POMÈS LAB

Computational Biophysics: Biomacromolecular Structure, Function, and Dynamics

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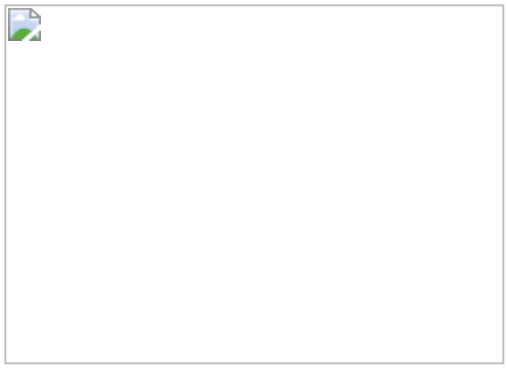
Research Synopsis:

To date, the development of most drug formulations proceeds largely by trial and error with no clear method of predicting which excipient or material is most appropriate. In this way, the selection of a suitable excipient or material can be a time consuming and expensive endeavor. There are certain physico-chemical criteria of drugs and excipients that have been shown to be important in terms of influencing the effectiveness or performance of a formulation including molecular weight, solubility, stability and compatibility. Recent advances in molecular modeling methods combined with theoretical approaches allow accurate calculation and prediction of important properties of many biological and chemical systems.

The solubility of drugs and the degree of interaction for drug-excipient pair are important properties that are commonly used to guide formulation design. In my study, semi-empirical methods and molecular dynamics (MD) simulations were employed to calculate the solubility parameters (δ) for drug and excipients as well as the Flory-Huggins interaction parameters (χFH) for excipient-drug pairs. The compounds of interest for my studies are the potent, hydrophobic anti-cancer agent docetaxel and the pharmaceutical excipients (i.e. tributyrin, tricaproin, tricaprylin, vitamin E and B-caryophyllene. Docetaxel has a limited aqueous solubility and is approved for use in the treatment of prostate, gastric, lung, breast and head and neck cancers. Cerius software and COMPASS force-field were employed for the MD simulations.

The values obtained from the MD simulations for the solubility of docetaxel in the various excipients were in good agreement with the experimentally determined values. The simulated values for solubility of docetaxel in tributyrin, tricaproin and vitamin E were within 2 to 6 % of the experimental values. MD simulations predicted docetaxel to be insoluble in B-caryophyllene and this result correlated well with experimental studies.

The MD model proved to be a reliable tool for selecting suitable excipients for the solubilization of docetaxel. At present, the MD method are employed to direct the design of drug delivery materials.



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