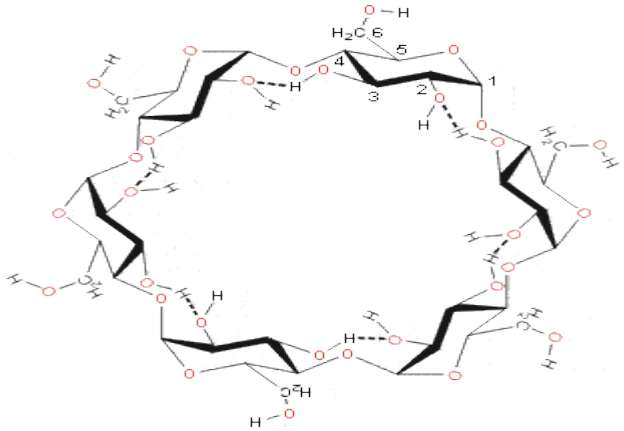
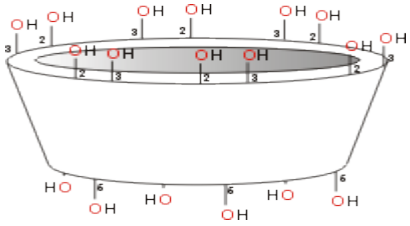
Cyclodextrins

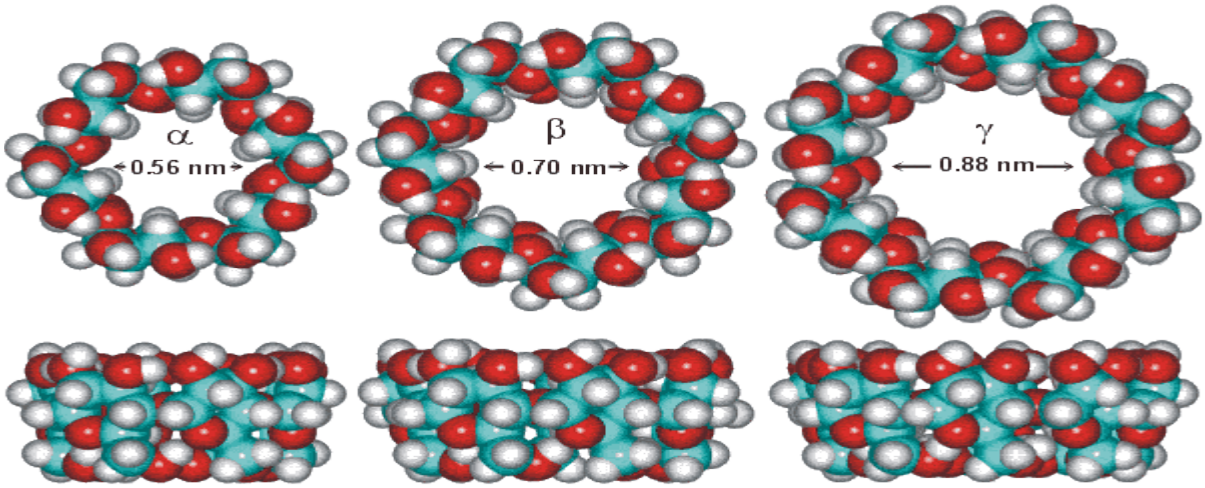
Cyclodextrins are non-reducing cyclic glucose oligosaccharides resulting from the cyclomaltodextrin glucanotransferase (E.C. 2.4.1.19; CGTase) catalyzed degradation of starch. Their structures [918] and use in the food industry [1576] have been reviewed. There are three common cyclodextrins with 6, 7 or 8 D-glucopyranonsyl residues (α-, β-, and γ-cyclodextrin respectively) linked by α-1,4 glycosidic bonds. The glucose residues have the $^4C_1$ (chair) conformation. All three cyclodextrins have similar structures (that is, bond lengths and orientations) apart from the structural necessities of accommodating a different number of glucose residues. They present a bottomless bowl-shaped (truncated cone) molecule stiffened by hydrogen bonding between the 3-OH and 2-OH groups around the outer rim. The hydrogen bond strengths are α-cyclodextrin < β-cyclodextrin < γ-cyclodextrin.



The flexible 6-OH hydroxyl groups are also capable of forming linking hydrogen bonds around the bottom rim but these are destabilized by dipolar effects, easily dissociated in aqueous solution and not normally found in cyclodextrin crystals. The hydrogen bonding is all 3-OH (donor) and 2-OH (acceptor) in α-cyclodextrin but flips between this and all 3-OH (acceptor) and 2-OH (donor) in β- and γ-cyclodextrins [918].



The cavities have different diameters dependent on the number of glucose units (empty diameters between anomeric oxygen atoms given in the diagram below). The side rim depth (shown below in the diagrams) is the same for all three (at about 0.8 nm).



Properties of the main cyclodextrins

Cyclodextrin	Mass	Outer diameter, (nm)	Cavity diameter (nm)		Cavity volume, (mL/g)	Solubility, g/kg H_2O[915]	Hydrate H_2O [915]	
			Inner rim	Outer rim			cavity	external
α, $(glucose)_6$	972	1.52	0.45	0.53	0.10	129.5	2.0	4.4
β, $(glucose)_7$	1134	1.66	0.60	0.65	0.14	18.4	6.0	3.6
γ, $(glucose)_8$	1296	1.77	0.75	0.85	0.20	249.2	8.8	5.4

Cyclodextrin rings are amphipathic with the wider rim displaying the 2- and 3-OH groups and the narrower rim displaying 6-OH group on its flexible arm. These hydrophilic groups are on the outside of the molecular cavity whereas the inner surface is hydrophobic lined with the ether-like anomeric oxygen atoms and the C3-H and C5-H hydrogen atoms. In aqueous solution, this hydrophobic cavity contains about 3 (α-DC), 7 (β-DC) or 9 (γ-DC) poorly held (but low entropy) and easily displaceable water molecules. This water in the cavities has low density as the cavities are large enough to accommodate several more molecules. Thus, the otherwise hydrophilic cyclodextrin molecules may bind non-polar suitably-sized aliphatic and aromatic compounds such as aroma compounds and lipophilic drugs. They may bind in 1:1, 2:1 and 1:2 ratios dependent on the molecules involved (for example, two molecules of γ-cyclodextrin bind well to single C_{60}-fullerene molecules [944]). The binding is driven by the enthalpic and entropic gain on the reduction in the hydrophobe-aqueous surface and the release of water molecules from the cavity to the bulk phase. Such binding also allows cyclodextrins to be used to increase the water solubility of normally hydrophobic compounds or minimize undesirable properties such as odor or taste in certain food additives. Cyclodextrin complexes are now widely used in the pharmaceutical, food and cosmetic and toiletry fields [919].

γ-Cyclodextrin is most flexible and easily hydrolyzed by α-amylases whereas α-cyclodextrin is most rigid and only very poorly hydrolyzed. The cyclodextrins, by themselves, are natural, non-toxic additives. The hydroxyl groups may be derivatized to modify the specificity, physical and chemical properties of the cyclodextrins. The 6-OH groups are most easily derivatized.

The low solubility of β-cyclodextrin, when compared to α- and γ-cyclodextrins presents a puzzle [915]. In a similar manner to the poor solubility of scyllo-inositol, it appears the stronger crystal structure (as with cellulose), due to better placed intramolecular hydrogen bonding, together with a similarly better fit with the structure of water, and consequential low entropy of hydration, are responsible.

Larger cyclodextrins such as cyclomaltononaose (δ-cyclodextrin) and cyclomaltodecaose (ε-cyclodextrin) are also found, if more expensive to produce, but as their ring size increases their stiffness diminishes and the ring becomes slightly twisted, so reducing its binding capacity. Also they becomes much more easily hydrolyzed by α-amylases.

Interactive structures are available (Jmol)

Source: http://www1.lsbu.ac.uk/water/cyclodextrin.html