A01

Design and synthesis a water-soluble group for ether-linkage of 10-hydroxycamptothecin prodrug

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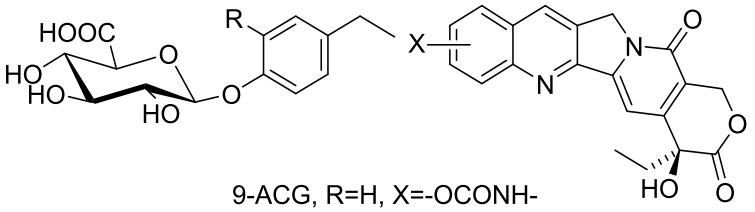
For selective cancer chemotherapy, we previously designed and synthesized two *β*-glucuronidase-activated prodrugs of camptothecin (**9-ACG** and **10-HCG**), which increased water solubility for camptothecins. In normal tissues, *β*-glucuronidase is localized primarily in lysosomes and thereby not available for activation of glucuronide prodrugs because these prodrugs are generally hydrophilic, thus rendering them impermeable to cell membranes. Therefore, glucuronide-based prodrugs can be used in prodrug monotherapy.

9-ACG was more soluble than **10-HCG** via oxycarbamate linkage, so **9-ACG** was more low toxicity than **10-HCG**. However, **10-HCG** was a good substrate for *β*-glucuronidase, which has ether linkage. In order to increase the solubility of **10-HCG**, we designed **10-HCPG**, which creates a hydrophilic group in link of prodrug. We predict that **10-HCPG** is soluble, low cytotoxicity and good a substrate for *β*-glucuronidase. We expect **10-HCPG**, which is a good candidate for selective cancer chemotherapy.



9-ACG, R=H, X=-OCONH-
10-HCG, R=-NO_2, X=-O-
10-HCPG, R=-CH_2-N(CH_2CH_2)$_2$-N-CH_3, X=-O-