Cavitron™ and Cavasol* hydroxypropyl-β-cyclodextrins

Product Overview

Unique solutions for pharmaceutical formulations

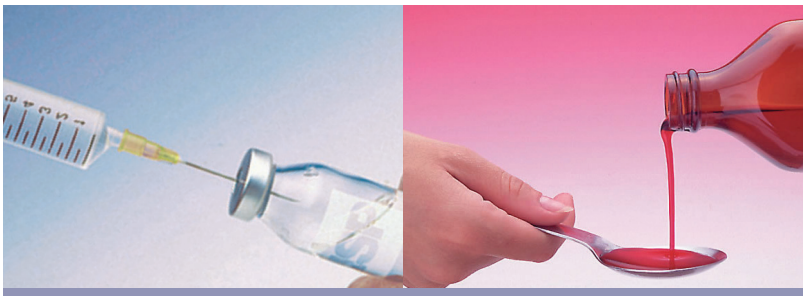
Cavitron and Cavasol cyclodextrin derivatives, like the native Cavamax* cyclodextrins, have the unique ability to act as molecular containers by entrapping guest molecules in their internal cavity. The resulting inclusion complexes are most commonly used to increase water solubility of poorly soluble drugs to improve bioavailability.

In addition to the Cavamax native cyclodextrins, Ashland offers and supports a range of 2-hydroxypropyl-β-cyclodextrin (HPBCD) products. The HPBCD products are manufactured by Wacker Chemie, for pharmaceutical applications around the world (Table 1). The alliance with Wacker combines Wacker's cyclodextrin manufacturing expertise with Ashland's technical sales and customer service capabilities to provide solutions for formulating pharmaceutical products.

Table 1
Ashland offers a range of 2-hydroxypropyl-β-cyclodextrin products

Product	Typical Degree of Substitution	Approximate Molecular Weight	Bacterial Endotoxin
Cavasol W7 HP Pharma cyclodextrin	4.1-5.1	~1410	Not tested
Cavitron W7 HP5 Pharma cyclodextrin	4.1-5.1	~1410	10 IU/g max
Cavitron W7 HP7 Pharma cyclodextrin	6.0-8.0	~1520	10 IU/g max

* Registered trademark owned by Wacker Chemie AG. Ashland acts as a worldwide distributor for Wacker.



Benefits

Increase bioavailability in oral, parenteral, ophthalmic and liquid dosage forms

Provide low endotoxin grades for use in parenteral and ophthalmic dosage forms

Offer grades with differing degrees of substitution

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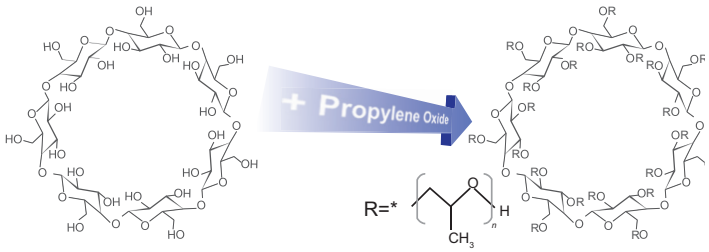
With good chemistry great things happen.™

The Cavitron™ hydroxypropyl-β-cyclodextrin grades are differentiated by degree of substitution. These grades are manufactured to control endotoxin levels and are acceptable for use in parenteral and ophthalmic applications, while the Cavasol* cyclodextrin grade is suitable for oral applications.

β-cyclodextrin derivatives

Hydroxypropyl-β-cyclodextrin is produced by reacting β-cyclodextrin with propylene oxide. The original bucket structure and cavity volume of the β-cyclodextrin remains intact. The propylene oxide reacts randomly with the hydroxyl groups of the β-cyclodextrin resulting in a mixture of compounds with respect to the amount (degree) and position of substitution of hydroxyl groups. By controlling the amount of propylene oxide used, the degree of substitution or average number of hydroxypropyl groups per each cyclodextrin molecule can be controlled.

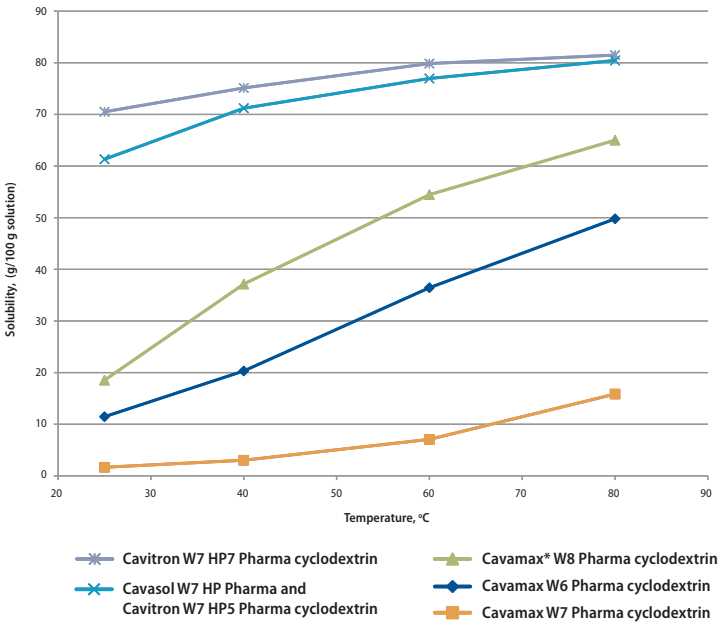
Figure 1: Cavitron and Cavasol cyclodextrins are derived from β-cyclodextrin



Increase in aqueous solubility

The hydroxyl groups and hydroxypropyl groups located on the exterior of the hydroxypropyl-β-cyclodextrin provide increased aqueous solubility (Figure 2). With its higher degree of substitution, Cavitron W7 HP7 Pharma HPBCD has slightly higher water solubility than Cavitron W7 HP5 Pharma HPBCD.

Figure 2
Hydroxypropyl-β-cyclodextrin has increased water solubility



Stable and compatible

Cavitron and Cavasol hydroxypropyl-β-cyclodextrins are stable in bases and weak organic acids, but are hydrolyzed by strong acids. The rate of hydrolysis depends on the concentration of acid and temperature.

The Cavitron and Cavasol cyclodextrins are also stable in the presence of glucoamylases or γ-amylase and β-amylase. The ability of amylases to hydrolyze Cavitron and Cavasol cyclodextrins is limited. The substitution provides steric hindrance resulting in less hydrolysis by the enzyme. The greater the degree of substitution or amount of substitution, the more resistant the hydroxypropyl-β-cyclodextrin is to hydrolysis.

Cavitron and Cavasol cyclodextrins are biocompatible and compatible with a wide range of ingredients commonly used in pharmaceutical applications.

Osmolality

Osmolality is important for formulating ophthalmic, nasal and injectable dosage forms. The osmolality of different concentrations of Cavitron cyclodextrins was determined using a cryoscopic osmometer (Table 2).

Table 2
Osmolality of aqueous Cavitron™ cyclodextrin solutions at 25°C

Product	Conc g/100 mL	mOsmol/kg
Cavitron W7 HP5 Pharma cyclodextrin	10	91
	20	221
Cavitron W7 HP7 Pharma cyclodextrin	10	87
	20	240

Safety and Regulatory

Cyclodextrins are derived from starch and are generally regarded as essentially non-toxic materials. Hydroxypropyl-β-cyclodextrin does not exhibit the nephrotoxicity associated with β-cyclodextrin. A complete toxicology summary is available on request.

Cavitron and Cavasol* cyclodextrins conform to current USP/NF and Ph. Eur. pharmacopeia monographs for hydroxypropylbetadex.

A Drug Master File (DMF) for Cavitron and Cavasol cyclodextrins is currently maintained with the United States Food & Drug Administration.

Cavitron and Cavasol cyclodextrins supplied to the pharmaceutical industry are manufactured in accordance with cGMP.

Applications

Cyclodextrins find use in a wide range of pharmaceutical applications. Many have been well studied and a significant amount of information exists in the technical literature. However, it is only recently that cyclodextrins have started to become commercially significant as process improvements have made them more economically available in large scale, and as formulators and regulatory agencies become more familiar with their benefits.

The primary application for hydroxypropyl-β-cyclodextrins is to form inclusion complexes with poorly soluble drug actives.[1] The resulting drug-cyclodextrin complex hides most of the hydrophobic functionality of the drug active in the interior cavity of the cyclodextrin while the hydrophilic hydroxyl groups on its external surface remain exposed to the environment. The net effect is a water-soluble cyclodextrin drug complex. By forming a cyclodextrin inclusion complex with the active, reactions induced by radiation, heat, oxygen, water and by other chemicals can also be reduced or minimized thus increasing the stability of the active.

[1] This application is potentially covered by patents in some countries. A patent review in the geographic markets of commercial interest is recommended.

Key Specifications

	Cavasol W7 HP Pharma HPB	Cavitron W7 HP5 Pharma HPB	Cavitron W7 HP7 Pharma HPB
Appearance of solution	Clear, colorless		
Molar substitution (per anhydro glucose unit)	0.59 - 0.73	0.59 - 0.73	0.86 - 1.14
% β-cyclodextrin	1 Maximum	1.5 Maximum	1.5 Maximum
% Loss on drying	10 Maximum	10 Maximum	10 Maximum
Bacterial endotoxin (IU/g)	Not tested	10 Maximum	10 Maximum

Full product specifications are available on request.

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