

UDK 615 (497.11)

ISSN 0004-1963 (Štampano izd.)
ISSN 2217-8767 (Online)

ARHIV ZA FARMACIJU

Godina 68

Broj 3

Beograd, 2018.

ČASOPIS SAVEZA FARMACEUTSKIH UDRUŽENJA SRBIJE

SPECIJALNI BROJ/SPECIAL ISSUE

VII Kongres farmaceuta Srbije sa međunarodnim učešćem

Zajedno stvaramo budućnost farmacije

Beograd, 10-14. oktobar 2018.

VII Serbian Congress of Pharmacy with international participation

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Radove objavljene u časopisu Arhiv za farmaciju indeksiraju: EMBASE i SCOPUS

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COLD LABELED TRASTUZUMAB-P-SCN-BN-DTPA AND TRASTUZUMAB-P-SCN-BN-1B4M-DTPA CONJUGATES- PREPARATION AND SPECTROSCOPIC ANALYSIS

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Emilija Janevik-Ivanovska¹**

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The importance of immunoconjugates in treatment of various cancers was motivation for us to formulate a stable cold labeled trastuzumab conjugates with two bifunctional chelators (BFCAs) (*p*-SCN-Bn-1B4M-DTPA(2-(4-isothiocyanatobenzyl)-6-methyl-diethylene-triaminepentaacetic acid and *p*-SCN-Bn-DTPA(2-(4-izothiocyanatobenzyl)-diethylenetriaminepentaacetic acid)). The labeling with non-radioactive LuCl₃ and YCl₃ is important to determine the possible physicochemical changes in the structure of immunoconjugates after metal binding. ATR-IR (Attenuated total reflectance-infrared) and Raman spectroscopy as powerful and non-destructive techniques are appropriate for verification of possible secondary structure changes of trastuzumab after conjugation and labeling.

Anti-HER2/neu monoclonal antibody trastuzumab was conjugated with *p*-SCN-Bn-DTPA, *p*-SCN-Bn-1B4M-DTPA in ratio of 1:10 and 1:50 and lyophilized to solid state. The freeze dried conjugates were labeled with cold LuCl₃ and YCl₃. The retained secondary structure of the antibody was proven by spectroscopic analysis with ATR-IR and Raman spectroscopy and compared with purified trastuzumab from commercial product Herceptin®. The ATR-IR and Raman spectra of four samples have shown the presence of characteristic amide bands and retained native IgG1 structure of the antibody principally composed of β-sheets. Characteristic amide I band at ~1670 cm⁻¹ and amide III band (1230-1300 cm⁻¹) were detected in Raman spectra. IR spectra also contain the amide I (1700-1600 cm⁻¹), amide II (1480-1575 cm⁻¹) and amide III bands (1255-1244 cm⁻¹) specific for secondary structure of the proteins.

No significant changes in antibody structure after cold labeling gives us a hope for further radiolabeling of immunoconjugates with ¹⁷⁷LuCl₃ and ⁹⁰YCl₃ and development of radioimmunotherapeutics and diagnostic products active against HER2 positive breast tumors.