Poster Presentation

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Cyclodextrin inclusion complexes of the antioxidant α-lipoic acid

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Owing to its potent antioxidant activity,α-lipoic acid (1,2-dithiolane-3-pentanoic acid) is widely used as a supplement and is recommended for treating a number of conditions including chronic liver disease and diabetes. The poor aqueous solubility of the acid (~0.003 M at 25 °C) has prompted studies of its interaction with cyclodextrins (CDs) as a possible route to improving its solubility. However, relatively few studies have focused on the isolation of solid CD inclusion complexes of the antioxidant, and in most cases the racemic form of the acid was employed. In the comprehensive study reported here, the bioactive (R)-(+)-enantiomeric form of the molecule was used exclusively, resulting in the isolation and structural characterization of its inclusion complexes with each of the native host CDs (α-, β- and γ-CD) as well as permethylated α-CD (TRIMEA), permethylated β-CD (TRIMEB) and 2,6-dimethylated-β-CD (DIMEB). The α-CD complex crystallizes in the trigonal system, space group R32, with three independent CD molecules in the asymmetric unit and is not isostructural with any known CD complex while the β-CD complex crystallizes in the monoclinic system (C2). With the host γ-CD, an orthorhombic (pseudo-tetragonal) inclusion complex was identified, an unusual result as γ-CD complexes generally crystallize in the tetragonal space group P4212. The complexes with TRIMEA and TRIMEB crystallize in the orthorhombic system (P212121), the modes of inclusion of the (R)-(+)-α-lipoic acid molecule in the respective hosts being reversed: the guest molecule is fully encapsulated by the former host with the dithiolane ring located at the secondary rim, while in the latter host, the dithiolane ring rests on the concave surface of the host cavity at the primary side. A significant level of guest disorder was detected in the inclusion complex with DIMEB (P21). Thermal and phase-solubility analyses complemented the X-ray structural studies.

Keywords: cyclodextrins, inclusion complex, lipoic acid