THERMODYNAMICS OF GUEST INCLUSION BY POLYMORPHS OF NATIVE CYCLODEXTRINS

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Cyclodextrins (CDs) are applied to encapsulate drugs, food additives, dyes, essential oils and many other target guests used in various applications. Typically, such encapsulation is performed in solid mixtures, slurries or paste-like systems where there is not enough water to fully dissolve cyclodextrin and guest. Such systems require a different approach than the classical CDs' complexation in aqueous solutions.

The key feature of guest inclusion in solid state is phase transition from solid CD to solid inclusion compound. This process involves a complex interplay between the size exclusion effect for guest inclusion, the cooperative activation of this process by a third component such as water (or organic solvent) additive, and the competition between the guest and water for the space inside CD cavity. As an additional factor, the newly discovered polymorphism of natural CDs can be used [1]. All these processes can be analyzed using classical thermodynamics.

To make a fair comparison of solid state and solution processes, they were analyzed using a thermodynamic activity scale [2]. This approach allowed us to estimate the quantitative contribution of the hydrophobic effect and other important factors affecting the stability of complexes, such as the shape of guest molecules, H-bonding, and repulsion of «high-energy» water molecules.

Fast scanning calorimetry (FSC) is state-of-the-art method which allowed to find the melting points and enthalpies for the natural CDs [1]. The obtaining of such data is possible due to extremely high heating rates up to 2,400,000 K/min, enabling a study of processes that are 'hidden' for the conventional methods of thermal analysis. Such data are essential for understanding structure-property relationships; for calculations on the energy of the crystal lattice for CD polymorphs, which has a crucial effect on inclusion properties; for evaluation of the temperature limits during modification of drug complexes by fast heating and cooling. Such data also give the innovative possibility to determine thermodynamic parameters of CDs liquid state which is essential for the understanding and the molecular modeling of guest inclusion by CDs.

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2. Gatiatulin A.K., Ziganshin M.A., Gorbatchuk V.V. Guest inclusion by native cyclodextrins in solid state and solutions: A review // Carbohydr. Polym. 2025. Vol. 349, 122962. https://doi.org/10.1016/j.carbpol.2024.122962

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