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Archaeal diether lipids dominate membrane behavior of DPPC

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Archaeal lipids are different from bacterial lipids. Archaeal lipids are ether-linked and have isoprenoid chains instead of alkyl chains. This is supposed to make archaea and their membranes more resistant to changes in temperature or pH.

This lead to the idea to use archaeal lipids in vesicles for oral drug delivery of pH-sensitive therapeutic compounds. To quantify the influence of the archaeal diether lipids (DELs) of *H. volcanii* (Hvo) on phosphoester lipid membranes, mixtures of DELs and DPPC were characterized. Both, mixed monolayers and mixed DPPC/DEL vesicles were examined by compression film balance experiments, differential scanning calorimetry, laurdan fluorescence, and attenuated total reflection infrared spectroscopy (ATR-IR).

Unsurprisingly, we found that DEL lipid chains generally have a lower order than DPPC chains. The lipid main phase transition temperatures of DPPC and transition enthalpies decrease with increasing DEL content, even at low ratios (5-20 %). At DEL contents of approximately 30% to 50%, the liquid-expanded to liquid-condensed transition of monolayers and the main phase transition in bilayers disappear. Already at low content, DELs have a dominant influence on DPPC membrane behavior.

In summary, it could be shown that the DEL lipids of *Haloferax volcanii* are potentially suitable for oral drug delivery. Next, the membrane permeabilization shall be studied.