Biophysical Properties of Model Membranes under the Effect of Daunorubicin

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Drug screening involves an assortment of steps. Drug design is followed by in vitro studies, usually in cells. However, cells are time consuming, expensive to maintain and include a variety of confounding factors, so the use of model membranes such as liposomes as a first front for drug screening could be immensely beneficial.

That being said, the aim of our study was to assess the effects of daunorubicin and on the lipid membranes of four LUV formulation models, two of them constituted by DMPC with and without cholesterol at pH 7.4, mimicking the normal cell membrane, and the other two simulating the tumoral cell membrane, constituted by a mixture of DMPC:DOPC:DPPS (3:1:1) also with and without cholesterol at pH 6.3.

Size, zeta potential, membrane location and fluidity were assessed for the four formulations of liposomes mentioned before. Membrane location and anisotropy techniques were also performed on tumoral cells, the line MDA-MB-231, to assess the validity of the designed models of mimicking the actual biomembranes.

Size and zeta potential results confirmed that the models were prepared as intended.
The drug partitions very well into all models except normal with cholesterol. While in this case cholesterol seems to impair partitioning, the opposite occurs in the tumoral models. Daunorubicin appears to localize between the acyl chains of phospholipids in the membrane but still interacting through electrostatic interactions with the polar heads, so it appears to locate at an intermediate region.

In terms of fluidity, the normal model with cholesterol appears to be the most rigid of all and remains unchanged by the drugs tested, while the normal model is highly fluid. Contrarily to what was expected, the tumoral model with cholesterol becomes less fluid with the presence of drug, which does not happen in the tumoral model without cholesterol. Similar results were found for tumoral cells. S

Summarily, it could also be observed that the designed model membranes, although simple, replicated biomembranes quite well. This study and follow-up work can be a big step towards the validation of liposomes as models for cell membranes, and in the future allow the facilitation of drug-interaction studies.

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