Rheological Services

Supportung Semi-Solid Product Development & Equivalence Testing

RaDes GmbH, 2026

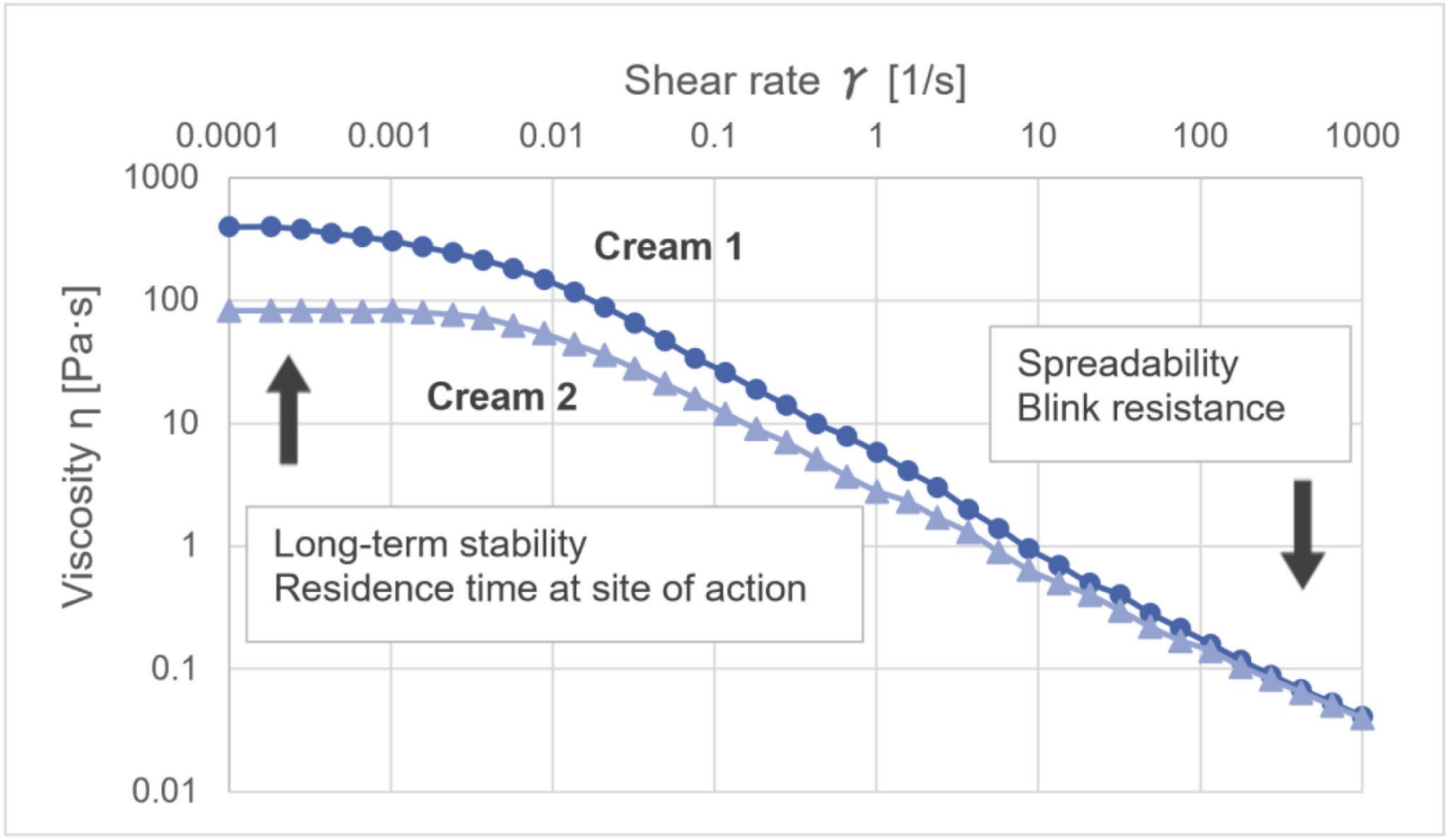
RATIONAL DESIGN
OF FORMULATIONS

How Rheology Supports Topical Product Development

How can rheology (using high performance rheometers) support product development and optimization?

- **Physical stability** during storage (sedimentation, creaming)
- Spreadability on the skin and other **sensory-related aspec**ts
- **Device compatibility** (e.g. pump dispensing)
- **Process Development:** Behaviour during filling processes or time to rebuild inner structure (thixotropy)
- Indications for physical **long-term stability** of inner structure (thermorheology)
- Rheological equivalence testing of **generic formulations** (e.g. according to **EMA** „Draft guideline on quality and equivalence of topical products“ (EMA/CHMP/QWP/708282) and **FDA** „Physicochemical and Structural (Q3) Characterization of Topical Drug Products Submitted in ANDAs“
- Ophthalmic formulations: **residence time**, blink resistence
- Rheological characterization as part of pharmaceutical development for **dossiers** (according to guidelines)
- **Exchangeability** of structure-determining excipients (e.g. petrolatum)

Viscosity in Design & Optimization of Formulations



Cream 1 and 2 feel the same when they are applied on the skin due to the same high shear viscosity

Cream 1 shows a 6-times better physical storage stability and a longer residence time on application site due to the differences in zero-shear viscosity (log scale!)

In ophthalmic application, both creams show a low blink resistence, but cream 1 would show a longer residence time on the eye.

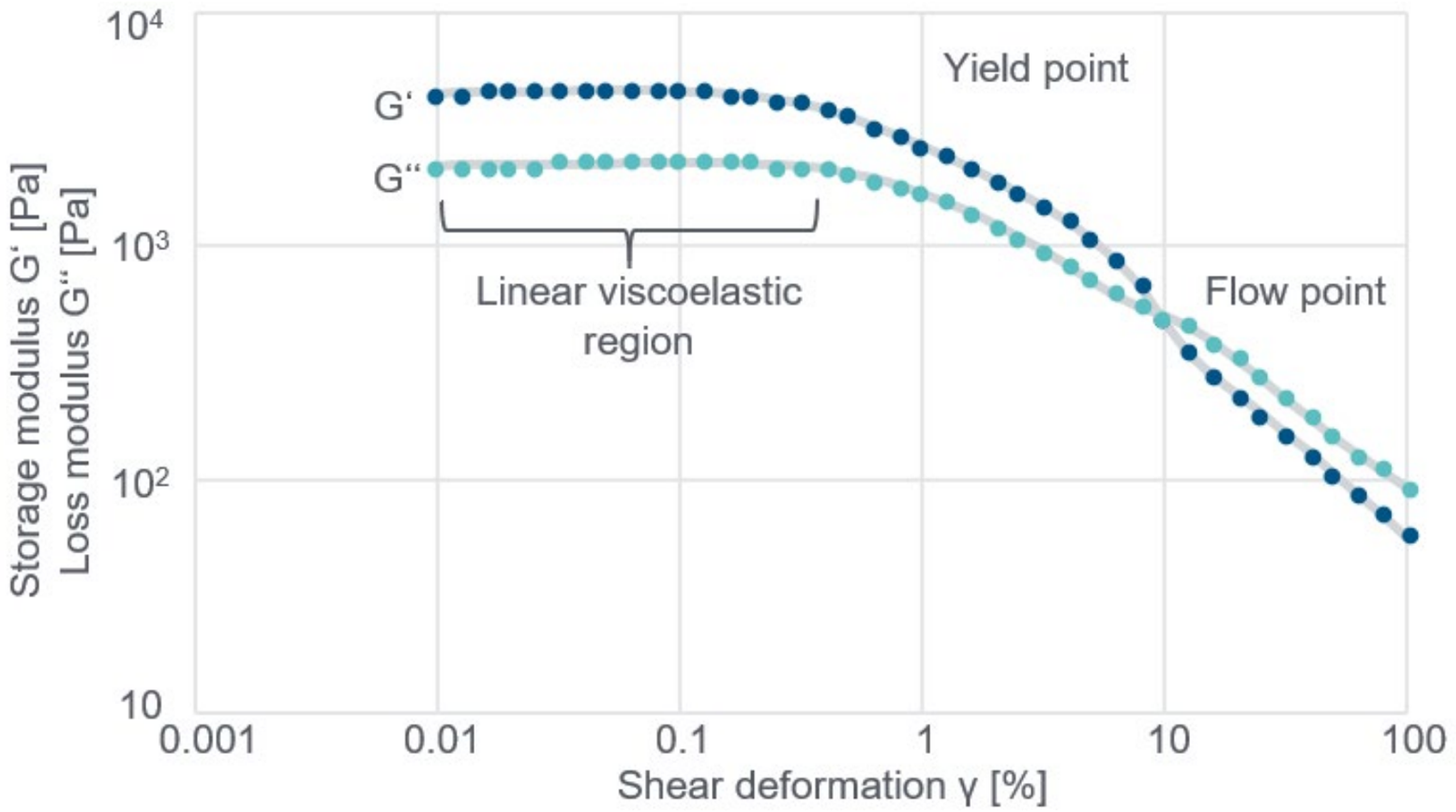
- Rheological methods help to understand, design, optimize and re-engineer formulations with regards to physical stability, manufacturing processes and patient/consumer relevant properties.

Herbig ME, Evers D-H, Gorissen S, Köllmer M. Rational Design of Topical Semi-Solid Dosage Forms-How Far Are We? *Pharmaceutics*. 2023; 15(7):1822

Oscillatory rheology

Amplitude sweep test:

- Insight into “the inner structure” of the formulation “at rest” can be obtained.
- The storage modulus G’ represents the elastic (solid-like) and the loss modulus G’’ the viscous (liquid-like) behavior. Also phase angle (viscous-liquid-ratio) and complex modulus G* (rigidity) can be obtained
- Stability and usage/consumer-related information (range of linear viscoelastic region, flow point, behavior of storage modulus at varying frequencies, phase angle, flow transition index).



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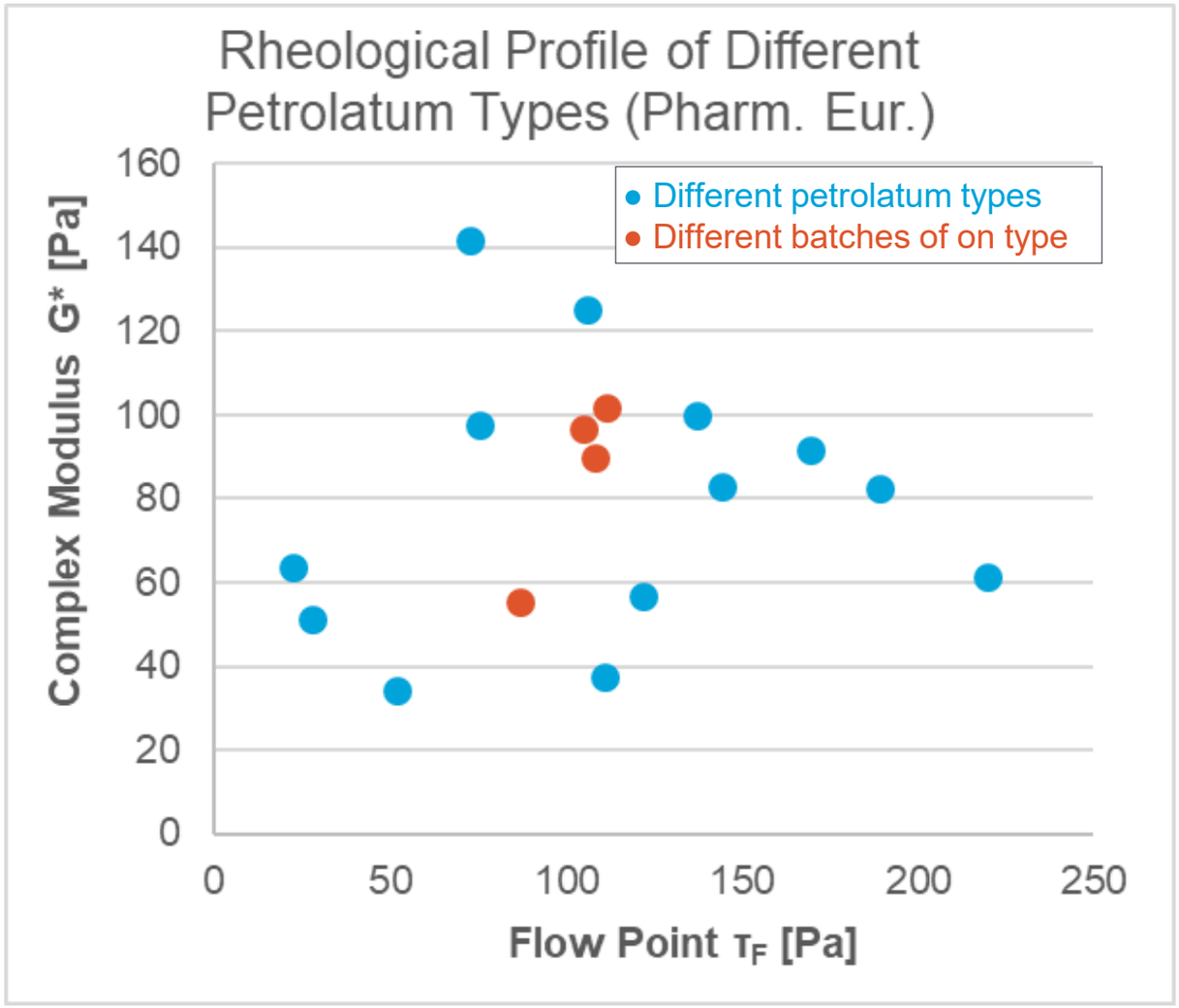
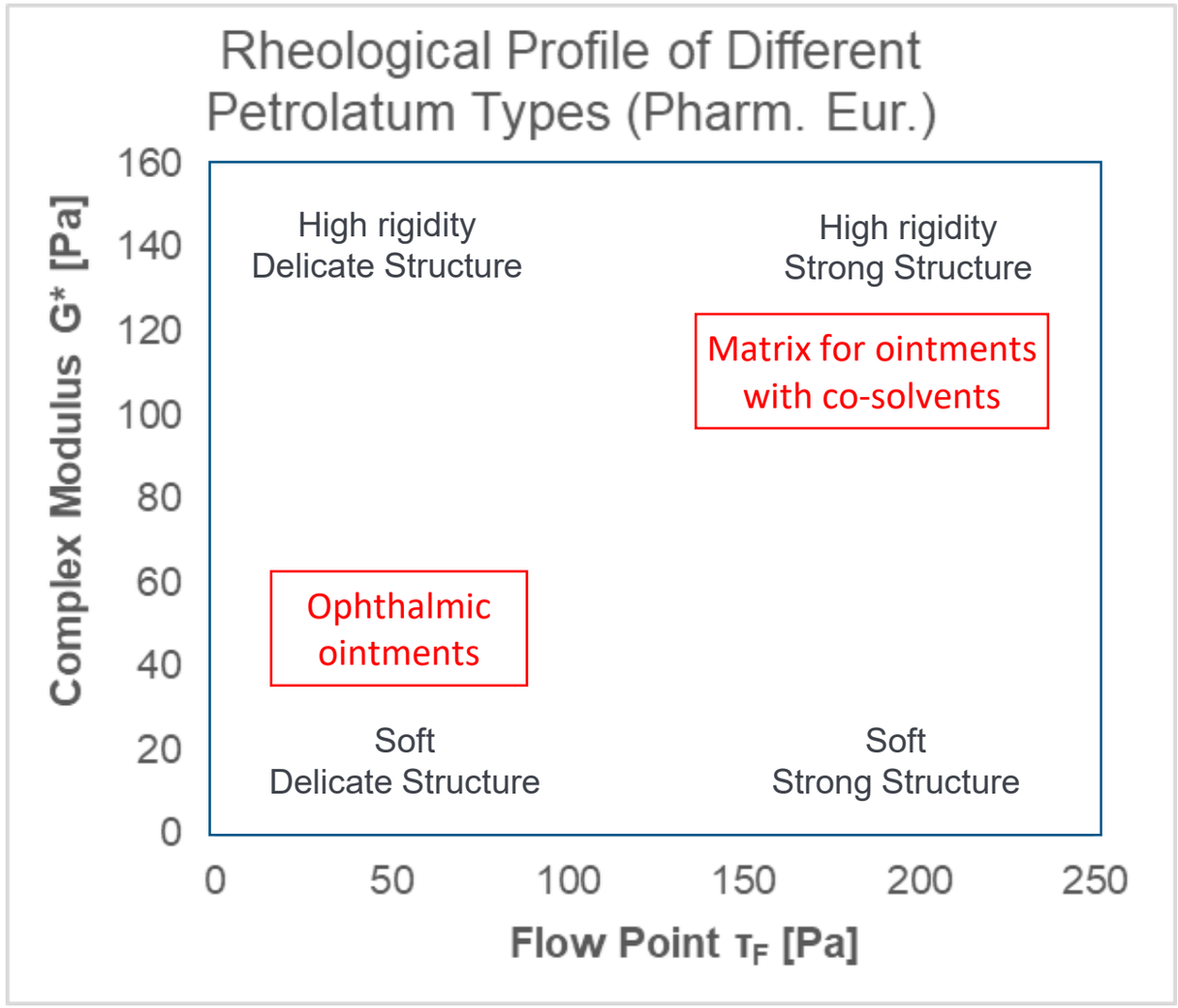
Oscillatory rheology

Rheological Profiling of Excipients :

- Even within the pharmacopoeial specifications, excipients may vary significantly in their rheological properties [1]
- These differences may impact critical formulation attributes and process parameters





[1] Herbig ME, Evers D-H, Gorissen S, Köllmer M. Rational Design of Topical Semi-Solid Dosage Forms-How Far Are We? *Pharmaceutics*. 2023; 15(7):1822

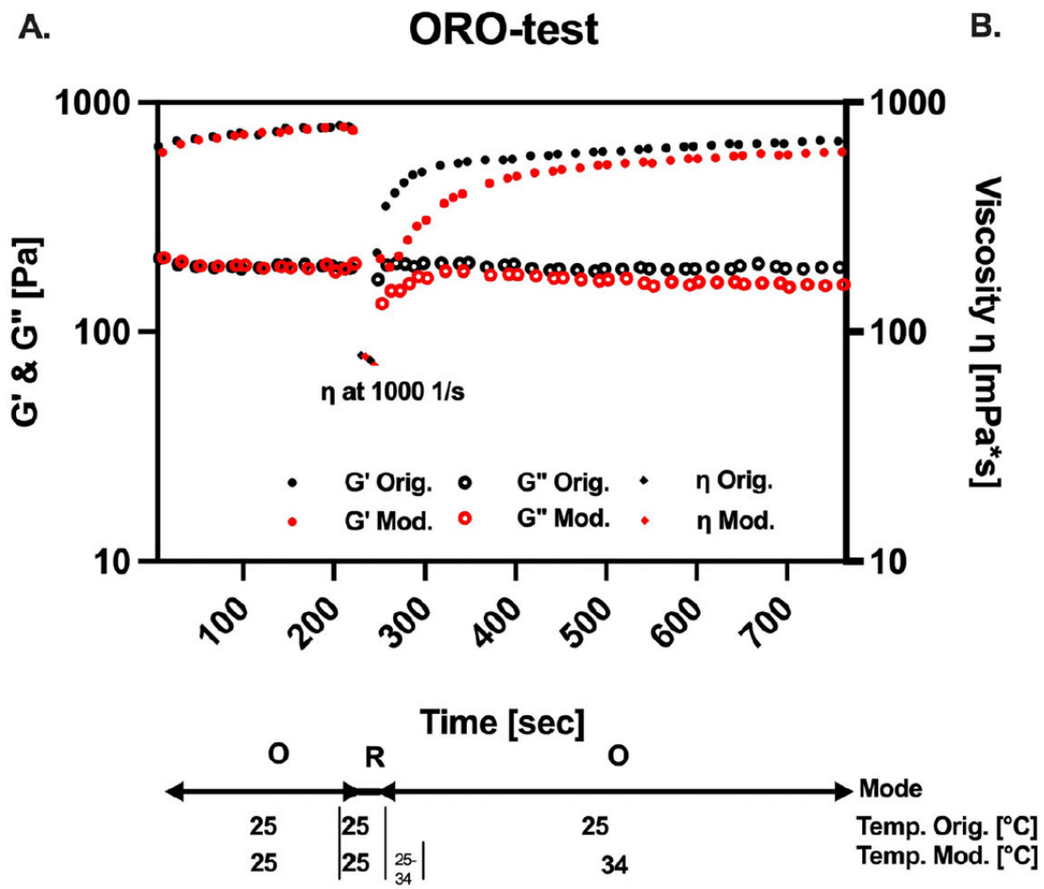
Oscillatory rheology

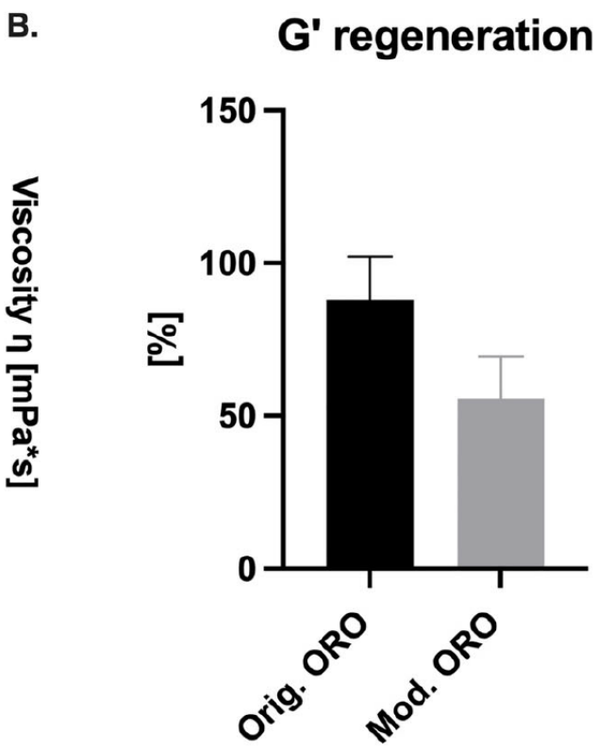
“ORO test” (= oscillation, rotation, oscillation):

Information on how quickly/to what extent the original viscosity recovers after exposure to strong shear forces (e.g. spraying)

Case study[1]: sprayable emulsion:

- During storage in the container, a high zero-shear viscosity is needed to prevent the emulsion from creaming
- Shear-thinning by shaking is required to make the emulsion sprayable
- A quick and strong thixotropic recovery helps to avoid running from nose



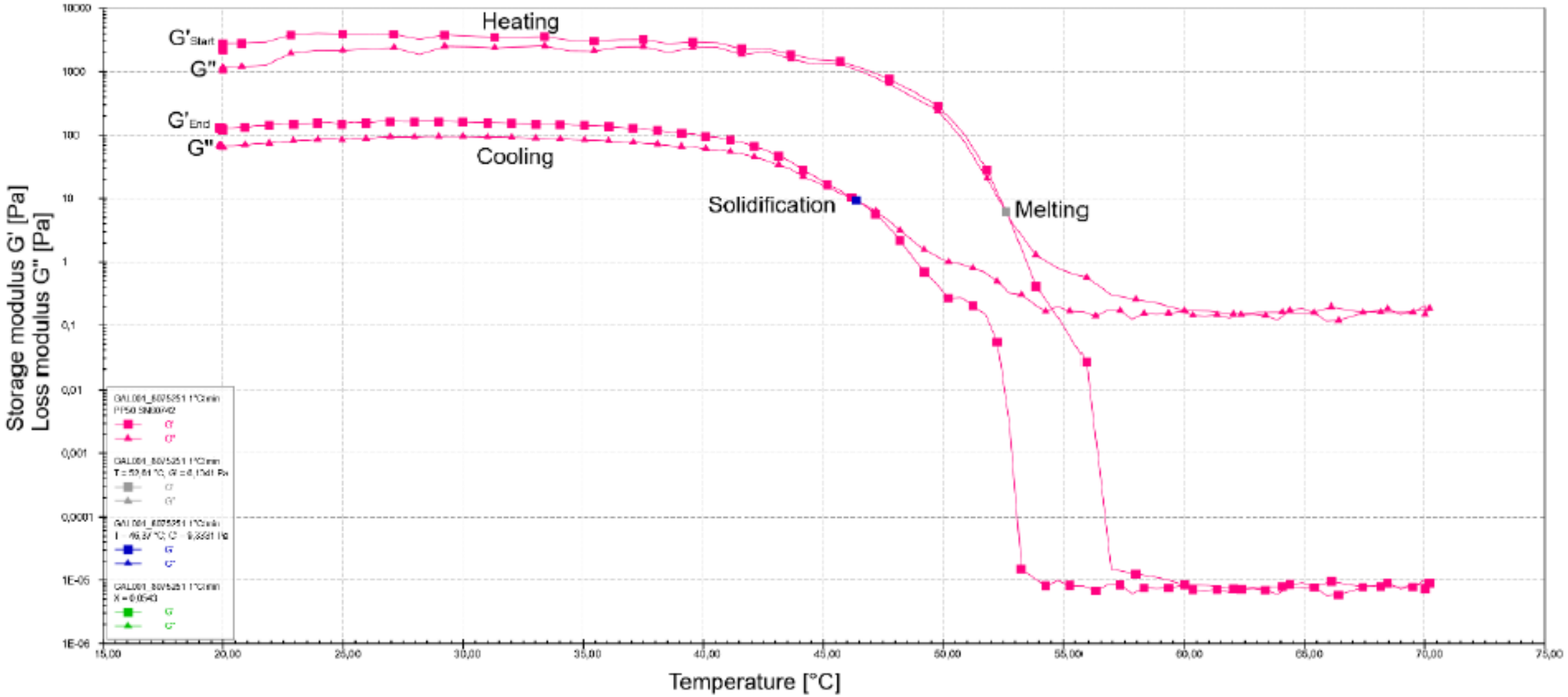


[1] Martin M. Sailer, Melanie Köllmer, Beatrice Masson, Fabio Fais, Ilja P. Hohenfeld, Michael E. Herbig, Assen K. Koitschev & Sven Becker (2023): Nasal residence time and rheological properties of a new bentonite-based thixotropic gel emulsion nasal spray – AM-301, Drug Development and Industrial Pharmacy, DOI: 10.1080/03639045.2023.2183724

Oscillatory rheology

Thermo-rheology (temperature sweep test):

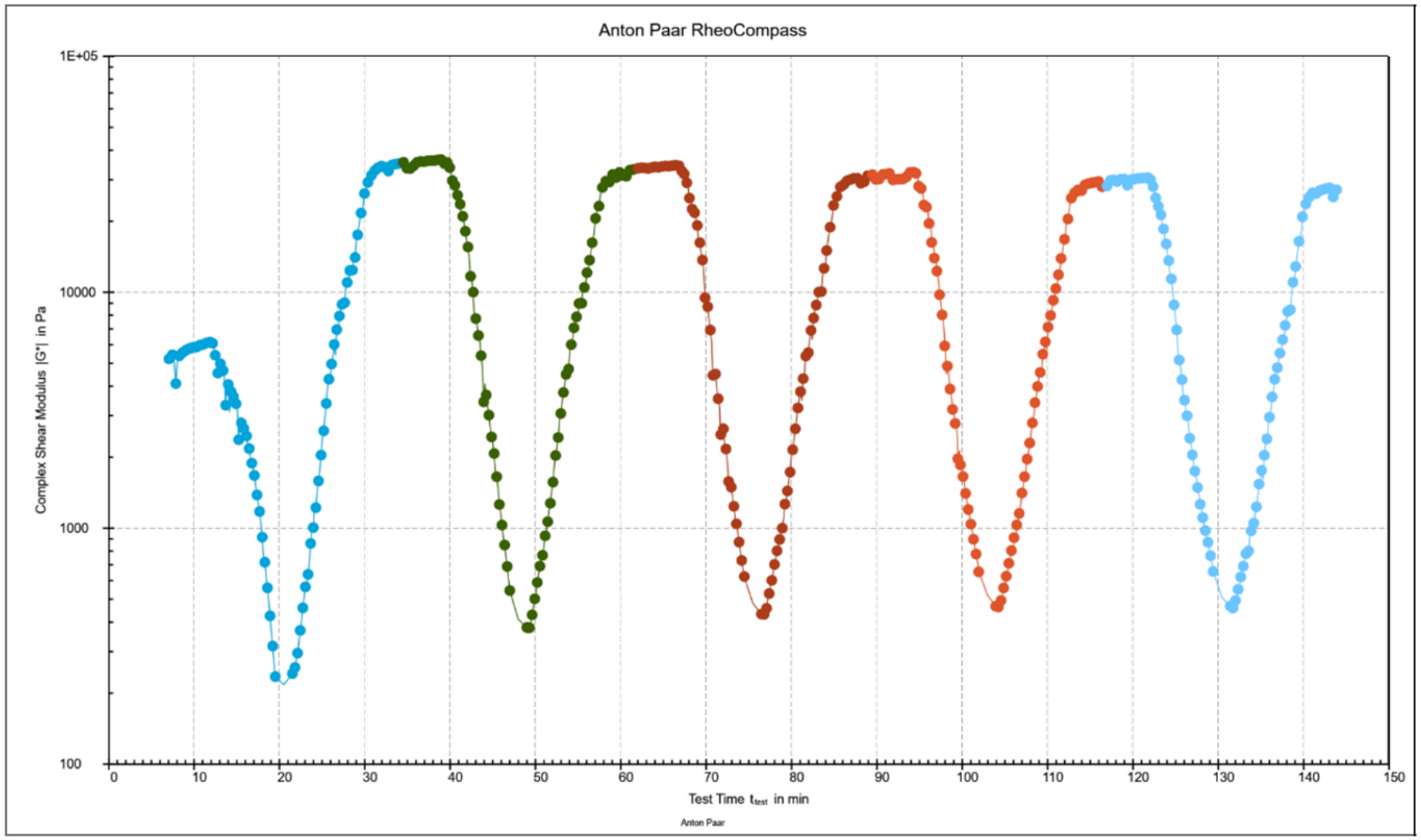
- The change of moduli as a function of temperature is monitored for a formulation or excipient
- It provides important process-relevant information on melting, solidification and structural changes
- It can simulate the cooling phase of a process which is often critical for product quality & stability

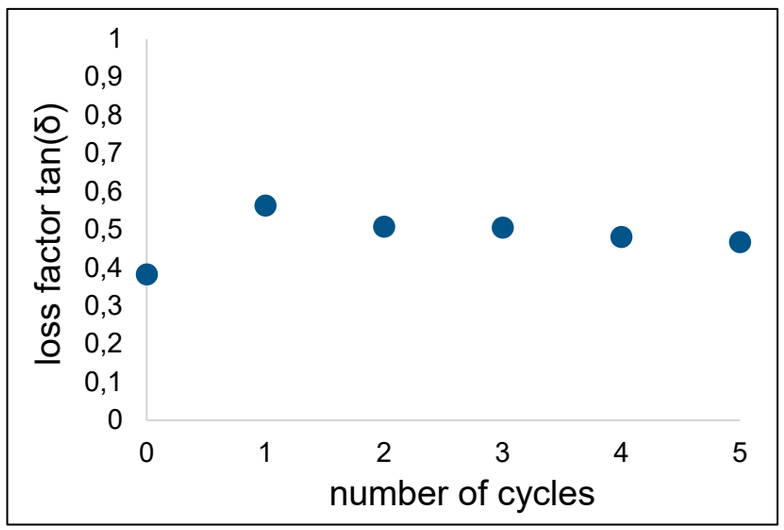


Oscillatory rheology

Temperature cycling (thermal loop test):

- Variation of temperature at constant strain & stress. Several heat-cool cycles
- Information on stability (prediction of long-term physical stability)
    - Good stability if loss factor tanδ (or G’ or G*) remains constant after several cycles





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Rheological equivalence testing according to EMA „Draft guideline on quality and equivalence of topical products”

The EMA “Draft guideline on quality and equivalence of topical products” [1] requests comprehensive rheological testing and statistical evaluation of test vs. reference product.

Example of rheological comparison of an originator and generic of a topical cream [2]:

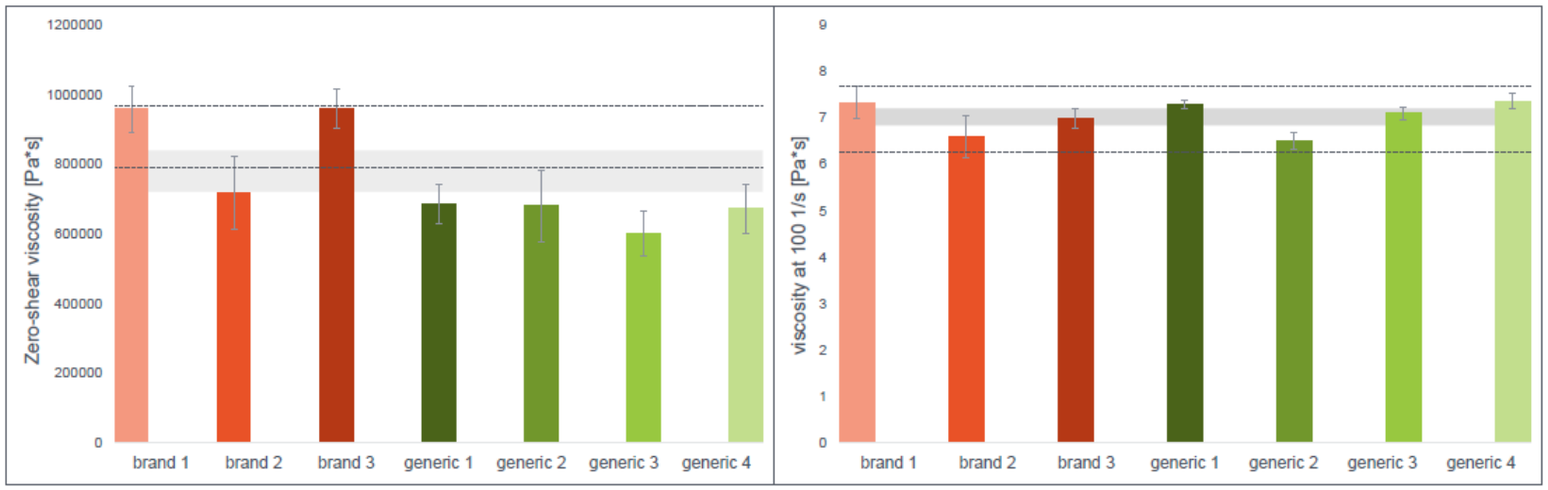

Figure 2. Viscosities at different shear rates

The dashed lines illustrate the +/- 10 % limits and the gray bar represents the 90% confidence interval.

Table 1. Confidence intervals of the observed rheological parameters.

Rheological parameter	Yield strain γ_L	Yield stress τ_y	Flow stress τ_f	Complex modulus |G*|	Flow transition index τ_f/τ_y	Phase angle δ	Zero shear viscosity η_0	Viscosity at 100 1/s η_{100}	Rel. thixotropy area S_R	Recovery after 480 s	*+/- 10 % range*
Confidence interval	0.923	0.778	0.810	0.826	0.923	0.974	0.821	0.981	1.100	0.950	***> 0.9***
	1.080	0.945	0.920	0.905	1.098	1.015	0.955	1.032	1.431	1.077	***< 1.1***
Passes the euqivalence criteria?	Yes	No	No	No	Yes	Yes	No	Yes	No	Yes	-

[1] EMA „Guideline on quality and equivalence of locally applied, locally acting cutaneous products” (EMA/CHMP/QWP/708282/2018 Corr.1*)

[2] Philipp Böhm, Melanie Köllmer, Michael Herbig. Equivalence testing of rheological parameters of generic and branded cream, facing criteria of EMA Draft Guideline 2019. Innovations in Dermatological Sciences Conference. Center for Dermal Research. New Jersey, September 28 th , 2022

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