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Multifunctional Dendritic Polyglycerol Nano- and Microgels for Encapsulation and Release of Functional Biomacromolecules

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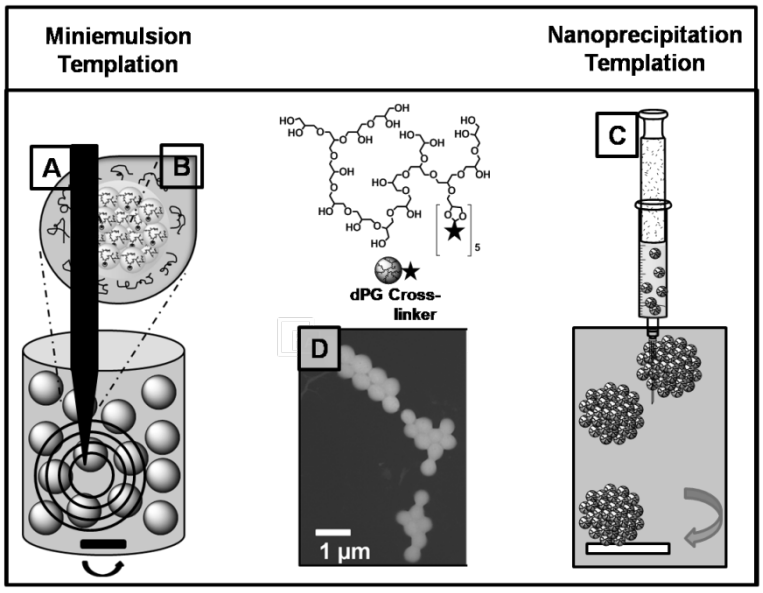
Nanogels, which are hydrogel particles on the nanometer scale, are highly water swollen scaffolds that exhibit similar properties as many biological objects, thus making them excellent candidates for biomedical applications. Nanogels are usually prepared by the templation of reactive monomers on the nanometer scale and subsequent crosslinking of the templates to obtain hydrogel nanoparticles. One of the most frequently used methods is the templation in miniemulsion droplets. The crosslinking of both dPG macromonomers and commercial glycerol-based monomers in miniemulsion nanodroplets yield biocompatible nanogels which show excellent cell penetration.[1] We also reported the preparation of disulfide-containing polyglycerol nanogels which degrade in the reductive environment of cells.[2] The need of high energy input and block-co-polymer surfactants, however, may hinder the in-situ encapsulation of bioactive guests into the nanogel network and nanogel preparation in high quantities might be difficult, using the miniemulsion technique.

The nanoprecipitaion technique has evolved as a powerful tool for the surfactant- and ultrasound free templation of hard polymer nanoparticles. Particles prepared by nanoprecipiation avoids the above mentioned downsides and allows hydrophobic drugs to be encapsulated. To the best of our knowledge, the nanoprecipitation technique has not been applied for the preparation of nanogels, made from hydrophilic polymers. Hence, we prepared for the first time water swollen nanogels by gelling in nanopricipitation templates (figure 1).[3] We have chosen dendritic polyglycerol (dPG) as nanogel building block, because of its excellent protein resistant properties. Additionally we were able to extend the size controlled synthesis of polyglycerol scaffolds up to the 100 µm range and to load these highly biocompatible microgels in situ with living cells.[4]



In conclusion, we have prepared dendritic polyglycerol nanogels and microgels by crosslinking in miniemulsion- and nanoprecipitation templates. Because surfactants and high energy input by ultrasonication are not required for the templation by nanoprecipitation, we believe that this technique is more suitable to prepare nanogels for biomedical applications. Currently we are applying these mild conditions for the encapsulation of various water soluble biomacromolecules.

Figure 1. Schematic representation of nanogel preparation by miniemulsion templation using strong ultrasonication (A: black bar) and block-co-polymer surfactants (B: black lines), nanogel preparation by templation using surfactant and ultrasound free nanoprecipitation technique (C), transmission electron micrograph of the optained nanogels by nanoprecipitation (D).

References

[1] A.L. Sisson, D. Steinhilber, R. Haag et al., Angew. Chem. Int. Ed. (2009) 7540-7545.
[2] D. Steinhilber, R. Haag et al., Adv. Funct. Mater. 20 (2010) 4133-4138.
[3] D. Steinhilber, Rainer Haag et al., J. Control. Release, accepted.
[4] D. Steinhilber, D. A. Weitz, R. Haag et al. Biomaterials 32 (2011) 1311-1316.