Investigation of the Structure, Stability, and Relative Solubility of Psilocybin in Water and Pure Organic Solvents

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Psilocybin is an indole-based secondary metabolite found naturally in mushrooms which possesses several pharmacological effects. Recently, a large number of experimental investigations have been conducted to characterize the pharmacology of psilocybin and its derivatives, and to develop synthetic pathways to manufacture psilocybin. Nonetheless, current research on the physical characterization of psilocybin is limited in part due to legal restrictions. In the present study, we investigate two unique tautomers of psilocybin as depicted in the 2D chemical structure of psilocybin presented in the recent literature. Using a combination of electronic structure calculations and molecular simulation, we are able to identify and characterize the thermodynamically preferred tautomer. We additionally computed the solvation free energy and investigated the solvation structure of psilocybin in water and 35 organic solvents. We find that hydrogen bonding between psilocybin and the solvent dominate the solvation process. Considering the thermodynamically preferred tautomer, we find that the solubility in water is greater than all of the studied organic solvents.