STUDY ON INCLUSION INTERACTION OF IBUPROFEN WITH β-CYCLODEXTRIN DERIVATIVES

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Abstract—The inclusion interaction of ibuprofen with hydroxpropyl-β-cyclodextrin (HP-β-CD), hydroxyethyl-β-cyclodextrin (HE-β-CD) and methyl-β-cyclodextrin (Me-β-CD) was investigated by fluorescence spectroscopy. Experimental conditions affecting the inclusion process, such as host molecule, HP-β-CD concentration and pH, were discussed in detail. The results suggested the formation of inclusion complexes with a stoichiometric ratio of 1:1 and HP-β-CD was more suitable to include neutral ibuprofen molecule. In addition, a phase solubility study was performed by mixing an excess amount of ibuprofen with aqueous solution containing increasing amount of β-CDs using UV-vis. The results indicated that the solubility of ibuprofen was increased by inclusion with β-CD derivatives, and HP-β-CD was most efficient among the three β-CD derivatives. Moreover, stable solid inclusion complexes were established and characterized by DSC.

Keywords—ibuprofen, β-CD derivatives, inclusion complex, fluorescence spectroscopy.

I. INTRODUCTION

Cyclodextrins (CDs) are macrocyclic compounds with several D-glucopyranoses residues linked by α-1,4-glycosidic bonds. α-, β- and γ-CD are the most common CDs, which have six, seven and eight glucose units, respectively. Their structures are shown in Fig. 1 (Szejt, 1998; Wenz, 1994; Harata and Kawano, 2002; Rek-harsky and Inoue, 1998). Because of the C6 chair conformation of each glucopyranose unit, the whole molecule has the shape of a hollow truncated cone. The interior of the cavity is composed of hydrogen atoms of C-3, C-5 and oxygen atoms of the glycosidic linkage which make the intracavity hydrophobic, while the exterior of the cavity is hydrophilic due to assembling large numbers of alcoholic hydroxyl groups. CDs can form host-guest inclusion complexes by weak intermolecular interaction with a wide variety of guest (Hapiot et al., 2006; Saenger and Noltemeyer, 1976; Sonoda et al., 2006; Harata, 1998).

Upon inclusion or partial inclusion of molecules within their hydrophobic interior, many properties of guest molecules are affected remarkably, such as chemical reactivity (Uekama et al., 1998), volatility (Tong, 2001), absorption spectrum (Aoyagi et al., 1997) and so on (Matsushita et al., 1997; Ueno, 1992). These changes in chemical and physical properties are of both theoretical and practical interest. CDs have been extensively studied in connection with various areas of chemistry, including the sensing of organic molecules, analytical chemistry, pharmaceuticals, food, encapsulation of drugs and other industrial areas (Jiang et al., 2004; Garcia-Rio et al., 1997; Fakayode et al., 2005; Csernak et al., 2006; Pacioni and Veglia, 2003). In particular, CDs were applied to increase the solubility, bioutility (Aigner et al., 1996), and stability (Uekama et al., 1998) of drugs.

Ibuprofen (IBU) is a non steroidal anti-inflammatory drug from the 2-arylpropionic acid family (Fig. 2). Because of its important anti-inflammatory activity, IBU is commercialized in several types of pharmaceutical preparations, such as tablets, capsules, suppositories and oral drops (Matkovic et al., 2005). However, IBU is not soluble easily in water. Therefore, formation of an inclusion complex with CDs can hopefully increase its aqueous solubility. At present, the interaction of CDs and IBU is limited to parent CDs which have poor water solubility and are unsafe due to its nephrotoxicity (Frank et al., 1976; Irie and Uekama, 1997). Therefore, several modified and relatively safe β-CDs have been used, such as HP-β-CD, HE-β-CD and Me-β-CD.

In our research, the inclusion behavior of IBU with HP-β-CD, HE-β-CD and Me-β-CD was investigated systematically by fluorescence spectroscopy. In addition, a phase solubility study was performed and stable solid inclusion complexes were established and characterized by DSC.

![Figure 1. Molecular structures of CDs](image1)

![Figure 2. The chemical structure of IBU](image2)