Preparation of ^{89}Zr-Oxalate Isotonic Solution for Nuclear Medicine

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Aim: The aim of this study is to develop handy procedure for production of ^{89}Zr-oxalate in physiologically acceptable form and evaluate its potential for using in PET radiopharmaceutical chemistry. The procedure should allow to obtain the chemically pure preparation with high molar activity and radionuclide purity. The solution should be isotonic (concentration of oxalate in it does not exceed 0.115 M) with shelf-life at least 10 days.

Materials and methods: All chemicals and solvents were of high-purity or pharmaceutical grade and were purchased from Sigma-Aldrich or Panreac. Quality control was carried out with TLC chromatography (iTLC-SG strips, different eluents; PET-MiniGita radio-TLC scanner). Dowex1, Chelex-100 (Sigma-Aldridge), ZR (Triskem), Chromafix-HCO_3 (Macherey-Nagel) resins were used. $^{89}ZrCl_4$ in 5 M HCl was purchased from Cyclotron Ltd, (Russia). *In vivo* experiments were carried out in BALB/C mice models with different pathologies. Wizard^{2}2480 gamma-counter and G4-microPET (Sofie) were used for biological evaluation.

Results: It was found that ZR resin allows to obtain ^{89}Zr-oxalate solution with highest yield and lowest metal impurities content. Chromafix-HCO_3 and Chelex-100 resins allow to obtain high purity as well, and Chelex-100 resin allows to formulate ^{89}Zr-oxalate in an acceptable form. However, ^{89}Zr-oxalate solution purified with ZR resin does not meet all the requirement for the PET radiopharmaceutical under development. Its virtues and shortcomings will be presented in detail. Thus, conjoint use of ZR and Chelex-100 resins allowed to develop the procedure for production of pH-neutral isotonic ^{89}Zr-oxalate solution with high purity and specific activity. Radiochemical yield of the preparation and purification procedure is ≥90%. ^{89}Zr complexes with other carboxylic acids were studied as well. Biological and toxicity tests were carried out as well. Experimental results will be presented in detail.

Conclusion: Handy procedure of production of ^{89}Zr-oxalate physiologically acceptable solution was developed. Oxalate concentration in final solution is ≤ 0.115 M and does not interfere with further reactions of ^{89}Zr complexation with chelating agents. On the other hand this concentration prevents hydrolysis effectively long enough. Its suitability for radiopharmaceutical preparations was evaluated. Moreover, this concentration of oxalic acid allows to obtain stable ^{89}Zr-solutions with different pH values (1-8), whereas it's impossible to achieve pH>2 with concentration of oxalic acid >0.27 M (due to precipitation of sodium oxalate).

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