INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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SHORT ABSTRACT

Hydrotropes are substances that improve the solubility of sparingly soluble solute molecules in water. Hydrotropic solubilization is new, simple, economic, safe method, and widely used to increase the solubility of sparingly soluble drugs. The mechanism by which hydrotrope molecules increase the solubility of insoluble solutes has been investigated. We focus on the effects of anionic, cationic and nonionic hydrotropes on the different hydrophobic as well as sparingly soluble drug molecules and put an effort to uncover the basic mechanism of hydrotropy. Chapters 2 deals with the hydrotropic action of anionic hydrotrope and is divided into two parts: Part A and Part B. In Part A, we investigate the self-aggregation behavior of hydrotrope sodium cumene sulfonate (SCS) in aqueous solution of increasing SCS concentration. The study reveals that SCS molecules start to self-associate at and above its minimum hydrotrope concentration (MHC) and with increasing concentration the self-aggregation propensity of hydrotrope SCS molecules also increases. The underlying mechanism behind the enhanced solubility of a solute in water (in presence of hydrotropes) has been explored in Part B. To examine the mechanism of hydrotropy we have used di-t-butyl-methane (DTBM) as a model hydrophobic solute and SCS as hydrotrope and the outcome is presented here. We find that above minimum MHC, the self-aggregation of SCS starts and the aggregated SCS creates a micellar like environment in which the hydrophobic tail part of SCS points inward while its hydrophilic sulfonate group points outward to make favorable contact with water molecules. Similar to the work in Chapter 2B, the effect of hydrotrope SCS on the solubility of a sparingly water-soluble drug, griseofulvin, is studied in Chapter 3. The main observations from this study are the following: (i) The SCS molecules self-aggregate through its small hydrophobic tail above the MHC causes the formation of micellar-like frameworks, and (ii) interestingly, though the drug griseofulvin drug molecule possesses both polar and nonpolar groups, it prefers to get encapsulated inside the hydrophobic core of SCS aggregates. In Chapter 4, we have examined the effects of cationic hydrotrope on the solubility of sparingly soluble drug molecule by means of classical MD simulation technique. We have used p-toluidinium chloride (PTOL) as hydrotrope molecule and gliclazide as drug molecule. Our cluster structure analysis results demonstrate that PTOL starts to self aggregate above its MHC. Further, these PTOL aggregates create a mixed micellar type framework in which the hydrophobic small tail parts of most of the PTOL molecules direct inside whereas in order to make favorable contact with water molecules its hydrophilic ammonium group points outward. The effect of non-ionic hydrotrope nicotinamide on the solubilization of sparingly soluble riboflavin drug molecule is investigated in Chapter 5. The calculation of orientational preference of aromatic planes constituting the nicotinamide with respect to the another nicotinamide or riboflavin molecule indicate that nicotinamide molecules selfassociate through stacking of their pyridine rings and they also form complexes with riboflavin molecules in 1:1 and 1:2 ratio. In Chapter 6, we have emphasized the drug releasing ability hydrotrope clusters. The goal of this study is to investigate the release of griseofulvin drug into situ. In brief, we investigated the binding of the drug griseofulvin molecule (after releasing from the hydrotrope cluster) to the different binding sites of the protein γ-tubulin via classical MD simulation and MM-GBSA method. In Chapter 7, we have discussed the results of each of the work and concluded.