LIVING FREE RADICAL POLYMERIZATION FOR THE SYNTHSIS OF POLYMER-DRUG CONJUGATES FOR CANCER TREATMENT

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ABSTRACT

As various forms of cancer are affecting people all over the world, there have been significant advances in the design of effective anti-tumour drugs. However, poor solubility and short circulation times present a challenge to the administration of these drugs.[1] The conjugation of drugs to synthetic polymers such as poly(ethylene glycol) has been shown to increase their circulation time and solubility.[2] We have investigated the synthesis of polymeric drug conjugates for cancer treatment in which hydrophobic anti-tumor drugs were conjugated to polymers made by living free radical polymerization (LRP). LRP techniques such as nitroxide mediated polymerization (NMP), atom transfer radical polymerization (ATRP) and reversible addition-fragmentation chain transfer (RAFT) polymerization have proved to be very useful techniques for producing polymers of well defined architectures and narrow molecular weight distributions. Of these techniques, RAFT seems the most promising to design polymer-drug conjugates, as it gives access to the widest range of functionalities and architectures.[3,4] Thus, polymer-drug conjugates were successfully synthesized by RAFT polymerization and characterized by size exclusion chromatography, NMR and Fourier transform infrared spectroscopy (FT-IR). The conjugates formed micellar aggregates in water with the hydrophobic anti-tumor drug in the core, which allows transportation of the drug within the human circulatory system. These micellar aggregates are expected to have long circulation times, which improve passive targeting of tumors via the enhanced permeation and retention (EPR) effect.[5]

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