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Pharmacokinetics of Lipid-Drug Conjugates Loaded into Liposomes

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Abstract

Drugs that are neither lipophilic nor suitable for encapsulation *via* remote loading procedures are generally characterized by low entrapment efficiencies and poor retention in liposomes. One approach to circumvent this problem consists in covalently linking a lipid to the drug molecule in order to permit its insertion into the vesicle membrane. The nature of the conjugated lipid and linker, as well as the composition of the liposomal bilayer were found to have a profound impact on the pharmacokinetic properties and biodistribution of the encapsulated drugs as well as on their biological activity. This contribution reviews the past and recent developments on liposomal lipid-drug conjugates, and discusses important issues related to their stability and *in vivo* performance. It also provides an overview of the data that were generated during the clinical assessment of these formulations. The marketing authorization of the immunomodulating compound mifamurtide in several countries as well as the promising results obtained with the lipid prodrug of mitomycin C suggest that carefully designed liposomal formulations of lipid-drug conjugates is a valid strategy to improve a drug's pharmacokinetic profile and with that its therapeutic index and/or efficacy.

Keywords: lipid-drug conjugates, liposomes, cancer, pharmacokinetics, release kinetics