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Comparing the biophysical properties of sterols in lipid membranes – what is special about cholesterol?

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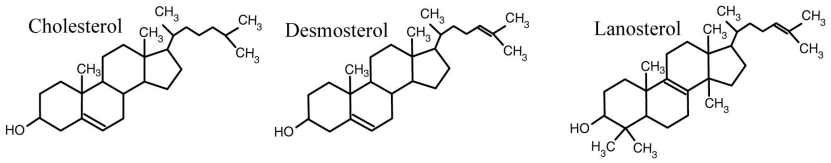
1. Introduction

Cholesterol is a major constituent of mammalian cell membranes. Its biophysical properties are essential for several membrane functions. However, a recently described generation of knock out mice, entirely lacking cholesterol [1], showed surprisingly mild phenotype changes. Since the cell membranes of these mice contained desmosterol, the direct precursor of cholesterol, we compared the biophysical properties of membranes containing cholesterol, desmosterol and lanosterol (a more distant precursor).



2. Membrane packing

Membrane packing properties were studied by ^{2}H NMR, fluorescence, and EPR spectroscopy. It was found that cholesterol and desmosterol showed a very similar behavior, while lanosterol produced significantly weaker effects [2].

3. Lateral Diffusion

We also investigated the effect of the sterols on the lateral diffusion of the lipids and of the sterols, respectively, by ^{1}H PFG MAS NMR spectroscopy [3]. In the liquid-crystalline phase, the phospholipid diffusion coefficients are decreased in the presence of all three sterols. In the l_o-phase this decrease strongly depends on the cholesterol concentration. Cholesterol mirrors the lipid behavior, but exhibits a slightly faster

diffusion. In the lanosterol and desmosterol containing membranes, the lipid diffusion rates are somewhat higher than those for cholesterol. While desmosterol diffusion rates are also only slightly higher than for the lipids, lanosterol diffusion rates significantly exceed lipid diffusion rates. This indicates weaker interactions between the lipids and lanosterol, which explains the weaker condensation effect of lanosterol.

4. Conclusion

Our results suggest that lipid-sterol interactions that determine the properties of membranes are very similar for cholesterol and desmosterol. Cell membranes need to contain sterols that condense lipids, to form lipid domains such as rafts, and provide the basis for a proper organization and function of membrane proteins. Our results show that, from the point of view of membrane biophysics, cholesterol and desmosterol are very similar sterols.

The weaker interactions between lanosterol and phospholipids must be related to the molecular structure of lanosterol. The additional methyl groups weaken the ability of lanosterol to form hydrogen bonds. The shifted double bond results in a less planar surface of lanosterol and may weaken van-der-Waals interactions with the phospholipids.

References

[1] Wechsler, A., Brafman, A., Shafir, M., Heverin, M., Gottlieb, H., Damari, G., Gozlan-Kelner, S., Spivak, I., Moshkin, O., Fridman, E., Becker, Y., Skaliter, R., Einat, P., Faerman, A., Bjorkhem, I., and Feinstein, E., *Generation of viable cholesterol-free mice*, Science 302*,* **(2003)**, 2087.

[2] Huster, D., Scheidt, H. A., Arnold, K., Herrmann, A., and Müller, P., *Desmosterol may replace cholesterol in lipid membranes*, Biophys. J. 88*,* **(2005)**, 1838-1844.

[3] Scheidt, H. A., Huster, D., and Gawrisch K., *Diffusion of Cholesterol and its Precursors in Lipid Membranes Studied by ^{1}H PFG MAS NMR*, Biophys. J. 89*,* **(2005)**, 2504-2512.