^{68}Ga- Schiff-bases as myocard tracers

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Introduction: Coronary artery disease (CAD) is the leading cause of death worldwide. Arteriosclerotic accumulations in the vessels lead to a minorperfusion of the heart (ischemia). After several years without any symptoms, arrhythmia, angina pectoris, heart failure and cardiac infarction may suddenly hit the patient.

Changes in the myocardial perfusion help to differ between ischemic tissue which can be vitalized again by re-vascularization and already scar tissue.

To obtain information about the state of the heart of the patient via positron emission tomography (PET) it is necessary to develop a lipophilic radiotracer which has a high first-pass extraction in the myocardial cells. Ideally, the uptake would be between 2-3% of the injected dose.

Experimental: Different aldehydes were coupled with a tetra-amino backbone. ^{68}Ga-Labeling was performed at 80°C for 10 min in HEPES-buffer. The radiotracer was purified via a C-18 cartridge and eluted with 0.5 mL of ethanol.

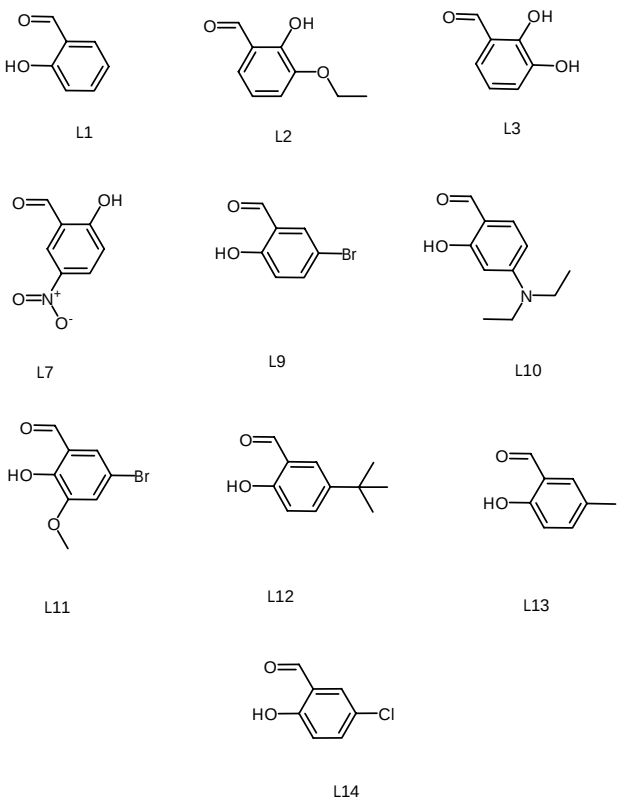

Figure 1. 10 different aldehydes which were used to attach to the tetra-amino backbone.

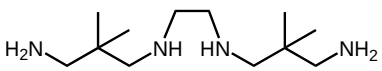

Figure 2. structure of tetra-amino backbone G1.

An *in-vitro* assay was set up to measure the uptake into myocardial cells. Therefore, HL-1 cells were grown on petri dishes and trypsin was used to solve them. Test tubes were equipped with more than 1 mio. cells per tube. To one half of the test tube the ionophor valinomycin was added to reduce the uptake in those cells. Around 100 µL of radiotracer (around 5 MBq) was added to the tubes. After incubation for 30 min at 37°C and centrifugation at 1200*g for 5 min, the activity levels of the supernatant and the pellet were measured.

Furthermore, the electric charge of tracer G1L9 was investigated. Therefore, electrophoresis was performed in different buffers. At pH 7.4 (to simulate physiological conditions) phosphate-buffer as well as PBS and NH_4PF_6-puffer were used. For an acid pH of 4.6 an acetic acid/sodium acetate buffer was used.

Results:

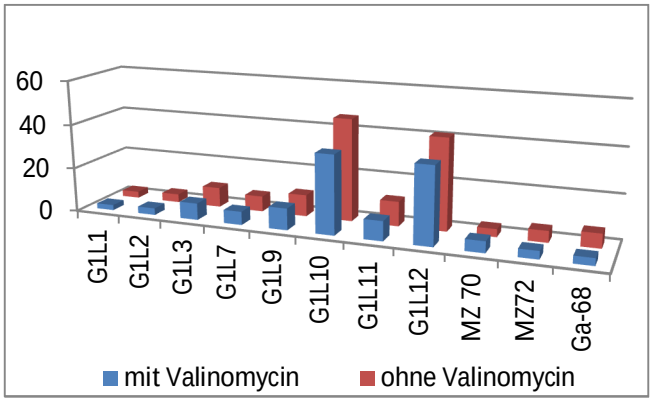

Figure 3. Results of the *in-vitro* cell tests.

The ^{68}Ga-tracers G1L10 and G1L12 show the highest uptake in the cell assay. The ionophor valinomycin represses the uptake into the cells.

The electrophoresis showed that at physiological pH the tracer seems to be charged negative. Therefore the pH was dropped to 4.6 and the acetic acid/sodium acetate buffer was used. At this pH the tracer is not charged at all and stays at the starting line.

In next experiments the electric charge of the other Schiff-base should be investigated.

Literatur:

[1] Hsaio, Mathias, Wey, Fanwick, Green, *Nucl. Med. Biol.*, *36*, **2009**, 39-45.