QUALITY CONTROL OF ^{99m}Tc – LABELLED HUMAN SERUM ALBUMIN FOR STUDIES OF THE HAEMODYNAMICS

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Radiopharmaceutical ^{99m}Tc-HSA(Sn) or P is prepared by addition of sterile pyrogen-free sodium ^{99m}Tc-pertechnetate, which is conveniently supplied by the ^{99}Mo/^{99m}Tc generator, to diagnostic composition (kit), containing a sterile, pyrogen-free lyophilised HSA(Sn) (MRRC RAMS). The kits must be prepared from HSA, which have been tested and found non-reactive for hepatitis B surface antigen (HBsAg) and HIV antibody.

The development of sensitive, reproducible methods and techniques for chemical and radiochemical quality control of ^{99m}Tc-HSA(Sn) seems appropriate. It was the purpose of our study. The main quality control tests of P in kits are: concentrations of Sn(II), albumin, the percentage of ^{99m}Tc unbound with HSA(Sn) (radiochemical impurity or RCI). We have tested all mentioned parameters except RCI in non radioactive kit.

Stannous ions content is one of the most important values, and the labelling efficiency with ^{99m}Tc depends on it. A spectrophotometric method has been developed for stannous ions determination in HSA(Sn). This method is based on measuring of absorption of red-orange Fe(II) complex with o-phenanthroline at 510 ± 2 nm. The linear correlation between the intensity of the absorption peak and the concentration of Sn(II) in the range of 0.5-6.0 μg/ml was observed. The errors of the spectrophotometric measurements did not exceed ± 3 %.

Protein content was determined by means of colorimetric method based on formation of the violet Cu(II) complex with protein peptide bonds in alkaline solution with absorption maximum at about 540 ± 2 nm. The accordance to the Lambert-Beer law was observed for the biuret complex of HSA(Sn) from 0.25 to 2.5 mg/ml. The specific extinction of 1% alkaline solution of HSA(Sn) found with biuret reagent was 2.8 ± 0.1 (n=20, P=0.95). The presence of tin in kit vial had no influence on the results of protein determination. The errors of the colorimetric measurements did not exceed ± 5 %.

RCI is one of the important values of quality control because radiochemical impurities in radiopharmaceutical, though would rarely produce a serious toxic reactions but, may lead to a serious errors in diagnosis. We have supposed that RCI or unbound technetium-99m could consist of different chemical ^{99m}Tc compounds such as pertechnetate $^{99m}TcO_4^-$, hydrolysed-

reduced ^{99m}Tc (H-R) and others. TLC and paper chromatography (PC) methods have been developed for the control of main radiochemical impurities in ^{99i}Òñ-HSA(Sn). Chromatographic conditions: Silicagel F_{254} (“Merck”), acetone-water (95:5) (TLC, RCI - $^{99m}TcO_4^-$); FN 17 (“Filtrak”), 25 % NH_3 – 2M NaCl (4:1) (PC, RCI - ^{99m}Tc (H-R)). In TLC the ^{99m}Tc-HSA(Sn) and ^{99m}Tc (H-R) remain at the starting-point and $^{99m}TcO_4^-$ ion migrates near to the solvent front. Not more than 5.0 % of the radioactivity due to ^{99m}Tc corresponds to free $^{99m}TcO_4^-$. In PC ^{99m}Tc (H-R) remain at the starting-point and ^{99m}Tc-HSA(Sn) with $^{99m}TcO_4^-$ migrates with the solvent front. Not more than 5.0 % of the radioactivity corresponds to ^{99m}Tc (H-R).

A number of ^{99m}Tc-HSA(Sn) products were tested for radiochemical impurity yield during 6 h standing and each product showed no increase in percentage of RCI. Kits have been stored up to 12 months at +2-10° C and have showed no change in chemical and radiochemical properties of the preparation ^{99m}Tc -HSA(Sn).

A sensitive, reproducible methods and techniques for chemical and radiochemical quality control of labelling kit and ^{99m}Tc-HSA(Sn) have been developed.