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Design of Novel Cytotoxic Compounds for a Selective Treatment of Cancer

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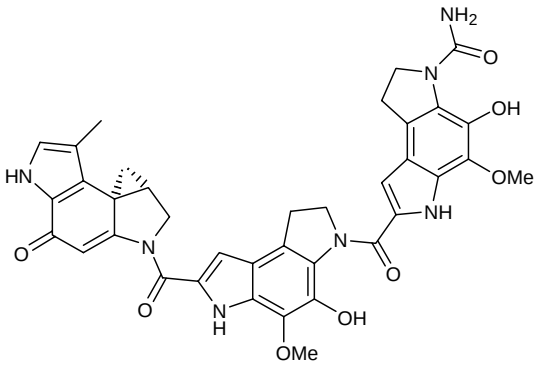
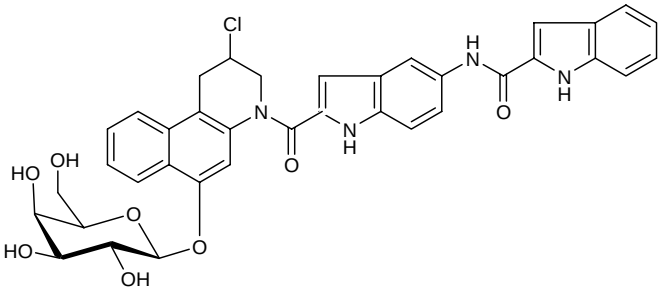
Tumour-selective chemotherapy must be based on the exploitation of phenotypic or genetic differences of malignant and normal cells. A promising approach is the antibody directed enzyme prodrug therapy (ADEPT) in which a conjugate of an enzyme and a monoclonal antibody binding to tumour associated antigens is used to convert a non-toxic prodrug into a toxic species selectively at the surface of malignant cells. We have developed novel glycosidic prodrugs such as **2** based on the biologically highly active antibiotic CC-1065 **1** which is a potent cytotoxic compound with an ED_{50} of about 30 pM.[1]



CC1065 **1**



Seco CBI-Galactoside **2**

This prodrug is up to 3000 times less toxic than the corresponding toxin in cell culture investigations. It does not show any systemic toxicity using therapeutic doses and is very effective also in the *in vivo* investigations employing mice. Novel techniques as Optical Imaging and Volume Computer Tomography allow us to localize the binding of the monoclonal antibodies and to determine the size of the tumors in living animals.

References:

Review: L.F. Tietze and T. Feuerstein, *Aust. J. Chem.* **2003**, *56*, 841-854.