JNM
The Journal of Nuclear Medicine

Meeting Report | Molecular Targeting Probes - Radioactive & Nonradioactive

In vitro response of ^{177}Lu-PSMA-617 with two different specific activities

Cristian Wieczorek Villas Boas, Jair Mengatti, Priscila Passos, Daniel Vieira and Elaine Bortoleti de Araujo

Journal of Nuclear Medicine May 2020, 61 (supplement 1) 624;

Abstract

624

Introduction: PSMA-617 radiolabeled with lutetium-177 has shown good results in compassionate studies around the world. Being a receptor-specific radiopharmaceutical, the specific activity (SA) of the preparation may represent an important factor for therapeutic efficacy. Lutetium-177 can be produced by two different routes: with ytterbium-176 (Non-carrier-added or NCA) and with lutetium-176 (Carrier-added or CA). The SA (MBq/ug) of the labeled PSMA varies accordingly to each lutetium. For NCA lutetium, the radiolabeling procedure is based on the SA of 74 MBq/ug. When the radiolabeling is performed with CA lutetium, SA is determined by the molar ratio of 2.1:1 (PSMA moles/lutetium moles declared in the certificate), resulting in lower SA than NCA. This work evaluated the influence of specific activity of 177Lu-PSMA-617 on *in vitro* specific binding assays (saturation, competition and internalization). **Materials and Methods:** Radiolabeling of PSMA-617 (ABX, Germany) with lutetium-177 was performed in heating block at 90°C for 30 minutes with sodium ascorbate (0.5 M pH 4.7) as buffer. For NCA lutetium (JSC, Russia) the radiopharmaceutical specific activity was 74 MBq/ug. For CA lutetium (IDB, Netherlands), the specific activity was 41 MBq/ug. The radiochemical purity was analyzed with HPLC. For all experiments, 6-well plates were used for adherence cells with 200,000 LNCaP per well. Molar concentration of saturation curves experiments were 0.01; 0.05; 0.6; 1.5; 3.0 and 3.5 for CA lutetium and 0.1; 0.6; 1.5; 2.0; 2.5 and 3.0 for NCA lutetium. After 1 hour of incubation at 8 ºC, supernatant was removed, then washed with PBS (phosphate buffer saline) and finally cells were burst with NaOH 1 M, and activity was measured in gama counter; the experiments were performed in octuplicate. Competition experiments were performed adding in all wells 5 nM of radiolabeled PSMA-617 and in the competition well (non-specific binding) were added an excess of 15 times (76 ug) of non

radiolabeled PSMA-617. After 1 hour of incubation at 8 ºC, supernatant was removed, then washed with PBS and finally cells were burst with NaOH 1 M, and activity was measured in gama counter, these experiments were performed in triplicate. The specific binding was obtained by the difference between total binding and non-specific binding. Internalization experiments were performed at Kd of NCA and CA lutetium. After 1 hour of incubation at 37 ºC, supernatant was removed, washed with PBS, then washed again with 0.05 M glycine solution pH 2.8 and finally cells were burst with NaOH 1 M. Activity was measured in gama counter, these experiment were performed in sextuplicate. **Results and discussion:** The radiochemical purity were 98% and 99% for labeling with NCA and CA lutetium, respectively. Saturation curve assay with NCA lutetium shown a Kd of 0.7 ± 0.15 nM and a Bmax of 857 ± 55.79 pMol/ng, and with CA lutetium resulted in a Kd of 1.71 ± 0.45 nM and a Bmax of 1156 ± 113.8 pMol/ng. The variation between both Kd curves were statistically different (P value = 0.0058). Competition assay demonstrated an effective blocking for both types of lutetium, for NCA unpaired T test shown a P value of 0.0011. For CA lutetium, the unpaired test disclosed a P value of 0.0258. The comparison between both results revealed a P value of 0.01 at the specific binding. Internalization assay shown for both types of lutetium similar results, 27.1 ± 2.45% and 30.6 ± 4.97%, for CA and NCA lutetium, respectively, and was not statistically significant (P value = 0.17)

Conclusions: These experiments demonstrated that the type of lutetium (CA or NCA) directly affects *in vitro* binding of ^{177}Lu-PSMA-617 to receptors expressed in LNCaP cells. It was statistically demonstrated that the higher specific activity of ^{177}Lu-PSMA-617, more radiolabeled peptide can bind to cells at saturation and competition assays. **Acknowledgments:** Grant 2018/12965-4, São Paulo Research Foundation (FAPESP) and National Commission of Nuclear Energy.

Previous

Back to top

In this issue

Journal of Nuclear Medicine

Vol. 61, Issue supplement 1
May 1, 2020

Table of Contents

Index by author