Albumin and Albumin-Drug Conjugates: Pharmacokinetics and Tissue Distribution Studies in Rats and Mice
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Purpose
Proteins such albumin are playing an increasing important role as a drug carriers with a number of albumin-based formulations already on the market. It has abeen demonstrated that binding of a therapeutic peptide or protein to albumin enhances its stability and half-life in vivo. More recently modified albumins have been developed in an attempt to further modify the half-life of the carrier molecule. Whilst the pharmacokinetics of albumin is generally well described within the native species (ie human albumin in man), there is a notable lack of data regarding the pharmacokinetics of albumins across species (ie human albumin in the rat). This study was performed to provide pharmacokinetic information for albumin in pre-clinical species.

Methods
Albumin (human, mouse and bovine) was labeled using [3H]-N-Succinimidyl Propionate.

Eight male Sprague-Dawley rats were dosed intravenously with [3H]-human albumin (6.25mg/kg) and were killed 0.25, 1, 3, 8, 24, 72, 120 and 240 hours post dose. Terminal blood samples were taken for preparation of plasma and carcasses retained for whole body autoradiography. One animal was placed in a glass metabowl and urine and faeces collected up to 240 hours post dose. Six male CD-1 mice were dosed intravenously with either [3H]-mouse albumin, or [3H]-bovine serum albumin (6.25mg/kg). Serial samples were taken 0.25, 1, 3, 8, 24, 72, 120 and 240 hours post dose for preparation of plasma

Results
The plasma half-life for [3H]-labeled human albumin in the rat was found to be about 25 hour. Autoradiograms showed radioactivity distributed throughout the animal with maximal tissue concentrations observed 3 hours after dose administration. The plasma half-life for [3H]-labeled mouse albumin in the mouse was found to be about 38 hours, whilst the plasma half-life for bovine serum albumin in the mouse was 72 hours.

Conclusion
The data obtained in this study provides basic pharmacokinetic information that can be used in the development of albumin drug conjugates. It has been shown that the half-life of albumin can vary dependent on the source and species used for testing.