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Optimized Method for the Radiochemical Purity Quality Control of ^{99m}Tc-Mertiatide - Nephromag™

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Abstract

^{99m}Tc-NephroMAG™ is a radiopharmaceutical which is used for dynamic renal imaging. The summary of product characteristics (SPC) specifies that the determination of radiochemical purity must be achieved via high pressure liquid chromatography or Sep-Pak™ C18 cartridge methods. To minimize the time required to test radiochemical purity, a method with radio-thin-layer chromatography (r-TLC) was used in radio pharmacy unit of Tours CHRU. However, this method on Whatman™ 3mm was too long and offered no optimized resolving parameters.

Methods: For each preparation (n=5), two strips r-TLC with Tec-Control™ #150-005 has been achieved, first with hydrophilic mobile phase (hMP) in order to highlight colloidal technetium (^{99m}TcO2), second with lipophilic mobile (lMP) to separate ^{99m}TcO4.

Results: The method with two kinds of mobile phase offers a better resolving power for both impurities searched and was more rapid to perform.

Conclusion: The simplified method is a reasonable alternative to the registered SPC methods and to the method with Whatman™ 3 mm chromatographic paper.

Keywords 99mTc-NephroMAG™; Analytic method; Radiochemical purity; Radio-thin-layer; Chromatography

Introduction

^{99m}Tc-NephroMAG™ is a radiopharmaceutical which is used for dynamic renal imaging. Isotopic nephrogram indications with ^{99m}Tc-NephroMAG™ include the evaluation of obstructive uro-/nephropathy, diagnosis of renovascular hypertension and the early follow-up of kidney graft quality [1,2]. Before patient injection, the radiochemical purity of the radiotracer must be determined. Analytical methods described in the summary of product characteristics (SPC) of ^{99m}Tc-NephroMAG™ (i.e. high pressure liquid chromatography or Sep-Pak™ C18 cartridge) are either too much time-consuming or too irradiating for operators. In radiopharmacy unit of Tours CHRU, a radio-thin-layer chromatography (r-TLC) method on Whatman™ 3 mm, with a length of 10 cm (Fisher Scientific) and with a mobile phase composed of CH3CN/water for injection (60:40, v/v) has been developed. Nevertheless, long duration of migration (# 30 min) and poor selectivity of the method to separate free technetium (^{99m}TcO4-) on Whatman™ chromatography paper required optimization of chromatographic parameters of this quality control.

Materials and Methods

99mTc-NephroMAG™ preparation

All radiopharmaceutical preparations (n=5) were prepared with ^{99m}Tc-pertechnetate eluted from a ^{99M}o-^{99m}Tc generator (Mallinckrodt). ^{99m}Tc-NephroMAG™ was prepared at 800 MBq in a 2 mL quantity of NaCl 0.9% after 15 minutes of incubation time then 2 mL of commercial buffer were added. All activities were measured with a Capintec CRC®-15R dose calibrator.

Radio-thin-layer chromatographic assays

All chromatographic solvents were obtained from Sigma-Aldrich. Quality control of radiochemical purity of ^{99m}Tc-NephroMAG™ was completed by r-TLC with Mini QC-Scan™ (Bioscan) with 0.25 mm.sec^{-1} speed of plate during 5 minutes, detection cut-off was 2 Mega shots per minute. Quantitative analysis of chromatograms (Tr=retention time; ω=width at the base of the peak) was completed by Chromoleon™ software. For each preparation, two strips r-TLC has been achieved, first with hydrophilic mobile phase (hMP) in order to highlight colloidal technetium (^{99m}TcO2), second with lipophilic mobile phase (lMP) to separate ^{99m}TcO4$^-$. The stationary phase was Tec-Control™ #150-005 systems (Biodex), with a length of 5.5 cm. hMP was sodium citrate. lMP used were ethyl acetate (EA), methyl ethyl ketone (MEK), mix EA/CH3CN and EA/MeOH (60:40, v/v). In lMP, 2 µL of a mix of ^{99m}Tc-NephroMAG™ (^{99m}Tc-NG) with ^{99m}Tc-pertechnetate (^{99m}TcO4$^-$) was extemporaneously prepared in

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order to bring out the resolving power of the method. Selectivity was calculated according to the equation (i)

Separation was considered acceptable based on resolving factor (Rf) greater than 2 and peak profile fitted with a Gaussian-like curve. Statistical results were expressed in terms of 95% confidence interval.

Results

With sodium citrate on Tec-Control™ chromatography system the mean Tr and the mean ω ^{99m}Tc-NG were 3.74 ± 0.16 and 1.31 min ± 0.05, respectively (Figure 1).

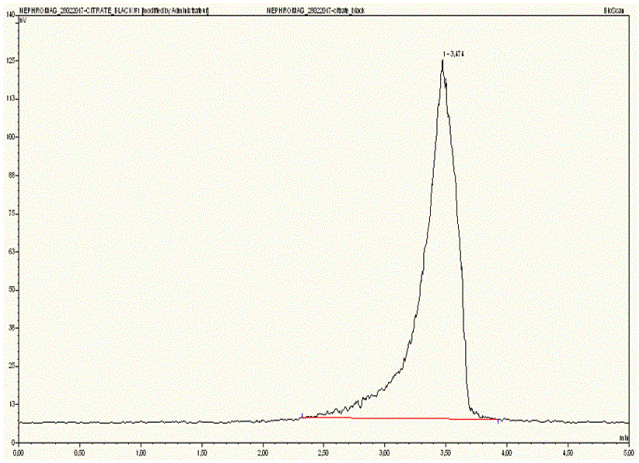

Figure 1: Radio-thin-layer chromatogram of ^{99m}Tc-NephroMAG in a hydrophilic mobile phase composed of sodium citrate on Tec-Control™ #150-005 strip. The peak at 3.47 min corresponds to ^{99m}Tc-NG.

From prior work, in this chromatographic conditions ^{99m}TcO2 showed mean Tr and ^{99m}TcO2 mean ω of 0.94 min ± 0.02 and 0.8 ± 0.02 min, respectively.

In lMP, only the mixture EA/CH3CN (60:40, v/v) provided satisfactory results. Indeed, the ^{99m}Tc-NG profile peak was not a Gaussian-like curve with the following lMP: MEK, mixture EA/MeOH (60:40, v/v). When EA was used like lMP, ^{99m}TcO4$^-$ exhibited a double-shouldered peak. Whereas in the mixture EA/CH3CN (60:40, v/v), the ^{99m}Tc-NG and ^{99m}TcO4$^-$ peak respected a Gaussian curve with mean Tr 1.05 ± 0.12 et 4.07 ± 0.13 min, respectively (Figure 2).

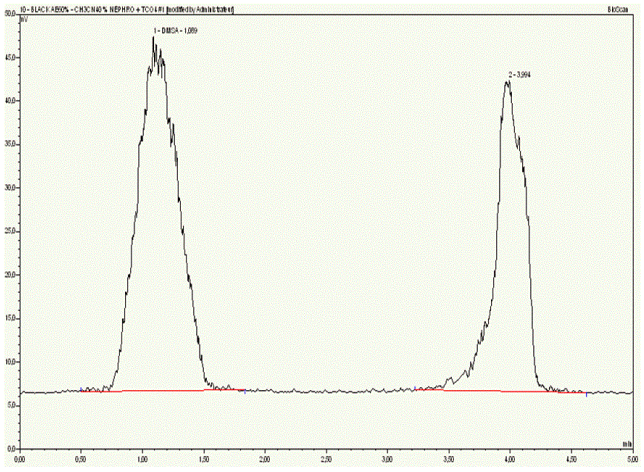

Figure 2: Radio-thin-layer chromatogram of a preparation of ^{99m}Tc-NephroMAG (^{99m}Tc-NG) contaminated by an addition of free technetium (^{99m}TcO4$^-$) in a lipophilic mobile phase composed of EA/CH3CN (60:40, v/v) on Tec-Control™ #150-005 strip. The first peak at 1.09 min corresponds to ^{99m}Tc-NG and the second at 3.99 min is ^{99m}TcO4$^-$.

According to the equation (i), the mean Rf was 3,23 ± 0.24 min. Concerning the time of quality control (migration + analysis), it was 27 ± 0.8 min for the method on Whatman™ 3 mm against only 15 ± 0.6 min for method on Tec-Control™ strip.

Table 1 summarizes and compares chromatographic conditions and results between quality control method on Whatman™ 3 mm paper and Tec-Control™ #150-005 system.

Table 1: Chromatographic conditions and results of the ^{99m}Tc-NephroMAG™ quality control with the two r-TLC methods. Rf: resolution factor; hMP: hydrophilic mobile phase; lMP, lipophilic mobile phase.

	Whatman™ 3 mm	**Tec-Control™ #150-005**
Stationary phase	Cellulose	Cellulose
Mobile phase	CH3CN/EPPI (60:40, v/v)	- Sodium citrate
		- EA/CH3CN (60:40, v/v)
Migration time	# 20 min	# 5 min
Analysis time	# 7 min	# 5 min (x2)
Rf (^{99m}Tc-NG & ^{99m}TcO2)	>>2	>>2 (hMP)
Rf (^{99m}Tc-NG & ^{99m}TcO4$^-$)	0.92 ± 0.09	3.23 ± 0.24 (IMP)

Discussion/Conclusion

At the opposite of ^{99m}Tc-MAG3™, another radiopharmaceutical used for dynamic renal scintigraphy, where analytical methods for determining radiochemical purity were published [3]; to our knowledge it is the first study that reported a r-TLC quality control method of radiochemical purity of ^{99m}Tc-NephroMAG™. Technescan MAG3™ is composed of betiatide and its preparation is more time-consuming than NephroMAG™ due to the radiolabeling requires heating. Concerning the determination of radiochemical purity of ^{99m}Tc-MAG3™ both techniques, with modified solid phase extraction cartridge procedure and instant thin-layer chromatography method has been developed [3]. The quality control of the radiochemical purity of ^{99m}Tc-NephroMAG™ via r-TLC with both mobile phase, hydrophilic (sodium citrate) and lipophilic (EA/CH3CN (60:40, v/v)) thanks to Tec-Control™ strip, is an interesting alternative to the method on Whatman™ 3 mm chromatographic paper. On the one hand, this new analytical method offers a better resolving power for both impurities searched. On the other hand, these chromatographic parameters allow reducing quality control time by half, making it easier to realize a discharge control of ^{99m}Tc-NephroMAG™.

References

1. Sfakianakis GN, Sfakianaki E, Georgiou M, Serafini A, Ezuddin S, et al. (2009) A renal protocol for all ages and all indications: mercapto-acetyl-triglycine (MAG3) with simultaneous injection of furosemide (MAG3-F0): a 17-year experience. Semin Nucl Med 39:156–173.
2. Taylor AT, Folks RD, Rahman AKMF, Polsani A, Dubovsky EV, et al. (2017) (99m)Tc-MAG3: Image Wisely. Radiology 15: 2311.
3. Seetharaman S, Sosabowski M, Ballinger J (2007) Validation of alternative methods of preparing 99mTc-MAG3. Applied Radiation and Isotopes 65: 1240–1243.

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