A GALA lipopeptide mediates pH- and membrane charge dependent fusion with stable giant unilamellar vesicles

Peptides capable of mediating fusion between lipid membranes are widely observed in nature, and have attracted considerable attention in the liposome drug delivery field. However, studies that are proving the benefit of small synthetic fusion peptides as components in drug delivery systems remain sporadic and there is a strong need to characterize and increase our understanding of the membrane fusion properties of these peptides. Many fusion studies have focused on the ability of free peptides in solution that mediate fusion between liposomes. For drug delivery purposes it is a necessity to attach the peptides to the surface of the liposome drug delivery carrier, without impairing the peptide functionality. Here we present the synthesis and characterization of a new diacylated derivative of the previously described fusion peptide GALA. Two myristoyl chains were attached to the GALA peptide through the 1,2-diamino propanoic acid (Dap) moiety, yielding the lipopeptide dimyristoyl-Dap-GALA (DMDGALA). We have investigated DMDGALA as a component in large unilamellar vesicles (LUVs) and demonstrate pH-triggered fusion of peptide containing LUVs with stable target giant unilamellar vesicles (GUVs), which were used as simple mimics of cell membranes. The number of fusion events was large at pH 5.0, which is a physiologically relevant pH-range for a drug delivery system.

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