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Hydroxyethyl Starch Based Smart Nanomedicine

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Abstract

Derived from waxy maize, which contains more than 95% of amylopectin, hydroxyethyl starch (HES) is therefore highly water soluble, keeps the branched structure of amylopectin, and has wide clinical use as plasma volume expander. HES can be categorized into various classes based on its molecular weight, mole substitution of hydroxyethyl, and substitution pattern (C_2/C_6 ratio). These parameters affect the endogenous α-amylase mediated degradation of HES in blood, thus determine the pharmacokinetics of HES, enabling convenient ways to tailor the in vivo fates of HES by simply adjusting these parameters. The good manufacturing practice, high water solubility, tailorability, biocompatibility, biodegradability, well defined in vivo safeties, and wide clinical applications make HES a promising drug carrier which warrants clinical translation explorations.

In this talk, we will present our progress of HES based smart nanomedicines. We prepared a novel redox-sensitive hydroxyethyl starch-doxorubicin conjugate, HES-SS-DOX, with diameter of 19.9 ± 0.4 nm, to alleviate the side effects and improve the antitumor efficacy of DOX. With HES-SS-PTX, we also obtained self-assembled nanoclusters (with diameter of 150 nm), which show dual α-amylase and redox responsive properties for enhanced tumor penetration and therefore improved antitumor efficacy. We conjugated HES with polylactide to afford HES-PLA, which self assembles to nanoparticles with varied sizes. The large sized HES-PLA nanoparticles (with diameter 700 nm) are applied to saturate the MPS system, while the smaller ones (150 nm) are loaded with DOX for enhanced drug delivery efficiency and improved anti-tumor efficacy. Moreover, both cytotoxic drug, for instance DOX, and immunomodulatory, for example TGF-β receptor inhibitor, can be loaded together within HES-PLA for inhibition of insufficient chemotherapy induced metastasis. Our researches collectively corroborate HES would be an excellent candidate for clinical applications.

Keywords: Hydroxyethyl starch; Smart nanomedicines; Drug delivery