THERMORESPONSIVE SYSTEMS CONTAINING SERICIN FOR TOPICAL DELIVERY: DLS AND RHEOLOGICAL CHARACTERIZATION

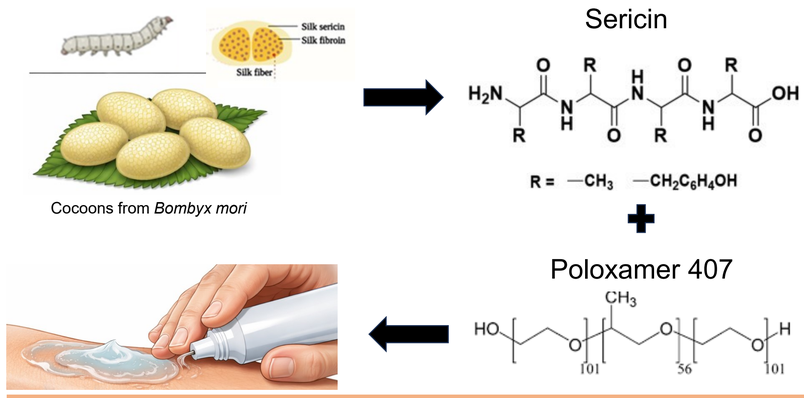
MARCOS L. BRUSCHI[1], MICHAEL T. COOK[2], GABRIELLI FURLAN[1]

[1]*Laboratory of Research and Development of Drug Delivery Systems, Postgraduate Program in Pharmaceutical Sciences, Department of Pharmacy, State University of Maringa, Maringa, PR, Brazil.*

[2]*UCL School of Pharmacy, University College London, 29-39 Brunswick Square, London, WC1N 1AX, England, United Kingdom.*

E-mail: mlbruschi@uem.br

INTRODUCTION



Sericin is a hydrophilic protein extracted from the cocoons of *Bombyx mori*, considered industrial waste. It has received increasing attention for its biological activities (i.e., antioxidant, anti-inflammatory, antimicrobial and healing potential). Sericin is used in biomaterials to enhance skin repair and regeneration [1]. However, its instability in aqueous media limits pharmaceutical use. The association of sericin with poloxamer 407 (P407) may be an innovative and efficient strategy for the development of topical formulations with healing action, aiming to obtain functional and stable systems capable of gelling at body temperature. The aim of this study was to prepare and perform the size and rheological analyses of systems composed of sericin and P407 aiming the topical administration.

MATERIALS AND METHODS

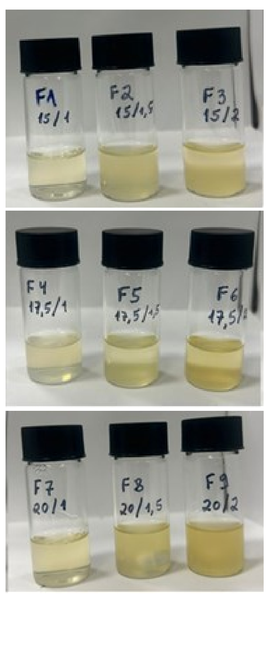
Formulations were prepared using a 3^2 factorial design (Table 1; Figure 1).

Table 1 - Matrix of factorial design 3^2 for systems composed of poloxamer 407 (P407) and sericin.

Independent variables	Levels		
	Low	Central	High
	(-1)	(0)	(+1)
X_1 = P407 (%, w/w)	15	17.5	20
X_2 = Sericin (%, w/w)	1.0	1.5	2.0

Standard run (Formulations)	X_1	X_2
F1	-1	-1
F2	-1	0
F3	-1	+1
F4	0	-1
F5	0	0
F6	0	+1
F7	+1	-1
F8	+1	0
F9	+1	+1

Figure 1 – Formulations.



✓ **Preliminary physicochemical stability** of systems was visually evaluated after preparation.

Zetasizer nano ZS (Malvern)

✓ **Dynamic light scattering (DLS) at 34 °C**:
- Micelle size;
- Polydispersity index (PDI);
- Zeta potential.

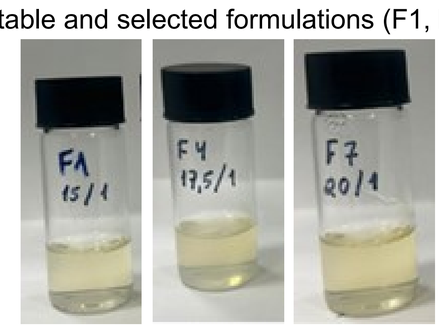
✓ **Rheology**:

Temperature sweep was carried out from 5 to 60 °C, at a frequency of 1.0 Hz and a heating rate of 10 °C/min, under a fixed shear stress (1 Pa), using a rheometer HR20 (Waters Instrument®), with cone and plate geometry. The sol-gel transition temperature ($T_{sol/gel}$) was determined as the point where the elastic modulus (G') was halfway between the values for the solution state and for the gel state with increasing temperature, followed by a significant increase in dynamic viscosity (η') [2].

RESULTS

Some systems showed instability after preparation with the visualization of sediments after 24 h of storage. Only formulations F1, F4 and F7 remained stable, both containing the lowest concentration of sericin (1%, w/w) and 15.0, 17.5 and 20 % of P407, respectively. These systems were used for further analyses.

Figure 2. Stable and selected formulations (F1, F4 and F7).



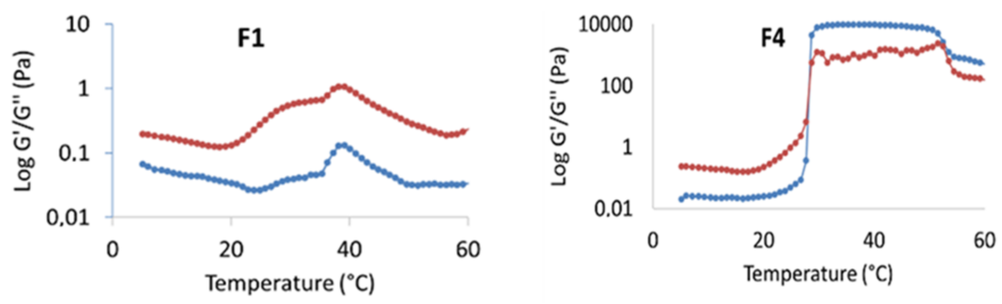
The DLS analysis showed that F4 and F7 both presented similar values for the analyzed parameters (Table 1), being within the expected range for P407 micelles, while F1 displayed larger size and PDI. The zeta is an indicator of electromagnetic stability: the lower the value in modulus, the greater the aggregation capacity of the systems, all systems presented low values for this parameter, which is expected for systems containing P407 (non-ionic polymer). F4 and F7 showed higher zeta potential, demonstrating greater repulsive capacity between the particles, while F1 showed a lower value indicating system instability.

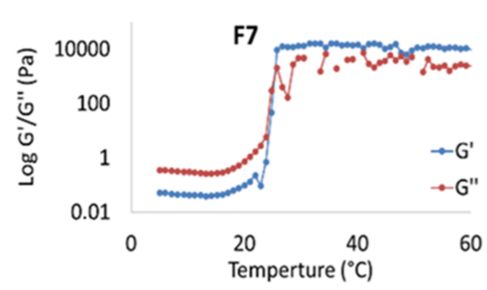
Table 1. Hydrodynamic diameter (Dh), polydispersity index (PDI) and zeta potential of systems at 34 °C

Systems	Dh (nm)	PDI	Zeta (mV)
F1	37.5 ± 0.9	0.58 ± 0.01	-3.48 ± 0.04
F4	27.2 ± 1.0	0.33 ± 0.01	-7.55 ± 0.24
F7	27.0 ± 0.1	0.35 ± 0.00	-6.46 ± 0.19

The $T_{sol/gel}$ was 28.17 ± 0.58 °C for F4 and 24.82 ± 0.70 °C for F7, the formulation with the average concentration of P407 (17.5%) was able to gel close to body temperature, being below the $T_{sol/gel}$ found in the literature for systems at this concentration (Figure 3).

Figure 3. Temperature sweep of selected formulations (F1, F4 and F7).





F1 did not present $T_{sol/gel}$, probably because it uses a P407 concentration below the minimum transition concentration (Figure 3).

CONCLUSION

Although F4 and F7 showed no major differences in the DLS analysis, the $T_{sol/gel}$ results indicated that F4 is the most promising formulation for topical application. Its thermoresponsive behavior makes it suitable for topical delivery, although additional analyses are required to better characterize the system's structure.

REFERENCES

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