International Journal of Bio-Inorganic Hybrid Nanomaterials

Nanoparticles of Cyclodextrins & Their Applications in Food Technology

Atena S. Mazloom[1*], Nazanin Farhadyar[2], Fatemeh Azarakhshi[2], S. Hesameddin Erfani[3]

[1] *M.Sc., Department of Food Science and Technology, Varamin-Pishva Branch, Islamic Azad University, Varamin, Iran*

[2] *Assistant Professor, Department of Chemistry, Varamin-Pishva Branch,Islamic Azad University, Varamin, Iran*

[3] *M.Sc., Department of Food Science & Technology, Science and Research Branch, Islamic Azad University, Tehran, Iran*

Received: 3 December 2013; Accepted: 7 February 2014

ABSTRACT

Cyclodextrins (CDs) are a family of cyclic oligosaccharides which are composed of α (1,4) -linked glucopyranose subunits. Thebest-characterized forms are α, β and γ CD which are consisted of six, seven and eight D-glucose units, respectively. Cyclodextrins are produced from starch by enzymatic degradation. These macrocyclic carbohydrates with polar internal cavities can form complexes with and solubilize many normally water-insoluble compounds. Cyclodextrins are useful molecular chelating agents. They are used in food industry as food additives, for stabilization of flavors, for elimination of undesired tastes or other undesired compounds such as cholesterol and avoiding microbiological contaminations and browning reactions. Also, the molecular encapsulation of lipophilic food ingredients with cyclodextrin improves the stability of flavors, vitamins, colorants and unsaturated fats, etc., both in physical and chemical sense leading to extended product shelf-life.

Keyword: Cyclodextrins; Inclusion complex; Nanoparticle applications; Encapsulation; Food industry.

1. INTRODUCTION

Cyclodextrins (CDs) are inexpensive enzyme-modified starch derivatives, which have been industrially produced. These starch derivatives are non-toxic ingredients, are not absorbed in the upper gastro intestinal tract, and are completely metabolized by the colon microflora. Cyclodextrins (CDs) are cyclic oligosaccharides composed of glucose units [1,2].

The best-characterized forms are α, β and γ CD consisting of six, seven and eight D-glucose units, respectively (Figure 1). β-Cyclodextrin (βCD) has been on the GRAS list since 1998, as a flavor carrier and protectant, at a level of 2% in numerous food products.

(*) Corresponding Author - e-mail: atena.mazloom@yahoo.com.

Cyclodextrins can be utilized in foods mainly as carriers for molecular encapsulation of flavors and other sensitive ingredients, considering that CDs are not hygroscopic, moreover, they are water-retention improving, homogeneous, pure substances and a very broad field of their utilization begins to assert itself.

The compounds having super molecular structures carry out chemical reactions which involve all intramolecular interactions where covalent bonds are not formed between interacting molecules, ions or radicals. Majority of all these reactions are of 'host–guest' type. Compared to all the super molecular hosts mentioned above, cyclodextrins are the most important. Because of their inclusion complex forming capability, the properties of the materials with which their complexity can be modified significantly [3].

As a result of molecular complexation phenomenon CDs are widely used in many industrial products, technologies and analytical methods. The negligible cytotoxic effects of CDs are an important attribute in applications such as rug carrier [4,5], food and flavors [6], cosmetics [7], packing [8], textiles [9], separation processes [10], environment protection [11], fermentation [12] and catalysis fields [13].

Cyclodextrins have been known for nearly 100 years. In 1881, Villiers first produced them by digesting starch with Bacillus amylobacter and in 1903, Schardinger demonstrated the cyclic structure of these compounds. Cyclodextrins macro cyclic, non-reducing malto-oligosaccharides composed of glucose units linked by α-(1,4) glycosidic bonds. CDs are naturally occurring water-soluble glucans. They are also known as cycloamyloses, cyclomaltoses and Schardinger dextrins. They are produced as a result of intramolecular transglycosylation reaction from degradation of starch by cyclodextrin glucanotrans-

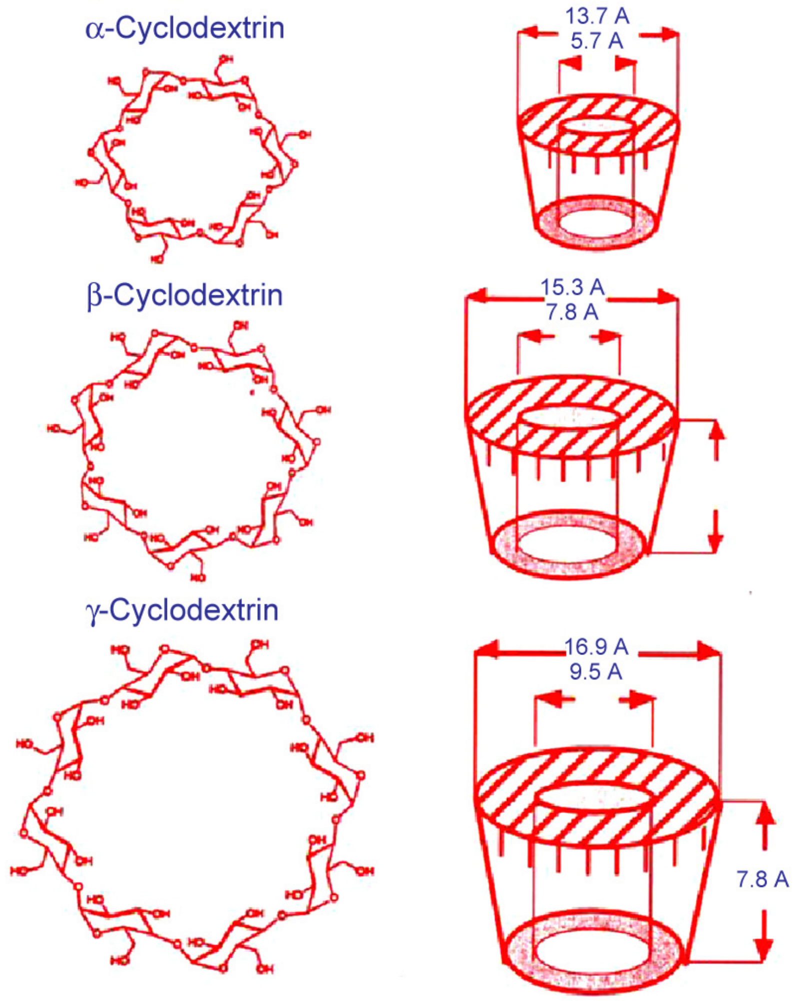

Figure 1: Cyclodextrins: α, β and γ-cyclodextrins.

ferase enzyme (CGTase) [3].

2. PROPERTIES OF CYCLODEXTRINS

2.1. α-cyclodextrin

The main properties are:

- Relatively irritating after i.m. injection
- Binds some lipids; some eye irritation
- Between 2% to 3% absorption after oral administration to rats
- No metabolism in the upper intestinal tract
- Cleavage only by the intestinal flora of caecum and colon [14].

2.2. β-yclodextrin

The main properties are:

- Less irritating than α-cyclodextrin after i.m. injection
- Binds cholesterol
- Very small amounts (1–2%) absorbed in the upper intestinal tract after oral administration
- No metabolism in the upper intestinal tract
- Metabolized by bacteria in caecum and colon
- Currently the most common cyclodextrin in pharmaceutical formulations and thus, probably the best studied cyclodextrin in human
- Application of high doses may be harmful and is not recommended, therefore bacterial degradation and fermentation in the colon may lead to gas production and diarrhea [14].

2.3. γ-cyclodextrin

The main properties are:

- Insignificant irritation after i.m. injection
- Rapidly and completely degraded to glucose in the upper intestinal tract by intestinal enzymes (even at high daily dosages, e.g. 10 – 20 g/kg)
- Almost no (0.1%) absorption (of intact γ-cyclodextrin) after oral administration
- Practically no metabolism after i.v. administration
- Probably the least toxic cyclodextrin (at least of three natural cyclodextrin)
- Actively promoted as food additive by its main manufacturers
- Complexion abilities [14].

3. INCLUSION COMPLEX FORMATION

The most notable feature of cyclodextrin is their ability to form solid inclusion complexes (host–guest complexes) with a very wide range of solid, liquid and gaseous compounds by a phenomenon of molecular complexation [15]. In these complexes, a guest molecule is held within the cavity of the cyclodextrin host molecule. Complex formation is a dimensional fit between host cavity and guest molecule [16]. The lipophilic cavity of cyclodextrin molecules provides a microenvironment into which appropriately sized non-polar moieties can enter to form inclusion complex [17]. No covalent bonds are broken or formed during formation of the inclusion complex [18]. The main driving force of complex formation is the release of enthalpy-rich water molecules from the cavity. Water molecules are displaced by more hydrophobic guest molecules present in the solution to attain an apolar-apolar association and decrease of cyclodextrin ring strain resulting in a more stable lower energy state [3]. The binding of guest molecules within the host cyclodextrin is not fixed or permanent but rather is a dynamic equilibrium. Binding strength depends on how well the 'host-guest' complex fits together and on specific local interactions, between surface atoms. Complexes can be formed either in solution or in the crystalline state and water is typically the solvent of choice. Inclusion complexation can be accomplished in co-solvent system, also in the presence of any non-aqueous solvent. Cyclodextrin architecture confers upon these molecules a wide range of chemical properties markedly different from those exhibited by non-cyclic carbohydrates in the same molecular weight range. Inclusion in cyclodextrins exerts a profound effect on the physicochemical properties of guest molecules as they are temporarily locked or caged within the host cavity giving rise to beneficial modifications of guest molecules, which are not achievable otherwise [19]. These properties are: solubility enhancement of highly insoluble guests, stabilization of labile guests against the degradative effects of oxidation, visible or UV light and heat, control of volatility and sublimation, physical isolation of incompatible compounds, chromatographic separations, taste modification by masking off flavors, unpleasant odors and controlled release of drugs and flavors. Therefore, cyclodextrins are used in food [20], pharmaceuticals [21], cosmetics [22], environment protection [23], bioconversion [24], packing and textile industry [9].

The potential guest list for molecular encapsulation in cyclodextrins is quite varied and includes such compounds as straight or branched chain aliphatics, aldehydes, ketones, alcohols, organic acids, fatty acids, aromatics, gases, and polar compounds such as halogens, oxyacids and amines [19]. Due to the availability of multiple reactive hydroxyl groups, the functionality of CDs is greatly increased by chemical modification. Through modification, the applications of cyclodextrins are expanded. CDs are modified through substituting various functional compounds on the primary and/or secondary face of the molecule. Modified CDs are useful as enzyme mimics because the substituted functional groups act in molecular recognition. The same property is used for targeted drug delivery and analytical chemistry as modified CDs show increased enantio selectivity over native cyclodextrins [15].

4. CYCLODEXTRINS AS MULTIFUNCTIONAL FOOD INGREDIENTS

The application of CD-assisted molecular encapsulation in foods offers the following advantages [25]:

- Protection of active ingredients against oxidation, light-induced reactions, heat-promoted decomposition, loss by volatility, sublimation.
- Elimination (or reduction) of undesired tastes/odors, microbiological contaminations, fibers/other undesired components, hygroscopicity, etc.
- Technological advantages that include typically stable, standardizable compositions, simple dosing and handling of dry powders, reduced packing and storage costs, more economical, technological processes, manpower saving.

5. CYCLODEXTRINSAS FLAVOUR CARRIERS

From functional standpoint, cyclodextrins can be considered as ‘empty capsules’ of molecular size, and thus the cyclodextrin complexation of flavors is an encapsulation process on molecular scale. The unique feature of the molecular encapsulation compared with traditional encapsulations is that, this novel technology provides an effective protection for every single flavor constituent present in a multicomponent food system. This molecular scale encapsulation inhibits or excludes molecular interactions between the different components of natural or synthetic composite systems like flavor concentrates essential oils, oleoresins, etc [26].

6. CYCLODEXTRINTO PROTECT AGAINST OXIDATION

The complete or partial entrapment of oxygen sensitive flavors or other food ingredients (unsaturated fatty acids, colourants, etc.) by cyclodextrins will, in most cases, result in improvement of chemical stability of the encapsulated agents. Such cyclodextrin-stabilized flavors were found to survive even extreme conditions as it is illustrated on the example of pure oxygen-stressed cinnamaldehyde and benzaldehyde [27]. The effect of oxygen stress on the flavour identity was performed using a Wartburg apparatus, monitoring manometrically the oxygen consumption of the test samples. The results of these experiments showed that CD complexation almost entirely prevented these oxydizable substances from chemical alterations even when stored in pure oxygen atmosphere [26].

7. CYCLODEXTRIN TO PROTECT AGAINST LIGHT-INDUCED DECOMPOSITIONS

Many of the components of flavors are known to be sensitive against different kinds of irradiation. For example, citral (a component responsible for fresh citrus odor) is reported to be cyclized under UV irradiation to ‘photocitral A’ and ‘photocitral B’ [27]. Besides the so called photocitrals the formation of p-cymene and other cyclic monoterpenes have been recently reported which, will cause significant taste modification in citrus flavor containing juices. However, when citral is molecularly entrapped by β-cyclodextrin, none of the above cyclic decomposition products was found after a 6-h exposure to UV light [28]. Similar promising light stability results were obtained with other β CD-complexed flavors upon storage in solid dry state under UV light [26].

8. CYCLODEXTRIN TO PROTECT AGAINST HEAT-INDUCED CHANGES

The CD complexes of volatile flavors and essential oils in solid, dry state were found to possess a remarkable resistance toward heat. In general, improved flavor retention is attained by employing cyclodextrins, compared to the traditional formulations [29]. It was demonstrated on the example of the free adsorbed and cyclodextrin entrapped forms of natural essential oils how powerfully the molecular encapsulation can protect the volatile active ingredients against evaporation. The special thermo analytical method-Evolved Gas Analysis-detects organic volatiles by FID detector released during a programmed heating of solid test samples. Similar encouraging results were obtained by isothermic heat treatments (accelerated stability test) at 60°C for 14 days [26].

9. PACKING AND TEXTILE INDUSTRY

Textile finishing is another area in which cyclodextrins are increasingly attracting attention. Fabrics can be imbued with novel properties by means of cyclodextrins. In order to permanently transfer the versatile properties of cyclodextrins to textiles, Wacker-Chemie(the world's largest producer of γ-CDs) covalently attached reactive CD derivative with monochlorotriazinyl (MCT) substituents to the fiber. This substituted CD provided excellent textile finishing for cottons, blended materials and wools. CDs are also incorporated to the fabrics to entrap and mask malodors from sweat and cigarette smoke. CDs are also used for dying fabrics to increase dye uptake by the fabric and reduce the amount of dye lost in the wastewater. Using hydrophobic tosyl derivative of β-cyclodextrins, 3-fold increase in the binding of fluorescent dye to the polyester fiber was attained [9]. CDs also play a major role in the packing industry. Cyclodextrin inclusion complex containing oily antimicrobial and volatile agents, are coated on a water-absorbing sheet with a natural resin binder, which is used for wrapping fresh products [30]. It was found that food-packaging bags manufactured by using CD with ethylene-tetracyclo-3-dodecane copolymer and hinokitol, showed no odor and good antifungal properties after 1 week of storage at room temperature, which proved useful for food-packaging materials [8].

10. CONCLUSIONS

The ability to hold, orient, conceal and separate guest molecules together with CDs' chirality and low toxicity place cyclodextrins in a unique class of building blocks for constructing novel molecular architecture. Cyclodextrins are not merely another group of excipients, extenders or bulking agents, but they are multipurpose technological tools that can be finely honed by chemical modification. CDs have a demonstrated biotechnological utility as modifiers of sub-microenvironment for solving a range of current problems. They act as molecular chelating agents of growing importance in food, pharmaceuticals, agriculture and chromatographic techniques. The versatility of CDs and modified CDs is demonstrated in their range of applications from cosmetics and food to drugs.

REFERENCES

1. Saenger W., *Angew. Chem.*, **19** (1980), 344.
2. Szetjli J., *Chem. Rev.*, **98** (1998), 1743.
3. Stella V.J., Rajewski R.A., *Pharm Res.*, **14** (1997), 556.
4. Matsuda H., Arima H., *Adv. Drug Deliv. Rev.*, **36** (1999), 81.
5. Mabuchi N., Ngoa M., *Japanese Patent JP* 2001, 128, 632.
6. Buschmann H.J., Schollmeyer E., *A review. J.Cosmet. Sci.*, **53** (2002), 185.
7. Hirose T., Yamamoto Y., *Japanese Patent JP* (2001), 55480.
8. Hedges R.A., *Chem. Rev.*, **98** (1998), 2035.

9. Lu X., Chen Y., *J.Chromatogr. A*, **955** (2002), 133.
10. Baudin C., Pean C., Perly B., Goselin P., *Int. J. Environ. Anal. Chem.*, **77** (2000), 233.
11. Kumar R., Dahiya J.S., Singh D., Nigam P., *Bioresour Technol.*, **28** (2001), 209.
12. Koukiekolo R., Desseaux V., Moreau Y., Marchis M.G., Santimone M., *Eur. J. Biochem.*, **268** (2001), 841.
13. Del Valle E.M., *A review. Process Biochem.*, (2004), 1033.
14. Eastburn S.D., Tao B.Y., *Biotechnol. Adv.*, **12** (1994), 325.
15. Munoz-Botella S., Del Castillo B., Martin M.A., *Ars. Pharm.,* **36** (1995), 187.
16. Loftsson T., Brewster M.E., *J. Pharm. Sci.*, **85** (1996), 1017.
17. Schneiderman E., Stalcup A.M., *J. Chromatogr. B*, **745** (2000), 83.
18. Schmid G., *Trends Biotechnol.*, **7** (1989), 244.
19. Fujishima N., Kusaka K., Umino T., Urushinata T., Terumi K., *Japanese Patent JP* 2001, 136, 898.
20. Hashemiravan M., Mazloom A.S., and Farhadyar N., *Int. J. Nanosci. Nanotechnol*, **9** (2013), 185.
21. Holland L., Rizzi G., Malton P., *PCT Int. Appl. WO*, **67** (1999), 716.
22. Lezcano M., Ai-Soufi W., Novo M., Rodriguez-Nunez E., Tato J.V., *J Agric. Food Chem.*, **50** (2002), 108.
23. Dufosse L., Souchon I., Feron G., Latrasse A., Spinnler H.E., *Biotechnol. Prog.*, **15** (1999), 135.
24. J. Szejtli, 1988. *Cyclodextrin technology, Dordrecht*, the Netherlands: Kluwer Academic.
25. Szente L., & Szejtli J., *Trends Food Sci Tech.*, **15** (2004), 137.
26. L. Szente, & J. Szejtli, 1987. *Stabilization of flavors by cyclodextrins*, In S. Risch, & G. Reineccius (Eds.), Flavor Encapsulation *Am. Chem. Soc. Symp.*, Series 370, 148. New Orleans: ACS.
27. Szejtli J., Szente L., & Banky-Elod E., *Acta Chimica Sci.*, **101** (1979), 27.
28. T.H. Furuta, T. Yoshii, A. Fujimoto, Y. Yasunishi, P.Linko, 1996. *A short cut method for estimating L-menthol retention included in cyclodextrin during drying a single drop,* In J. Szejtli, & L. Szente, (Eds.), *Proc. Intl. Symp.,* OnCyclodextrins, Budapest, the Netherlands: Kluwer Academic.
29. Ishibashi M., Kashikura A., Ozaki S., Kawakubo H., *Japanese Patent JP,* **11** (1999), 285, 368.