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SYNTHESIS OF DENDRONIZED POLYMERIC CHELATING AGENTS USING HYDRAZONE LIGATION STRATEGY

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Abstract

A practical protocol has been designed to synthesize dendronized polymeric chelating agents containing 1,4,7,10-tetraazacyclododecane-*N,N',N'',N'''*-tetraacetic acid (DOTA) ligand. The efficiency of suggested approach was verified by grafting of *N*-vinylpyrrolidone-acrolein P(VP-Ac) copolymer with dendrons containing several DOTA residues as compared to acylation of *N*-vinylpyrrolidone-vinylamine P(VP-VA) copolymer with active ester of DOTA. It was shown that attachment of pre-synthesized branched building blocks using hydrazone ligation strategy is an efficient method to increase the payload of carrier molecule. A similar methodology was applied for the preparation of polymer grafted by dendrons bearing DOTA complexes with paramagnetic ions (Gd^{3+} and Mn^{2+}). Obtained results evidenced that polymer-metal complexes possess high relaxivity values and can be considered as promising candidates for MRI contrast agents. The presented results demonstrate utility of hydrazone ligation strategy for the synthesis and screening of dendronized polymeric carriers of different nature.

Keywords: polymer grafting; dendronized polymers; DOTA; hydrazone ligation; MRI contrast agents

Abbreviations: EPR, enhanced permeability and retention effect; DTPA, 2-[bis[2-[bis(carboxymethyl)amino]ethyl]amino]acetic acid; TFA, trifluoroacetic acid; Fmoc, 9-fluorenylmethoxycarbonyl; DMF, *N,N*-dimethylformamide; DCM, dichloromethane; OPfp, pentafluorophenyl ester; TIS, triisopropylsilane; DIC, *N,N'*-diisopropylcarbodiimide, 6-Cl-HOBt, 1-Hydroxy-6-chloro-benzotriazole; i-Pr-OH, isopropyl alcohol.

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