

**MOLECULAR INTERACTIONS IN LOMEFLOXACIN-LIPOSOME SYSTEMS**

MARIANNA BUDAI<sup>1\*</sup>, RÉKA PALLAGHY<sup>1</sup>, ZSÓFIA SZABÓ<sup>1</sup>,  
ANDREAS ZIMMER<sup>2</sup> and PÁL GRÓF<sup>1</sup>

<sup>1</sup>Semmelweis University, Institute of Biophysics and Radiation Biology H-1088  
Budapest, Puskin u. 9, Hungary, <sup>2</sup>Karl-Franzens University, Institute of  
Pharmaceutical Chemistry and Pharmaceutical Technology, A-8010 Graz,  
Schubertstr. 6, Austria

The antibacterial efficacy of the broad spectrum fluoroquinolone antibacterial drug lomefloxacin (LMFX) has been investigated in a wide variety of clinical infections. An alternative approach to the classical delivery of antibacterial drugs consists in associating the drug to a liposomal carrier. It seems clear that liposomal encapsulated antibiotics allow increased drug concentration at infected sites but reduce drug toxicity.

Our goal was to design a liposomal LMFX formulation and to investigate the molecular interactions of the lipid with LMFX. The effect of LMFX on DPPC-liposomes was examined by electron spin resonance spectroscopy (EPR) using 5- and 16- doxyl stearic acid spin labels in small unilamellar vesicles (SUV) and multilamellar vesicles (MLV) at three characteristic pH values: 5.0, 6.8 and 8.0. The size distribution of the preparations and its stability were checked by dynamic light scattering. Zeta potential measurements were carried out to investigate the effect of LMFX on the surface charge. The chemical structure of the lomefloxacin possesses two protonable groups. The EPR spectra can be influenced by the relative concentrations of the three microspecies (zwitterionic, nonionic and monocationic forms) which exist predominantly at the investigated pH values. From our measurements we concluded that lomefloxacin interacts with the lipids close to the head-group region, resulting in a decrease in the fluidity and also a specific protonation of the doxyl-stearic spin label molecule takes place. Our observations may direct attention to investigate the specific interactions of LMFX with other protonable compounds of the liposomal/biological membranes which can lead to similar protonation reactions.

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\* E-mail: [budaimarianna@freemail.hu](mailto:budaimarianna@freemail.hu)