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## Evaluation of Y-90 labeled PANAM dendrimers of the 1st and 4th generations

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Radiolabeled monoclonal antibodies and their fragments represent promising agents for radioimmunotherapy of cancers. For labeling with radiometals, macrocyclic chelating agents with high complex stability are usually attached to the biomacromolecule. To achieve specific activity of the antibody sufficient for a cancer treatment, large numbers of chelating groups have to be conjugated to a single macromolecule that usually results in a drop of its immunoreactivity. The problem could be overcome by an employment of biocompatible dendrimer-based agents. Dendrimers are hyperbranched artificial macromolecules with tree-like structure enabling multifunctional modification of their surface. The purpose of this study was to optimize the procedure for radiolabeling with Y-90 of PANAM dendrimers of the first (G1) and fourth generation (G4) conjugated with a DOTA derivative DO3A-py/NO-C/ (10-/4-carboxy-1-oxidopyridin-2-yl/methyl-1,4,7,10-tetraazacyclododecane-1,4,7-triacetic acid) and to analyze stability of the labeled products. 8 and 57 chelators were conjugated to a single G1 and G4 molecule, respectively. For the analysis, thin-layer chromatography and size exclusion chromatography were used. Results showed that 90Y-labeled dendrimers G1 and G4 conjugated with DO3A-py/NO-C/ can be prepared with a high specific activity and radiochemical purity at 37°C. Radiolabeled species were stable for at least 24 hrs both in saline and in plasma. Our results indicate that an employment of dendrimer-radiometal chelate conjugates represents a prospective way for radiolabeling of antibodies and their fragments to obtain markedly high specific activity and minimal loss of their immunoreactivity.

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