Investigating the effect of cholesterol and melatonin in model lipid membrane

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Alzheimer's disease (AD) is a neurodegenerative disease which progresses with age and is commonly associated with dementia. AD is characterized by the formation of insoluble amyloid fibrils (plaques) composed of proteins in β-sheet conformation found on the surface of neuron plasma membrane. Recently, several research contributions have highlighted the importance of the lipid membrane as a key target for amyloid fibril formation and toxicity (1,2). Small molecules such as cholesterol and melatonin may alter the physical properties of lipid membrane and thus affect amyloid fibril formation and toxicity. Cholesterol is a well known sterol and plays an important role in lipid raft formation. Melatonin is a pineal hormone that is produced in the human brain during sleep and it sets the sleep-wake cycle (and circadian rhythm) (3). In human and animal studies, it has a protective role and slows the development of AD (4,5). In contrary to melatonin protection it has been shown that cholesterol when present in a membrane can enhance the amyloid binding and fibril formation (6).

Dipalmitoylphosphatidylcholine (DPPC) and dioleoyl-sn-glycero-3-phosphocholine (DOPC) are the two of most important lipids found in neuron membranes with the presence of cholesterol and melatonin. Pure and mixed lipid membranes with cholesterol or melatonin have been investigated by 2 neutron scattering techniques to complement AFM experiments. Small angle neutron diffraction (SAND) from the stacks of oriented multilayers and small angle neutron scattering (SANS) from the dispersion of unilamellar vesicles were used to see the changes in bilayer thickness (7,8). Lipid membrane thickness is parameter required to accurately determine bilayer structure, lipid-lipid, and lipid-protein interactions in biomembranes. Our results confirm the well known effect of cholesterol on lipid bilayers, according to which bilayer thickness increases with the addition of cholesterol (see Figure 1A). This is most likely a result of increased order of lipid chains due to the interactions with cholesterol. Interestingly, our results reveal the opposite effect caused by the addition of melatonin (Figure 1B). This result helps to determine the mechanism by which cholesterol and melatonine affect the properties of biological membranes, and could be utilized to understand the development of amyloid fibril formation.

References

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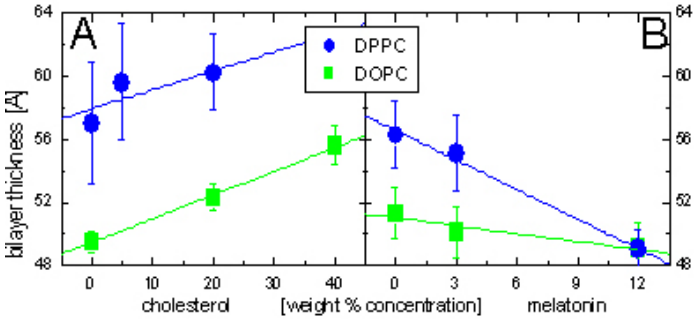

Fig. 1 The thickness of bilayers made of DPPC (blue circles) or DOPC (green squares) with the addition of cholesterol (A) or melatonin (B).