PHARMACEUTICAL

Viscosity at high shear rate for assessing drug injectability

- *Adapting the injection system for a specific formulation* -

Introduction

Injectability and syringeability are major parameters that must be optimized during the development phase of injectable drugs. These key features notably encompass the ability of drug to be filled into a syringe and administered to the patient. Therefore, the force needed to pump solution through the needle must be carefully considered during formulation. In this study, we show how viscosity measurements using a microfluidic device - Fluidicam^{Rheo} can be used to rationalize and speed-up injectable drug development without the need of direct force measurements.

KEY BENEFITS

HIGH SHEAR RATE

LOW VOLUME

PRECISE

Reference:

1. *Cilurzo, Francesco, Francesca Selmin, Paola Minghetti, Marco Adami, Elisa Bertoni, Sara Lauria, and Luisa Montanari. 2011. 'Injectability Evaluation: An Open Issue'*
2. *Watt, R. P., Khatri, H. & Dibble, A. R. G. Injectability as a function of viscosity and dosing materials for subcutaneous administration.*
3. *Burckbuchler, V. et al. Rheological and syringeability properties of highly concentrated human polyclonal immunoglobulin solutions.*
4. *Allmendinger, A. et al. Rheological characterization and injection forces of concentrated protein formulations: An alternative predictive model for non-Newtonian solutions.*

Reminder of the technique

Fluidicam^{RHEO} uses a co-flow microfluidic principle to measure viscosity. The sample and a reference solution are simultaneously introduced into the microfluidic channel (typically 2.2mm X 150µm) with controlled flow rates. This results in a laminar flow where the interface position between sample and reference relates the viscosity ratio and flow rates.

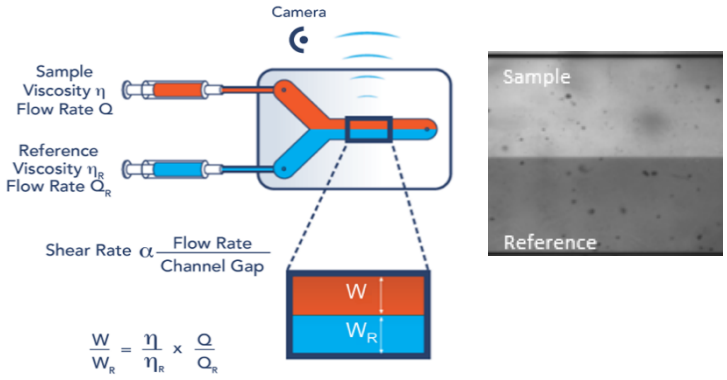


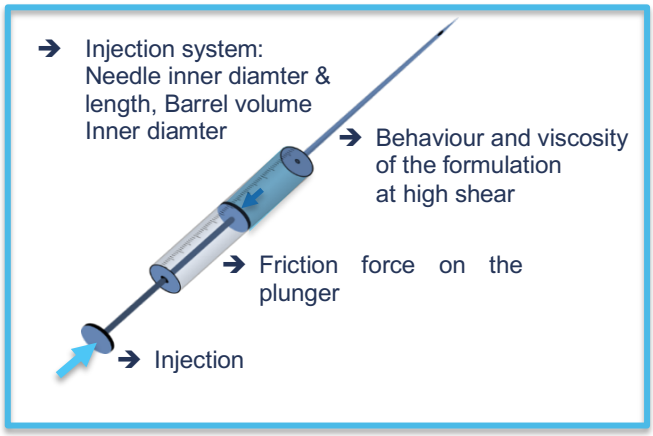
Figure 1: Fluidicam measuring principle

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

What impacts injectability

As mentioned earlier, the force is an important parameter to optimize and ensure injectability. The required force to pump or eject injectable from a syringe is dependent on both physical properties of the injectable solution and the 'geometric' parameters of the injection system to be used. Namely these parameters are:

- Barrel radius (Rs), needle length (L), needle. inner diameter (R_N), piston friction…
- Formulation viscosity (at given temperature).



Conventional injection needles have gauge sizes ranging from ~20G (ID = 603 µm) to ~31G (ID=133 µm), but some speciaized applications such as pen injectors can range even up to gauge 34 (ID = 82.6 µm).

Downsizing of the needle gauge can help achieve better patient tolerance to pain. However it also highly influences back-pressure during injection as the flow can reach very high wall shear rate, typically ranging from 30 000 to 100 000 s^{-1} [4].