EuroSciCon

17th Edition of International Conference and Exhibition on

Pharmaceutics and Novel Drug Delivery Systems

October 04-06, 2018
Moscow, Russia

Int J Drug Dev & Res 2018, Volume 10
DOI: 10.21767/0975-9344-C1-003

Functionalized amphiphilic alternating copolymer targets 3D multicellular tumor spheroids

Myron R Szewczuk
Queens University, Canada

Chemically engineering a smart delivery system of hydrophobic chemotherapeutic drugs to tumor cells is a novel approach for cancer treatment. The efficacy of this cancer treatment approach is to enhance and prolong circulation time, specifically by targeting cancer cells with controlled drug release. One of the important challenges in drug delivery systems is the inherent difficulty in the full encapsulation and retention, followed by long-term and targeted delivery of hydrophobic chemotherapeutics at a tumor site. To this end, we tested the efficiency of a smart delivery carrier targeting multicellular tumor spheroids (MCTS), a promising 3D tumor model platform which resembles the 3D architecture of avascular tumors. A pH-responsive, smart active polymeric delivery system was fabricated using folate functionalized amphiphilic alternating copolymer poly(styrene-alt-maleic anhydride) (FA-DABA-SMA) via biodegradable linker 2,4-diaminobutyric acid (DABA). This alternating copolymer was designed to be an active pH-responsive polymer, forming amphiphilic nanostructures at pH 7 and allowing the simple loading of hydrophobic drugs in its inner core. Here, we tested this delivery system on MCTS, generated using the novel cyclo-RGDfK peptide and its modification with triphenyl phosphonium cation (TPP), known hereafter as cyclo-RGDfK (TPP) peptide method, to determine whether our delivery system penetrates the inner core of human pancreatic (PANC-1) and breast (MDA-MB231) cancer spheroids. The FA-DABA-SMA copolymer was quantitatively tested for its drug encapsulation efficacy and release profiles using curcumin as a hydrophobic drug mimetic at various concentrations and pH values. Using standard clinical chemotherapeutic hydrophobic drugs, paclitaxel and 5-fluorouracil (5-FU) loaded FA-DABA-SMA, we tested their therapeutic killing efficacy on PANC-1 using the WST-1 cell proliferation assay. The polymeric drug carrier shows potential as an active smart tumor-targeting drug delivery system to internalize hydrophobic drugs, releasing the chemotherapeutics in acidified endosomes for effective elimination of cancer cells. The FA-DABA-SMA encapsulated with chemotherapeutics effectively penetrated the inner core of pancreatic and breast cancer MCTS and reduced spheroid volume in a time-dependent manner.

szewczuk@queensu.ca