or chemical properties of different families of guest molecules and complex forming ability with other CDs and their derivatives.

Connors (1997) summarized a collection of K_{11} values from CD literature. Treated as statistical populations, the complex stabilities appear to be reasonably described as normal distribution in log K_{11}, with the mean log K_{11} value equal to 2.11, 2.69, and 2.55 for α-β-, and γ- CDs, respectively.

Thermodynamics of Complexation

The standard free-energy decrease associated with formation of CD inclusion complexes is generally due to a negative standard enthalpy change ($\Delta H°$) accompanying the inclusion process. The standard entropy change ($\Delta S°$) can be either positive or negative, although the majority of guest molecules that have been studied appear to have negative $\Delta S°$ values.

Several intermolecular interactions have been proposed as being responsible for the formation of CD inclusion complexes in an aqueous solution (Matsui et al. 1985; Connors 1997). They are (a) hydrophobic interaction; (b) van der Waals interaction mainly induction and dispersion forces; (c) hydrogen bonding and dipole-dipole interactions; (d) the release of *high energy water* from the cyclodextrin cavity upon substrate inclusion; and (e) the release of conformational strain in a CD-water adduct, together with the formation of a hydrogen bonding network around the O(2), O(3) side of the CD macrocycle upon substrate inclusion.

Because the values of $\Delta H°$ and $\Delta S°$ for complex formation vary over such a wide range, it is reasonable to conclude that the various intermolecular interactions described earlier act simultaneously, and the extent to which these interactions contribute may largely depend on the nature of host and guest molecules.

For most other non-inclusion molecular complexes, the driving forces responsible for complex formation include London dispersion, dipolar (including hydrogen bonding), ionic, π-bonding, and hydrophobic effects (Higuchi and Connors 1965). Most small molecules that have been reported to form complexes exhibit molecular features that permit intermolecular hydrogen bonding. In addition, most molecules whose complex exhibits a substantial planar aromatic moiety, and data strongly suggest that such compounds stack together in a plane-to-plane configuration (Higuchi and Kristiansen 1970).

COMPLEXATION BY CYCLODEXTRINS

There are many examples to demonstrate the effect of CDs on the solubility, dissolution rates and the bioavailability of poorly water-soluble compounds (Uekama et al. 1985; Green and Guillory 1989; Szejtli 1994; Uekama et al. 1994; Thompson 1997; Emara et al. 2002; Patel et al. 2005; Lahiani-Skiba et al. 2006; Yao et al. 2014). Concerning bioavailability, both the rate and extent of absorption are typically enhanced: Not only is the blood concentration higher, with its peak occurring sooner, but the area under the curve is also larger. These results can be obtained, for example, after the oral administration of inclusion compounds of digoxin:γ-CD in the dog (Uekama et al. 1981), diazepam:γ-CD in the rabbit (Uekama et al. 1983c), and allobarbital, amobarbital, barbital, pentobarbital or phenobarbital:β-CD in the rabbit (Koizumi and Kidera 1977). A similar result is obtained following the oral administration in humans of the inclusion compounds salicylic acid:β-CD (Frömming and Weyermann 1973) or prednisolone: β-CD (Uekama et al. 1983a).

Many CDs have been successfully used to solubilize insoluble drugs, here are a partial list of CD derivatives reported in the literature: HP-β-CD, SBE-β-CDs, randomly methylated-β-cyclodextrin (RM-β-CD), 2,3,6-partially methylated-β-CD (PM-β-CD), glucosyl-β-CD (G1-β-CD), maltosyl-β-cyclodextrin (G2-β-CD), hydroxyethyl-β-cyclodextrin (He-β-CD), diethyl-β-cyclodextrin (DE-β-CD), O-carboxymethyl-O-ethyl-β-cyclodextrin (CME-β-CD), (2,6-di-O-methyl)-β-cyclodextrin (DOM-β-CD), 2-hydroxypropyl-γ-cyclodextrin (HP-γ-CD).