Preparation and stability of rhenium $^{188}$Re sulfide suspension with different particle size distributions

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Two different dispersion methods were studied in order to obtain rhenium $^{188}$Re sulfide suspension with different particle size distributions. The manufactured swirling device offers Suspension I with larger particles (55%<5 μm, 19%>10 μm). However, ultrasonication can only produce Suspension II with smaller particles (93%<5 μm, 0.3%>10 μm). Stability tests indicated that deposition appears after 6 and 15 minutes for Suspensions I and II, respectively. Radiochemical purity and particle size distribution did not change distinctively within 24 hours. So, both suspensions can be used in animal tests to find out the optimal particle size ranges for intra-articular injection.

Introduction

Radiation synovectomy is an attractive alternative to surgery in the treatment of rheumatoid arthritis, and has been developed in Europe since many years.1,2 This procedure consists of the intra-articular injection of a radionuclide in colloidal or particulate form in order to alter or ablate the inflamed synovium.3 However, it is not widely used because of the unnecessary and unacceptable radiation delivered to non-targeted organs due to leakage of radioactive material from the treated joints. Radiation leakage can presumably be reduced by many methods.4,5 Choosing a radionuclide with a shorter half-life would help minimize the cumulative radiation dose.6 In addition, immobilization of the treated joints has been shown to reduce particle leakage.3

Numerous experimental evidences have indicated that radiolabeled particle size is of great importance to the undesirable radioactivity leakage.5,7,8 In earlier studies of $^{198}$Au radionuclide with the majority of particles less than <1 μm, 5% to 48% of the dose delivered to the target cavity eventually leaked through the draining lymph glands.2 Leakage of the rhenium sulfide colloid prepared using hydrogen sulfide gas was about 40% between 5 hours and 2 days.9 The high leakage was due in part to the large amount of particles of less than 0.5 μm labeled with $^{186}$Re.9 Many particle ranges from 1 to 10 μm,2 to 5 μm,11 5 to 10 μm,9 and >10 μm4 were investigated on animal models or patients. It is suggested that the appropriate particle range from 2 to 10 μm is available for intra-articular administration.2

Therefore, we developed two methods to produce particles mainly ranged from 2–10 μm. Particle analysis showed that they still have different size distributions.

After injection of two medicines with different particle sizes to normal rabbit knees, biodistribution experiments follow to find out the different tissue uptake and joint leakage.9,12,13 $^{188}$Re has suitable properties for therapy usage. Many experimental and clinical results indicated that it could be an effective radiotherapy agent.9,12,13 In this study, we labeled rhenium sulfide suspension with $^{188}$Re, and then produced two different particle-size suspensions through two dispersion methods. Stability tests indicated that both suspensions could be used in animal tests to select the optimal particle size ranges for intra-articular injection.

Experimental

Materials

KReO$_4$ was provided by Johnson Matthey Chemicals, Ltd., England. Particle size was measured by an optical microscope (BX51, Olympus, Japan) and measured by ImagePro Soft. Radiochemical purity was determined by scanning radiochromatography (AR-2000, BioScan, USA).

Methods

Preparation of rhenium $^{188}$Re sulfide suspension: The rhenium sulfide suspension was prepared through a kit in which potassium perrhenate and sodium thiosulfate have been quantitatively freeze-dried.14 The kit was radiolabeled by the addition of 0.2 ml of HCl and 0.8 ml of eluted sodium perrhenate solution [Na$^{188}$ReO$_4$], which was obtained from an $^{188}$W/$^{188}$Re generator. The mixture was heated in a boiling water bath for 30 minutes, and then cooled for a few minutes.

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Addition of 1 ml of polyvinyl pyrrolidone (PVP) and sodium hydroxide solution was necessary in order to obtain a stable and neutral suspension.

Dispersion of the suspension: The vial was placed on the operation plate through the column cover and shaken for 1 minute by means of a vortex mixer. The obtained product was called Suspension I. Figure 1 shows the sketch of the swirling device.

The vial was put in the operating pool of the ultrasonicator and ultrasonicated for 30 minutes. This product was called Suspension II.

Sedimentation tests of the suspension: After the dispersion procedure, 20 μl of the supernatant was removed at intervals of 0, 3, 6, 9, 12, 15 and 30 minutes and measured using a γ-counter. After 30 minutes the suspensions were again mixed shaken for a few seconds, and γ-counted.

Stability of radiochemical purity and particle size: At the preset sampling times of 0, 4, 8, 12, 24, 36, 48 and 72 hours, radiochemical purity was evaluated by paper chromatography (XinHua 1# chromatography paper) using 0.9% saline solution as the developing solvent. Particle size distribution was observed by a microscope and calculated through ImagePro Soft.

Results and discussion

Particle size distribution of the suspension

Figure 2 shows the particle size distribution of Suspensions I and II which were dispersed by the vortex mixer and ultrasonication, respectively. The size distribution of Suspension II showed that 93% of the particles were within the range of <5 μm. 55% of particles of Suspension I were >5 μm, and 19% were >10 μm. On the other hand, less than 7% of particles of Suspension II were >5 μm and ignorable 0.3% were >10 μm. Pictures obtained by the optical microscope are shown in Fig. 3.

![Fig. 1. Swirling device: 1 – screw, 2 – column cover, 3 – operating salver, 4 – vortex mixer](image1)

![Fig. 2. Particle size distribution of Suspensions I and II](image2)