Abstract

MOLECULAR INTERACTIONS IN INCLUSION OF COMPLEXES WITH CYCLODEXTRINS

by

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Most case studies of Thai traditional drugs (herbal products) have shown a similar problem of the substance degradation that can cause the instability in the active compounds, including Plumbagin. Basically, encapsulation technique is adopted to address this problem and widely employed to improve the stability of numerous compounds in diverse industries. Binding energy is an important value in the inter-molecular interaction between host and guest molecules, that can directly affect the drug efficiency from the release of active compound to the target cell. *Ab initio* investigation of the binding energy is an important tool to provide useful theoretical predictions. Density Functional Theory (DFT) is most suited to do this. However, its dependence on the exchange-correlation (XC) functionals means that it is necessary to assess the strengths and weaknesses of these functionals for the relevant system. This is the main objective of this study.

To consider the molecular and organic system, B3LYP functional is generally viewed as the most suitable XC functional. However, it is unable to properly account for inter-molecular interaction, of which dispersion forces (and therefore, dispersion-corrected functionals) is a vital part. A total of five dispersion-corrected functionals were assessed in this study: CAM-B3LYP, B3LYP-GD3, CAM-B3LYP-GD3, M06-2X, and M06-2X-GD3. The conventional hybrid DFT (B3LYP) provides positive binding energy, which means it cannot capture the dispersion force from an inter-molecular interaction. Dispersion correction functionals, meanwhile, give negative values of binding energy, with DFT-GD3 providing the precise and lowest binding energies. These *ab initio* results are compared also with those

of semi-empirical methods. Of these, the PM7 method presents the lowest binding energy, though we observe significant overestimations.

Keywords: Cyclodextrins, Encapsulation, Inclusion complex, DFT, Dispersion functional