# Phospholipid Membrane Properties Determining Drug Permeation

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The relevance of order and dynamics of phospholipid bilayer membranes as detected with fluorescent probe molecules embedded in the membranes for describing the permeability of solutes across the membranes was studied. Order parameters (S) and rotational diffusion coefficients ($D_\perp$) of 1,6-diphenyl-1,3,5-hexatriene (DPH) and 1-(4-trimethylammoniumphenyl)-6-phenyl-1,3,5-hexatriene (TMA-DPH) in unilamellar vesicles were determined by time-resolved fluorescence spectroscopy. Vesicles consisting of combinations of 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphatidylcholine, 1,2-dimyristoyl-sn-glycero-3-phosphatidylcholine, egg sphingomyelin and cholesterol were studied at 288, 298 and 308°K. Permeability coefficients (P) of the model permeant D-[$^{14}$C]mannitol were determined. A model is proposed for correlating P with both S and $D_\perp$, whereas S is linked to the average free surface area per lipid molecule and $D_\perp$ reflects lipid thermal motion and, thus, redistribution rate of free surface area of the bilayer. P values ranging from 0.9 to 12.4 $*10^{-11}$cm/s were well described by the model. This supports the notion that permeation depends on membrane structural and dynamic properties. While changes in both S and $D_\perp$, at relative significance varying with the situation, appeared responsible for the effect of lipid composition on permeability, the effect of temperature on P was related primarily to $D_\perp$. P correlated better with S and $D_\perp$ obtained with TMA-DPH rather than DPH. The location of the fluorescent probe molecules within the membranes is discussed as the cause for this difference.

## References

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