Light-Induced Drug Release to Interfaces with Lipid Monolayers

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Light-induced drug release using photoresponsive nanocarriers is increasingly explored for targeted therapeutic applications. While most studies characterize release in bulk aqueous environments, transport of a drug across aqueous-organic interfaces is equally important. That is because these interfaces represent the drug's entry point into cells. We recently demonstrated light-induced drug release to air-water interface as a simplified model for the cell membrane interface.[1,2] However, passive diffusion of anticancer agents across lipid membranes is a key transport mechanism, yet direct quantitative data on drug-lipid interactions and their influence on release remain limited.

In this contribution, we report on using photoswitchable arylazopyrazole (AAP) amphiphiles as micellar nanocarriers and doxorubicin (Dox) as a representative anticancer drug and study how the composition of the lipid monolayers governs light-induced drug release to the interfacial layer. This is done by studying Lipid monolayers in a Langmuir-Pockels trough though interface-specific vibrational sum-frequency generation (SFG) spectroscopy as a function of the available mean molecular area. Using SFG spectroscopy, we quantitatively estimate drug release to lipid monolayers at air-water interfaces as (our) model membrane. To systematically address the specific effects of the lipid headgroup, we have studied DMPC, DMPG, DMPS, and DMPE which share identical alkyl tails but differ in charge and polarity of their headgroups. As nanocarriers, we use micelles of octyl-AAP sulfonates which can be photoisomerize between E and Z states, with the E form being substantially more surface active than Z form. In addition, E/Z photoisomerization can be utilized to change the critical micelle concentration dramatically from 0.1 mM (E isomer) to 1 mM (Z isomer). This gives rise to effective encapsulation of Dox in micelles of the E isomer and effective release of Dox after E (micelles) to Z (monomers) photoisomerization e.g. at a octyl-AAP concentration of 0.3 mM. Note, the latter has been found to cause substantial release to the air-water interface without a lipid being present [1,2]. In comparison, water surfaces with DMPC, DMPG, DMPS, and DMPE lipids exhibit a selective release of Dox mostly to anionic lipid (DMPS, DMPG) interfaces while the release to interfaces with zwitterionic lipids (DMPC, DMPE) was neglectable.

These results will elucidate how lipid-drug interactions modulate release efficiencies at membrane-like interfaces, providing insights relevant to the design of photoresponsive nanocarrier systems for targeted drug delivery.

Keywords:
Lipid monolayer, interface spectroscopy, adsorption, photoswitchable surfactants, nanocarriers, micelles

References:

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[2] Ipsita Pani, Christina Spruck, Johannes Walter and Björn Braunschweig. *J. Coll. Int. Sci.* 703, 139030 (**2026**).

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