Hydroxyethyl-β-cyclodextrin

1 Nonproprietary Names

None adopted.

2 Synonyms

2-HE-β-CD; HE-β-CD; HEBCD; 2-hydroxyethyl-β-cyclodextrin; (2-hydroxyethyl)-β-cyclodextrin; hydroxyethyl-SS-cyclodextrin.

3 Chemical Name and CAS Registry Number

β-Cyclodextrin, 2-hydroxyethyl ether [128446-32-2] and [98513-20-3]

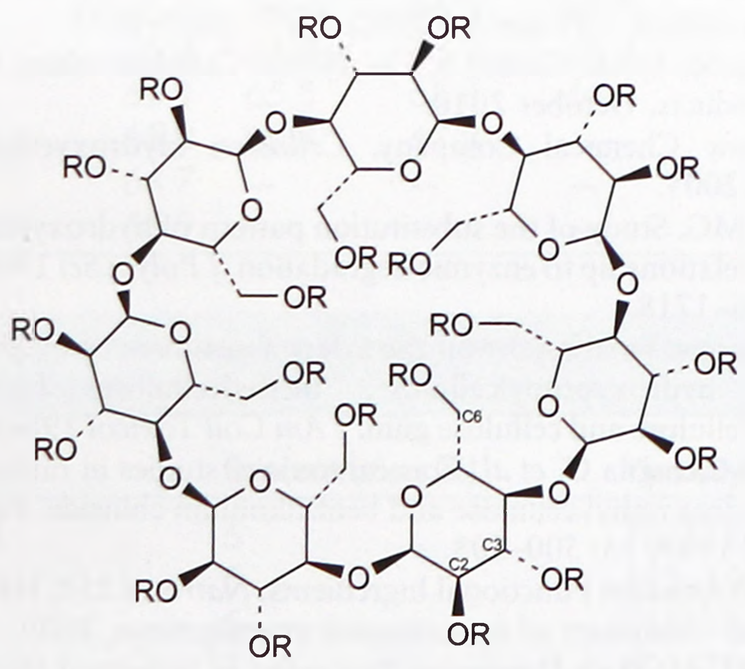
H

4 Empirical Formula and Molecular Weight

$C_{42}H_{70}O_{35}(C_2H_4O)_x$ (where x = molar substitution)

The molecular weight depends on the degree of substitution. The molecular weight of unsubstituted β-cyclodextrin is 1134.98.

5 Structural Formula



R = H or CH_2CH_2OH for 2-hydroxyethyl cyclodextrin depending on degree of substitution.

6 Functional Category

Complexing agent; modified-release agent; microencapsulating agent; solubilizing agent; tonicity agent.

7 Applications in Pharmaceutical Formulation or Technology

Hydroxyethyl-β-cyclodextrin is used to improve dissolution, solubility, bioavailability, and stability of poorly water-soluble drugs through the formation of inclusion complexes in oral,[1,2] topical[3,4] and ophthalmic[5] pharmaceutical formulations. It is used in applications similar to those for β-cyclodextrin (*see* Cyclodextrins), and is more water-soluble than the unsubstituted β-cyclodextrin.

8 Description

Hydroxyethyl-β-cyclodextrin is a nonionic hydroxyalkyl β-cyclodextrin derivative. It occurs as a white crystalline powder.

9 Pharmacopeial Specifications

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10 Typical Properties

Density (bulk) 0.681 g/cm^3
Density (tapped) 0.916 g/cm^3
Density (true) 1.378 g/cm^3
Hygroscopicity Hydroxyalkyl β-cyclodextrin derivatives have low hygroscopicity compared with the parent β-cyclodextrin, and dissolve in the presence of high humidity (>90%).[6]
Melting point 260°C
Solubility Greater than 1 in 2 parts of water at 25°C
Surface tension 68.0–71.0 mN/m (68–71 dynes/cm) at 25°C

11 Stability and Storage Conditions

Hydroxyethyl-β-cyclodextrin is stable in the solid state if protected from high humidity.

Store under inert gas in a cool, dry and well-ventilated place.

12 Incompatibilities

Hydroxyethyl-β-cyclodextrin is incompatible with strong oxidizing agents.

13 Method of Manufacture

Hydroxyethyl-β-cyclodextrin is produced by the condensation reaction of β-cyclodextrin with a hydroxyalkylating agent such as 2-chloroethanol, in alkaline medium.[6,7] The degree of substitution of hydroxyethyl groups can vary.[8]

14 Safety

Hydroxyethyl-β-cyclodextrin is considered to be of low toxicity for use as an excipient.[9] However, direct contact with the material may cause irritation.

Hydroxyethyl-β-cyclodextrin has been reported to be more toxic in mice than hydroxypropyl-β-cyclodextrin, although it was found to be the least potent cyclodextrin derivative in terms of hemolysis.[10]

The International Agency for Research on Cancer (IARC) reports that no component of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen.[11]

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled.

Avoid contact with skin and eyes, and avoid breathing vapors, mist or gas. Gloves and eye protection are recommended. Handle in a well-ventilated environment.

16 Regulatory Status

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17 Related Substances

Betadex sulfobutyl ether sodium; cyclodextrins (α, β and γ-cyclodextrin); dimethyl-β-cyclodextrin; hydroxypropyl betadex; trimethyl-β-cyclodextrin.

18 Comments

Hydroxyethyl-β-cyclodextrin may be used in foods to prolong shelf-life and as a taste-masking agent, and in cosmetic formulations.[12]