COMPRESSION AND PROTEIN-PROTEIN INTERACTIONS AS TRIGGERS FOR AGGREGATION OF MONOCLONAL ANTIBODIES AT INTERFACES

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Aggregation of biopharmaceuticals triggered by interfaces is a challenge at various levels from upstream processing to patient application. We specifically investigated the air-liquid interface. A combination of Langmuir-Blodgett Trough experiments, Infrared Reflection-Absorption Spectroscopy, Brewster Angle Microscopy, Atomic Force Microscopy and Profile Analysis Tensiometry could demonstrate that the film formed by monoclonal antibodies (mabs) at the interface can be substantially condensed upon compression due to interface movement. Protein-protein interactions subsequently are a key element which determines whether large aggregates result from this phase upon decompression.

Thus, not only addition of surface active molecules is a remedy to solve the problem of surface induced aggregation. Additionally, factors which strongly affect the protein-protein interactions, specifically pH and ionic strength are starting points.

Furthermore, the protein film formation itself depends on the monoclonal antibody properties. In a series of mabs the drug candidate which was most stable against shaking stress showing the most repulsive A2 values and the least hydrophocity was the one which adsorbed the slowest at the air-liquid-interface.

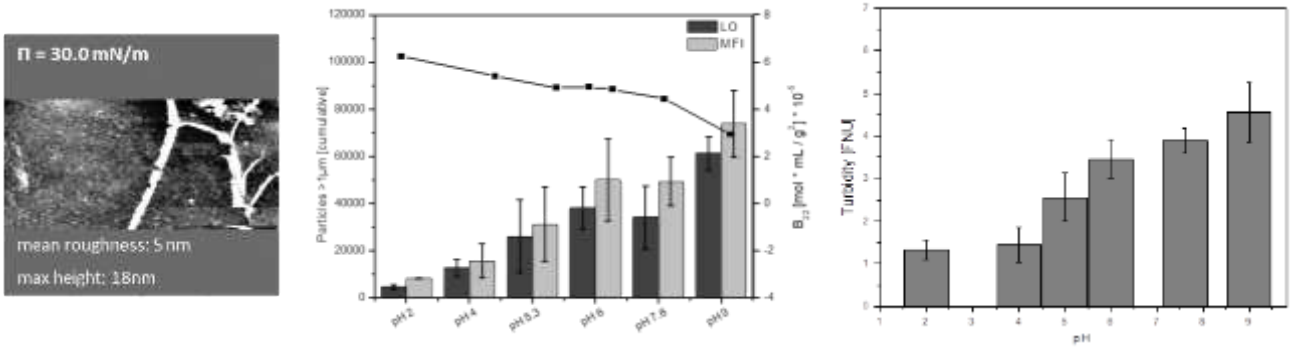

Figure 1 – Submerse AFM of blotted, compressed mab film; subvisible particle formation and turbidity upon stressing as well as B22 as a function of pH

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