# Structure evolution of phase-separated biopolymer films for controlled drug delivery

P. Carmona[1,2], M. Röding[1,3], A. Särkkä[3], E. Olsson[2], N. Lorén[1,2]

*[1]Unit Product Design, Department Agriculture and Food, Division Bioeconomy and Health, RISE Research Institute of Sweden, Gothenburg, Sweden., [2] Division Nano-and BioPhysics, Department of Physics, Chalmers University of Technology, Gothenburg, Sweden., [3]Department of Mathematical Sciences, Chalmers University of Technology, Gothenburg University, Gothenburg, Sweden.*

**INTRODUCTION:** Porous phase-separated ethylcellulose / hydroxypropylcellulose (EC/HPC) films are used to control drug transport in pharmaceutical pellets. The drug transport rate is determined by the 3D structure of the porous films that are formed as the water-soluble HPC leaches out. The films are applied on pharmaceutical pellets using fluidized bed spraying. However, a detailed understanding of the structure evolution of the phase-separated films is lacking. In this work, we have investigated EC/HPC films produced by spin-coating[1], which mimics the industrial manufacturing process. The aim of this work was to understand the structure evolution and coarsening kinetics during solvent evaporation and formation of the phase separated films.

**METHODS:** The in-plane and cross-sectional structure evolution was characterized using confocal laser scanning microscopy (CLSM) and Fourier image analysis.

**RESULTS:**

A new method to slow down the process of solvent evaporation to follow the structure evolution in situ during phase separation has been developed. Furthermore, a new image analysis procedure to monitor the time-dependent evolution of the curvature of the EC/HPC interface in bicontinuous structures has been implemented. Figure 1 shows two examples of structure evolution during phase separation of EC/HPC thin film, that can be monitored with CLSM. Results on the time-dependent evolution of the characteristic length scale of the structure, the time dependence of the domain's growth rate and the curvature evolution (see Figure 1b) has been obtained. With the findings, it is possible to correlate structure evolution to the governing phase separation and coarsening mechanisms[2].

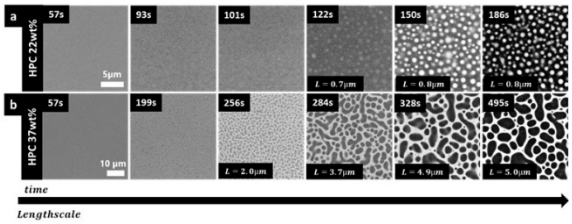


*Fig. 1: Overview of the structure evolution for two EC:HPC ratios, showing (a) a discontinuous structure with EC:HPC 78:22 wt% and (b) a bicontinuous structure with EC:HPC 63:37 wt% (HPC is bright, EC is dark). The x-axis corresponds to the key positions of the phase separation. Where applicable, the characteristic length scale L(t) is displayed on the corresponding micrograph.*

**DISCUSSION & CONCLUSIONS:** The findings of this work provide a good understanding of the mechanisms responsible for the morphology development and open for further tailoring of thin EC/HPC film structures for controlled drug release.

**ACKNOWLEDGEMENTS:** The Swedish Foundation for Strategic Research (SSF grant FID16-0013), the Swedish Research Council (VR grant 2018-03986), and the Swedish Research Council for Sustainable Development (grant 2019-01295) are gratefully acknowledged for the funding. AstraZeneca is acknowledged for the financial support and materials.

**REFERENCES:**

[1]P. Carmona, M. Röding, A. Särkkä, C. Von Corswant, E. Olsson and N. Lorén, Soft Matter, 2021, 17, 3913-3922, DOI: 10.1039/d1sm00044f.

[2]P. Carmona, M. Röding, A. Särkkä, C. Von Corswant, E. Olsson and N. Lorén, Soft Matter, 2022, 18, 3206-3217, DOI: 10.1039/d2sm00113f,.