PARTICLE SIZE OF COLLOIDAL RADIOPHARMACEUTICAL LIVER SCANNING AGENTS BY PHOTON CORRELATION SPECTROSCOPY

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Colloidal particles are removed from the circulation by the liver and the spleen and such particles labelled with the generator-produced, gamma emitting, short half-life radionuclide, technetium-99m, are widely used as liver scanning agents for diagnostic purposes. Uptake by the liver depends primarily on particle size, the optimum size being in the range 0.1 - 2μm.

Frier and Vennart (1976) discussed the use of electron microscopy and observed physical appearance changes with time for the sulphur colloid. Warbick et al. (1977) evaluated sizing methods for radiopharmaceutical colloids but did not consider the use of photon correlation spectroscopy. Lim et al. (1979) used photon correlation spectroscopy on a fractionated sulphur colloid after the decay of the technetium-99m activity i.e. not during the period when the agent is used in practice. Other intravenous colloidal injections e.g. liposomes, have been sized using this technique (Baillie et al. 1979).

Using photon correlation spectroscopy, changes in particle size from the time of preparation up to 6hr have been followed: the method is rapid and non-perturbing and with the introduction of commercial instruments specifically for quality control purposes (e.g. Coulter Nanosizer; Malvern 4400) this technique will become more widely available.

Technetium-99m labelled sulphur colloid has been the most widely used liver scanning radiopharmaceutical: other agents in use include rhenium sulphide colloid, antimony sulphide colloid and a technetium-99m labelled tin colloid has been introduced by The Radiochemical Centre, Amersham.

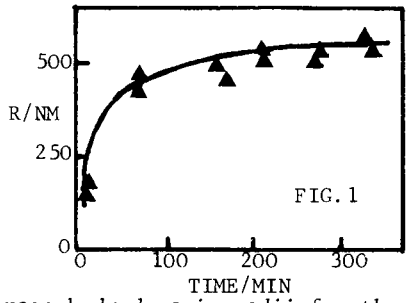

FIG. 1

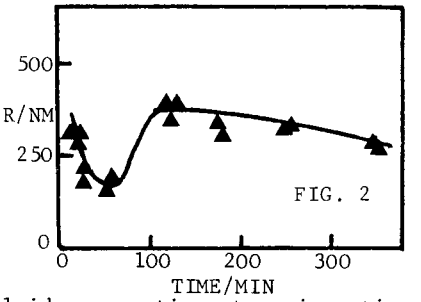

FIG. 2

Average hydrodynamic radii for the tin colloid preparation at various times after preparation are shown in Figure 1. The initial solution of 1mg sodium fluoride plus 0.125mg stannous fluoride in 8ml saline is rapidly hydrolysed and the earliest measurements possible after preparation (t=2min) show radii of 120-150nm. Growth of the particles continues for ca. 60 min after which time the particle size stabilises at 500-600nm. The system is polydisperse with values of the normalised variance of the distribution in the range 0.3-0.4.

The sulphur colloid preparation shows more complex behaviour: the average radius varying in the range 200-400nm (Figure 2); the initially polydisperse system becomes monodisperse at 15-18 min after preparation with a particle radius of 230nm. The system then becomes polydisperse again.

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Frier, M. and Vennart, W. (1976) J. Pharm. Pharmacol., 28 (Suppl.) 42P
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