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ACCEPTED MANUSCRIPT

EFFICIENT SYNTHESIS OF cRGD FUNCTIONALIZED POLYMERS AS BUILDING BLOCKS OF TARGETED DRUG DELIVERY SYSTEMS

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ABSTRACT

Synthetic peptides with cyclic arginine-glycine-aspartate motif (cRGD) play an important role

in cell recognition and cell adhesion. cRGD-decorated soluble polymers and polymeric

nanoparticles have been increasingly used for cell-specific delivery of antitumor drugs. While

the significance of cRGD modification for tumor cell-specific targeting of polymeric carriers

is well-accepted, straightforward procedures ensuring the fidelity of cRGD modification of

polymeric systems are still lacking. Herein, we have reported an in-situ polymerization

approach for synthesis of cRGD-end-functionalized well-defined polymers as potential

building blocks of targeted drug delivery systems. A new cRGD peptide functionalized RAFT

agent was synthesized as confirmed by MALDI-TOF and ¹H NMR spectroscopy. The ability

of this RAFT agent to control polymerizations was then tested using two different monomers

oligoethyleneglycol acrylate and t-butyl methacrylate. The RAFT-controlled character of

polymerizations and the living characteristic of the synthesized polymers were investigated

through a series of kinetic experiments. The cytotoxicity and targeting capability of cRGD-

functionalized OEGA polymers were investigated using cell lines expressing $\alpha_v \beta_3$ integrins at

varying extents.

Keywords: RGD, RAFT polymerization, end-group functionalization, targeted drug delivery

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