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Key Words

Liposomes

Targeting

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Tissue distribution

Tissue Distribution of Asialofetuin-labeled Liposomes in Rats

ABSTRACT

Targeting of drugs or therapeutic agents to hepatocytes may efficiently deliver these agents to improve the effectiveness of treatment. Asialoglycoprotein receptor (ASGP-R) is present on the plasma membrane of liver parenchyma cells. Liposomes (LP) grafted with asialoglycoprotein can be specifically directed to parenchyma cells based on a receptor mechanism and may facilitate hepatic uptake of liposomally entrapped materials. This study prepared asialofetuin-labeled liposomes (AFLP) and investigated their targeting efficiency in vivo. Anionic liposomes, (-)LP, and noncharged liposomes, (o)LP, were grafted with asialofetuin (AF) to form (-)AFLP and (o)AFLP, respectively. ^{14}C -cholesterol in the lipid bilayer and ^3H -inulin in entrapped aqua served as tracers. Wistar rats were treated with 1 ml of liposomes by an intravenous bolus injection. Plasma samples were collected on a time schedule up to 60 min after the injection. Immediately after the last blood sampling, the rats were sacrificed and their kidney, liver, lung, pancreas and spleen were excised to measure the radioactivity of ^{14}C and ^3H . The results showed that the areas under the plasma elimination curves within 1 to 60 min ($\text{AUC}_{0-60 \text{ min}}$) of ^{14}C and ^3H from AFLP were significantly smaller than that from LP regardless of liposomal charge. In all cases, the distributions of ^{14}C and ^3H in kidney, lung, pancreas, and spleen were negligible as compared with those in liver. The liver-to-plasma concentration ratios of ^{14}C and ^3H were > 172 fold for LP and > 338 fold for AFLP. 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. (N. Taipei J. Med. 2001; 3:101-106)

INTRODUCTION

Liposomes have emerged as a promising new entity for various biological applications, including drug delivery and gene transfection, because of their ability

to encapsulate both hydrophilic and hydrophobic substances, with the potential for site-specific delivery in vivo. Interactions of liposomes with cells by endocytosis or fusion have led to the use of liposomes as a vehicle for intracellular delivery.^{1,2} Some drug treat-

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