

Contribution of various instrumental methods to transformation/metamorphosis assessment of hydrophilic gels during skin application

Andžela Tošić, Tanja Ilić, Snežana Savić, Ivana Pantelić

University of Belgrade-Faculty of Pharmacy, Department of Pharmaceutical Technology and Cosmetology,

Vojvode Stepe 450, Belgrade, Serbia

Correspondence: andjela.tosic@pharmacy.bg.ac.rs

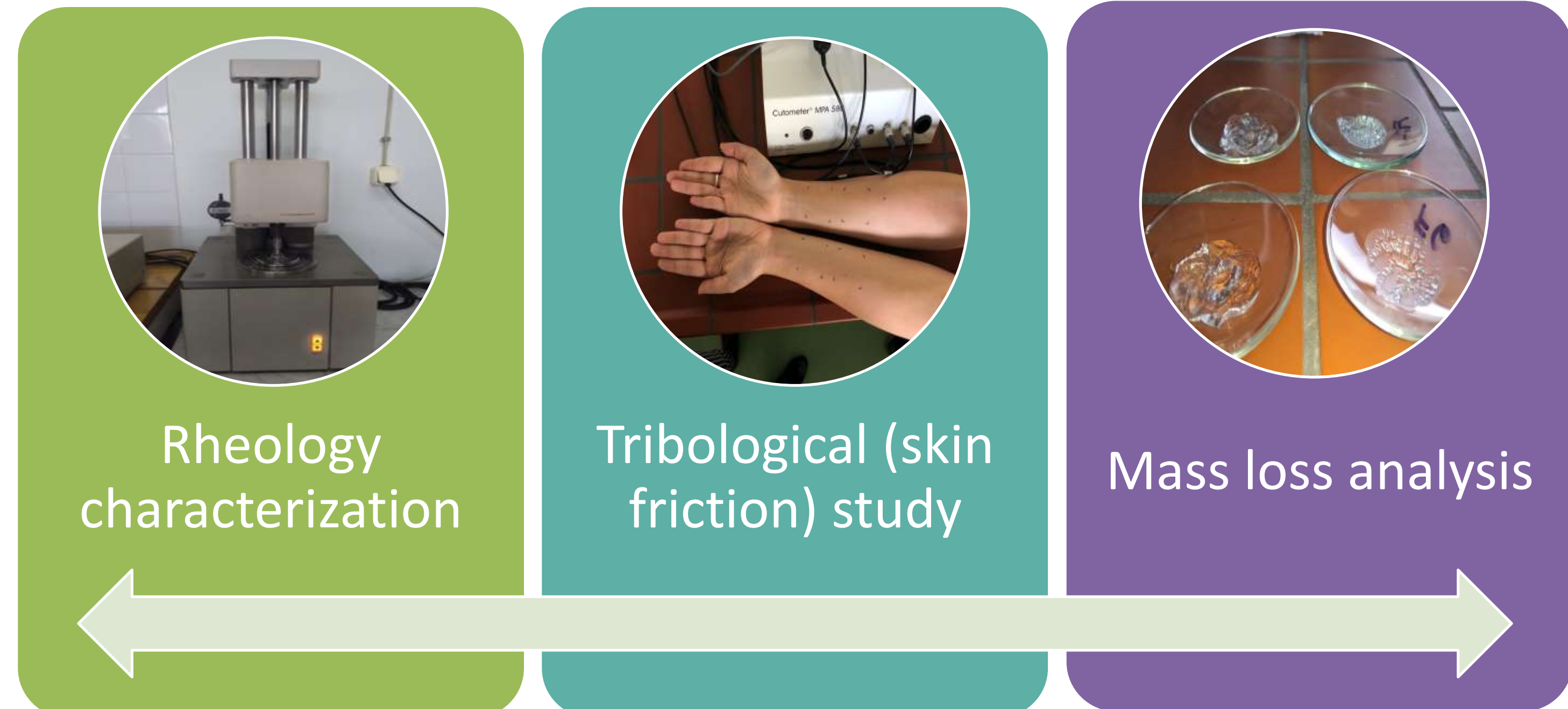
Conclusions

All three methods: rheology characterization, tribology study and mass loss analysis in a certain sense contributed to the examination of the metamorphosis of carbomer gels. Certain time points during mass loss and friction tests correlate well in terms of the exact onset of each transformation phase!

Introduction

The vehicle metamorphosis has a significant impact on the efficacy and quality of topical products (1,2), which has been recognized by the regulatory bodies (Figure 1; ref.3). Scientific community suggests only two methods for metamorphosis assesment, which requires very expensive, sofisticated equipment (4). The aim of this work was to examine the contibution of more accessible methods.

Methods



The concentration of **isopropanol**, as a model easily volatile ingredient, was varied in the range 0-15% (w/w). In the sample F1, the concentration of the gelling agent was also varied, as another parameter of interest for valid transformation analysis.

Results

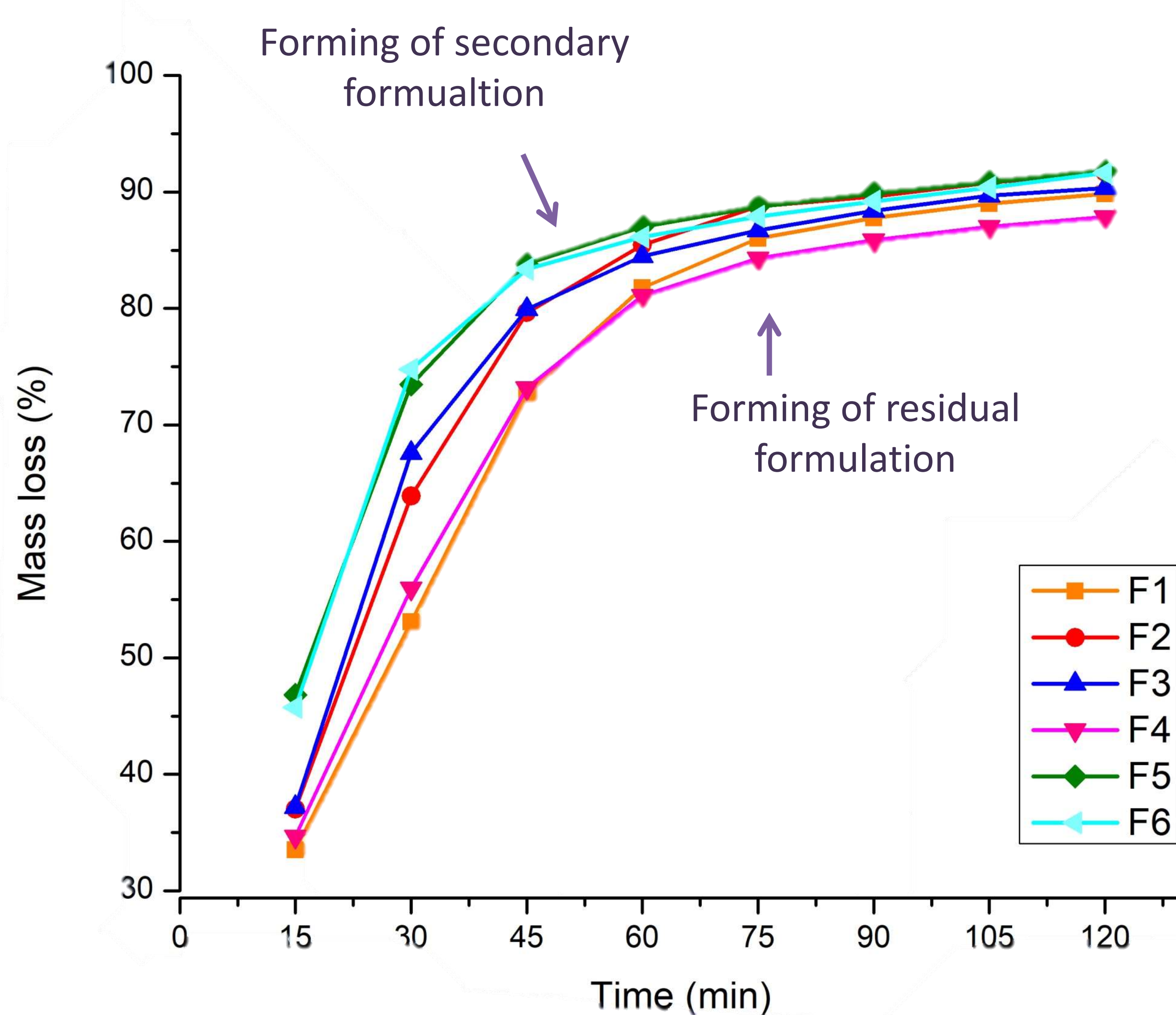


Figure 2 - Mass loss curves

The biggest potential for vehicle metamorphosis assessment has been demonstrated by the mass loss analysis, which enabled spotting the exact time interval of formation secondary and residual formulation. The slope between various time points has perspective to become a quantitative parameter of transformation rate (Figure 2). Tribology study carried out under finite dose conditions gave informative results. The friction value was directly correlated with the amount of volatile ingredients, and show the biggest oscillations in the samples F5-F6 (Figure 3). Irreversible changes which samples go through transformation process can be detected also with rheology characterization, as shown by the descending parts of flow curves for samples F4-F6 (Figure 4).



Figure 1 - Regulatory guideline requesting description of drug product transformation

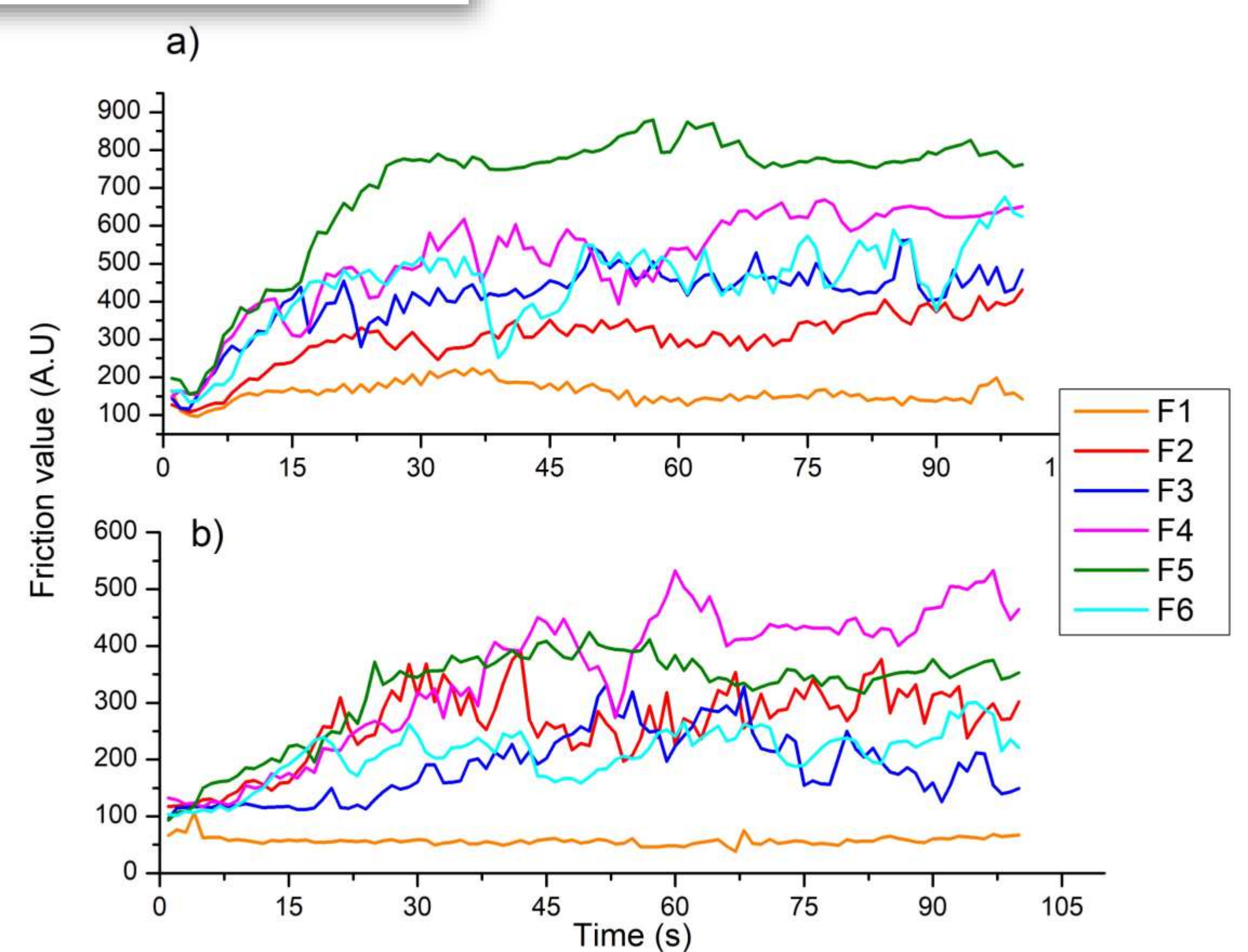


Figure 3 - Friction curves obtained after a) finite dosing; b) infinite dosing conditions

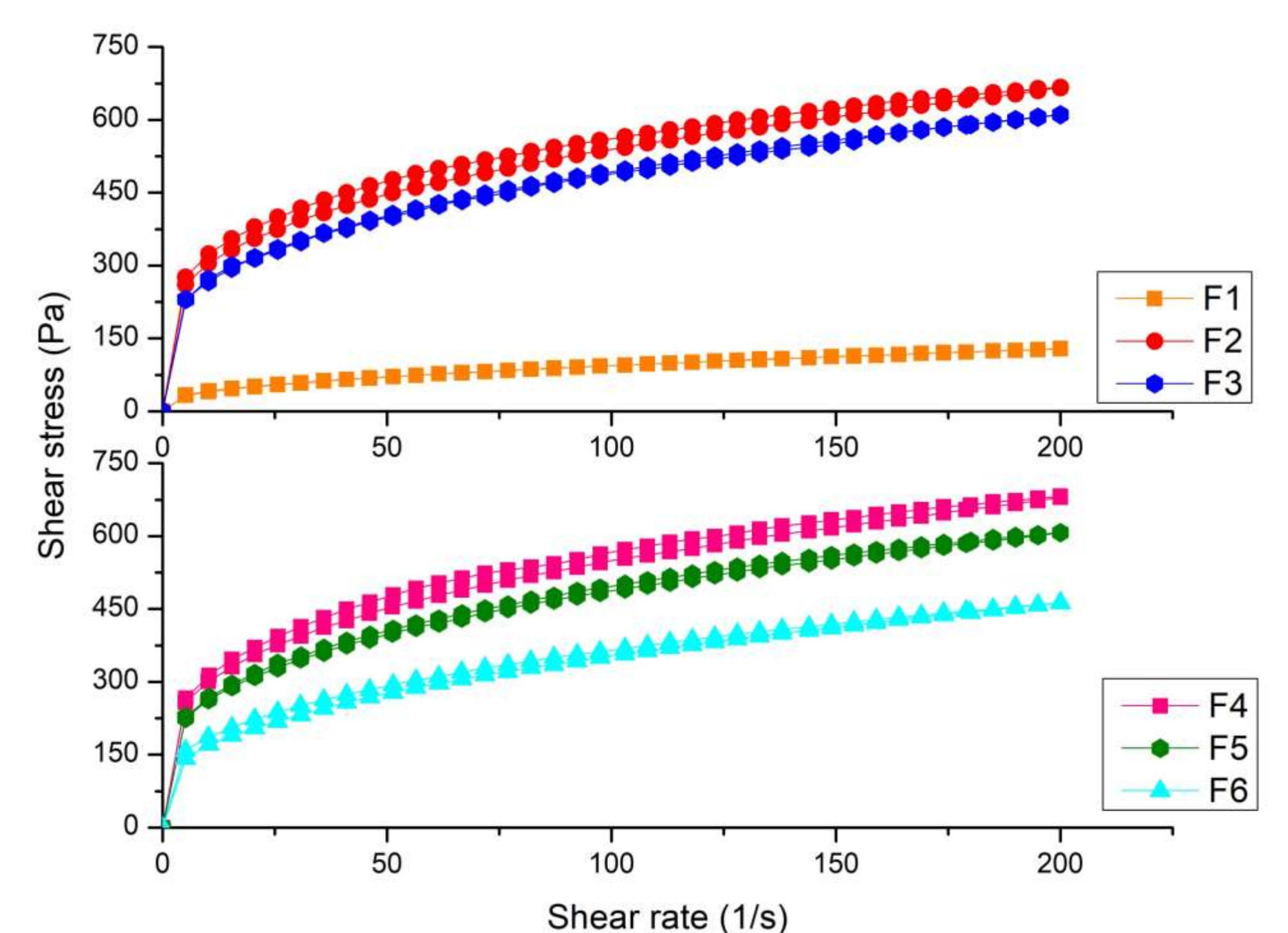


Figure 4 - Flow curves

1. Fantini, A., Padula, C., Nicoli, S., Pescina, S., Santi, P. The role of vehicle metamorphosis on triamcinolone acetonide delivery to the skin from microemulsions. *Int J Pharm.* (2019); 565:33-40.

2. Surber, C., Knie, U. Metamorphosis of Vehicles: Mechanisms and Opportunities. *Dermatology. Curr Probl Dermatol.* Basel: Karger. (2018); 54:152-165.

3. CHMP/QWP/708282/2018. Draft guideline on quality and equivalence of topical products. CHMP, EMA (2018).

4. Goh, C. F., Moffat, J. G., Craig, D. Q. M., Hadgraft, J., Lane, M. E Monitoring drug crystallization in percutaneous penetration using localized nano-thermal analysis and photothermal microspectroscopy. *Mol Pharm.* (2019); 16(1):359-370.

This research was funded by the Ministry of Education, Science and Technological Development, Republic of Serbia through Grant Agreement with University of Belgrade-Faculty of Pharmacy No: 451-03-68/2022-14/200161.