MPCE 013

SYNTHESIS OF RITUXIMAB IMMUNOCONJUGATES FOR SUBSEQUENT RADIOLABELING

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In order to increase the therapeutic efficacy unmodified monoclonal antibodies (mAbs) are associated with drugs, toxins and radionuclides. This immunoconjugates are examples of mAbs specifically designed to deliver their toxic loads directly to cancer cells. In general, one target-specific radioimmunoconjugate consists of three parts: biomolecule-carrier (mAb), bifunctional chelating agent (BFCA) and radionuclide (radiometal, M). The development of pharmaceutical formulation of an antibody "ready to label" with different radioisotopes (Lu-177, Y-90), we believe that can be of a major clinical impact. The aim of this work was to perform conjugation of mAb rituximab, with three different BFCAs, *p*-SCN-Bn-DOTA, *p*-SCN-Bn-DTPA and 1B4M-DTPA in a form of ready-to-label kit formulations. Conjugation of rituximab with selected BFCA's, was made by mixing the purified antibody diluted in phosphate buffer saline (0.1 M, pH = 8.0) and appropriate BFCA in ratio 1:20. Mixture was incubated 18 hours at 2-8 °C, with constant slight stirring. The BFCA's used for conjugation are derivatives of tetraazacyclododecane tetraacetic acid (DOTA) and diethylenetriamine pentaacetic acid (DTPA). The conjugation process undergoes reaction of the active ester group of the chelator with the neutral form of the amines of the antibody. Specifically, bonds of thiourea type with ε-amino groups of lysine residues of the antibody are formed. The resulting rituximab immunoconjugates were purified with ultrafiltration and subjected to the lyophilization process by using Labconco Free Zone Stoppering Tray Dryer, (USA). These immunoconjugates can be a good basis for conducting further experiments with radiolabelled formulations in order to develop promising new radiopharmaceutical.

Key words: rituximab, bifunctional chelating agents, immunoconjugates.