ABSTRACT IN ENGLISH

In this study, X-ray crystallographic and neutron scattering experiments have been performed in order to comprehend the negative solubility coefficient in water of methylated cyclodextrins (CDs). X-ray analyses have been carried out for two crystal forms of both heptakis(2,6-di-*O*-methyl)-β-CD (DIMEB) and octakis(2,3,6-tri-*O*-methyl)-γ-CD (TRIMEG) which were grown from cold water at 291 K, and neutron scattering measurements for aqueous solutions of DIMEB, TRIMEG, and γ-CD at 287–323 K.

In DIMEB·2H_2O and DIMEB·15H_2O, the DIMEB molecules adopt "round" conformations stabilized by interglucose O3(n)–H$\cdots$O2($n+1$) hydrogen bonds. While the former has 2 water molecules, one being included in the cavity and one in the intermolecular space, the latter has 15 water molecules which are all located outside the cavity and form a channel clathrate hydrate host structure enclosing the guest DIMEB. The abundance of 15 host-guest hydrogen bond interactions give rise to high thermal stability of the DIMEB·15H_2O crystal. (4TRIMEG)·19.3H_2O and TRIMEG·4.5H_2O which have no interglucose O3(n)–H$\cdots$O2($n+1$) hydrogen bonds (because all O–H groups are methylated) are more flexible and the molecular structure of TRIMEG is notably different. In (4TRIMEG)·19.3H_2O, all four TRIMEG molecules adopt "elliptical" conformations with two diametrically opposed glucose units 1 and 5 flipped by $\approx 180^\circ$ (*anti* orientation). The 19.3 water molecules are distributed over 27 positions both inside and outside the TRIMEG cavities and are hydrogen bonded in different patterns to the four TRIMEG molecules. This contrasts TRIMEG·4.5H_2O in which the molecular structure is "round" with all glucoses orientated *syn* and the 4.5 water molecules are accommodated in its cavity. The highly hydrated crystal forms of DIMEB·15H_2O, (4TRIMEG)·19.3H_2O, and TRIMEG·4.5H_2O grown from cold water indicate that the hydration may be associated with the high solubility of these methylated CDs in cold water.

This is evidenced by neutron scattering results showing that in aqueous solution at 287 K, DIMEB and TRIMEG are hydrated by a large number of water molecules and diffuse slowly as indicated by a broad quasielastic peak which is characteristic of diffusive motion in the liquid state. As the temperature rises to 305 K, the hydration number decreases, DIMEB and TRIMEG diffuse faster. When the temperarure reaches the crystallization point at 323 K, the hydration number decreases rapidly, DIMEB aggregates and crystallizes as shown by a sharp elastic peak which indicates very slow motion of larger, solid state particles. For comparison, for γ-CD (with normal solubility behavior), the diffusion mobility increases with increasing temperature and the hydration number decreases and converges to an asymptotic value at higher temperature.