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Diagnostic kit for blood pool imaging

One of the methods employed in the past to image the blood pool for diagnostic purposes involves the intravenous administration of 99m Tc serum albumin which is available commercially and is a sterile pyrogen-free solution of albumin labelled with Technetium 99m having an activity of greater than 100 microcuries/ml.

In utilizing this method of blood pool imaging, it is important to predose the patient immediately prior to the attempted visualization of the blood pool, since the 99m Tc serum albumin is very rapidly lost from the blood stream by exchange in the kidney.

Another method used in the past for imaging blood pools is the *in vitro* labelling of red blood cells (outside the host animal) followed by reinjection of the cells into the vascular system of the selected animal. By this method, it is possible to visualize both heart blood pools plus major peripheral vessels up to 3 hours after injection of the labelled cells. As can be seen, this is a complicated procedure, and therefore is a more time-consuming and expensive method.

Still another procedure for imaging blood involves the injection of stannous pyrophosphate followed by injection of 99m Tc-pertechnetate. This technique is reported as successful in producing satisfactory imaging of blood pools.

US Patent Specification No. 4 027 005 discloses *inter alia* an *in vitro* prepared radioactive diagnostic composition comprising a pertechnetate, stannous chloride dihydrate and a glucoheptonate salt, the preferred minimum weight of glucoheptonate being 200 times that of the stannous compound. This composition is primarily for use in examination of the kidneys.

In accordance with the present invention, there is provided a diagnostic kit suitable for the radioactive labelling of red blood cells *in vivo*, thus making possible the imaging of blood pools within the circulatory system of the patient being examined. As an integral part of the diagnostic kit of the present invention, there is also provided a novel chemical composition comprising a lyophilized mixture of a glucoheptonate salt and a pharmaceutically acceptable stannous salt in the ratio of 25 parts by weight of glucoheptonate salt to 3 parts by weight of stannous salt measured as calcium glucoheptonate and stannous chloride dihydrate or approximately 22.9 parts of glucoheptonate ion to 1.32 parts of tin calculated as available stannous ion.

An important feature of the present invention is the provision of an individual diagnostic kit containing a non-toxic stannous salt capable of supplying an amount of stannous ion equivalent to at least 2.5 mg and no more than 4.0 mg of stannous chloride dihydrate. Less than 2.5 mg of the stannous chloride does not provide sufficient stannous ion to effect a satisfactory degree of labelling of red blood cells. Because of the known toxicity of stannous salts, no more than 4 mg of stannous chloride dihydrate or a stannous salt containing an equivalent amount of stannous ion should be incorporated in an individual dosage kit.

The present invention also includes the process for the preparation of the novel chemical composition and the diagnostic method for imaging blood pools in patients suspected of having abnormalities in the circulatory system.

In accordance with the process of the present invention, a sterile solution of a non-toxic pharmaceutically acceptable salt of glucoheptonic acid, e.g., calcium glucoheptonate, is mixed with a non-toxic stannous salt in a ratio of 25 parts by weight of glucoheptonate salt to 3 parts by weight of stannous salt, calculated as calcium glucoheptonate and stannous chloride dihydrate.

The solution is adjusted to a neutral pH 6—8, subdivided, and lyophilized to produce individual vials containing a dry, sterile mixture comprising 25 mg. calcium glucoheptonate and 3 mg. stannous chloride dihydrate.

In utilizing the kit of the present invention for imaging the blood pools of a patient to diagnose abnormalities in the cardiovascular system, a vial containing the dry, sterile mixture of calcium glucoheptonate and stannous chloride dihydrate is reconstituted by mixing with 2—8 ml. of a USP saline solution. The reconstituted solution is then used for injection of the patient to be examined. After a period of 30 minutes, a second injection of 2—8 ml. of a sterile saline solution of sodium pertechnetate is made. Following the injection of sodium pertechnetate, it is possible, after waiting from 30 seconds to 2 minutes, to image the blood pools in the patient being examined. This *"in vivo"* labeling of the red blood cells is exceptionally stable and approximately 95% of the radioactivity is retained by the red blood cells for at least 6 hours following injection. This simple procedure avoids the instability of the human serum albumin/99m Tc injection of the prior art as well as the expense and inconvenience of the *in vitro* labeling of the red blood cells noted as an alternate prior art method.

Example 1

Blood Pool Imaging Kit

A solution is prepared under sterile conditions with 25 g. of calcium glucoheptonate in sterile pyrogen-free water which has been purged with nitrogen. The solution of calcium glucoheptonate is stored and purged under nitrogen. In a separate container, 3 g. of stannous chloride dihydrate is dissolved in 1 ml. of

hydrochloric acid, and the resulting solution diluted with nitrogen-purged, sterile water to a volume of 10 ml. The stannous chloride dihydrate solution is then added to the calcium glucoheptonate with stirring and flushing with nitrogen. The solution is mixed thoroughly, and the pH is adjusted to neutrality with a solution of sterile 1N sodium hydroxide solution. The volume is then adjusted to 2000 ml. with sterile, nitrogen-purged water and subdivided into vials, each containing 2 ml. of the solution. The vials are then lyophilized and sealed under nitrogen. Each vial contains 25 mg. of calcium glucoheptonate and 3 mg. of stannous chloride dihydrate.

Example 2

Method of Using Blood Pool Imaging Kit

A solution of sodium chloride for injection USP (2 ml.) is added to a vial containing a lyophilized mixture of 3 mg. of stannous chloride dihydrate and 25.0 mg. calcium glucoheptonate. The resulting solution is used for the intravenous injection of patients for the purpose of imaging the blood pools for diagnostic purposes. The amount of solution used is based on the weight of the patient and sufficient volume is used so that 30 mcg./kg. of stannous ion, measured as stannous chloride dihydrate, is injected. It is recommended that no more than the contents of one vial be administered to any patient. After waiting a period of 30 minutes, a sterile saline solution of sodium pertechnetate-Tc99m (2—20 mCi) is injected. This tags the red blood cells and permits imaging of the blood pools of the patient being examined almost immediately (from 30 seconds to 2 minutes).

Claims

1. A diagnostic kit used for blood pool imaging comprising a sterile sealed vial containing a lyophilized mixture of a non-toxic pharmaceutically acceptable salt of glucoheptonic acid and a non-toxic pharmaceutically acceptable stannous salt in a ratio of 22.9 parts by weight of glucoheptonate ion to 1.32 parts of stannous ion, provided that the individual dose of stannous ion is from 2.5 to 4 mg, calculated as stannous chloride dihydrate.

2. A kit according to claim 1 in which the salt of glucoheptonic acid is calcium glucoheptonate and the stannous salt is stannous chloride dihydrate.

3. A kit according to claim 2 that comprises a lyophilized mixture of 3 mg of stannous chloride dihydrate and 25 mg of calcium glucoheptonate.

Revendications

1. Dispositif diagnostique utilisé pour la visualisation d'hématomes, comprenant un flacon scellé stérile contenant un mélange lyophilisé d'un sel non toxique pharmaceutiquement acceptable de l'acide glucoheptonique et d'un sel stanneux non toxique pharmaceutiquement acceptable dans un rapport de 22,9 parties en poids d'ion glucoheptonate à 1,32 partie en poids d'ion stanneux, à condition que la dose individuelle d'ion stanneux soit de 2,5 à 4 mg, calculée sous forme de chlorure stanneux.

2. Dispositif selon la revendication 1, caractérisé en ce que le sel de l'acide glucoheptonique est le glucoheptonate de calcium et le sel stanneux est le chlorure stanneux dihydraté.

3. Dispositif selon la revendication 1, caractérisé en ce qu'il comprend un mélange lyophilisé de 3 mg de chlorure stanneux dihydraté et de 25 mg de glucoheptonate de calcium.

Patentansprüche

1. Diagnostischer Kit zur Verwendung für die Darstellung von Blutansammlungen, enthaltend ein steriles verschlossenes Fläschchen, das ein lyophilisiertes Gemisch eines nicht-toxischen, pharmazeutisch brauchbaren Salzes von Glucoheptonsäure und eines nicht-toxischen, pharmazeutisch brauchbaren Stannosalzes in einem Verhältnis von 22,9 Gew.-Teilen Glucoheptonation zu 1,32 Teilen Stannoion enthält, vorausgesetzt, dass die individuelle Dosis des Stannoions 2,5 bis 4 mg, berechnet aus Stannochloriddihydrat, beträgt.

2. Kit nach Anspruch 1, in dem das Salz der Glucoheptonsäure Calciumglucoheptonat ist und das Stannosalz Stannochlorid-dihydrat ist.

3. Kit nach Anspruch 2, enthaltend ein lyophilisiertes Gemisch von 3 mg Stannochloriddihydrat und 25 mg Calciumglucoheptonat.