Accelerating Topical Drug Development Through Initial Excipient Selection

Benjamin GAVINET[1*], Benoît SOUYRI[1], Emilie TONGLET[1], Maïté CAVAILLÈS[1], Alice DANESHVAR[2]

[1] Seppic Research & Innovation, 127 chemin de la Poudrerie 81105 Castres FRANCE
[2] Seppic S.A., 50 boulevard National 92257 La Garenne Colombes FRANCE
[*] Corresponding Author: benjamin.gavinet@airliquide.com

Introduction

Novel topical drug development will require multiple formulation adjustments from the initial formulation studies to the registration phase [1].

Common issues encountered are API chemical instability, API lack of solubility, dosage form instability, optimization of the skin delivery, mitigation of side-effects…

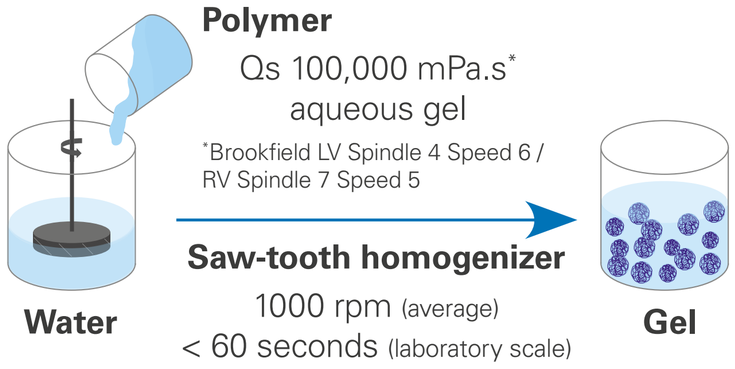
pH adjustment and change of nature or concentration of solvents, penetration enhancers and emollients can be relevant adjustments [2]. However, each adjustment is at risk of disrupting polymeric and surfactant systems, causing further delay in formulation and drug development [3].

There is a need for stabilizing excipients able to provide the same performance independently from formulation changes.

Material & Method

Thickening / Stabilizing Polymer

Acrylamide / Sodium Acryloyldimethyl Taurate Copolymer in inverse emulsion



pH adjustment

Lactic Acid — Qs pH 2 - 4
Triethanolamine — Qs pH 8-10-12
pH/effect response: viscosity and stability (7 days, RT).

Solvent addition

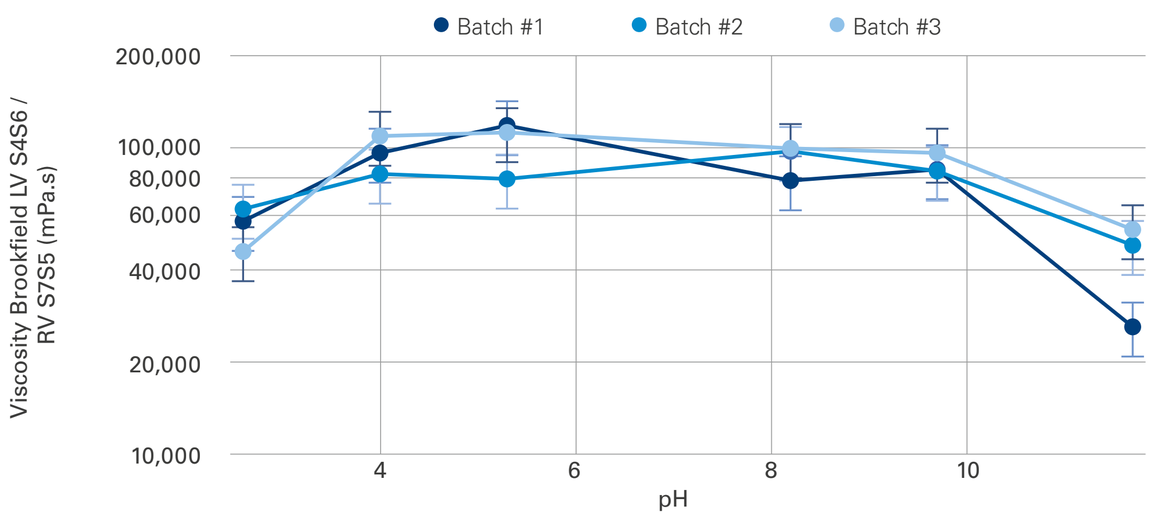
Dose/effect response: viscosity, pH and stability (1 month, RT).

Emollient addition

Dose/effect response: viscosity, pH and stability (1 year, RT and 3 months, 45°C).

Stability to formulation adjustments

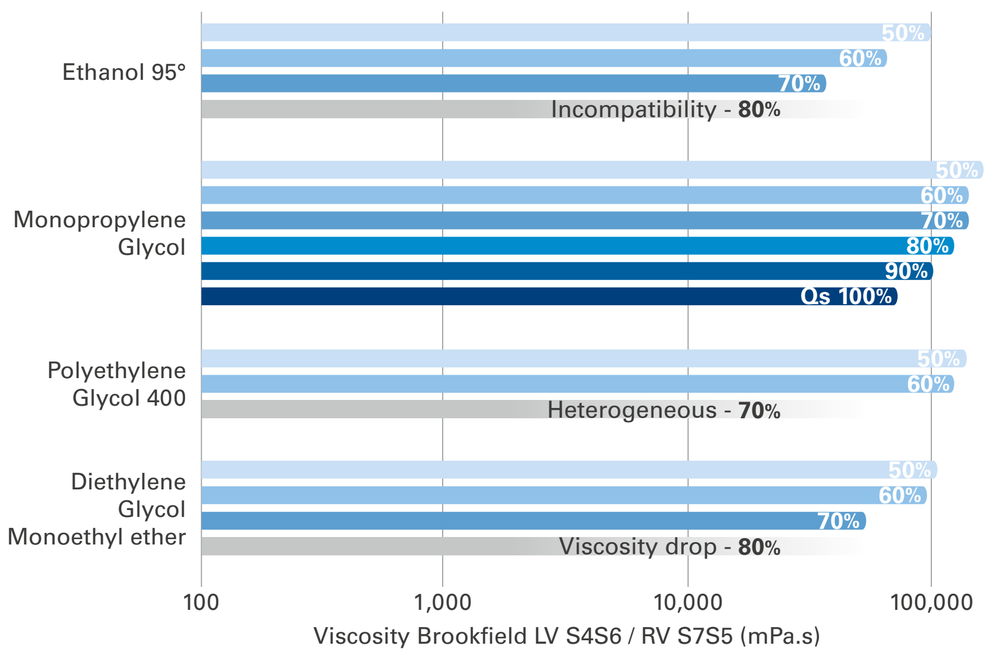
Impact of pH adjustment on the polymer network



☑ From pH 4 to 10, the gels obtained have comparable viscosities with no impact even with pH adjustment. The Acrylamide / Sodium Acryloyldimethyl Taurate Copolymer shows a good batch-to-batch reproducibility.

Extreme acid or basic pH tend to decrease the gels viscosity. An increase of polymer concentration can compensate for this viscosity loss.

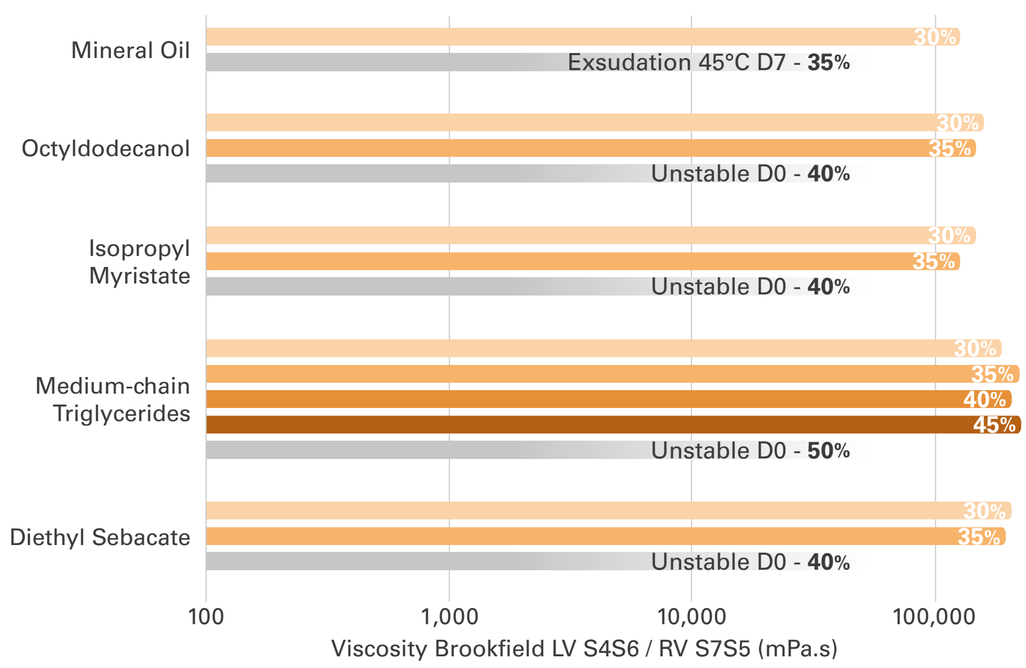
Solvent concentration stabilized



☑ The gels of Acrylamide / Sodium Acryloyldimethyl Taurate Copolymer can stabilize at least 60% of tested solvents with close resulting viscosities.

At higher solvent concentration, Ethanol shows the most viscosity impact, while PEG-400 from 70% concentration causes phase segregation.

Emolient concentration stabilized



☑ Acrylamide / Sodium Acryloyldimethyl Taurate Copolymer gels can stabilize at least 30% of tested emollient with comparable resulting viscosities.

Change of oil nature have limited impact on the dosage form stability, though higher emollient concentrations can be reached with medium-chain triglycerides.

REFERENCES

[1] Brown, M. B., Turner, R., & Lim, S. T. (2011). Topical Product Formulation Development. In Topical and Transdermal Drug Delivery (p. 255-286). John Wiley & Sons, Ltd. https://doi.org/10.1002/9781118140505.ch14

[2] Lamba, S., & Lebwohl, M. (2001). Combination therapy with vitamin D analogues. British Journal of Dermatology, 144(s58), 27-32. https://doi.org/10.1046/j.1365-2133.2001.144s58027.x

[3] Modi, D., Sharma, H., & Campbell, G. (2020). Accelerate development of topical cream drug product using a common platform base formulation. Pharmaceutical Development and Technology, 25(6), 767-778. https://doi.org/10.1080/10837450.2020.1741617

Conclusion

- Acrylamide / Sodium Acryloyldimethyl Taurate Copolymer in inverse emulsion exhibits a strong and reproducible thickening and stabilizing performance over a wide range of pH, nature and concentration of solvents and emollients.
- Significant formulation time gain is expected in drug development, not having to switch or adapt the polymeric and surfactant systems for each formulation adjustment.
- Viscosity loss with extreme pH or high solvent concentration can be compensated by higher polymer dose.

SEPPIC | A company Air Liquide HEALTHCARE