On-line process rheology for pharmaceutical semi-solid dosage forms

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AIM

The aim of this study was to investigate an on-line apparatus (based on pressure difference) for the measurement of rheological parameters with pharmaceutically relevant model system. Rheological properties (Fig.1) have an impact on stability, patient perception and production equipment [1].

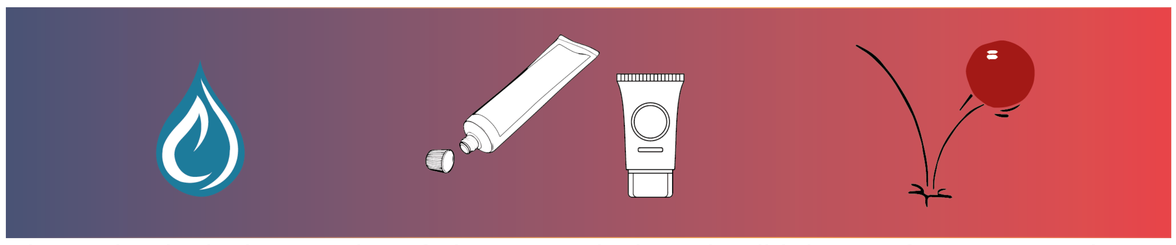

Fig.1: Rheological properties of pharmaceutical semi-solid dosage forms are a mixture of a viscous (G") and an elastic (G') component and are usefully determined with a standard rotational rheometer.

METHODOLOGY

Hydroxyethyl cellulose (HEC) gels were produced in six different concentrations and measured with the pressure difference apparatus (RheoStream®, Fluidan, Denmark) and a standard rheometer (Physica MCR300, Anton Paar, Germany). A calibration model was established based on half of the data set and verified by using the second half. Pressure signals obtained were converted to rheological parameters (see Fig. 2), using an established method by which empirical constants are derived as previously described [2].

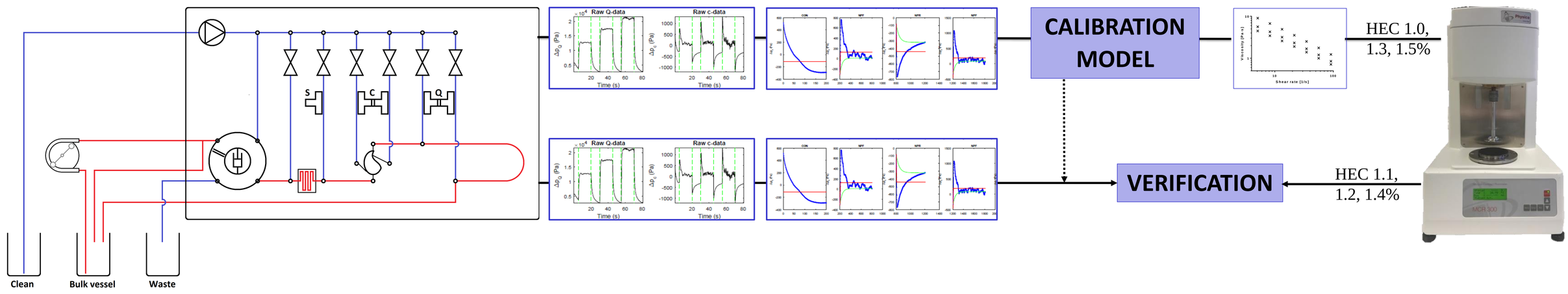

Fig.2: The pressure difference apparatus (left) and standard rheometer (right) was compared to make a calibration model. The calibration model was subsequently used to convert the pressure differences into rheological parameters of HEC gels, which were not part of the calibration.

RESULTS

The HEC gels behaved non-Newtonian and showed a shear thinning region in the flow curve (Fig. 3). The shear thinning does not show linear concentration dependence. The investigated shear area and frequencies reflect the typical conditions during production of the gel.

The G' (the elastic component) dominated at higher frequencies independent of concentration, while G'' (the viscous component) dominates at lower frequencies (Fig. 4-5). The cross over of G' and G'' depend on polymer concentration. The decline of moduli with frequencies were similar for all concentrations.

VISCOSITY

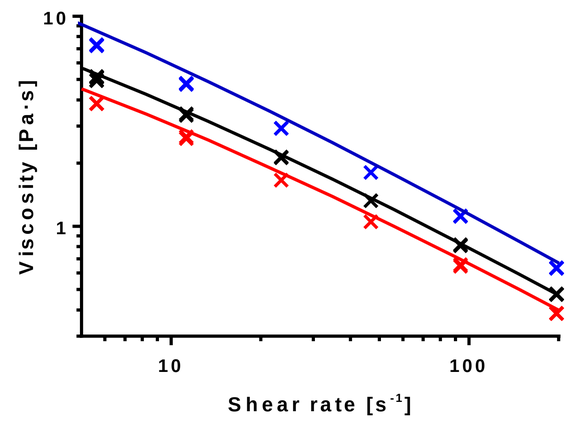

Fig.3: Verification the flow curves

G'

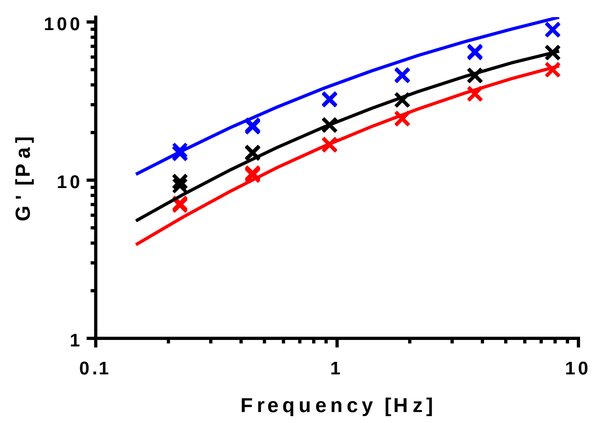

Fig.4: Verification the G'

G''

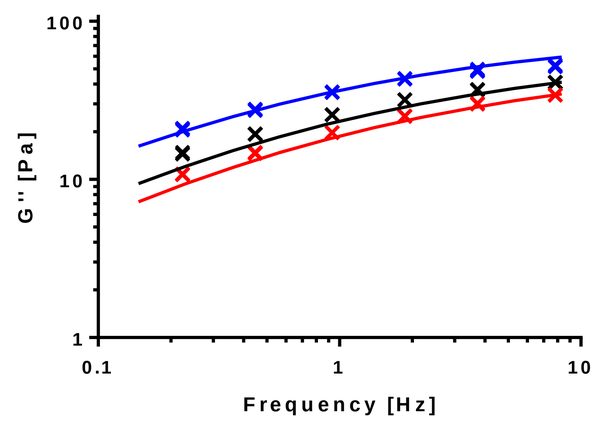

Fig.5: Verification the G"

HEC gels, 1.1% red, 1.2% black and 1.4% blue measured on the pressure difference apparatus (x) and standard rheometer (line).

CONCLUSION

The rheological data including viscosity, G' and G'' of the different formulations were shown to be comparable between the pressure difference apparatus and the standard rheometer.

FUTURE PERSPECTIVES

The calibration model could in future experiments be used to utilize the real-time data, which could be a part of a control strategy during scale up and production of typical pharmaceutical semi-solid dosage forms.

Acknowledgments
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References

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Information

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