Characteristics of DSPE-PEG2000 Self Assemblies in Pure Water and Isotonic Buffer Solution

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Statement of Purpose: Our laboratory has been investigating the use of micelles formed by DSPE-PEG_{2000} in isotonic HEPES buffer as a drug delivery system for more than a decade. At 1-5 mM these micelles have a diameter of ~15 nm[1]. This study was performed to examine the self-assemblies of DSPE-PEG_{2000} in pure water and isotonic buffer at different concentrations, by dynamic light scattering and viscosity measurements.

Methods: DSPE-PEG_{2000} was directly dissolved in either pure water or 10 mM isotonic HEPES buffer. Lipid concentrations ranged from 10.0-45.0 mM and 10.0-40.0 mM in water and HEPES buffer, respectively. The solutions were flushed with Argon gas and equilibrated for 4 hours in the dark at 25°C. The presence of micelles was detected by dynamic light scattering (Agilent 7030 NICOMP DLS/ZLS). The viscosities of the lipid solutions were measured using a Brookfield DV-II+ Viscometer with a cone and plate geometry.

Results: In both pure water and buffer, self assembled particles were detected in all the lipid concentrations studied. Micelle size was smaller in pure water compared to buffer and stayed the same in all concentrations studied (Figure 1). The smaller size of the micelles in pure water is most probably due to increased PEG chain folding in the absence of NaCl. When the lipid concentration was increased in isotonic HEPES buffer the apparent size of the micelles decreased as seen in Figure 2, but this change was reversible upon dilution. The apparent size decrease of the micelles in the buffer is most likely due to micelle-micelle interactions causing the PEG to fold, whereas the constant micelle size in the water is due to less number of micelles at the studied lipid concentration. At low lipid concentrations in pure water the micelle peak was lower and not dominant and smaller particles were also detected.

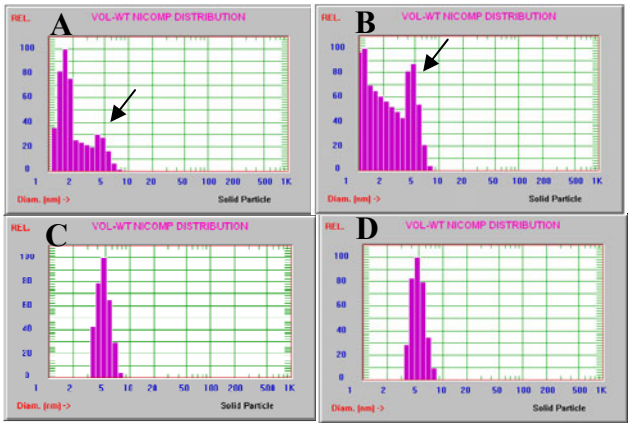

Figure 1: DSPE-PEG_{2000} in pure water **A**) 10 mM, **B**) 20 mM, **C**) 35 mM, **D**) 40 mM, arrows point to micelle peak in 10 and 20 mM graphs

The solution viscosity of DSPE-PEG_{2000} in pure water and HEPES buffer increased exponentially with increase in lipid concentration, as shown in Figure 3. As the number of micelles increased in both systems the viscosity also increased, as expected. But, the viscosity was higher at every concentration and increased at a higher rate in the pure water samples. This is most likely because of the greater number of lipid monomers, long flexible structures, in pure water because of the higher critical micelle concentration.

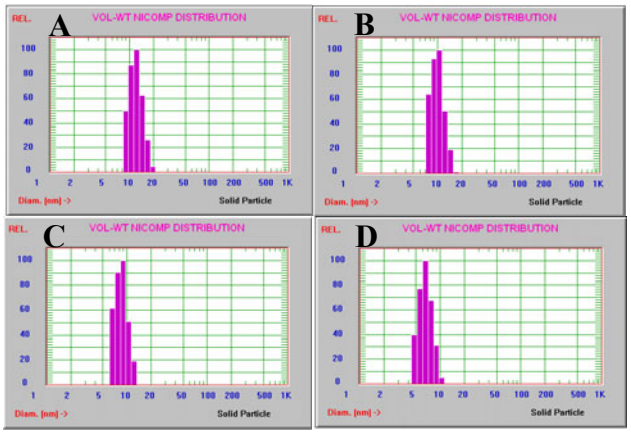

Figure 2: DSPE-PEG_{2000} in 10 mM isotonic HEPES buffer **A**) 10 mM, **B**) 20 mM, **C**) 30 mM, and **D**) 40 mM

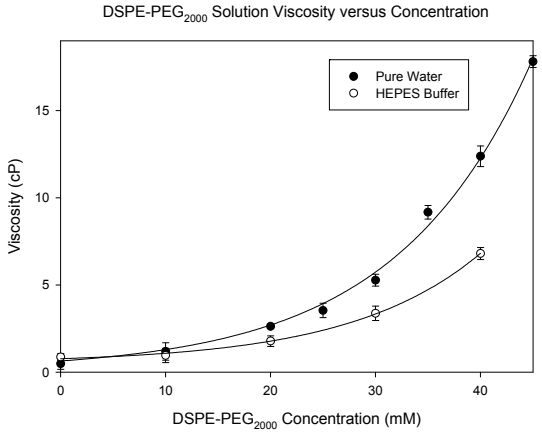

Figure 3: DSPE-PEG_{2000} solution viscosity versus lipid concentration in pure water and HEPES buffered saline

Conclusions: DSPE-PEG_{2000} behaves differently in the presence of buffer salts and at varying concentrations. These properties should be considered when preparing PEGylated lipid micellar formulations.

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References:

[1]Ashok B, et al. *J. Pharm. Sci.* (2004) 93.10:2476-87