Preparation, characterization, and radiolabeling of [68Ga]Nodaga-pamidronic acid: a potential PET bone imaging agent

ABSTRACT

Early diagnosis of bone metastases is crucial to prevent skeletal-related events, and for that, the non-invasive techniques to diagnose bone metastases that make use of image-guided radiopharmaceuticals are being employed as an alternative to traditional biopsies. Hence, in the present work, we tested the efficacy of a gallium-68 (68Ga)-based compound as a radiopharmaceutical agent towards the bone imaging in positron emitting tomography (PET). For that, we prepared, thoroughly characterized, and radiolabeled [68Ga]Ga-NODAGA-pamidronic acid radiopharmaceutical, a 68Ga precursor for PET bone cancer imaging applications. The preparation of NODAGA-pamidronic acid was performed via the N-Hydroxysuccinimide (NHS) ester strategy and was characterized using liquid chromatography-mass spectrometry (LC-MS) and tandem mass spectrometry (MSn). The unreacted NODAGA chelator was separated using the ion-suppression reverse phase-high performance liquid chromatography (RP-HPLC) method, and the freeze-dried NODAGA-pamidronic acid was radiolabeled with 68Ga. The radiolabeling condition was found to be most optimum at a pH ranging from 4 to 4.5 and a temperature of above 60 °C. From previous work, we found that the pamidronic acid itself has a good bone binding affinity. Moreover, from the analysis of the results, the ionic structure of radiolabeled [68Ga]Ga-NODAGA-pamidronic acid has the ability to improve the blood clearance and may exert good renal excretion, enhance the bone-to-background ratio, and consequently the final image quality. This was reflected by both the in vitro bone binding assay and in vivo animal biodistribution presented in this research.

Keyword: [68Ga]Ga-NODAGA-pamidronic acid; Radiopharmaceuticals; Positron emitting tomography (PET); Contrasting agents; Bone metastases; Ion suppression; Bisphosphonate