PHARMACEUTICAL

Quantifying protein denaturation inhibition with viscosity

Introduction

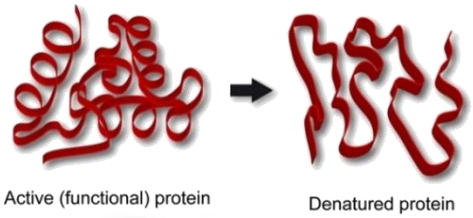
The advent of protein-based drugs brings along new challenges in term of stability and formulation. Indeed, proteins have a strong tendency to denature and/or aggregate, depending on parameters such as temperature, shear, solvent composition, etc. This instability affects the shelf life and can alter the drug efficiency. Moreover, their high molecular weight, associated to a low permeability, prevents oral administration, meaning protein-based drugs often have to be injected. In term of formulation, injecting implies a low viscosity and a small volume, so a high protein concentration

KEY BENEFITS

FAST

SMALL SAMPLE VOLUME

ACCURATE



Various compounds may be considered as additives in order to prevent protein denaturation. Most commonly studied are: Arginine and Histidine, susceptible of stabilizing protein structures and so preventing increase of viscosity.

Reminder on the technique

FLUIDICAM uses a co-flow microfluidic principle to measure viscosity. Sample and reference standard are pushed together to the microfluidic channel (typically 2.2mm X 150µm) under controlled flow rates. In this laminar flow, interface position between sample and reference relates the viscosity ratio between the two to the flow rates.

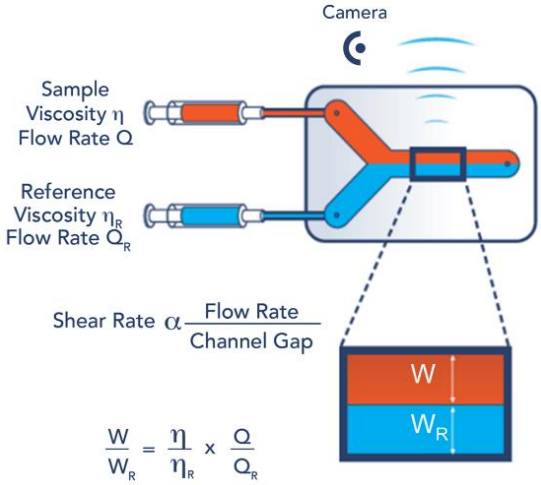
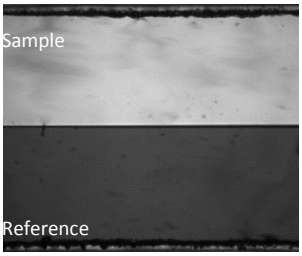


Fig. 1: Fluidicam measuring principle

Images acquired during the measurement allow to calculate the position of the interface and plot directly an interactive flow curve.



Method

Several BSA solutions were prepared in this study, two concentrations of additives were considered (50 and 200mM), and two natural protein solutions one in water and the other in PBS – phosphate buffer solution. In order to determine the influence of additive on protein unfolding and thus protection efficiency, the viscosity was measured after subjecting the solutions to high temperatures (60°C for 4h and 25°C for 48h).