Characterization of Model Membranes under the Effect of Anticancer Drugs

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Abstract

Cancer is a pathology that affects a large portion of the world's population [1]. It is an assembly of diseases with various symptoms that significantly decreases the patient's life quality and has a high rate of mortality [2]. One of the most commonly used treatments for this pathology is chemotherapy, involving the use of combinations of drugs to kill cancer cells. Since these drugs either act directly on the membrane or have to cross it to reach their targets, the interactions between anticancer drugs and biological membranes are of high importance.

The structure of biological membranes consists of a phospholipid bilayer. In healthy cells, phosphatidylcholine (PC) and phosphatidylserine (PS) are some of the most common lipids, the PS being found on the inner leaflet, but cancer cells' membranes usually present higher heterogeneity in constitution and the PS exposed to the extracellular media [3]. The complexity of the membrane and all the variables associated with the cells' functions makes it a very difficult model to study. As such, artificial model membranes like liposomes might present a viable alternative, being a simpler and easier to manipulate model that accurately simulates the cell membrane's constitution and behaviour.

That being said, the aim of our study was to assess the effects of two anthracyclines used in chemotherapy, daunorubicin and doxorubicin, on the lipid membranes of four LUV formulation models, two of them constituted by DMPC with and without cholesterol, 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. Hepes buffer at pH 7.4 and Tris buffer at pH 6.3 were used to mimic the normal and tumoral tissue's external pH, respectively. The effects of the drugs on the different models were assessed by size and zeta potential measurements, partition coefficient (Kp) determination, drug location and membrane fluidity studies. The four formulations were then validated as model membranes for healthy cells and cancer cells. This was achieved through the study of similar properties in lines of healthy and cancer cells under the influence of the same drugs.

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