Study of specific interactions in inclusion complexes of amine-terminated PAMAM dendrimer/flavonoids by experimental and computational methods

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Polyamidoamine (PAMAM) dendrimers have a multifunctional structure, able to encapsulate molecules for pharmacological applications. We evaluated the specific interaction that govern the encapsulating and affinity of one group of natural and synthetic flavonoids into the G5-PAMAM dendrimers. The complexation and capture percent of one flavonoid series into G5-PAMAM dendrimers, under neutral and acid pH conditions, were studied through UV?Vis spectroscopy. Additionally, only three of the flavonoids (two synthetic and one natural) were studied by high-performance liquid chromatography (HPLC) and molecular dynamic (MD) simulation, at neutral pH to calculate the affinity constants (Kd) and binding free energies (?Gb). From spectroscopic results, we observed that the encapsulation was much more rapid at low pH than at neutral pH, which was attributed to a greater number of cavities inside the dendrimer. The MD simulations suggested that the more compact molecular structure at neutral pH reduces the capture kinetics. Finally, the relative binding free energies calculated using MD simulations showed the same tendency as the experimental data for the three complexes. These affinities appear to be due to a complex balance of different contributions, which cannot be attributed to hydrogen bonds or charge?charge interactions alone. Nevertheless, we suggest that a protocol including UV?Vis, HPLC, and MD simulation can be a powerful predictive tool to determine the affinity of drug binding to nanocarriers.

Dendrimers

flavonoids

Hill model

MM-GBSA

molecular modeling simulation

Binding energy

Bins

Flavonoids

Free energy

High performance liquid chromatography

Hydrogen bonds

Liquid chromatography

Molecular dynamics

Affinity constants

Binding free energy

Charge interactions

MM-GBSA

Molecular modeling simulations

Multi-functional structures

Polyamidoamine dendrimers

Specific interaction

Dendrimers