Peptide-loaded microgels as carriers of antimicrobial peptides

Lina Nyström1; Randi Nordström1; Shalini Singh1; Brian R. Saunders2; Rubén Álvarez-Asencio3,4; Mark W. Rutland3,5; Bruno Borro6; Martin Malmsten1,6

1. Department of Pharmacy, Uppsala University, P.O. Box 580, SE-752 32 Uppsala, Sweden
2. School of Materials, The University of Manchester, MSS Tower, Manchester, M13 9PL, United Kingdom
3. Department of Surface and Corrosion Science, School of Chemical Science and Engineering, KTH Royal Institute of Technology, SE-100 44 Stockholm, Sweden
4. Institute for Advanced Studies, IMDEA Nanoscience, 28049 Madrid, Spain
5. SP Technical Research Institute of Sweden, SP Chemistry, Materials and Surfaces, SE-114 86 Stockholm, Sweden
6. Department of Pharmacy, University of Copenhagen, DK-2100 Copenhagen, Denmark.

Microgels are weakly cross-linked polymer colloids, which can be designed to display responsive volume transitions triggered by a range of parameters. In the context of drug delivery, microgels are of particular interest as carriers for biomacromolecular drugs, such as peptides and proteins. In order to elucidate factors affecting the functional performance of microgels in this context, we here investigate effects of microgel charge density, conformationally induced peptide amphiphilicity, and PEGylation on antimicrobial peptide loading and release, using nuclear magnetic resonance (NMR) structural studies combined with a battery of other physicochemical methods. In parallel, consequences of peptide loading and release for membrane interactions and antimicrobial effects were investigated, as was protection of microgel-incorporated peptides by infection-related proteases. Furthermore, we elucidate factors determining volume transitions of electrostatically triggered surface-bound microgels, as well as their use as delivery systems for peptides. In doing so, we investigate effects of microgel charge density, pH, and ionic strength on microgel volume transitions at surfaces, surface-induced microgel deformation and nanomechanical properties.

Figure 1. Factors affecting peptide loading into, and release from, microgels was investigated with regards to microgel and peptide properties, as well as to ambient conditions. The consequences of such effects for the function of antimicrobial peptides are addressed as well.

References

1. L. Nyström et al., Biomacromolecules, 2016, 17, 669-678
2. L. Nyström et al., ACS Appl. Mater. Interfaces, 2016, 8, 27129-27139