From lanosterol to cholesterol: Structural evolution and differential effects on lipid bilayers

Cholesterol is an important molecular component of the plasma membranes of mammalian cells. Its precursor in the sterol biosynthetic pathway, lanosterol, has been argued by Konrad Bloch (Bloch, K. 1965. Science. 150:19-28; 1983. CRC Crit Rev Biochem. 14:47-92; 1994. Blochs in Venetian Paintings, the Nine-Banded Armadillo, and Other Essays in Biochemistry. Yale University Press, New Haven, CT.) to also be a precursor in the molecular evolution of cholesterol. We present a comparative study of the effects of cholesterol and lanosterol on molecular conformational order and phase equilibria of lipid-bilayer membranes. By using deuterium NMR spectroscopy on multilamellar lipid-sterol systems in combination with Monte Carlo simulations of microscopic models of lipid-sterol interactions, we demonstrate that the evolution in the molecular chemistry from lanosterol to cholesterol is manifested in the model lipid-sterol membranes by an increase in the ability of the sterols to promote and stabilize a particular membrane phase, the liquid-ordered phase, and to induce collective order in the acyl-chain conformations of lipid molecules. We also discuss the biological relevance of our results, in particular in the context of membrane domains and rafts.