[^{68}Ga]HHDPD: A potential imaging agent for tumours and arteriosclerotic plaques

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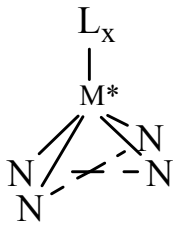
Introduction: Generator-derived gallium-68 is highly relevant for molecular imaging strategies by means of position emission tomography (PET). The trivalent radiometal is used in a variety of current radiopharmaceutical developments. In this context, an effective post-processing of the generator-eluted gallium-68 plays a key role for following labelling procedures. This study reports a convenient method for ^{68}Ga-labelling of lipophilic porphyrin derivatives under anhydrous conditions using solid-phase derived gallium-68-acetylacetonate (^{68}Ga(acac)$_3$) in a microwave-enhanced radiosynthesis. Porphyrin derivatives accumulate in tumour tissue and atheromatous plaques and are established in photodynamic therapy (PDT).

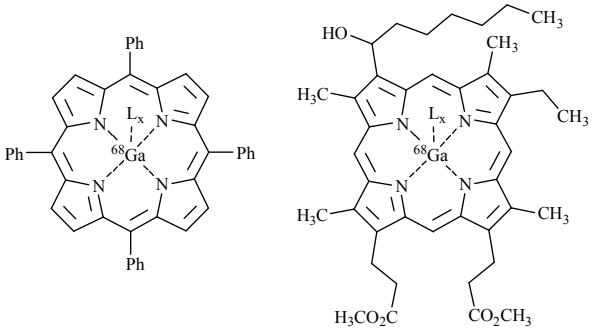
Experimental: ^{68}Ge/^{68}Ga-radionuclide generators utilizing TiO_2 to adsorb ^{68}Ge(IV) were used. The initial aqueous eluate was transfered online onto a cationic exchange resin to quantitatively absorb ^{68}Ga. From this resin, ^{68}Ga was eluted with different acetone–based, non-aqueous solvent systems providing n.c.a. ^{68}Ga(acac)$_3$ as labelling synthon. ^{68}Ga-labelling of porphyrin derivatives was performed in chloroform in a focused microwave synthesis system.

Results: More than 95% of the initially eluted ^{68}Ga was eluted form the cationic exchange resin with only 600 µl of a 98% acetone / 2% acaetylacetone mixture. Two different porphyrin derivatives, the simple symmetric meso-tetraphenyl-porphyrin and (3-(1-hydroxyheptyl)deuteroporphyrin dimethylester (HHDPD, FZ.MZ), were labelled in yields of >90% within 5 minutes using the ^{68}Ga(acac)$_3$ and diverse co-ligands in chloroform. Radiochemical purities of >95% were achieved by solid-phase extraction.

Conclusion: Two lipophilic porphyrin derivatives were rapidly labelled in high yields in a microwave-enhanced radiosynthesis. ^{68}Ga-labelling was achieved using solid-phase derived ^{68}Ga(acac)$_3$ as synthon under anhydrous conditions. Gallium complexation inside the macrocyclic tetrapyrrol-system was realised by diverse co-ligands.
The novel ^{68}Ga-labelled porphyrin compounds are currently under investigation concerning their medical potential. Despite the synthesis of ^{68}Ga-porphyrin complexes, however, the procedure of online synthesis of ^{68}Ga(acac)$_3$ as a synthon for labelling reactions under non-aqueous conditions may be of general interest.



Scheme 1: Tetragonal pyramidal coordination of the five-coordinate metalloporphyrin (L_x: axial co-ligand, M*: trivalent metal ion)



[^{68}Ga]Tpp [^{68}Ga]HHDPD

Scheme 2: Structure of [^{68}Ga]Tpp and [^{68}Ga]HHDPD (L_x = phenol, gentisic acid.

References

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