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QUALITY CONTROL PROCEDURES FOR IODINATED RADIOPHARMACEUTICALS ^{131}I-HIPPURAN AND ^{131}I-RISA

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ABSTRACT

A rapid miniaturized chromatography system was developed for fast determination of the proportion of inorganic radioactive iodide from radiopharmaceuticals ^{131}I-Hippuran and ^{131}I-Risa.

The technical parameters associated with miniaturized chromatography system were evaluated. One of the problems found in this system was the movement of the ^{131}I-Risa from the origin with consequent overestimation of the inorganic iodide.

A correct spot placement eliminated this problem.

PROCEDIMENTOS PARA CONTROLE DE QUALIDADE DOS RADIOFÁRMACOS ^{131}I-HIPPURAN E ^{131}I-RISA

RESUMO

Desenvolveu-se um sistema de cromatografia miniaturizada para determinação rápida da proporção de iodeto inorgânico radioativo nos radiofármacos Hippuran ^{131}I e Risa ^{131}I.

Avaliaram-se os parâmetros técnicos associados com o sistema cromatográfico miniaturizado. Um dos problemas encontrados neste sistema foi o deslocamento da Risa^{131} a partir da origem com consequente erro na determinação do iodeto inorgânico.

Uma aplicação correta da amostra elimina este problema.

INTRODUCTION

Organic compounds labelled with a radioiodide for use in medical diagnosis generally contain inorganic radioiodide as their main impurity.

Paper electrophoresis and classical chromatography have come to be accepted very generally as methods of determining the purity of labelled compounds in the field of radiopharmaceuticals[2,6].

The paper electrophoresis technique used for ^{131}I-Hippuran depends on the different migration rates of charged molecules in an electric field. Migration is primarily influenced by polarity and magnitude of charge on a molecule and its size and shape and also by the applied voltage, distance between electrodes and duration of separation.

The classical paper chromatography, used for ^{131}I-RISA is an effective way of analysing the inorganic radioiodide impurities, but this technique, although very accurate, is probably too time-consuming for routine quality control.

With the advent of miniaturized chromatography systems[1,7] quality control procedures for radiopharmaceuticals are becoming very quick and also easy to perform. However, variations in the results have been observed for several ^{99m}Tc preparations by some investigators, because artifactual results are produced when improper technique is used[5,3]. Careful technique is necessary in miniaturized chromatography system to analyse ^{99m}Tc radiopharmaceuticals.

In our laboratory, the routine analysis of the radiopharmaceuticals ^{131}I-Rose Bengal and ^{131}I-Bromosulphthalein have usually provided rapid and accurate results independent of the technical parameters associated with the chromatography quality control procedures.

Similar results were obtained with ^{131}I-Hippuran, but for ^{131}I-RISA the results of a large number of experiments developed in our laboratory indicated that when increasing amounts of sample are applied to the paper, a definite tailing off in the direction of the solvent front is produced. It is important to find artifacts through which the conditions that produce this tailing are recognized so that true separation can be obtained.

MATERIAL AND METHODS

The miniaturized chromatographic procedures were developed using Whatman 3MM (6.5 cm x 1.0 cm) paper strip as support and chloroform: glacial acetic mixture (1.00:0.05 v/v)and 0.9% sodium chloride as solvent for ^{131}I-Hippuran and ^{131}I-RISA, respectively.

With this system, ^{131}I-Hippuran migrated in close proximity to the solvent front, whereas the inorganic iodide remained at the origin. For ^{131}I-RISA, it remained in a narrow peak at the site of application while the inorganic iodide moved away from it.

The papers were spotted 1.0 cm from the bottom. The strips were placed in a vial containing approximately 1.0 ml of a chloroform: glacial acetic mixture (1.00:0.5 v/v) for ^{131}I-Hippuran, and 1.0 ml of 0.9% sodium chloride for ^{131}I-RISA.

The chromatogram was developed for a distance of 5.0 cm during 10 minute for both radiopharmaceuticals. The strips then were removed, dried and may be cut midway between the origin and solvent front portions and each piece counted separately in a well-type scintillation counter (ANSR Gamma Counter Abbot Lab.).

Preliminary scanning is advisable even if the strips are cut between the two peaks.

The counts of each section were expressed as a percentage of the total-counts of the two sections.

The spot sizes, sample volume and drying before developing had no effects on the results of analysis when Whatman 3MM paper was used. One important finding was that significant errors are produced, only for ^{131}I-RISA, when increasing amounts of the radiopharmeutical is used.

RESULTS AND CONCLUSIONS

The percentual of inorganic iodide of the two radiopharmaceuticals, ^{131}I-Hippuran and ^{131}I-RISA, are shown in Table I and II. The mean values of the iodide determination were in agreement with the data obtained by classical paper electrophoresis for ^{131}I-Hippuran with correlation coefficient $r = 0.9905$, and by classical chromatography for ^{131}I-RISA with correlation coefficient $r = 0.9889$. The excellent correlation coefficient results between the classical methods and the miniaturized chromatography system indicated the accuracy of the method.

Table I

Comparison of Percentual Values of Inorganic Iodine in the Analysis of ^{131}I-Hippuran Samples by Electrophoresis and Miniaturized Chromatography

Date	Percentage of Inorganic Iodide	
	Classical Electrophoresis	Miniat. Chromatography
11.07.84	2.58	2.35
31.07.84	2.74	2.80
14.08.84	1.41	1.52
21.08.84	1.60	1.72
05.09.84	2.78	2.60
12.09.84	1.58	1.56
19.09.84	1.47	1.53
25.09.84	2.58	2.42
03.10.84	1.68	1.69
09.10.84	4.10	4.09
		correlation coefficient r = 0.9905

Table II

Comparison of Percentual Values of Inorganic Iodide in the Analysis of ^{131}I-RISA Samples by Classical Chromatography and Miniaturized Chromatography

Date	Percentage of Inorganic Iodide	
	Classical Chromatography	Miniat. Chromatography
10.07.84	1.65	1.67
24.07.84	1.32	1.29
06.08.84	1.55	1.56
14.08.84	1.46	1.41
21.08.84	1.70	1.75
28.08.84	1.36	1.32
19.09.84	1.16	1.25
25.09.84	1.22	1.27
09.10.84	1.42	1.63
16.10.84	2.92	2.78
		correlation coefficient r = 0.9889

Table III indicated the percentual of inc nic iodide obtained in 10 preparations of ^{131}I-Hippuran and 10 preparations of ^{131}I-RISA when differents total-counts in the sample were used. For ^{131}I-Hippuran, as indicated in this Table, increasing total-counts did not significantly change the percentages of inorganic iodide.

On the other hand, for ^{131}I-RISA it was necessary to test the minimum amount of sample to permit only negligible tailing of radioactivity along the path of migration since the albumin which contains relatively large amount of radioactivity, has the tendency to adsorb to paper[4].

As indicated in Table III a completely false overestimation of the percentual of inorganic iodide level was obtained when the total-count of the strip was greater than 800,000 cpm.

The reproducibility of the method in ideal work condition (which use the same with simultaneos runs) is illustrated by the data shown in the Table IV with coefficient of variation CV = 2.73% for ^{131}I-Hippuran and CV = 2.45% for ^{131}I-RISA.

The miniaturized chromatography system provided a rapid and easy method to assess the radiochemical purity.

Table III

Effect of Varying Total-counts on the Strips of Chromatographic Determination of Inorganic Iodide in a Preparation of ^{131}I-RISA and ^{131}I-Hippuran

^{131}I-RISA		^{131}I-Hippuran	
Total-counts cpm	Inorg. Iodide %	Total-counts cpm	Inorg. Iodide %
30,290	1.37	22,146	1.52
283,287	1.36	289,737	1.58
475,320	1.53	366,996	1.50
510,039	1.50	495,890	1.54
722,448	1.48	791,039	1.68
883,390	*6.60	966,033	1.54
1,464,892	*21.72	1,363,437	1.62
1,583,304	*17.09	1,608,983	1.62
1,600,400	*19.00	1,807,592	1.63
1,971,211	*20.00	2,052,322	1.56
			X = 1.58
			S = 0.057
			CV = 3.6

* Spuriously high percentual of inorganic iodide level is produces if the applied spot is a large amount of radioactivity.

Table IV

Reproducibility of the Method Obtained With the Same Sample and Simultaneous Runs(20) for ^{131}I-Hippuran and ^{131}I-RISA

Runs	Percentage of Inorganic Iodide	
	^{131}I-Hippuran	^{131}I-RISA
1	1.72	2.42
2	1.76	2.34
3	1.76	2.38
4	1.69	2.40
5	1.70	2.44
6	1.74	2.50
7	1.63	2.34
8	1.62	2.42
9	1.69	2.37
10	1.75	2.36
11	1.72	2.48
12	1.72	2.43
13	1.64	2.37
14	1.72	2.44
15	1.63	2.52
16	1.63	2.44
17	1.72	2.43
18	1.69	2.37
19	1.68	2.51
20	1.75	2.53
	X = 1.70	X = 2.42
	S = 0.0465	S = 0.0594
	CV = 2.73	CV = 2.45

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