

Short Research Article

Development of (^{67}Ga)2-acetylpyridine 4,4-dimethyl thiosemicarbazone for detection of malignancies[†]

AMIR R. JALILIAN^{1,*}, FARIMA HAGHIGHI MOGHADAM^{1,2}, ALI NEMATI² and Mohammad Abedini²

¹Cyclotron and Nuclear Medicine Department, Nuclear Research Center for Agriculture and Medicine (NRCAM), Moazzen Blvd., P.O.Box: 31485-498, Rajaeeshahr, Karaj, Iran

²Inorganic Chemistry Department, Faculty of Sciences, Tehran University, Tehran, Iran

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Introduction

Gallium-67 is used for single photon emission computed tomography. Gallium-68 and gallium-66 are positron emitters, mostly used in the research studies through the world. The most practically used gallium radiopharmaceutical is gallium-67 citrate, capable of detecting inflammation and/or infections and certain tumors. Thiosemicarbazone gallium complexes have shown interesting anti-proliferative activity *in vitro* and *in vivo*.

The most studied compounds are pyridine-based compounds, this is possibly due to their resemblance to pyridoxal metabolites that attach to co-enzyme

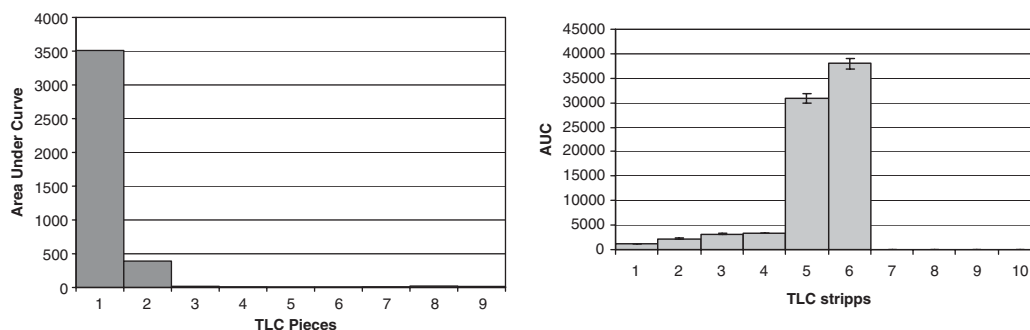
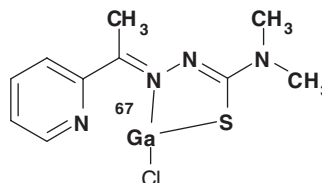


Figure 1 TLC of the final [^{67}Ga]APTSM₂ solution (right) and Ga³⁺ (left) eluted by ammonium acetate 10%: MeOH (1:1). AUC: area under curve of 184 keV peak in gamma spectrum.

*Correspondence to: Amir R. Jalilian, Cyclotron and Nuclear Medicine Department, Nuclear Research Center for Agriculture and Medicine (NRCAM), Moazzen Blvd., P.O. Box: 31485–498, Rajaeeshahr, Karaj, Iran. E-mail: ajalilian@nrcam.org

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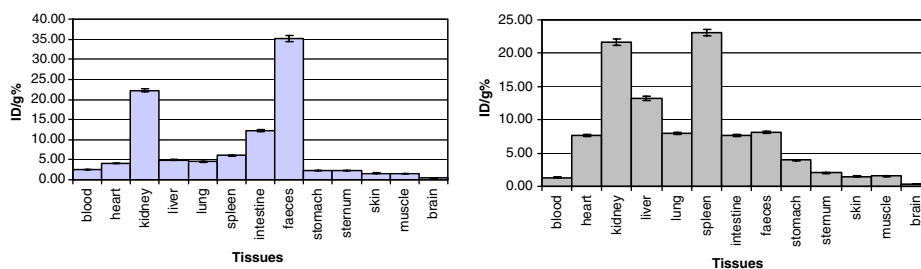


Figure 2 Biodistribution of [⁶⁷Ga]APTSM₂ (1.85 MBq, 50 μCi) in normal rats 2 h (left) and 22 h (right) after iv injection via tail vein.

B₆-dependant enzymes and cause enzyme inhibition. Due to the importance of pyridine thiosemicarbazones in anti-neoplastic activity and the necessity of gallium complexation in most of these compounds for enhancement of their activity, the idea of developing a possible tumor imaging agent using SPECT by incorporating ⁶⁷Ga into a suitable chelate, i.e. APTSM₂ was investigated.

Results and discussion

The reaction of 2-acetylpyridine *N*-dimethylthiosemicarbazone (HL) with GaCl₃ in absolute ethanol in 1:1 molar ratio has yielded the complex [Ga]⁺. The reaction was optimized for time, temperature and solvent. The labeling was not satisfactory when water was present in the solvent. The solution was stable at room temperature up to 4 days post-formulation, allowing

performance of biological experiments. Incubation of [⁶⁷Ga]APTSM₂ in freshly prepared human serum for 2 h at 37°C showed no loss of ⁶⁷Ga from the complex. The radiochemical purity of complex remained at 99% for 2 h under physiologic conditions. The lipophilicity of [⁶⁷Ga]APTSM₂ compound was measured using octanol/water partition coefficient, *P* (≈ *P*=12). The lipophilicity is over 1.07 followed by biodistribution studies (Figure 1), (Figure 2).

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