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RADIOCHEMICAL QUALITY CONTROL OF ^{67}Ga-CITRATE RADIOPHARMACEUTICALS

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A rapid, miniaturized chromatography system has been developed to determine the possible contaminants of ^{67}Ga-citrate. This method is simple, inexpensive and suitable for laboratory routine tests. By classical paper chromatography the analysis takes several hours to complete.

INTRODUCTION

Chromatography procedures for ^{67}Ga-citrate radiopharmaceuticals are an important part of the quality control program in nuclear medicine. The ^{67}Ga radioisotope has been widely used in Medical diagnosis for the localization of a variety of malignant human tumors. It is a radioisotope of great value in clinical investigation and a useful radionuclide in research as an energy and efficiency calibration[1] source for detectors. ^{67}Ga is obtained in cyclotron and has a relatively short half-life (78.6 h).

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Classical paper chromatography used for ^{67}Ga is an effective way of analyzing impurities, but this technique[2,3], although very accurate, is probable too time-consuming for becoming a routine quality control method.

Miniaturized chromatographic[4,5] quality control procedures for radiopharmaceuticals are becoming very rapid and also easy to perform.

A number of solvents was tested on Whatman No. 1 and No. 3 MM chromatographic paper with the purpose of finding a system capable of resolving gallium in its different chemical form.

The migration of an individual compound in a sample is conveniently characterized by its Rf values.

Rf values were established for gallium hydroxide, gallium chloride and probable impurities in the chromatographic system used for quality control, by running each compound in parallel with the mixture of ^{67}Ga-citrate.

MATERIALS AND METHODS

The ^{67}Ga-citrate radionuclide was produced at the Instituto de Pesquisas Energéticas e Nucleares - CNEN - São Paulo.

The determination of ^{67}Ga radiochemical[2] purity was studied in ascendent chromatographic paper. The mobile phase solvent was pyridine and ethanol in addition to water in the proportion of 1:2:4. Chromatographic paper strips (2x20 cm) were used for the classical method and Whatman No. 1 and No. 3 (6.5x1.0 cm) for the miniaturized system as supporting medium.

^{67}Ga was spotted 2.0 cm and 1.0 cm from the botton to the paper.

For the classical method the strip was placed in a measuring cylinder containing 100 ml of the solvent,

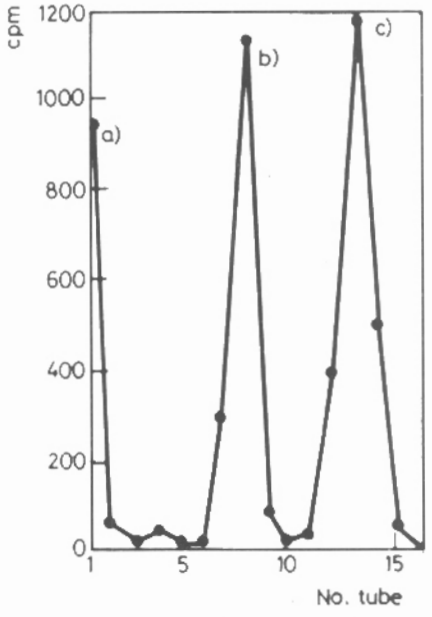

Fig. 1. Radiochromatograms of a - $GaCl_3$, b - $Ga(OH)_3$ and c - ^{67}-Ga-citrate in solvents pyridine: ethanol:water 1:2:4

while in the miniaturized system the paper was placed in a 10 ml vial containing 1 ml of solvent.

The chromatogram was developed until the solvent front had traveled 16 cm and 5.5 cm, and the development time was about 1.30 h and 20 min, respectively.

The strip was removed, dried and cut in strips of 1.0 cm and 0.5 cm length.

Each strip was measured with an ANSR Gamma Counter (Abbot Lab.).

RESULTS AND DISCUSSION

Figure 1 present the radiochromatograms obtained for $GaCl_3$, $Ga(OH)_3$ and ^{67}Ga-citrate, respectively. With this system ^{67}Ga-citrate migrates in the proximity of the

TABLE 1

Rf value on Whatman No. 1 and No. 3 MM radiochromatogram paper. The mobile phase used contained pyridine, ethanol and water (1:2:4)

Compound	Classical	Miniaturized
$GaCl_3$	0.00	0.00
$Ga(OH)_3$	0.50	0.40
^{67}Ga-citrate	0.80	0.80

TABLE 2

Comparison of percent values of $GaCl_3$ in the analysis of ^{67}Ga-citrate by classical and miniaturized chromatography

Classical	Miniaturized
1.44	1.45
1.66	1.68
1.10	1.02
1.12	1.09
1.72	1.75
2.30	2.35
1.45	1.48
1.15	1.20
1.04	1.06
1.28	1.25

solvent front, whereas gallium chloride remaines at the origin.

Table 1 presents the Rf values obtained in this study and those obtained by the classical method.

Table 2 shows the percent values of $GaCl_3$ obtained in the analysis of ^{67}Ga-citrate samples by classical and a

TABLE 3

Reproducibility of the method obtained with the sample and simultaneous runs (n = 11) for ^{67}Ga-citrate

N	$GaCl_3$	^{67}Ga-citrate
1	1.29	98.71
2	1.32	98.68
3	1.26	98.74
4	1.30	98.70
5	1.35	98.65
6	1.27	98.73
7	1.38	98.62
8	1.25	98.75
9	1.33	98.67
10	1.36	98.64
11	1.27	98.73
	$\bar{X}$ = 1.31	S = 0.044 CV = 3.34

Where: $\bar{X}$ = mean value, S = standard deviation, CV = variation coefficient.

miniaturized chromatography technique. The excellent correlation coefficient, r = 0.9974, between the classical method and the miniaturized chromatography system indicates the accuracy of the latter method.

Table 3 illustrates the reproducibility of the method using the same conditions with simultaneous runs (n = 11, $\bar{X}$ = 1.31) and a coefficient of variation of 3.34%.

Gallium is a labile element, i.e. it will reache chemical equilibrium rapidly and the reaction on the paper will be completed almost immediately after contact with the solvent front.

CONCLUSION

For routine control, the miniaturized chromatography system was choosen because it is a rapid and easy method to evaluate radiochemical purity.

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