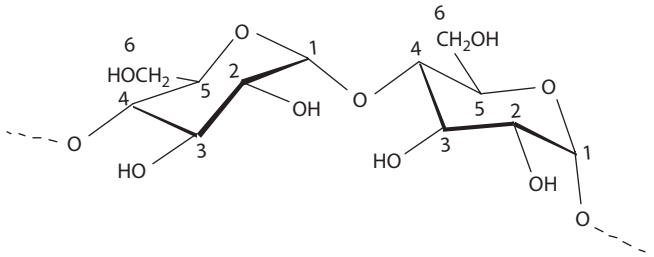

FIGURE 8.1 Conformation and numbering of the cyclodextrins (CDs).

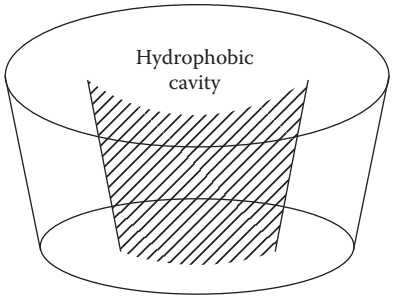

FIGURE 8.2 Physical shape of the cyclodextrin (CD) molecule.

solubility. The solubility of β-CD in water is only 1.85 g/100 mL, compared to 15 g/100 mL for α-CD and 23 g/100 mL for γ-CD. Suitable chemical modification leads to amorphous or at least partially crystalline CD derivatives with high aqueous solubility and considerable reduced parenteral toxicity, depending on the type, degree, and patterns of substitution. The two modified CDs that have received the greatest attention are the HP-β-CDs and SBE-β-CDs, mainly as (SBE)7M-β-CD (Stella and Rajewski 1997; Ammar et al. 2006). The solubility of underivatized CDs generally increases with increasing temperature. On the other hand, the aqueous solubility of methylated CDs is inversely proportional to temperature. An increase in temperature may cause the dehydration of methylated CDs in a manner similar to nonionic surfactants (Uekama 1985).

The physical dimensions of inner cavity of HP-β-CD, that is, 7–8 Å, should be similar to those of its parent. The other dimensions such as height of the torus, diameter of the periphery, and effective volume of the cavity, can only be estimated to fall within a broad range, because of the freely rotating nature of the hydroxypropyl adducts. In the case of SBE-β-CDs, the long hydrophobic groups with an ionic head in the substituent are expected to align themselves to reduce interactions with the aqueous environment similar to micellar formation, resulting in an extended hydrophobic cavity. Because the anionic sulfates repel each other, the opening of the cavity is still maintained.

CDs are fairly stable in alkaline media, whereas they are hydrolytically cleaved by strong acids to give linear oligosaccharides (Bender and Komiyama 1978). The acid-catalyzed ring-opening rate depends upon the cavity size; the larger the cavity, the greater the rate will be. The presence of guest molecules has been showed to decelerate the ring-opening rate of β-CD (Uekama et al. 1994). The authors attributed this to inhibition of access of catalytic oxonium ions to the glycosidic bond, because the CD cavity is occupied by guests.