

Table 2. The AUC_{1-60 min} (min. % of dose/ml) of Liposomal Radioactivity in Plasma

Liposomes	¹⁴ C	³ H
(-)LP	11.68 ± 2.90*	29.43 ± 5.32*
(-)AFLP	4.38 ± 1.15	4.29 ± 2.39
(o)LP	15.17 ± 3.47	19.83 ± 4.45*
(o)AFLP	13.13 ± 2.88	5.85 ± 1.74

Data are the mean ± SD of 3 determinations.

* Significantly different from that of AF-labeled liposomes, $p < 0.05$.

plasma, kidney, lung and pancreas were all below 0.08%, and those in the spleen were below 0.5% of dose/g wet tissue. Concentrations of both ¹⁴C and ³H in liver were obviously the highest among the tissues examined, and the AF-labeled liposomes gave significantly higher concentrations of ¹⁴C and ³H than did plain liposomes.

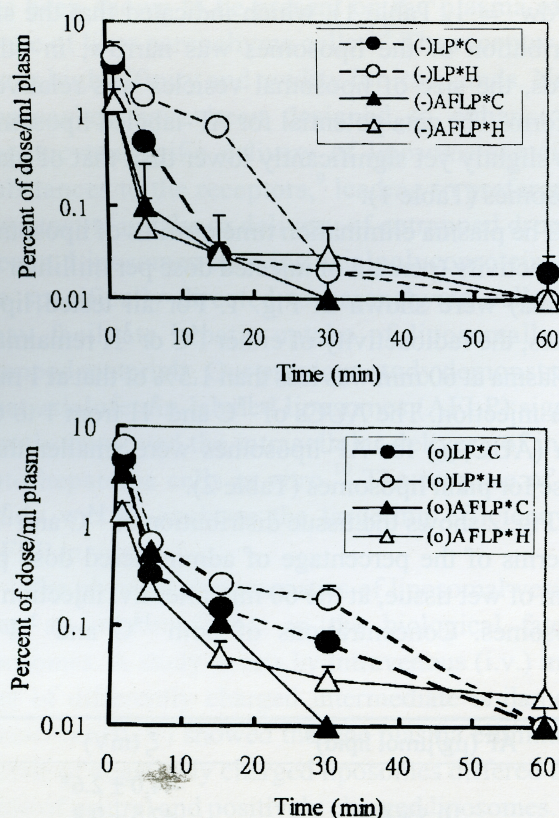


Fig. 1. Plasma elimination curves of liposomal ³H and ¹⁴C in rats after i.v. injection. Each point represents the mean with SD of 3 determinations. Key: (●, ▲) = ¹⁴C, (○, △) = ³H.

DISCUSSION

Plasma elimination of liposomes was rapid after i.v. injection, and the amount of liposomes remaining in plasma at the 60th min was less than 1.5% of that of the first min. The AUC₁₋₆₀ of ³H and ¹⁴C were not affected by liposomal charge but were affected by labeling with AF. The AUC₁₋₆₀ of AF-liposomal ³H and ¹⁴C were lower than those of plain liposomes. These results suggest that the extravascular distribution of AF-liposomes may be higher than that of plain liposomes regardless of liposomal charge.

The importance of the physical characteristics of the liposomal vehicle with respect to the biological fate of the encapsulated substance has been demonstrated. Liposomal vesicle size is an important determinant of the plasma clearance rate.¹⁷ Liposomes in circulation are taken up to a large extent by organs rich in cells of the reticuloendothelium system (RES). Small liposomes are taken up less rapidly than large ones, and when those small unilamellar

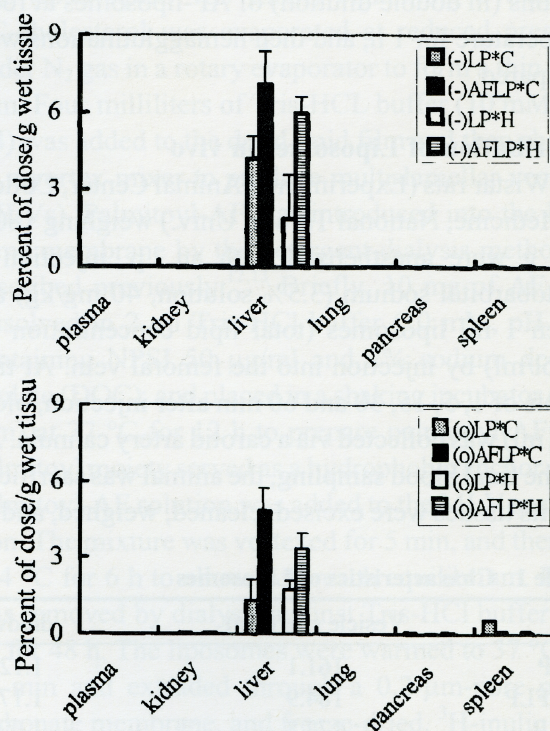


Fig. 2. Liposomal ³H and ¹⁴C in rat tissues 60 min after i.v. injection. Each column represents the mean with SD of 3 determinations.