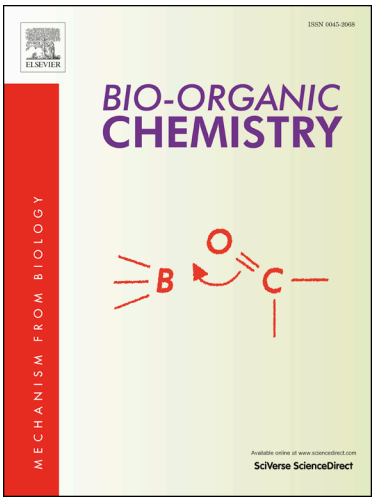

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Development of pyrrolo[2,1-*c*][1,4]benzodiazepine β-glucosideprodrugs for selective therapy of cancer

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Abstract:

Cancer chemotherapy has several limitations such as often insufficient differentiation between malign tissue and benign tissue. The clinical utility of the pyrrolo[2,1-*c*][1,4]benzodiazepines (PBDs) are inadequate because of the lack of selectivity for tumor tissues, high reactivity of the pharmacophoric imine functionality, low water solubility, and stability. To address these limitations two new β-glucoside prodrugs of PBDs have been synthesized and evaluated for their potential use in selective therapy of solid tumors by ADEPT. The preliminary studies reveal the prodrugs are much less toxic compared to the parent moieties. These prodrugs are activated by β-glucosidase to produce the active cytotoxic moiety signifying their utility in ADEPT of cancer. The prodrugs **1a** and **1b** were evaluated for their cytotoxic activity in three human cancer cell lines, i.e, A375, MCF-7 and HT-29 by employing MTT assay. The results reveal that the prodrugs have shown significant cytotoxic activity in the presence of enzyme. Another important property of these molecules is their enhanced water solubility and stability, which are essential for a molecule to be an effective drug.

Keywords:pyrrolo[2,1-*c*][1,4]benzodiazepine,prodrugs,β-glucoside, cytotoxicity, selective therapy.

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