addition, CDs are used as a packaging material for controlling ripening and antibacterial treatment. Furthermore, the effect of supplementation of α-CD as a dietary fibre has recently been attracting attention. CD incorporation in foods is expected to become more widely used as a key method in food development to maintain and improve the quality of life and health.

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Chapter 2
Solid Encapsulation Method: Ethylene Gas Encapsulation into Amorphous Alpha-Cyclodextrin Powder

Thao M. Ho, Kamornrath Sungkaprom, Binh T. Ho, and Bhesh R. Bhandari

2.1 Introduction

Ethylene (C_2H_4) gas is a well-known olefin with a simple structure of two carbons symmetrically linked to each other by a double bond (CH_2=CH_2) (Sundaram et al. 1991). It is an odorless and colorless gas, which occurs naturally and can also be created by man-made sources from industrial activities such as car exhausts from internal combustion engines and gas pipes (Wills et al. 2007). It is a very reactive molecule which can be involved in various chemical reactions, such as polymerization addition, oxidation, and hydration. Biologically, C_2H_4 is a gaseous hormone and is involved in many physiological processes during plant development. The largest producers of C_2H_4 compound are plant and plant products, for example, fruits, vegetables, and floral products, which produce it within their tissues and release it into the surrounding atmosphere. Fruits, vegetables, and flowers contain receptors which serve as binding sites to absorb free atmospheric C_2H_4 molecules (Saltveit 1999; Sundaram et al. 1991). For commercial uses, C_2H_4 gas is usually stored in pressurized cylinders. However, safety is a significant issue in its handling, transport, and storage due to its flammability.

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Table 2.1 The beneficial and detrimental effects of C_2H_4 gas on fresh products (adapted with permission from Saltveit 1999)

Beneficial effects	Detrimental effects
• Promotes color development in fruits • Stimulates ripening of climacteric fruits • Promotes de-greening of citrus • Stimulates dehiscence in nuts • Alters sex expression in the cucurbitaceae • Promotes flowering in bromeliaceae (e.g. pineapple) • Reduces lodging of cereals by inhibiting stem elongation	• Accelerates senescence • Stimulates chlorophyll loss and yellowing • Enhances excessive softening of fruits • Stimulates sprouting of potatoes • Promotes abscission of leaves and flowers • Stimulates phenylpropanoid metabolism • Promotes discoloration (e.g. browning) • Hastens toughening of vegetables

C_2H_4 gas is a naturally produced gaseous plant hormone that plays a significant role in plants' physiology, development, and metabolism. It accelerates senescence, stimulates yellowing, enhances excessive softening, and other undesirable effects on fruits and vegetables. Despite its deleterious effects, it can be used to improve fruit quality by promoting uniform ripening of batches of fruits (Saltveit 1999). Table 2.1 summarizes the beneficial and the detrimental effects of C_2H_4 on quality of fresh fruits and vegetables.

There are many ways that C_2H_4 gas can be used for ripening and other applications in postharvest technology. For instance, the utilization of C_2H_4 generators where a liquid, comprising of ethanol and catalyzing agents, is heated to produce C_2H_4 gas, in the addition of measured quantities of C_2H_4 for gas cylinders and the use of C_2H_4-releasing chemicals such as Ethephon (Barry and Giovannoni 2007). However, the utilization of C_2H_4 in postharvest and plant growth regulation is limited due to its high volatility, safety issues, and the needs for strict handling protocols (Ho et al. 2011a; Ho 2013).

Cyclodextrin (CD) powders have been increasingly employed in food technology as encapsulating agents to form inclusion complexes with a wide variety of hydrophobic guest molecules. Among three common types of CDs, α-CD has the smallest cavity dimension comparing with other CDs, being able to complex with guest molecules having five carbons or less (including gases) more easily than β- and γ-CDs (Dodziuk 2006). The encapsulation of various gases using α-CD has been well described in Chap. 3 of this book. C_2H_4 gas is an appropriate structure, with its apolar characteristic and small size (C=C and C–H lengths of 132 and 108.2 pm, respectively) (Djedaïni-Pilard and Bonnet 2007) to form complexes with α-CD.

The studies have shown that C_2H_4 gas can be converted into a powder form of C_2H_4-α-CD inclusion complex (Bhandari and Ho 2014). Powder form produced by encapsulation of C_2H_4 gas into α-CD could provide several benefits which are easy and safe in handling as compared to gaseous form of C_2H_4, and being able to be

delivered in smallest portion as required. Moreover, the product is convenient to transport, which could also be in favor of choice over gaseous state. This has also been effective in in-transit ripening of fruits in trucks or fruit-transport vehicles (Ho et al. 2016a). Thus, the usage of powder form of C_2H_4-α-CD inclusion complex as the novel product is relatively simple way of managing fruit ripening and other C_2H_4 regulated plant processes such as seed germination (Ho et al. 2011a; Ho 2013). The powdered form of C_2H_4-α-CD is usually produced by following liquid encapsulation method, whereby the complexation takes place under the pressure of the gas in a saturated solution of the α-CD. In this liquid encapsulation, precipitation or crystallization of the inclusion complex occurs slowly, with the recuperation of the crystallized complexes being done in a batch in several days. Thus, this is a time consuming and low yielding process because the crystallization and diffusion processes are time dependent. In addition, there will be a significant amount of residual uncomplexed CD remaining in the liquid. The yield of complexed C_2H_4-α-CD is normally around 50% (Ho 2013). An innovative approach for encapsulating C_2H_4 gas into solid α-CD directly with expectation of shortened process and 100% yield, would have potential practical application and demand. Commercial α-CD exists in crystalline structure. The molecular structure of the crystalline form is tightly packed in a long-range order. That would be relatively difficult for C_2H_4 gas to be included into the α-CD molecule in the crystalline solid, as the molecules are tightly packed, making the cavity less accessible, resulting in the difficulty of C_2H_4 gas penetration (Dodziuk 1994). Amorphous structure of α-CD molecule is more porous, anarchial and tangled (Bhandari and Hartel 2005). The CD cavities in the amorphous structure would potentially be more accessible to interact with external molecules than would be the case for the crystalline structure. Solid encapsulation was used to encapsulate tea tree oil (TTO) by Shrestha et al. (2017). They added ethanol to the mixture of TTO and amorphous β-CD at 1:2 and 1:3 TTO:ethanol ratios. This resulted in the inclusion of 94.3 and 98.45 mg of TTO/g β-CD, respectively, which was similar to that of TTO encapsulated in the conventional paste method (95.56 mg TTO/g β-CD), suggesting an effective amorphous solid encapsulation method. Solid complexation by direct compression of carbon dioxide (CO_2) gas into amorphous and crystalline α-CD in solid state was also reported by Ho et al. (2015b) and Ho (2017). The results indicated that amorphous α-CD powder was more effective in the complexation with CO_2 at low pressure and short time than crystalline α-CD powder. For instant, complexation at 0.4 MPa for 4 h, amorphous α-CD powder encapsulated about 0.60 mol CO_2/mol α-CD whereas crystalline α-CD powder entrapped only 0.05 mol CO_2/mol α-CD.

In this chapter, we report the encapsulation of C_2H_4 gas in amorphous α-CD structure to increase the yield of entrapped C_2H_4 gas in the complexes, and qualitative characterization of the amorphous C_2H_4-α-CD complexes. Amorphous CD powders can be successfully produced by freeze drying (Li et al. 2002), ball milling (Kaminski et al. 2012; Tabary et al. 2011), and spray drying (Ho et al. 2015a, 2017; Ho 2017; Shrestha et al. 2017; Frieler et al. 2019). Details about production of amorphous CD powders and their properties can be found in Sect. 1.4, Chap. 1 of this book.

2.2 Complexation of C_2H_4 and Amorphous α-CD Powder

The encapsulation of C_2H_4 gas into α-CD allows for the conversion of C_2H_4 gas into a powder form that is easier to handle and use. This encapsulation technique relates to the incorporation of guest molecule physically into the core of a carrier molecule (Ho et al. 2011a). The C_2H_4-α-CD inclusion complex prepared by liquid encapsulation are in crystalline form. There are two different patterns of crystalline CD inclusion complex form, the cage and the tunnel type. The types of crystal formation can be responsible for further locking up of the guest molecule and release property of complexed gas (Saenger et al. 1998). Thus, C_2H_4 gas, olefin with two carbons symmetrically linked to each other by double bond, can be easily incorporated into α-CD. Although Ho et al. (2011a) had accomplished encapsulation of C_2H_4 gas into α-CDs to produce solid form inclusion complex crystals, there was some problems from crystalline molecule such as yield of complexed and uncomplexed C_2H_4 gas in crystallization technique. There is also little research of encapsulation of C_2H_4 gas using α-CDs into amorphous form.

Encapsulation of C_2H_4 gas into amorphous α-CD can be simply done in a pressure vessel. Amorphous α-CD powder is added into a multi-layered plastic container which is then placed inside the chamber of the pressure vessel. C_2H_4 gas is flushed into the vessel at set pressures and times. In the encapsulation process, the amorphous powder is exposed to C_2H_4 gas under the pressure without agitation. The complexation between α-CD and C_2H_4 occurs at the interface. In this case, the complexation is dependent on the penetration of the C_2H_4 gas into the CD molecular cavity. Figure 2.1 showed that an increase in encapsulation time results in significantly higher concentration of C_2H_4 in the amorphous C_2H_4-α-CD inclusion complexes. Meanwhile, in liquid encapsulation where C_2H_4-α-CD inclusion complex crystallises due to the low of solubility of complex compound, increasing pressure and time of encapsulation does not cause a profound increase (as compared to data

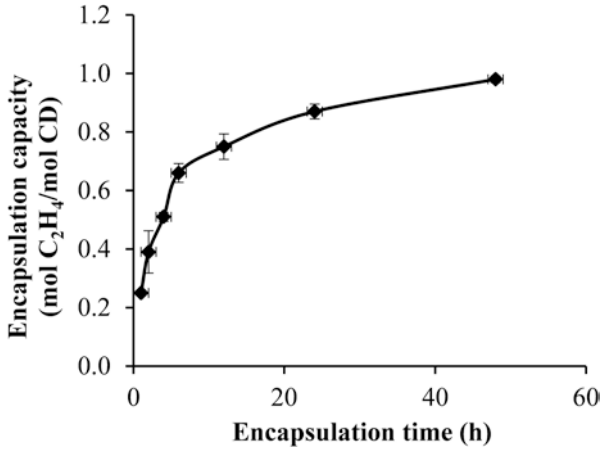

Fig. 2.1 C_2H_4 concentration (mol C_2H_4/mol α-CD) in amorphous C_2H_4-α-CD inclusion complexes encapsulated at 1.5 MPa at various time points