

**IN VIVO BEHAVIOR AND DISPOSITION OF <sup>3</sup>H-CHOLESTERYL  
ETHER LABELED LIPOSOMES FOLLOWING INTRAVENOUS  
ADMINISTRATION TO MICE: COMPARISON WITH AN  
INCORPORATED <sup>14</sup>C-INULIN AS AN AQUEOUS PHASE MARKER**

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The blood clearance kinetics and tissue distribution of liposomes prepared by sonication (disterylphosphatidylcholine [DSPC] and Cholesterol in a ratio of 3:1) when administered intravenously into CD-1 mice has been evaluated utilizing <sup>3</sup>H-cholesteryl ether as a lipid phase marker and compared to that using <sup>14</sup>C-inulin as an aqueous phase marker, at 0.25-48 hours post-administration. Liposomes biodistribution was calculated as a percentage of the administered dose per organ or whole blood volume. The size and the encapsulation efficiency of these liposomes were 219.4 (weight by number) nm  $\pm$  35.4 nm and 3.18 %  $\pm$  .008 % respectively. At times up to 48 hours post-administration the disposition of both markers was nearly similar in all organs. The highest levels of <sup>3</sup>H-cholesteryl ether and <sup>14</sup>C-inulin were found to be in the liver and spleen, respectively, with peak levels occurring after 3 hours (71.86 %  $\pm$  9.39 *versus* 77.67 %  $\pm$  10.30 in the liver and 5.05 %  $\pm$  1.07 *versus* 5.36 %  $\pm$  1.09 in the spleen) and falling off gradually to 48 hrs. However, only 0.29 %  $\pm$  0.03 (<sup>3</sup>H-cholesteryl ether) *versus* 0.28 %  $\pm$  0.03 (<sup>14</sup>C-inulin) of the administered dose was found in the blood after 3 hours. The lowest levels of <sup>3</sup>H-cholesteryl ether and <sup>14</sup>C-inulin were found to be in the heart where the values climbed to a peak of 0.32%  $\pm$  0.093 and 0.28%  $\pm$  0.109 after 1 hour and fell off to 0.16%  $\pm$  0.18 and 0.19%  $\pm$  0.024 at 48 hours. The kidneys showed rapid peaks of 1.11%  $\pm$  0.692 and 0.77%  $\pm$  0.432 for <sup>3</sup>H-cholesteryl ether and <sup>14</sup>C-inulin respectively after 0.25 h and then fell off to 0.4%  $\pm$  0.081 and 0.47%  $\pm$  0.055 where those levels were maintained for 48 hours. The lungs showed maximum values of 1.17%  $\pm$  0.236 and 0.91 %  $\pm$  0.178 at 0.25 hours after which the values gradually fell off to 0.3%  $\pm$  0.02 and 0.39%  $\pm$  0.017 after 48 hours.

In conclusion, it appears that the liposomes still intact and slowly release its contents. The disposition of <sup>14</sup>C-inulin as an aqueous phase marker is similar to that of liposomes.

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