Implementing an alternative method for iobenguane (^{123}I) radiochemical purity determination

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Keywords: radiopharmaceuticals, radiochemical purity, TLC.

The iobenguane (^{123}I) is a weekly produced radiopharmaceutical at the Nuclear Engineering Institute (IEN). Radiochemical purity determination is one of the sets of assays performed in this radiopharmaceutical quality control. The standard analytical method used in this determination is based on the High Pressure Liquid Chromatograpy technique associated to a NaI(Tl) radioactive detector [1]. Whenever the equipment is out of service, analysts must use an alternative method and the ones that include the Thin Layer Chromatograpy (TLC) technique is appropriate, as they well fulfill this purpose. In the standard method, ethanol, a low toxic solvent, is used as the organic modifier [1] Zimmer's method [2] allows ^{123}I and iobenguane (^{123}I) separation applying 6 µL of sample and NaCl 0.9 %, a nontoxic saline solution, as the mobile phase. Silica strips (0.7 x 6 cm) were used as the stationary phase. We adopted this alternative analytical method and the variations in the procedures are outlined as follows: Larger silica gel 60 aluminum based (3 x 13 cm) was applied to provide 20 µL aliquot elution. An ionization chamber was used to measure the activity of the unbound ^{123}I (R_f = 0.7 – 0.8) and iobenguane (^{123}I) (R_f = 0.4). These analites were quantified by the normalization method. As this method is not part of any Pharmacopoeia compendia, its validation was mandatory. The National Agency of Sanitary Vigilance (ANVISA) provides a specific validation guideline [3]. According to this regulation, the following criteria were evaluated: specificity, linearity, range, accuracy, quantitation limit, repeatability and robustness. The former and the latter criteria were performed applying an iobenguane 1 mg.mL^{-1} standard solution prepared according to the European Pharmacopoeia reference standard, while radioactive solutions of iobenguane (^{123}I) were applied to the other ones. Both analites activities measurements occurred in an interval of 30 seconds. Iobenguane showed a brown color in the presence and absence of the matrix, which is in accordance with the expected result for the specificity criterion (Figure 1). The linearity of the method ranges from 2.8 to 14.3 µCi.mL^{-1}. Method robustness was attended under the proposed variation method conditions. Table 1 shows the validation results for the radioactive solutions.

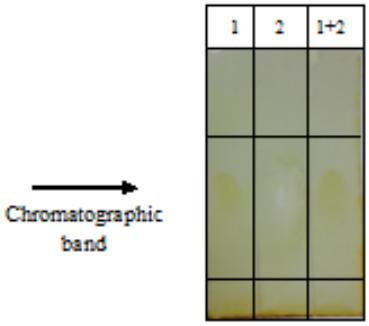

Figure 1. The chromatogram obtained for the specificity criterion. 1 = standard, 2 = sample

Table 1 - Validation results for the criteria performed with iobenguane (^{123}I). Decay correction was not necessary for the linearity criterion. The intermediate and maximum concentration values of linearity curves matched the accuracy expected interval

Criteria	Expected value or interval	Obtained value
Linearity	> 0.99	0.9999
Repeatability	< 5%	2,9%
Accuracy	95 to 105%	101.18 and 97.62%
Quantitation limit	-	1.82 µCi.mL^{-1}

Once standard and alternative methods are validated, their reliabilities are known. The next step is to prove method equivalence through statistics measurement.

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