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Radioiodine D amino acids labeling of rituximab, a new method for enhancing the radiopharmaceutical targeting and biostability

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View references (١٣)

Abstract

Introduction: Radioimmunotherapy (RIT) is a very promising new therapy for the treatment of recurrent B-Cell non-Hodgkin's lymphoma (NHL). Iodine-١٣١ is the most frequently used nuclide in clinical RIT, but its usefulness has been limited by dehalogenation of monoclonal antibodies labeled via conventional methods. To circumvent this problem, we have synthesized a tri-peptide consisting of non-metabolizable D amino acids attached to N-Hydroxysuccinimide (NHS). Methods: Tri-peptide was synthesized by standard Fmoc solid phase synthesis on tritylchloride resin. Labeling of tri-peptide was performed using the chloramine-T method and the conventional extraction. Radioiodination of tri-peptide was followed by conjugation to anti-CD٢٠ antibody. In vitro stability of labeled antibody in serum and phosphate buffered saline (PBS) was measured for ٤٨hr by (thin layer chromatography) TLC. Raji cell line was used to test cell binding of the labeled anti-CD٢٠. Results: The chemical purity of synthesized peptide as assessed by analytical (high performance liquid chromatography) HPLC was ٩٥٪. Labeling of tri-peptide resulted in a radiochemical yield of ٥٠-٧١٪ with radiochemical purity of > ٩٥٪. At Rituximab concentration of ١٠mg/ml, coupling efficiencies of ٦٥-٨٠٪ was obtained with radiochemical purity of ٩٥٪ and Specific activity (SA) of ١٨٥MBq/mg (٥mCi/mg). Conclusion: This study showed that labeling monoclonal antibodies with radioiodine by non-metabolizable D amino acids will improve bio-stability of the product.

Reaxys Database Information

Author keywords

D amino acid; Dehalogenation; Iodine-١٣١; Radioimmunotherapy

Indexed Keywords

EMTREE drug terms: dextro amino acid; n hydroxysuccinimide; radioactive iodine; radiopharmaceutical agent; rituximab; rituximab i ١٣١; tripeptide; unclassified drug

EMTREE medical terms: article; drug conjugation; drug stability; high performance liquid chromatography; human; human cell; in vitro study; isotope labeling; peptide synthesis; radiochemistry; radioiodination; Raji cell; solid phase synthesis; thin layer chromatography

Chemicals and CAS Registry Numbers: n hydroxysuccinimide, ٦٠٦٦-٨٢-٦; rituximab, ١٧٤٧٢٢-٣١-٧
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