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EFFECT OF HYDROPHOBICITY ON ENTRAPMENT EFFICIENCY OF DENDRIMERS

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Dendrimers are highly branched macromolecules having potential applications in medicine as drug delivery vehicles. In order to design new dendrimer molecules with high drug loading capacities, it is important to understand their structure-property relationships. Hydrophobic-hydrophilic interactions between the drug and the dendrimer plays a major role in drug loading. However, understanding the hydrophobic effect is difficult due to the limitations of conventional experiments. In this study, the effect of hydrophobicity on the entrapment efficiency of dendrimers using molecular dynamics simulations is reported. Simulations were performed with parameters derived from the force field developed by Shinoda, DeVane and Klein, for dendrimers of generation 2, 3 and 4 with a range of hydrophobicity. Hydrophobicity was varied with a parameter ζ (zeta), which was defined with $0 < \zeta < 1$; for the hydrophobic end of the range, ζ was defined as 0, and for the hydrophilic reference, $\zeta = 1$ was assigned. Phenol was used as the loading molecule and drug analogue. First, phenol was overloaded to the dendrimer by simulating the dendrimer in a phenol box. In order to see the entrapment capabilities, phenol overloaded dendrimer was simulated in a water box, allowing the overloaded phenol to release with time. By extrapolating the releasing behaviour, the equilibrium entrapment capacities were determined. It was found that entrapment capacity decreases with increasing hydrophilicity of the dendrimer for generation 2 and 3 dendrimers. However, for the generation 4 dendrimer, the highest entrapment capacity is observed for $\zeta = 0.3$. Analysis of the radius of gyration and root mean square separation of branch points clearly shows the coil-to-globule transition from $\zeta = 0.6$ to $\zeta = 0.8$ for all dendrimers. According to this study, entrapment capacity depends on many factors, such as hydrophobic interactions between drug and dendrimer, size of the dendrimer and solvent environment. This study provides valuable data to design new dendrimers with high loading capacities which were unable to access previously using conventional wet-lab experiments.

Keywords: Coil-to-globule transition, Dendrimers, Entrapment efficiency, Hydrophobicity