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Preclinical assessment of 68Ga-PSMA-617 entrapped in a microemulsion delivery system for applications in prostate cancer PET/CT imaging

Vusani Mandiwana[1,5], Lonji Kalombo[1], Yolandy Lemmer[1], Philip Labuschagne[1], Boitumelo Semete-Makokotlela[1], Mike Sathekge[2], Thomas Ebenhan[2, 3], Jan Rijn Zeevaart[4, 5]

[1] Centre for Polymers and Composites, Council for Scientific and Industrial Research, Pretoria, 0001, South Africa
[2] Department of Nuclear Medicine, University of Pretoria, Pretoria, South Africa
[3] Preclinical Imaging Facility, NuMeRI, Pelindaba, South Africa
[4] Radiochemistry, South African Nuclear Energy Corporation, Pelindaba, Pretoria, 0001, South Africa
[5] DST/NWU, Preclinical Drug Development Platform, North West University, Potchefstroom, South Africa

Abstract

It has in recent years been reported that microemulsion (ME) delivery systems provide an opportunity to improve the efficacy of a therapeutic agent whilst minimising side effects and also offer the advantage of favourable treatment regimens. The prostate-specific membrane antigen (PSMA) targeting agents PSMA-11 and PSMA-617, which accumulate in prostate tumours, allow for [68 Ga]Ga3+ -radiolabelling and positron emission tomography/computed tomography (PET) imaging of PSMA expression in vivo. We herein report the formulation of [68 Ga]Ga-PSMA-617 into a ME ≤40 nm including its evaluation for improved cellular toxicity and in vivo biodistribution. The [68 Ga]Ga-PSMA-617-ME was tested in vitro for its cytotoxicity to HEK293 and PC3 cells. [68 Ga]Ga-PSMA-617-ME was administered intravenously in BALB/c mice followed by microPET/computed tomography (CT) imaging and ex vivo biodistribution determination. [68 Ga]Ga-PSMA-617-ME indicated negligible cellular toxicity at different concentrations. A statistically higher tolerance towards the [68 Ga]Ga-PSMA-617-ME occurred at 0.125 mg/mL by HEK293 cells compared with PC3 cells. The biodistribution in wild-type BALB/C mice showed the highest amounts of radioactivity (%ID/g) presented in the kidneys (31%) followed by the small intestine (10%) and stomach (9%); the lowest uptake was seen in the brain (0.5%). The incorporation of [68 Ga]Ga-PSMA-617 into ME was successfully demonstrated and resulted in a stable nontoxic formulation as evaluated by in vitro and in vivo means.