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Synthesis and biodistribution studies of iodine-١٣١ D-amino acid YYK peptide as a potential therapeutic agent for labeling an anti-CD٢٠ antibody

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Abstract

A major drawback of conventionally radioiodinated monoclonal antibodies for radioimmunotherapy is in vivo dehalogenation of iodine as a result of deiodinase recognition. To solve this problem we have synthesized a YYK tri-peptide consisting of non-metabolizable D-amino acids modified with the N-succinimidyl (N-Succ) function. The chemical purity of the synthesized peptide as assessed by analytical high performance liquid chromatography was ٩٥٪. Labeling of the Fmoc-D-Tyr(tBu)-D-Tyr(tBu)-D-Lys(Boc)-N- Succ was performed using the chloramine-T method and the conventional extraction, resulting in a radiochemical yield of ٥٠-٧١٪ and a radiochemical purity of >٩٥٪. Radioiodination of the peptide was followed by conjugation to anti-CD٢٠ antibody with ٦٥-٧٥٪ labeling efficiency and ٩٠٪ radiochemical purity. The effect of radioiodinated peptide on the biological behavior of the conjugate was evaluated through biodistribution studies in normal Lewis rats. Thyroid and stomach levels from Rituximab labeled with [^{١٣١}I]-YYK- peptide were two- to four-fold less than those with directly labeled [^{١٣١}I]-Rituximab, suggesting low recognition of its D-iodotyrosine residue by endogenous deiodinases. The favorable in vitro/in vivo stability and biodistribution profiles suggest that this radioiodine-labeled YYK peptide is a good candidate for further exploration of its potential clinical application. Copyright © ٢٠٠٩ John Wiley & Sons, Ltd.

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Indexed Keywords

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