Novel self-assembled polymeric nanoparticles for drug delivery

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Technology

Particles made of nanoscale can more easily transport with their entrapped drug molecules through biological barriers, thus increasing drug bioavailability. The controlled manner of drug release from the nanoparticles (NPs) can also prolong the therapeutic efficacy while reducing local and systemic adverse effects. **Here, a new polymeric system and production process was generated for self-assembled drug-loaded NPs.** In addition to increase treatment efficacy of the NPs compared to unencapsulated drugs, the current invention also can offer ease and reproducibility of preparation, ease of storage and administration in a sterile form, satisfying drug-loading capacity, low toxicity, and feasibility for scale-up production. The novel spherical soft NPs are based on calcium crosslinked carbomer (50-500 nm). These were synthetized using a water-in-oil microemulsion as a template and calcium ions as cross-linkers. The manufacturing process combined cross-linking of carbomer within a W/O microemulsion followed by a phase-separation technique to avoid using organic solvents for extraction. The microemulsion was prepared from pharmaceutically acceptable components, such as widely used non-ionic surfactants, while neither acetone nor alcohols were used in any step of the process. The production was simple and easy, and the manufacturing process was short and robust.

Doxorubicin (DOX) was selected for proof-of-concept drug for assessment of the NPs. DOX is widely used drug in treatment for various malignance. Despite its potent activity DOX has a non-specific cell-cytotoxicity, long terminal half-life, and a high volume of distribution (i.e., low plasma concentrations). These disadvantages may lead to side effects. Cytotoxic studies were done *in vitro* on MCF-7 cells (cell line of breast cancer). NPs loaded with anticancer drug was more efficacious than the drug in plain solutions. Dose response behavior of DOX-loaded and unloaded NPs vs. solutions at various concentrations after 24-h and 48-h incubation was demonstrated. It could be noted that due to the slow-release manner of the drug from NPs, the effect of the NPs is expressed only from minimum 4-5 g/ml, compared with the solution which is highly cytotoxic at 1 g/ml. The DOX-NPs was also examined *in vivo* in mice inoculated with melanoma B16F0 cells subcutaneously. The mice were assigned for untreated control animals, treated animals with DOX-HCl solution, and treated animals with DOX- NP (s.c. administration). The most pronounced tumor growth inhibition was observed in mice treated with DOX-NPs, demonstrating the efficacy of NP encapsulation. While examine animal mortality, treatment apparently increased animal survival (day 18: untreated 27% survival; DOX-HCl 58% survival; DOX-NPs 67% survival)

Application

Drug delivery system for different active agents, including anti-neoplastic and anti-infective drugs.

Advantages

- Platform that can adjust for various therapeutic agents
- More effective treatment than unencapsulated drugs
- Low toxicity
- Ease and reproducibility of preparation – short & robust
- Feasibility for scale-up production
- The microemulsion was prepared from pharmaceutically acceptable components

Patent

WO2016/110839A1