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The Anti-Bladder Cancer Effects Exerted by Hyaluronan Nanoparticles Encapsulated Heteronemin Isolated from Hippospongia Sp.

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Abstract : Anti-tumor effects of natural products, like compounds from marine sponges and soft corals, have been investigated for decades. Polymeric nanoparticles prepared from biodegradable and biocompatible molecules, such as Hyaluronan (HA), Chitosan (CHI) and gelatin have been widely studied. Encapsulation of anti-cancer therapies by the biopolymeric nanoparticles in drug delivery system is potentially capable of improving the therapeutic effects and attenuating their toxicity. In the current study, the anti-bladder cancer effects of heteronemin extracted from the sponge Hippospongia sp. with or without HA and CHI nanoparticle encapsulation were assessed and evaluated in vitro. Results showed that IC50 (half maximal inhibitory concentration) of heteronemin toward T24 human bladder cancer cell viability is approximately 0.18 μg/mL. Both plain and HA nanoparticles-encapsulated heteronemin at 0.2 and 0.4 μg/mL significantly reduced T24 cell viability ($P<0.001$) while HA nanoparticles-encapsulated heteronemin showed weaker viability-inhibitory effects on L929 fibroblasts compared with plain heteronemin at the identical concentrations. HA and CHI nanoparticles-encapsulated heteronemin exhibited significantly stronger inhibitory effects against migration of T24 human bladder cancer cell than those exerted by plain heteronemin at the same concentrations ($P<0.001$). The flow cytometric results showed that 0.2 μg/mL HA and CHI nanoparticles-encapsulated heteronemin induced higher early apoptosis rate than that induced by plain heteronemin at the same concentration. These results show that HA and CHI nanoparticle encapsulation is able to elevate anti-migratory and apoptosis-inducing effects exerted by heteronemin against bladder cancer cells in vitro. The in vivo anti-bladder cancer effects of the compound with or without HA/CHI nanoparticle encapsulation will be further investigated and examined using murine tumor models. The data obtained from this study will extensively evaluate of the anti-bladder cancer effects of heteronemin as well as HA/CHI-encapsulated heteronemin and pave a way to develop potential bladder cancer treatment.

Keywords : heteronemin, nanoparticles, hyaluronan, chitosan, bladder cancer
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