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Determination of Radiochemical Purity of Radioactive Microspheres by Paper Chromatography

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Abstract

Simple methods to quantify radiochemical impurities existing in glass microspheres were tested. A system of two solvent mobile phases (acetone and 0.9% NaCl) were used with Whatman no. 3 paper strips as the stationary phase. Paper chromatography was used to identify radiochemical impurities in the radioactive microspheres. These impurities were found to be <0.01% for Azer spheres in saline and acetone solution. The results confirmed that glass microspheres prepared using the new procedures are convenient for radiotherapy purposes.

Keywords: Microspheres; Radioactive; Paper chromatography

Introduction

Chromatography is the collective term for a set of laboratory techniques for the separation of mixtures into their components. All forms of chromatography work on the same principle. They all have a stationary phase (a solid or a liquid supported on a solid) and a mobile phase (a liquid or a gas). The mixture is dissolved in a fluid called the mobile phase, which carries it through a structure holding another material called the stationary phase. The mobile phase flows through the stationary phase and carries the components of the mixture with it. The various constituents of the mixture travel at different speeds, causing them to separate. The separation is based on differential partitioning between the mobile and stationary phases. There are different types of chromatography, including column chromatography and paper chromatography [1-10].

Paper chromatography is a solid-liquid form of chromatography where the stationary phase is a specially manufactured porous paper and the mobile phase can be a single solvent or a combination of solvents. Paper chromatography is a method used to separate mixtures into their different parts [1-10]. Paper chromatography has been most commonly used to separate pigments, dyes and inks.

Chemists frequently use paper chromatography to follow the progress of a reaction by monitoring the disappearance of a reactant or the appearance of a product. Autoradiography can be used to investigate the distribution of radioactive materials [11].

Radiochemical purity is an important quality parameter for radiopharmaceuticals [12]. The radiochemical purity (RCP) of compounded radiopharmaceuticals should be monitored before administration to patients [13]. A number of analytical methods can be used to detect and determine the radiochemical impurities in a given radiopharmaceutical. Particularly important are precipitation, paper, thin-layer, and gel chromatography, paper and gel electrophoresis, ion exchange, solvent extraction, high performance liquid chromatography and distillation [8].

Thin-layer and paper chromatography is mostly used in a hospital environment. In paper and thin-layer chromatography, a volume equal to that described in the monograph is deposited on the starting-line. After development, the support is dried and the positions of the radioactive areas are detected by autoradiography or by measurement of the radioactivity over the length of the chromatogram using suitable collimated counters or by cutting strips and counting each portion. The positions of the spots or areas permit chemical identification by comparison with the solutions of the same chemical substance (non-radioactive) using a suitable detection method.

In the present study, paper chromatography was used to separate Y^{3+} ions into different structures. Depending on their molecular structures and interactions with the paper and mobile phase, they adhered to the paper more or less than the other compounds to allow quick and efficient separation. Autoradiography was used to investigate the distribution of radioactive Y^{3+} ions. This study developed a type of paper chromatography to determine the radiochemical purity of radioactive microspheres.

Materials and Method

Microsphere preparation

The present study developed a type of paper chromatography for determination and comparison of the radiochemical purity of radioactive yttrium-90 microspheres produced by sol gel method and different composition 1) TEOS: H_2O: HCl (Azer spheres) [14,15], 2) TEOS: CH_3COOH:H_2O (Azar spheres) [16], 3) TEOS: H_2O: H_3PO_4, (Az spheres) [17].

Neutron activation

For this procedure, 200 mg of each microsphere powder was poured into a quartz ampoule (6 cm in height, 0.7 cm in diameter) and the ampoule was sealed using an oxygen flame. The sample was irradiated inside a sealed aluminum container (7 cm in height, 3 in cm diameter) for 10 h in the research reactor. The medium neutron flux was about 3.0 $\times 10^{13}$ n/(s.cm^2).

After cooling for 3 d, the sealed aluminum container was cut and the quartz ampoule was crushed. These microspheres were subsequently added to a 10 ml vial with 5 ml of saline to form an elution. These

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radioactive microspheres were then analyzed to determine their radiochemical purity.

Radiochemical purity

Paper chromatography was used to determine the radiochemical impurities in the radioactive microspheres. The radiochemical purity of a radiopharmaceutical is defined as the fraction of total activity in the desired chemical form in the sample [18-20]. These impurities arise from incomplete labeling, breakdown of the labeled products over time caused by instability, and introduction of extraneous labeled ingredients during synthesis. Impurities can cause altered *in vivo* bio distribution after administration which can result in an unnecessary radiation dose to the patient. For these reasons, the US Pharmacopeia and US Food and Drug Administration have set limits on impurities in different radiopharmaceuticals that must not be exceeded in clinical operations.

Radiochemical impurities were checked using the two-solvent system: (a) saline solution (NaCl 0.9%) as the mobile phase on Whatman no. 3 paper; (b) acetone solution on Whatman no. 3 paper. The Whatman no. 3 chromatography paper sheets were cut into 1 cm × 8 cm strips and placed into empty 10 ml glass pharmaceutical vials. Approximately 1 ml of the appropriate solvent was placed into the vial and two droplets of radioactive solution were dropped onto it, forming a spot about 1 cm in diameter. After drying the droplets, the strips were placed in the appropriate solvent and the solvent was allowed to migrate until it reached the top of the strip.

This procedure generally requires 30 min. After the strip had dried, it was cut into eight 1 cm pieces and the radioactivity of each segment was measured in an alpha and beta counter (LB123 UMO Berthold) for 1 min. The data was expressed in counts per minute (cpm). The chromatography spectra are shown in Figures 1 and 2 and indicate low levels of impurities for these microspheres. The impurities were calculated by expressing the percentage of activity corresponding to the total activity on the plate (Tables 1 and 2).

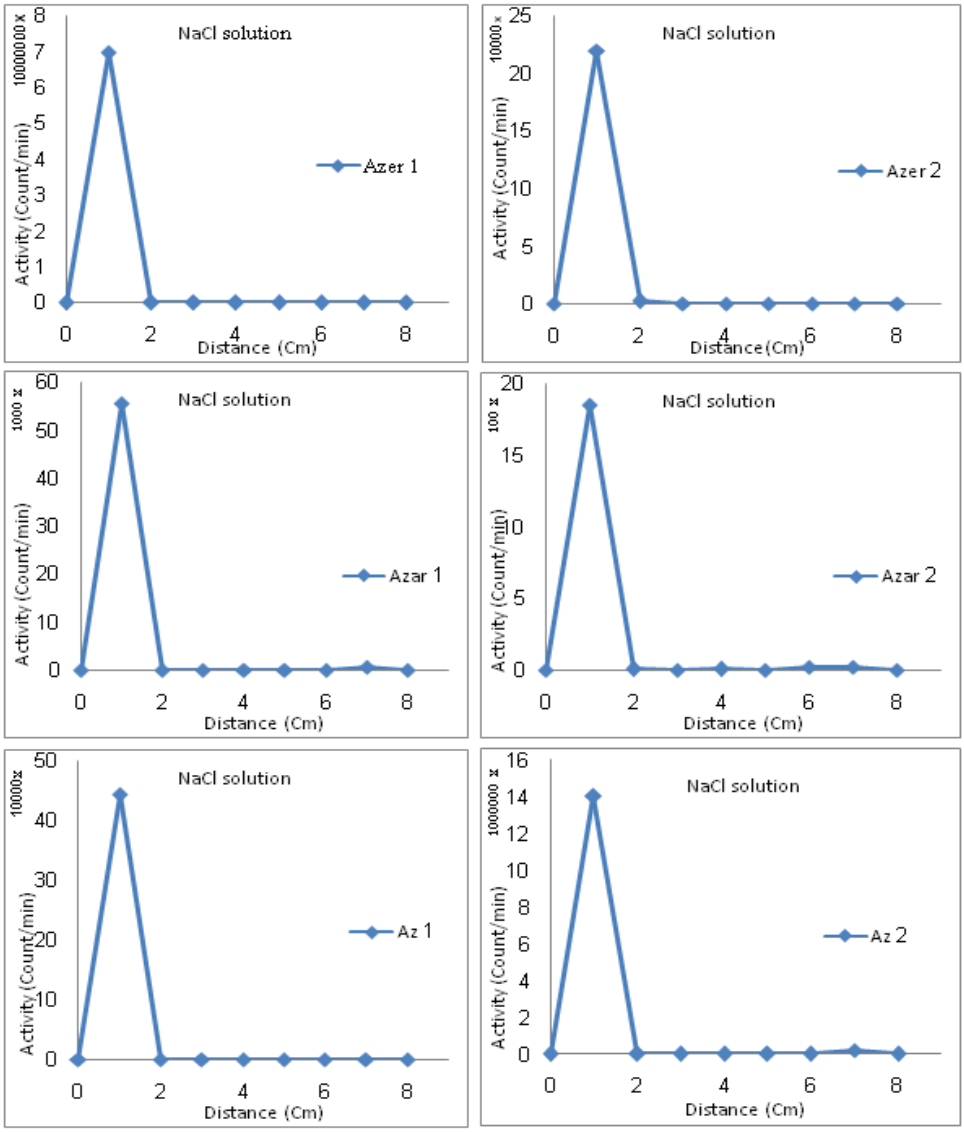

Figure 1: Chromatography analysis of different microspheres in saline solution.

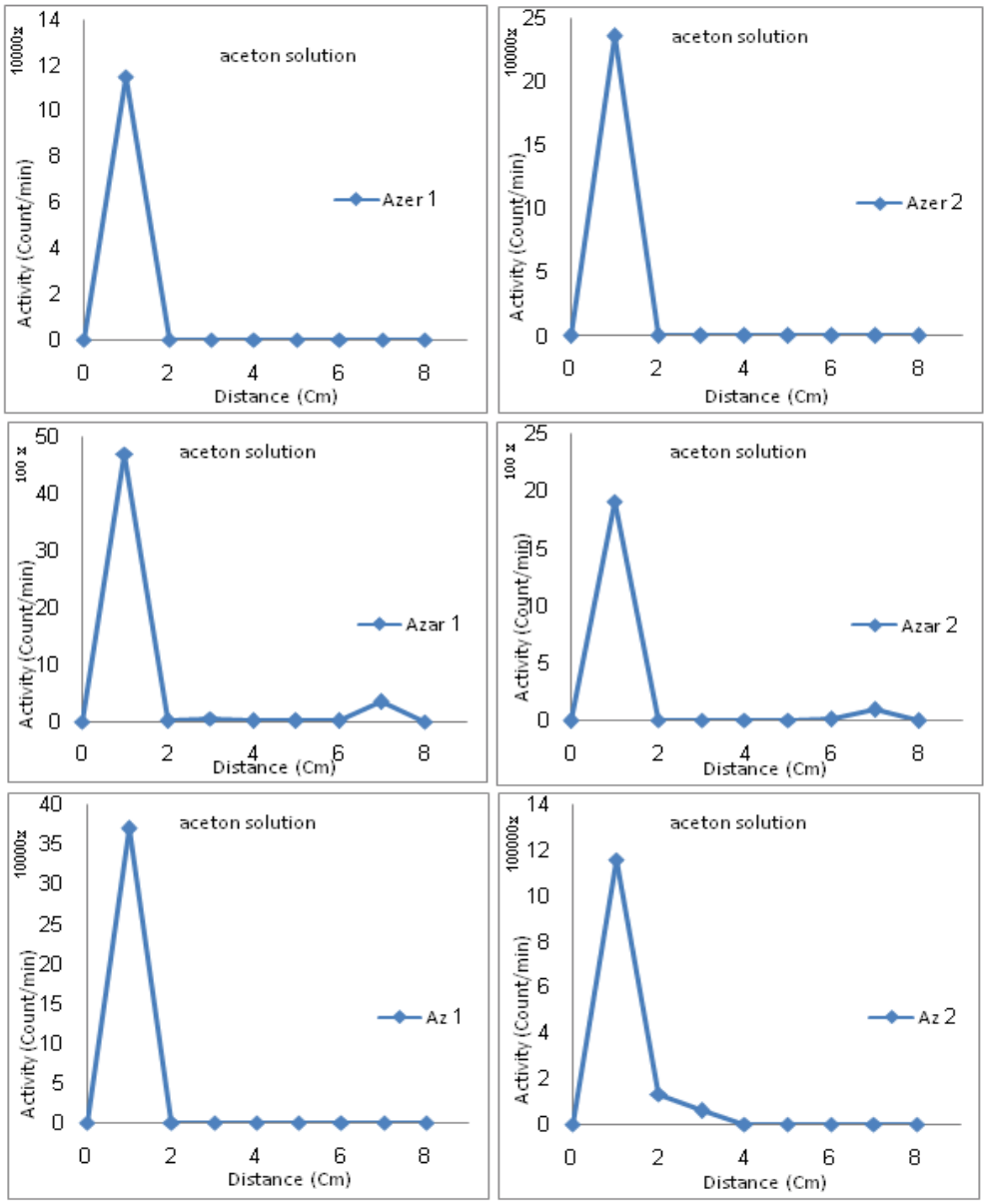

Figure 2: Chromatography analysis of different microspheres in acetone solution.

	Net activity of 1/3 strip in origin (Count/min)	*All activity of strip* (Count/min)	*Radiochemical Purity*
Azer-spher 1	115005	115008.7	0.9999
Azer-sphere 2	236030	236035	0.9999
Azar-sphere 1	4712	5121	0.9201
Azar-sphere 2	1919	2040	0.9407
Az-sphere 1	370015	370022.4	0.9999
Az-sphere 2	1290000	1339992	0.9627

Table 1: Radiochemical purity of different microspheres in saline solution.

For protection from ingestion, inhalation and irradiation of the radioactive product, these processes were performed in a box made of Plexiglas.

Results and Discussion

The chromatography spectra shown in Figures 1 and 2 indicate low levels of impurities for these microspheres. The impurities were calculated by expressing the percentage of activity corresponding to the total activity on the plate.

The chromatography spectrums of Azer sphere 1, Azar sphere 1 and Az sphere 1 and those for free Al Azer sphere 2, Azar sphere 2 and Az sphere 2 are shown in Figures 1 and 2. The radiochemical purity was found to be more than 99% for the Azer spheres in saline and acetone solution. And it was less than 95% for the Azar spheres in

	Net activity of 1/3 strip in origin **(Count/min)**	***All activity of strip*** **(Count/min)**	***Radiochemical Purity***
Azer-sphere 1	70000700	70000707.7	0.9999
Azer-sphere 2	222400	222446.6	0.9998
Azar-sphere 1	55605	56316	0.9874
Azar-sphere 2	1853	1898	0.9763
Az-sphere 1	445019	445092	0.9998
Az-sphere 2	14000035	14213742	0.9849

Table 2: Radiochemical purity of different microspheres in acetone solution.

saline solution. The radiochemical purity of Az sphere 1 was more than 99% in the saline and acetone solutions.

Conclusion

The results indicate that the low level of chemical impurities in the Azer and Az spheres make them suitable for medical applications. Paper chromatography with acetone and 0.9% NaCl was shown to be a simple and quick method for routine quality control of radiopharmaceuticals. It confirmed that glass microspheres prepared by the new procedure are a radiopharmaceutical of high efficiency and radiochemical purity with a satisfactory number of particles of the required size. These qualities promise good results for applications in radiotherapy where the radiochemical purity for radiopharmaceutical products must be higher than 95% [9].

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