Fabrication of nano-prodrugs composed of hinokitiol-modified podophyllotoxin

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In recent years, nanomedicines made by the usage of nanocarriers such as liposome, polymer micelle, and protein have been applied to drug delivery system for cancer treatment. However, the conventional formulation strategy can lead to several problems, such as undesirable side effects caused by the carriers themselves or their metabolites. To overcome these problems, our group have proposed "nano-prodrugs" which is novel designed nano-drugs without using carriers. We had reported some nano-prodrugs composed various substituent-modified drugs.[1]

In this study, we synthesized hinokitiol-modified anticancer drugs as heterodimeric prodrugs and fabricated their nano-prodrugs by reprecipitation method.[2] Hinokitiol, a natural monoterpenoid, is known for its antibacterial activity and some anticancer activities.[3] These nano-prodrugs possessed high drug loading capacity, and *in vitro* cell cytotoxicity revealed that depends on the length of the carbon chain linker (Figure 1). These nanoparticles also possessed good dispersion stability, and further research revealed that the tropone skeleton of hinokitiol is the key structure for the dispersion stability in our prodrug design.

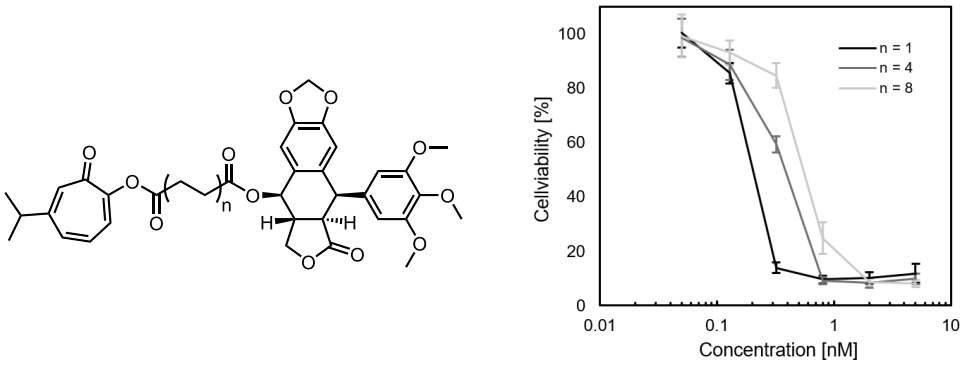

Figure 1. *in vitro* cytotoxicity of hinokitiol-conjugated PPT linked via dicarboxylic acid
All results are indicated as mean ± standard deviation (n = 3).

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