

PRODUCTION AND QUALITY CONTROL OF ^{99m}Tc -GLA (GLUCARIC ACID).

Castanheira CE; Bernardes DML; Muramoto E; Fukumori NTO; Matsuda MMN; Barboza MF; Mengatti J; Ramos CD.

Radiopharmacy Directory – IPEN-CNEN/SP.

Previous studies have showed that ^{99m}Tc labeled glucaric acid (GLA) is emerging as a promising metabolic marker of myocardial viability as it shows high affinity for necrotic myocardial tissue, acute cerebral injury and tumors. GLA is a 6-carbon dicarboxylic acid that has been proposed as a potentially useful SPECT imaging agent for myocardial infarction. This paper describes the production and quality control process of GLA in lyophilized form, under GMP condition, for labeling with Tc-99m. The process was performed under vacuum and low temperature in the Super Modulyo–“Edwards” lyophilizator and each lyophilized vial contained: 12.0 mg of GLA; 0.5 mg of gentisic acid and 0.5 mg of $\text{SnCl}_2 \cdot \text{H}_2\text{O}$, pH = 5.0. The radiochemical purity was determined by two paper chromatography systems in Whatman 3MM paper (1 x 8 cm), using acetone and saline (0.9% NaCl) as solvents. Sterility tests were performed by the microbiology procedures outlined in the pharmacopoeias and pyrogen test by the “in-vitro” Limulus test. Biological distribution in Wistar rats was evaluated 30 minutes after intravenous dose of 7.4–11.1 MBq/0.1 mL of ^{99m}Tc -GLA in different organs (% injected dose/organ). The radiochemical purity was > 95%. Sterility and pyrogen tests were negative in all the delivered lyophilized vials. The biological distribution of ^{99m}Tc -GLA in rats showed low uptake in lung and heart (< 1%) and low activities in liver and muscle (< 5%). Scintigraphic images of ^{99m}Tc -GLA were performed in 4 patients (Campinas University) with symptoms highly suggestive of acute myocardial infarction. The patients were injected with 740 MBq of ^{99m}Tc -GLA, 3 to 9 hours after the onset of chest pain and images were obtained 2 hours later. At rest, images from ^{99m}Tc -MIBI were also obtained for comparison. Acute infarction was confirmed in 2 patients with focal ^{99m}Tc -GLA uptake. In one patient without ^{99m}Tc -GLA uptake, myocardial infarction was finally excluded. The fourth patient injected 9 hours after the onset of chest pain had a final acute infarction diagnosis and a negative ^{99m}Tc -GLA scan. We concluded that ^{99m}Tc -GLA is a promising radiopharmaceutical for the diagnosis and localization of acute myocardial infarction and should be injected in less than 9 hours of the onset of chest pain. More studies are necessary to determine the accuracy of the method. The lyophilized form and quality control procedures of GLA labeled with Tc-99m have been developed and validated at Radiopharmacy Directory of IPEN-CNEN/SP.