Nature's Solution for Cancer: Enediynes – Understanding Enediyne-DNA Complexes from Binding to Apoptosis

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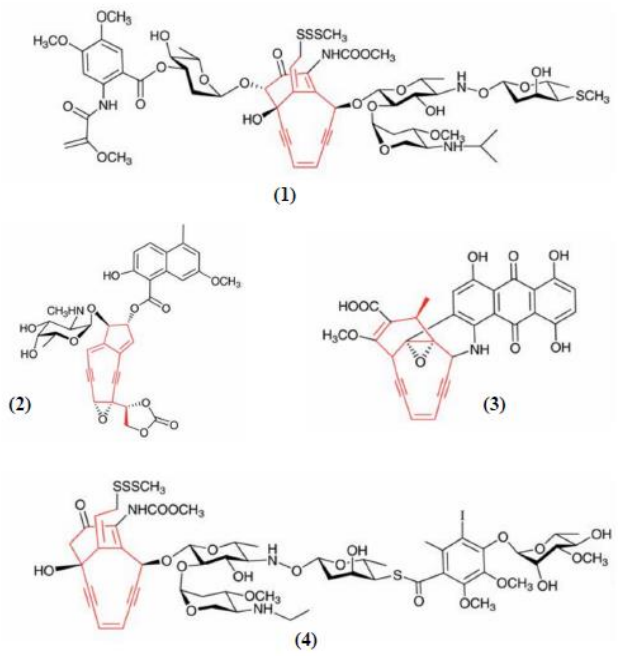
Abstract

Under the influence of heat or light, enediynes convert to para-benzenes via the Bergman cyclization reaction. The resulting para-benzyne moiety can abstract hydrogen atoms from DNA leading to DNA unraveling and subsequent cell death. Neocarzinostatin, Esperamicin, Calicheamicin, and Dynemicin are the major classes of natural compounds that contain an enediyne core. In order to evaluate the effectiveness of the enediyne compounds as a cancer drug, we utilized computational chemistry to evaluate the mechanism whereby these compounds undergo the Bergman cyclization and abstracts H atoms in the presence of DNA. We used docking methods available in GLIDE to generate initial poses, as well as published crystal structures, which were subsequently subjected to long time scale molecular dynamics to explore the conformational flexibility and binding affinity of the Enediyne-DNA complex. This study will allow us to see both the interaction of various potential cancer drugs with DNA as well as the energy necessary to influence the Bergman cyclization reaction.



Various Naturally Occurring Enediyne Molecules. (1) Esperamicin A_1, (2) Neocarzinostatin Chromophore, (3) Dynemicin A, (4) Calicheamicin γ_1^I. The enediyne core has been highlighted in red.