Molecular Dynamics Simulation on the Structural Stability and Solvation of Irinotecan in Water and Organic Solvents

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ABSTRACT

Irinotecan is a synthetic drug that belongs to a group of medications called topoisomerase 1 inhibitors. It is used in the treatment of several types of cancer, including colorectal, lung, and ovarian cancer. Despite its effectiveness, irinotecan is associated with several challenges, such as limited solubility, poor bioavailability, and toxicities. Recent studies have aimed to improve the drug's pharmacological properties, but little attention has been given to its solvation and conformation behavior. Understanding these properties is crucial for unlocking irinotecan's full potential in drug design and discovery. To investigate this, we study the influence of solvents on the drug's physicochemical properties. Using a combination of connection matrix and radial distribution function, we are able to perform structural analysis. Additionally, we computed solvation-free energy and investigated the solvation-free energy of irinotecan in water and 10 organic solvents. Our structural analysis shows that hydrogen bonding between irinotecan and solvents dominates the solvation process. We find that the drug's solubility and structural stability depend on the type of solvent used. Polar solvents were found to be better than non-polar solvents in terms of solubility and stability. Additionally, we observe that irinotecan bends and extends in polar solvents, while it only extends in non-polar solvents. Moreover, we find that the drug is more stable in cyclohexane than in water and studied organic solvents, as suggested by its more negative solvation-free energy (-395.380 J/mole in cyclohexane versus -339.150 J/mole in water). These findings reveal that cyclohexane is the best solvent for the solvation of irinotecan than in water other studied solvents. Additionally, irinotecan solubility is not only contributed by solute-solvent interactions as we normally think but also solute-solute interactions play a significant role.

Through our findings of solvents, we have gained valuable and comprehensive insights into the solubility and structural stability challenges of irinotecan in cancer treatment, which will significantly enhance its therapeutic efficacy.

Keywords: Irinotecan, Solubility, Solvation Free Energy