56P

DEVELOPMENT OF RADIOLABELLED ALBUMIN MICROSPHERES FOR CLINICAL USE: A COMPARISON OF GAMMA-EMITTING RADIOISOTOPES OF IODINE AND INDIUM

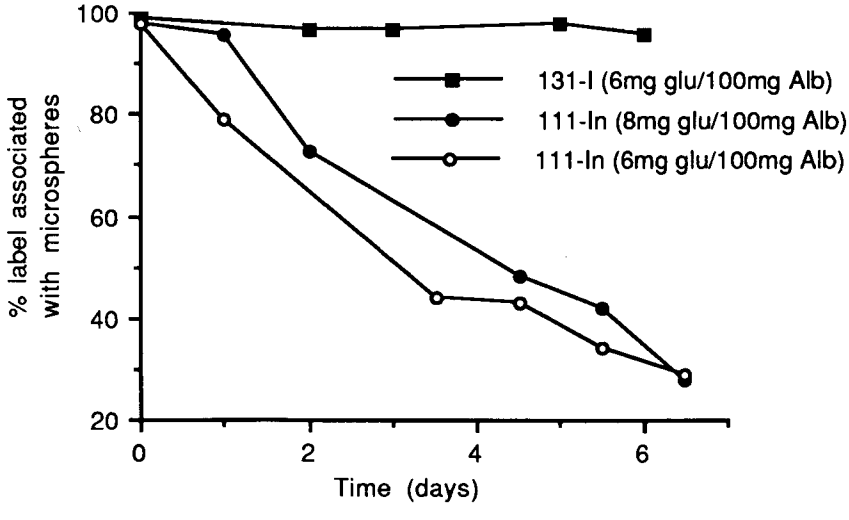
R. Carlton[1], T. Murray[2], Y.Chen[1], N. Willmott[1], J. Goldberg[3], R. Bessent[4] and J.McKillop[4], 1. Dept. of Pharmacy, University of Strathclyde,Glasgow, 2. Radioisotope Dispensary, Western Infirmary, Glasgow, 3. Dept. of Surgery and 4. Dept. of Nuclear Medicine, Royal Infirmary, Glasgow, UK.

Biodegradable protein microspheres (20-40μm diameter) were developed to localise cancer therapeutic agents via embolisation in desired organs (Goldberg et al., 1990) and to prolong residence at the site of action. Release of incorporated agents in vivo is governed inter alia by rate of biodegradation of protein matrix : this work describes comparative formulation and stability studies on the radionuclides ^{131}I and $^{111}In/^{113m}In$ in microspherical form designed to select a radiopharmaceutical for clinical investigations on biodegradation rate of embolised microspheres. ^{111}In or ^{113m}In (10-38MBq) was chelated to albumin (20 mg) using the cyclic dianhydride of the bifunctional chelate DTPA (Paik et al, 1985) and free separated from bound radionuclide on Sephacryl S-200 HR Coupling efficiency was typically 60-70%. Chelation of indium was sensitive to presence of Zn^{2+} and Fe^{3+} ions (50% inhibition at 38 and 7 ppm respectively) but preformed chelate was more stable. ^{131}I covalently bound to human albumin (37MBq/3-6mg protein) was purchased from Medgenix (Belgium). Albumin bound to both radionuclides was incorporated into microspheres prepared by stabilisation with glutaraldehyde of the aqueous phase of a w/o emulsion containing protein (Willmott *et al* , 1985). It was found that 32%(n=3) of the indium chelated to albumin was incorporated into microspheres compared to 63% (n=2) for iodine covalently bound to albumin. Moreover, ^{131}I-labelled microspheres were considerably more stable in plasma than those labelled with indium (see Figure).

It is concluded that protein microspheres labelled with ^{131}I will give a more reliable estimate of in vivo biodegradation : clinical studies involving administration of this radiopharmaceutical via the hepatic artery in patients with intrahepatic tumour indicate a median biological half-life of 2 days in tumour tissue (Ethics Committee and ARSAC approval obtained).

Goldberg, J.A., et al (1990) Br.J.Cancer, In press.
Paik, C.H. et al (1985) J.Nucl.Med., 26: 482-487.
Willmott, N. et al (1985) Biopharm. and Drug Disposition, 6: 91-104

Stability of ^{131}I and ^{111}In labelled albumin microspheres in vitro.



Key indicates amount of glutaraldehyde (glu) used in albumin (alb) micropshere preparation.