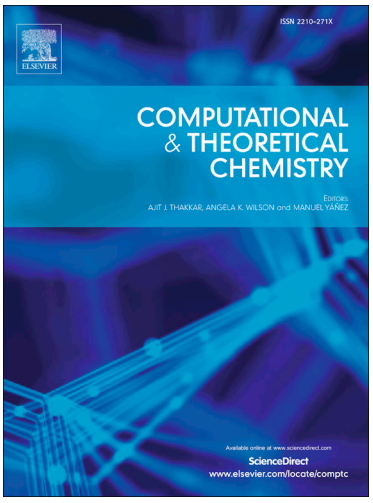


# DFT studies of camptothecin aggregation in solutions

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# DFT studies of camptothecin aggregation in solutions

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Dedicated to Prof. Andrej Staško in honor of his 80th birthday.

Abstract

The structures of camptothecin (CPT) lactone head-to-tail π-aggregates up to tetramers were optimized in DMSO and aqueous solutions using various DFT functionals with cc-pVDZ basis sets. Solvent effects were estimated using the Integral Equation Formalism Polarizable Continuum Model. The calculated reaction equilibria indicate that the higher π-aggregates formation is more preferred in DMSO than in aqueous solutions. TD-B3LYP calculated electron transitions ascribe two strong peaks over 300 nm in UV-Vis spectra to the CPT monomer (at lower wavelength) and to higher CPT head-to-tail π-aggregates (at higher wavelengths). Only B3LYP with D2 dispersion correction of Grimme and ωB97XD functionals are able to produce reliable results.

Keywords: DFT calculations; long-range and dispersion corrections; solvent effects; reaction equilibria; electron transitions

## 1. Introduction

The quinolone alkaloid camptothecin (CPT), (S)-4-ethyl-4-hydroxy-1h-pyrano[3‘,4‘:6,7]-indolizino-[1,2-b]-quinoline-3,14-(4h,12h)-dione, has been isolated from the bark and stem of the chinese tree *Camptotheca acuminata* (*Nissaceae*) [1-3]. A potent anticancer drug targeting intracellular Topoisomerase I corresponds to its lactone form (Fig. 1) which is stable at pH < 5.5. Under biological conditions the lactone hydrolyses to an inactive carboxylate form (stable at pH > 9) and the equilibrium is obtained after ca 2 hours [4]. The low lactone form concentration in