

Morphological and aggregation behavior of PEG-PPS block copolymers

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INTRODUCTION: Block copolymers are composed of covalently bound hydrophilic and hydrophobic polymer chains. Due to their amphiphilic character when put in a specific solvent they are able to associate and form a wide variety of aggregates¹. In this study we characterize the relationship between block copolymer composition and kind of aggregate formed in water by cryo TEM² technique and by measuring the critical aggregation concentration (cac) of a series of poly(ethylene glycol-*bl*-propylene sulfide) (PEG-PPS) block copolymers. Depending on the block ratios, nanoparticle, spherical micelles, rods, or unilamellar vesicles similar to liposomes can be formed. Our goal is to be able to optimize the design of these materials for use in the diagnosis and treatment of disease.

METHODS: The synthesis of the PEG-PPS diblock copolymer used in this study was performed as shown in the literature.² The polymer aggregates were prepared in two ways, first, preparing a concentrated solution of the polymer in THF then diluting few μl of it in water, second, using the standard thin film hydration technique followed by extrusion through a 200nm membrane. The resultant aggregates were then visualized using the cryo-TEM technique.³ For the cmc measurements we used the pyrene fluorescence technique as described elsewhere³. The results are reported respect to the hydrophilic fraction (f_{PEG}) and respect to the hydrophobic block, (nPPS).

RESULTS: Different aggregates are formed by increasing the nPPS of the polymers, showing also lower cac (easier aggregation) for more hydrophobic polymers. This follows the well established pattern already studied for similar block copolymer systems, Pluronics (PEO-PPO).⁴ The aggregation is in both cases driven by the hydrophobic effect. Depending on the specific polymer, different or same kind of aggregates could be formed in water, from either of the two ways used to form the aggregates, indirectly from THF or directly from simple hydration. Analysis of a specific triblock copolymer showed that the aggregates formed from THF are

thermodynamically stable, while those formed from water are kinetically trapped.⁴

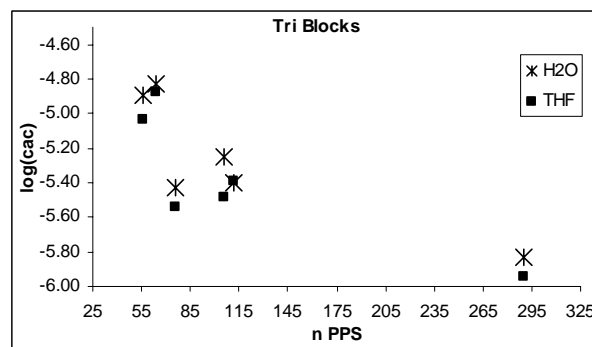


Figure 1 cac of a series of PEG-PPS triblock copolymers calculated by fluorescence technique. An increase in the hydrophobic block makes the cac decrease.

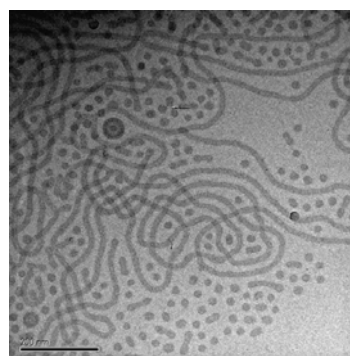


Figure 2 Example of aggregates formed by the E45S76E45 triblock copolymer at 1wt% in water

DISCUSSION & CONCLUSIONS: The study of the relationship between f_{PEG} , MW, hydrophobicity and the different aggregates formed in water, are of key importance for the rational design of block copolymers for different applications. One of the examples of particular interest is the vesicular structure, which could be useful in the drug delivery field.

REFERENCES: ¹ S. Jain et al (2003) *Science*, **300**:460-464. ² Napoli; N.Tirelli; G.Kilcher; J.A.Hubbell (2001) *Macromolecules*, **34**: 8913-8917. ² Dubochet, J.et al. P. Quaterly Review of Biophysics, **1988**, 21, 129-228. ⁴S. Cerritelli et al. (2005), *Macromolecules*, in printing.