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Assesing the effect of Ursolic Acid on Lipid Droplet biogenesis using a Langmuir model system

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According to the latest Lipid Droplet (LD) biogenesis models, interfacial tension plays a critical role on such process, determining the shape of the budding LD from the ER. We have previously presented triglyceride (TG) “lenses” at the air-water interface as a model system for studying LD biogenesis. The performance of Langmuir monolayers of mixed phosphatidylcholine (EPC)/TG in coexistence with TG microlenses (*i.e.* an excluded TG phase floating in the surface) and the characterization of their lenses´ thickness by Brewster Angle Microscopy (BAM) allow evaluating the proneness of TG lenses to form a LD. This is done by characterizing the associated thermodynamics and the resulting shape of the TG lenses. Here, we evaluated the modulation of TG lenses tendency to detach from the interface by the presence of a third component with interfacial activity. For this purpose, we choose Ursolic Acid (UA), a natural pentacyclic triterpenoid with many biological effects and a clear interfacial activity. We found that UA slightly diminished the surface pressure at which TG phase separation occurs (*i.e.*, lenses appearance) in composition dependent manner (both %UA and PC/TG relation). Such effect may be correlated with the dependency of UA interfacial partitioning on lipid composition. On the other hand, BAM analysis showed a lower reflectivity of lenses in the presence of UA. Assuming a negligible effect of UA on the refractive index of TG lenses, this implies a thinning of such structures. Additionally, the decreased radii of lenses observed allowed us concluding that the contact angle of the lenses is lower in the presence of UA. In conclusion, this experimental model allowed the detection of an interfacial active compound, like UA, affecting both the energy necessary to form the TG lenses and its shape, leading to structures of lower curvature and radii. These results are in accordance with observed effects of UA on LD in cells: a decrease in LD number and radii.

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