Evaluation of alternative methods for radiochemical purity testing of indium-111 capromab pendetide

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Abstract

Objective: To evaluate alternative methods for radiochemical purity testing of indium (In)-111 capromab pendetide after the discontinuation of instant thin-layer chromatography silica gel (ITLC-SG) strips.

Design: Descriptive experimental study.

Setting: United States in 2009.

Participants: Not applicable.

Intervention: Paper chromatography using Whatman 3MM strips, paper chromatography using Whatman 31ET strips, and mini-column chromatography using silica Sep-Pak cartridges were evaluated in the radiochemical purity testing of 13 consecutive vials of In-111 capromab pendetide prepared for clinical patient imaging procedures. These methods also were evaluated by testing seven aliquots of In-111 capromab pendetide that had been spiked with 5% to 15% In-111 pentetate (diethylene triamine pentaacetic acid).

Main outcome measures: Correlation coefficients, radiochemical purity values for each method compared with ITLC-SG, and procedure times.

Results: Correlation coefficients of 0.988, 0.996, and 0.979 were found for ITLC-SG compared with Whatman 3MM, Whatman 31ET, and silica Sep-Pak, respectively. Compared with ITLC-SG, mean (±SD) radiochemical purity values differed by –0.8 ± 0.8 (range –2.5 to 0.4) for Whatman 3MM, –0.8 ± 0.6 (–2.3 to 0) for Whatman 31ET, and –0.5 ± 1.2 (–3.6 to 0.7) for silica Sep-Pak. The approximate time required to develop the chromatography strip or elute the mini-column was 3, 14, 5, and 6 minutes for ITLC-SG, Whatman 3MM, Whatman 31ET, and silica Sep-Pak, respectively.

Conclusion: All three methods evaluated were acceptable alternatives to ITLC-SG for radiochemical purity testing of In-111 capromab pendetide. Based on its slightly higher correlation to ITLC-SG, slightly tighter SD and range, and slightly shorter development time, Whatman 31ET is preferred in our facility.

Keywords: Radiochemical purity, paper chromatography, radiopharmaceuticals, quality control, nuclear pharmacy.

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As described in its package insert[1] and *United States Pharmacopeia* (*USP*) monograph,[2] radiochemical purity testing of indium (In)-111 capromab pendetide involves the use of instant thin-layer chromatography silica gel (ITLC-SG) strips (Pall Life Sciences, Ann Arbor, MI). Because the manufacture of ITLC-SG strips was recently discontinued,[3] alternative methods for radiochemical purity testing are needed.

Objective

Other common methods that have been used for radiochemical purity testing of particular radiopharmaceuticals include paper chromatography using Whatman 3MM strips,[4] paper chromatography using Whatman 31ET strips,[4,5] and mini-column chromatography using silica Sep-Pak cartridges.[5] These methods were evaluated as potential alternatives to the standard ITLC-SG method for radiochemical purity testing of In-111 capromab pendetide.

Methods

Paper chromatography using Whatman 3MM strips (Whatman International, Maidstone, UK), paper chromatography using Whatman 31ET strips (Whatman International), and mini-column chromatography using silica Sep-Pak cartridges (Waters, Milford, MA) were evaluated in the radiochemical purity testing of 13 consecutive vials of In-111 capromab pendetide prepared for clinical patient imaging procedures. Because all of these preparations possessed radiochemical purities substantially greater than the minimum acceptable value of 90%,[2] the three test methods also were evaluated by testing seven aliquots of In-111 capromab pendetide that had been spiked with 5% to 15% In-111 pentetate (diethylene triamine pentaacetic acid [DTPA]) to evaluate their usefulness for preparations with borderline (i.e., slightly above or below 90%) radiochemical purity. Radiochemical purity values for each test method were compared with values for the standard ITLC-SG method for all 20 preparations.

Immediately before radiochemical purity testing, a small sample (i.e., several drops) of the In-111 capromab pendetide preparation was mixed with an equal volume of 0.05 mol/L DTPA, as described in the package insert[1] and *USP* monograph,[2] to chelate any free, cationic, unlabeled In-111 impurity.

For the chromatography strip methods, a small drop of the mixture was placed as a spot 1.5 cm from the bottom of a 1.7 × 10–cm strip and developed in 0.9% sodium chloride to a height of 8.5 cm (i.e., solvent front 7 cm beyond the origin[6]). Rather than simply cutting the strip in half as recommended,[1,6] each strip was cut into eight 1-cm segments starting at 1 cm (Figure 1). Each of these eight segments was counted with a scintillation well counter. Radiochemical purity was calculated as the

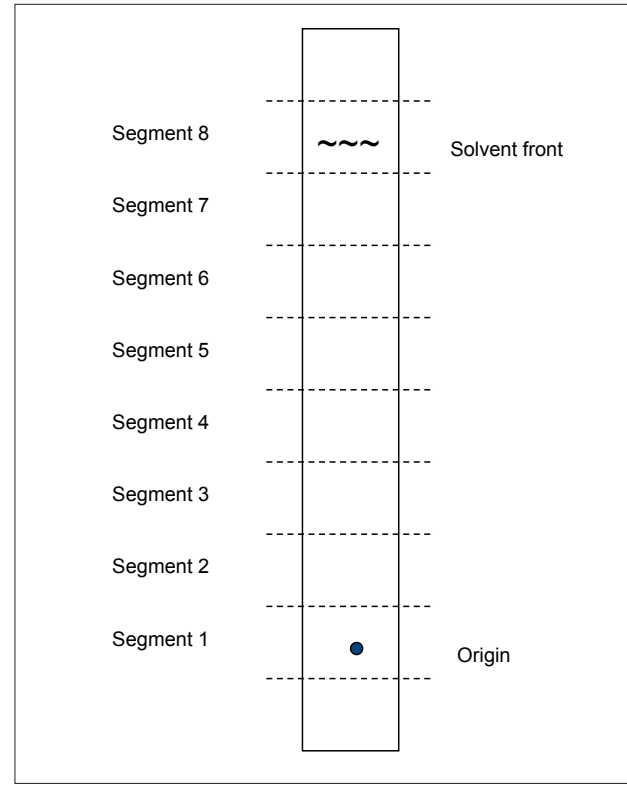

Figure 1. Segmentation of a 1.7 × 10–cm chromatography strip with the origin at 1.5 cm from the bottom and the solvent front at 7 cm above the origin.

At a Glance

Synopsis: Alternative methods for radiochemical purity testing of indium (In)-111 capromab pendetide were evaluated, as production of instant thin-layer chromatography silica gel (ITLC-SG) strips has been discontinued. Paper chromatography using Whatman 3MM strips and Whatman 31ET strips and mini-column chromatography using silica Sep-Pak cartridges were evaluated in the radiochemical purity testing of 13 consecutive vials of In-111 capromab pendetide prepared for clinical patient imaging procedures. The results showed that all three methods were acceptable alternatives to ITLC-SG, with Whatman 31ET strips performing slightly better than the other two methods.

Analysis: *The primary characteristic to consider when selecting an alternative radiochemical purity testing method is accuracy. All three test methods provided excellent separation of free In-111 (as In-111 diethylene triamine pentaacetic acid) from In-111 capromab pendetide. Compared with the standard ITLC-SG method, all three test methods demonstrated mean radiochemical purity values that were slightly low; therefore, even in cases of borderline radiochemical purity, these test methods offer a slight cushion for avoiding a falsely acceptable result. The Whatman 31ET and Sep-Pak cartridge methods may be preferred over the Whatman 3MM method because they can be performed more quickly. All of the methods involve relatively small amounts of radioactive samples and nontoxic support media and solvents and therefore are considered safe.*