Design and In vitro Evaluation of Gemcitabine Loaded in Targeted Chitosan-Agglutinin Conjugated Nanoparticles

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Abstract

Introduction: Cancer is one of the major causes of death in many industrialized countries and its incidence is continually increasing. The most effective treatment for tumor is chemotherapy that lead to severe side effects due to their effects on normal non-targeted organs. Nanoparticulate carriers perform as vehicle, protecting the therapeutic agent from the biological milieu and improve cellular uptake and accumulation inside tumor sites. Chitosan nanoparticles (NPs) can be considered suitable vehicles for site-specific delivery of gemcitabine. Wheat germ agglutinin (WGA) is one of the least immunogenic lectins and putative nontoxic that has been demonstrated as somewhat more specific to intestinal cell lines of human origin, human colonocytes and prostate cancer cells.

Methods and Results: Nanoparticles were generated by adding tripolyphosphate (TPP) to chitosan in acetic acid containing 1mg drug under magnet stirring and centrifuged at 30,000 rpm, then lyophilized. To conjugate the surface of NPs with WGA, NPs were incubated in tow repeatable cycles with anhydrous acetone containing carbonyldiimidazole (CDI). Then, the activated bead were suspended in borate buffer, pH 9.0 to which 0.1 mg of WGA was added under vortexing. After washing, NPs dispersed in water, freeze-dried and stored at 4° C.

Gemcitabine-loaded NPs conjugated by WGA were prepared with a mean size of 160 nm, gemcitabine encapsulation efficiency of 63% and yield of 60%. These NPs had superior in vitro anti proliferation activity against the Caco2 and HT29. Conjugated NPs in comparison with unconjugated NPs and free drug exhibit better selectivity for target cells and tissues.

Conclusions: NPs conjugated WGA by enhanced cytotoxicity could be considered as a good candidate for oral delivery of anticancer drug. However other studies should be performed to evaluate in vitro test of these NPs.

Key words: Gemcitabine, Chitosan, WGA, Targeted-drug delivery, Nanoparticle