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Progesterone Modulates Membrane Biophysical Properties in a Different Way Than Cholesterol

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The functionality of steroid hormones is intrinsically linked to their interaction with cell membranes, due to the location of signal receptors. Steroids have the capacity to act non-specifically, resulting in the active alteration of membrane biophysical properties, such as fluidity. The present study focused on female sex hormones, particularly progesterone. Employing fluorescence confocal microscopy and fluorescence spectroscopy, we were able to analyse structural and dynamic parameters of the biomimetic lipid membranes composed of phosphatidylcholine (14:1 PC), sphingomyelin (SM), and selected steroid. It was observed that the addition of progesterone resulted in the disruption of the phase separation process within the membrane. Furthermore, progesterone exerts an influence on the rigidity of the membrane, although the alterations observed in the monophasic membrane formed with PC are minimal in comparison to those induced by cholesterol. Nevertheless, the LD phase of phase-separated membranes in the case of either PC:SM:progesterone or PC:SM:cholesterol exhibits analogous fluidity parameters. This indicates that the mechanism of interaction between the two steroid molecules with the membrane is markedly different. This finding was further substantiated by diffusion coefficient measurements. To substantiate these observations, molecular dynamics simulations were conducted.