vesicles (SUVs) do go to the liver, there is a higher proportion entering the hepatocytes rather than Kupffer cells. Our previous study demonstrated that the splenic (RES-rich organ) uptake of liposomes was decreased by reducing the vesicle size to < 0.25 μm.[17] The low concentrations of liposomal $^{3}H$ and $^{14}C$ in rat spleen in this study suggest that the vesicle size of the injected liposomes is below the threshold for RES uptake.

The very low distribution of liposomal inulin in tissues except the liver implies little extravasation of liposomes from circulation except in liver. The fenestrated property of sinusoidal endothelial cells in the liver allows free diffusion of a large spectrum of substances between Disse's spaces and the sinusoids.[18] The vesicle diameter of liposomes in the present study was around 170 nm. A portion of liposomes in circulation could pass through the fenestrae into Disse's spaces, and thus facilitate the access to hepatocytes. Free inulin is not subject to degradation in circulation and is rapidly removed from circulation following i.v. administration. Free inulin does not diffuse through cell membrane into cells.[10] Therefore, the $^{3}H$ present in the liver can be ascribed to the $^{3}H$-inulin molecules delivered by liposome encapsulation,[10] but not the degradation part of $^{3}H$-inulin, or the free inulin leaked from liposomes.

The higher $^{3}H$ and $^{14}C$ values with AFLP than with plain liposomes in the liver allow assessment of the targeting property of AFLP. This result is in agreement with the result of an in vitro study,[10] which determined that the enhanced uptake of AFLP resulted from receptor-mediated transfer via ASGP-R.

In conclusion, grafting liposomes with AF enhances liver uptake. The preferential liver distribution of AFLP suggests a useful hepatocyte-targeting approach for drug delivery and gene transfection.

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