IN VIVO EVALUATION OF COLLOIDAL DOSAGE FORMS INTENDED FOR INTRAMUSCULAR USE

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The potential of colloidal systems as controlled drug release parenteral injections has been recognised for some time, and the release of drugs from emulsions (Higuchi 1964), liposomes (Gregoriadis 1973) and albumin microspheres (Kramer 1974) has been demonstrated by previous workers. Formulation factors such as the nature of the colloidal particles, the surface charge and the particle size have been shown to influence the colloid fate in vivo. Gamma scintigraphy is a non-invasive technique and so allows the time-course for disposition and fate of colloidal systems to be followed in animal models with minimal intervention to normal physiology. Its use to investigate the injection site clearance of various colloidal systems administered by the intramuscular route is presented, together with complementary histological and autoradiographical studies at the injection site. The different colloidal systems were produced using conventional techniques and were labelled with suitable gamma ray emitting radionuclides (Table). In the majority of cases the colloid itself was labelled and the stability of the label was evaluated in vitro to ensure that the label provided a true representation of the location of the system. The radiodiagnostic agents Iodohippuran and ^{75}Se-methylselenomethylnorcholinesterol were used as model drug substances and were incorporated into the appropriate disperse phases. The solutions administered IM leave the injection site rapidly (the delayed effect with indium chloride reflects tissue binding), whereas colloidal systems are cleared much more slowly, and also modify the local clearance of incorporated model drugs. The size and nature of the material are critical factors; the biodegradable materials have times for 50% clearance from 0.2-200 hours, whereas the inert materials such as polystyrene stay at the injection site considerably longer. The stability of the colloid in vivo can also determine its influence on the release of tracer substances; unstable colloidal systems do not modify the clearance pattern as effectively as a system that maintains its integrity in vivo

Table Clearance of colloid systems from intramuscular injection site (3 animals per group - mean results)

Colloid System	Particle size (μm)	Radionuclide as label	Time for 50% clearance (hr)
Sodium iodide solution	-	^{123}I	0.08
Iodohippuran solution	-	^{123}I	0.23
Indium chloride solution	-	^{113m}In	5.8
Polystyrene microspheres	1.09	^{131}I	6250
Human serum albumin microspheres	2.00)	^{111}In	32.4
	16)		68.2
	34)		92.6
Liposomes (dipalmitoyl lecithin)	6	^{131}I	204

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0022-3573/81/120048P-01$02.50/0