PHARMACOKINETICS OF LIPOSOMES DESIGNED TO CARRY GLUCOCORTICOIDS

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Over the past decade, particulate drug formulations have been successfully employed to reduce undesired side effects and improve drug biodistribution. Despite numerous experimental data, there are relatively few theoretical studies regarding the pharmacokinetics of such formulations. A quantitative pharmacokinetic description of particulate drug forms requires serious adjustments in existing theoretical approaches, due to formulation size. Thus, blood vessel permeabilization and the immunological system need to be accounted for. In this paper, we present a pharmacokinetic model intended to describe the distribution of glucocorticoid (prednisolone phosphate) encapsulated in long-circulated liposomes and its qualitative analysis. In order to achieve qualitative and quantitative agreement with experimental patterns of time-dependent liposome concentration changes in blood, liver and spleen, the existence of two hypothetical liposome populations was assumed. The two populations differ in their accumulation capacities, dosage and time constants. The first population is accumulated in the liver with a time constant of 50 s⁻¹ and a saturation level of 0.005 µmol/animal, whereas the second with 0.003 s⁻¹ and 50 µmol/animal, respectively. Such liposome parameterization results from the theoretical model used, however, it may have a physiological foundation. If the two opsonin and/or macrophage types that interact with the liposomes are assumed to have different characteristics, then the pharmacokinetic data obtained experimentally in an animal model can be described correctly.

Key words: pharmacokinetics, glucocorticoid, liposome, uptake

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