Interaction of Olanzapine, a Psycotropic Drug, on Lipid Monolayers.

Signe Steinkopf, Anita Sundal Ivarsflaten, Lene Therese Lindaas, Marit Elisabet Aardal, Torill Regine Sandvik Nilsen, Anja Underhaug Gjerde* and Holm Holmsen*.
Department of Biomedical Laboratory Science, Bergen University College,
*Department of Biomedicine, University of Bergen.
Bergen, Norway.

Olanzapine (OLP) is widely used as an antipsychotic agent. The activety of membrane proteins bound to lipid bilayers can be influenced by changes in phospholipid composition of the bilayer. Therefore, it is likely that perturbation of the lipid bilayer by amphiphilic OLP molecules can influence the activity of bilayer-bound proteins, even without direct interaction between the protein and the amphiphile. Consequently, some of the effects of OLP on dopaminergic receptors could be due to OLP perturbation of the lipid bilayer that contains the receptor.

This work is carried out on OLP interaction with lipid monolayers composed of 1,2-dipalmitoyl-*sn*-glycero-3-phosphatidylserine (DPPS), 1,2-dipalmitoyl-*sn*-slycero-3-phosphoethanolamine (DPPE), 1,2-dipalmitoyl-*sn*-glycero-3-phosphatidylcholine (DPPC) and cholesterol by the Langmuir monolayer technique. In principle, the lipid monolayer is half of the lipid bilayer building the cell-membrane and is therefore highly relevant in attributing OLP effects on the cell-membrane.

At the physiological pH of 7.4, OLP is present as two species, a positively charged one and a neutral one. This work shows that both presence of OLP and the monolayer´s lipid composition affect lipid packing in the monolayer, i.e. the monolayer structure. OLP increases the molecular area of all lipids studied with the exception of cholesterol. Furthermore, OLP demonstrates largest effect on a lipid monolayer of pure DPPS, contrasting the smallest OLP effect found on a cholesterol monolayer. The results show that OLP might induce formation of domains in DPPE containing monolayer. The results clearly show that the OLP effect of an increased lipid molecular area in the monolayer depends on the lipid composition.