Development of asymmetric liposomes to mimic plant plasma membrane using cyclodextrins as lipid carriers – Influence of phospholipid fatty acid chains.

Although liposomes can be criticized in terms of relevance to mimic real biological membranes, they give access to information at molecular or atomistic levels that are difficult to study *in cellulo*. In biophysical studies on liposomes, the asymmetric nature of the lipid distribution is often overlooked despite its role in several biological mechanisms. However, in the last decades, the preparation of asymmetric liposomes has been developed especially through protocols based on lipid-exchange lead by cyclodextrins, hemifusion or inverted emulsion phase transfer approaches. These strategies focused on human plasma membrane (PM) whereas the field of plant PM asymmetric liposomes remains unexplored. One difference between these two membranes concerns their phospholipids fatty acid compositions where linoleoyl chain is widely found in plants. Hence, phospholipids containing these chain (e.g. PLPC) is favoured to build artificial plant PM in comparison with those having oleoyl structure (e.g. POPC). The main objective of this work was to elaborate preliminary asymmetric liposomes mimicking plant PM and containing charged and uncharged phospholipids. We developed asymmetric models containing phosphatidylcholine and phosphatidylserine or phosphatidylcholine and phosphatidylglycerol using methyl-β-cyclodextrins as lipid carrier. The asymmetry has been controlled using F2N12S, a fluorescent probe sensitive to outer leaflet surface charge and lipid order. We found that the exchange efficiency is directly impacted by the nature of hydrophobic chains. Indeed, asymmetric liposomes have been prepared using exchanges between phospholipids with oleyl chain whereas no exchange has been observed in the case of phospholipids containing linoleoyl chain. Based on these results, we discussed on the relevance of the cyclodextrin mediated lipid exchange strategy to produce asymmetric liposomes mimicking plant PM.