Cyclodextrins

1 Nonproprietary Names

BP: Alfadex
Betadex

PhEur: Alfadex
Betadex

USP–NF: Alfadex
Betadex
Gamma Cyclodextrin

2 Synonyms

Cyclodextrin *Cavitron*; cyclic oligosaccharide; cycloamylose; cycloglucan; *Encapsin*; Schardinger dextrin.

α-*Cyclodextrin* alfadexum; alpha-cycloamylose; alpha-cyclodextrin; alpha-dextrin; *Cavamax W6 Pharma*; cyclohexaamylose; cyclomaltohexose.

β-*Cyclodextrin* beta-cycloamylose; beta-dextrin; betadexum; *Cavamax W7 Pharma*; cycloheptaamylose; cycloheptaglucan; cyclomaltoheptose; E459; *Kleptose*.

γ-*Cyclodextrin* *Cavamax W8 Pharma*; cyclooctaamylose; cyclomaltooctaose.

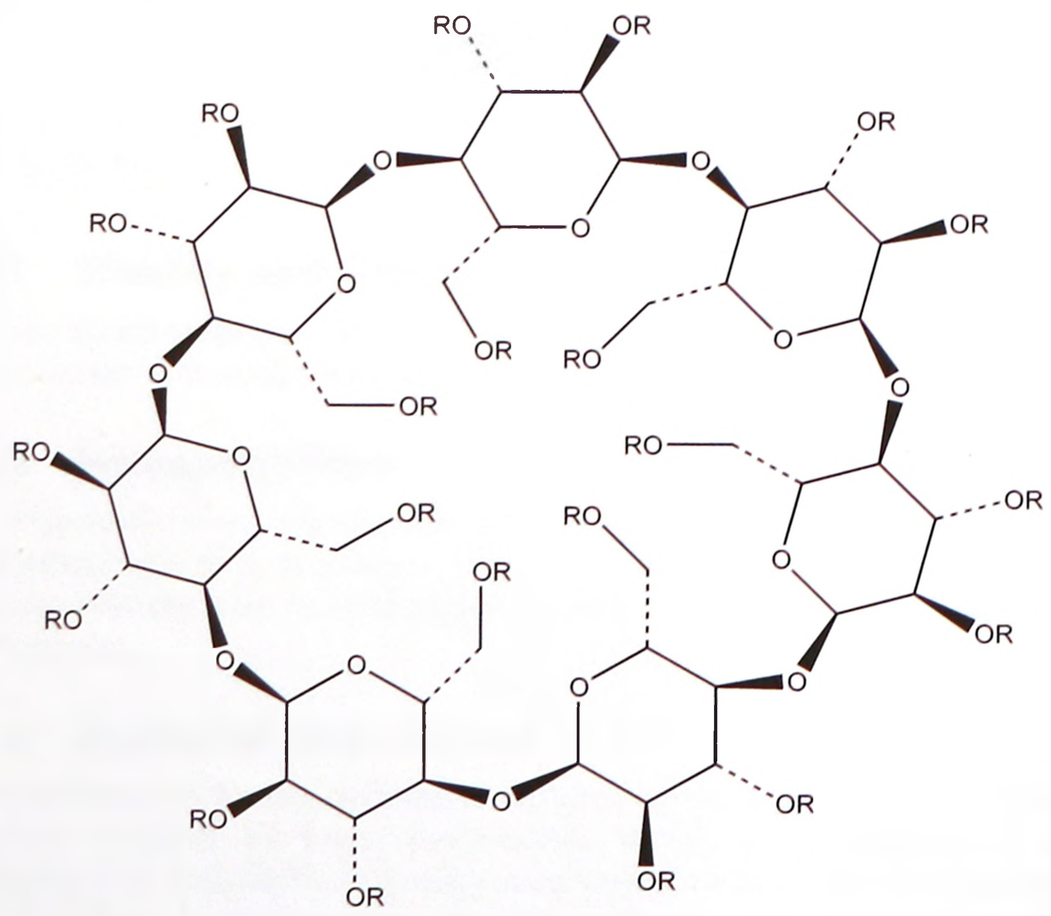
3 Chemical Name and CAS Registry Number

α-Cyclodextrin [10016-20-3]
β-Cyclodextrin [7585-39-9]
γ-Cyclodextrin [17465-86-0]

4 Empirical Formula and Molecular Weight

α-Cyclodextrin	$C_{36}H_{60}O_{30}$	972
β-Cyclodextrin	$C_{42}H_{70}O_{35}$	1 135
γ-Cyclodextrin	$C_{48}H_{80}O_{40}$	1 297

5 Structural Formula



Note: the structure of betadex (β-cyclodextrin) with 7 glucose units is shown.

R = H for 'natural' α, β, and γ-cyclodextrins with 6, 7, and 8 glucose units, respectively

R = H or CH_3 for methyl cyclodextrins

R = H or $CHOHCH_3$ for 2-hydroxyethyl cyclodextrins

R = H or $CH_2CHOHCH_3$ for 2-hydroxypropyl cyclodextrins

6 Functional Category

Complexing agent; solubilizing agent.

7 Applications in Pharmaceutical Formulation or Technology

Cyclodextrins are 'bucketlike' or 'conelike' toroid molecules, with a rigid structure and a central cavity, the size of which varies according to the cyclodextrin type; *see* Section 8. The internal surface of the cavity is hydrophobic and the outside of the torus is hydrophilic; this is due to the arrangement of hydroxyl groups within the molecule. This arrangement permits the cyclodextrin to accommodate a guest molecule within the cavity, forming an inclusion complex.

Cyclodextrins may be used to form inclusion complexes with a variety of drug molecules, resulting primarily in improvements to dissolution and bioavailability owing to enhanced solubility,[1] photostability,[2,3] and improved chemical and physical stability; *see* Section 18. Cyclodextrin inclusion complexes have also been used to mask the unpleasant taste of active materials[4] and to convert a liquid substance into a solid material.

β-Cyclodextrin is the most commonly used cyclodextrin, although it is the least soluble; *see* Section 10. It is the least expensive cyclodextrin; is commercially available from a number of sources; and is able to form inclusion complexes with a number of molecules of pharmaceutical interest.[5–8] However, β-cyclodextrin is nephrotoxic and should not be used in parenteral formulations; *see* Section 14. β-Cyclodextrin is primarily used in tablet and capsule formulations.

α-Cyclodextrin is used mainly in parenteral formulations, and has also been used in supramolecular polymer gels in a controlled drug release system.[9] However, as it has the smallest cavity of the cyclodextrins it can form inclusion complexes with only relatively few, small-sized molecules. In contrast, γ-cyclodextrin has the largest cavity and can be used to form inclusion complexes with large molecules; it has low toxicity and enhanced water solubility, and has been used in topical,[10] ophthalmic,[11] and parenteral[12] formulations.

In oral tablet formulations, β-cyclodextrin may be used in both wet-granulation and direct-compression processes. The physical properties of β-cyclodextrin vary depending on the manufacturer. However, β-cyclodextrin tends to possess poor flow properties and requires a lubricant, such as 0.1% w/w magnesium stearate, when it is directly compressed.[13,14]

In parenteral formulations, cyclodextrins have been used to produce stable and soluble preparations of drugs that would otherwise have been formulated using a nonaqueous solvent.[15]

In eye drop formulations, cyclodextrins form water-soluble complexes with lipophilic drugs such as corticosteroids. They have been shown to: increase the water solubility of the drug; enhance drug absorption into the eye; improve aqueous stability; and reduce local irritation.[16] Developments in ophthalmic formulations have included the use of cyclodextrins in gel and colloidal systems for controlled drug delivery and improved drug solubility, stability and/or ocular bioavailability.[17,18]

Cyclodextrins have also been used in the formulation of solutions,[19,20] suppositories,[21,22] and in nanoparticles,[23–25]