Doxorubicin and daunorubicin interplay with monolayers: the importance of lipid composition

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Antracyclines (doxorubicin, daunorubicin) are among the most used drugs in cancer treatment. In order to be conducted to the desired intracellular targets (for example, the DNA), these chemotherapeutic agents need to cross multiple barriers, including biological membranes. Drug-membrane interactions are inevitable, play essential roles in drugs' therapeutic activity and profoundly influence the chemotherapy efficacy. Biological membranes comprise different lipids that are usually not homogeneously distributed but can form microdomains, such as lipid rafts. In fact, it has been recognized that lipid domains enriched in sphingomyelin (SM) and cholesterol (Chol) are involved in different important cellular functions and act as functional platforms (together with proteins) for several signaling cascades.

For that reason, this work focus on the influence of doxorubicin and daunorubicin in lipid monolayers composed of DPPC, DPPC:SM [4:0.9] and DPPC:SM:Chol [4:0.9:1] in order to mimic the aforementioned lipid rafts.

A combination of different biophysical experimental techniques such as Langmuir isotherms, Brewster angle microscopy (BAM) and polarization modulation infrared-absorption spectroscopy (IRRAS), were used in order to obtain detailed information at the molecular level regarding anthracyclines interactions with lipids, at physiologic conditions.

The overall results obtained contributed to unveil the importance of drugs-membrane interactions in antineoplastic therapeutic action and side effects, as well as in the multi-drug resistance problem, responsible for therapy failure.

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