Macedonian Pharmaceutical Bulletin, 72 (Suppl 1) 43 - 44 (2026)
Online ISSN: 1857-8969
DOI: 10.33320/maced.pharm.bull.2026.72.03.019
Short communication

Optimization of hydrogel inks for semi-solid extrusion 3D printing

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Introduction

Three-dimensional (3D) printing enables fabrication of personalized dosage forms with complex geometries, tailored drug release, and the ability to combine incompatible active pharmaceutical ingredients within a single dosage form, reducing polypharmacy burden and improving patient adherence (Goole and Amighi, 2016). Rheological properties of pharmaceutical inks are critical for print quality, as the balance between elastic and viscous forces directs filament formation, while rapid structural recovery after extrusion ensures layer integrity (Barrulas et al., 2023). The aim of this study was to evaluate the effect of Poloxamer P407 concentration on the rheological behaviour of cefixime-loaded hydrogels and to correlate these properties with filament formation and the quality of 3D printed tablets.

Materials and methods

Materials

Poloxamer P407 (BASF, Germany), microcrystalline cellulose Avicel PH-102 (FMC BioPolymer, USA), and cefixime (kindly donated by Alkaloid AD, North Macedonia) were used for the preparation of the hydrogel formulations.

Preparation of hydrogels

Three P407 based hydrogel formulations containing cefixime as a model drug were prepared using the cold method. Each formulation contained 2% Avicel PH-102 and 50% cefixime, with P407 concentrations of 12.5% (F1), 17.5% (F2), and 22.5% (F3). The P407 and Avicel were dispersed in cold distilled water under continuous stirring and refrigerated overnight at 4°C to allow complete hydration and gel formation, after which cefixime was incorporated into the hydrogel base and mixed until homogeneous dispersion was achieved.

Rheological characterization

Rheological behaviour was analyzed using a modular compact rheometer (MCR 92, Anton Paar, Austria) equipped with a CP50-1 cone geometry (gap 0.104 mm) and Peltier temperature control at 25 ± 0.1°C. Two tests were performed: (i) amplitude sweep (angular frequency 10 rad s^{-1}, shear strain 0.1–100%, 31 data points over 500 s) to measure storage modulus (G′), loss modulus (G″), loss factor (tan δ), complex viscosity (η*), shear stress, and torque (Dutta et al., 2021); and (ii) thixotropy test

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comprising three consecutive intervals: a pre-shear oscillatory interval, a high-shear flow interval (500 s^{-1}, 60 s), and a recovery oscillatory interval to assess structural recovery after deformation.

Filament formation and printing 3D tablets

Hydrogels were loaded into 3 mL pneumatic cartridges and extruded through a 22G nozzle on a BioX 3D bioprinter (Cellink, Sweden). Each formulation was extruded for 3 seconds, the filaments were photographed and their morphology was evaluated. Subsequently, cylindrical tablets (13 × 7 mm) were printed for each formulation and assessed under stereomicroscope (ZEISS Stemi 305) for clearly defined interlayer boundaries and distinct separation between adjacent layers (O'Connell, et al., 2020).

Results and discussion

Amplitude sweep analysis demonstrated a clear concentration-dependent effect of P407 on the viscoelastic properties of the formulations. At low strain, all three formulations exhibited a linear viscoelastic region where $G' > G''$, confirming gel-like behaviour. F1 showed the lowest storage modulus (G' ~10000 Pa) and complex viscosity (η^* ~2×10^6 mPa·s), indicating a weak gel network. F2 exhibited higher values (G' ~29000 Pa, η^* ~6×10^6 mPa·s), while F3 had the highest G' (~29000 Pa) and η^* (~4×10^6 mPa·s), reflecting the most structured system. The crossover point ($G' = G''$, $\tan \delta = 1$) shifted with polymer content, with F1 showing $\tan \delta$ ~1.69 at the first measurement point, indicating proximity to the sol–gel transition.

Thixotropy testing showed the weakest recovery for F1 (G' ~9000 Pa), intermediate recovery for F2 (~60000 Pa), and the strongest for F3 (>80000 Pa), confirming superior structural rebuilding at higher polymer concentration.

Printability assessment confirmed the rheological implications. F1 produced only a drop at the nozzle, and the tablets exhibited layer fusion with no distinct structure, consistent with its predominantly viscous, low-modulus rheology. F2 extruded a nearly straight but slightly curved filament, while printed tablets showed slight layer fusion, indicating insufficient elastic recovery between layers. F3 produced a perfectly straight filament and printed tablets with well-defined layer separation and clear boundaries.

These findings establish that G', η^*, and structural recovery rate are the key rheological determinants of SSE printability in P407 based hydrogels, and that a minimum P407 concentration of approximately 17.5-22.5% is required to achieve acceptable filament formation and adequate 3D printed tablets.

Conclusion

P407 concentration critically governs both the rheological profile and 3D printing performance of cefixime loaded hydrogels. Increasing polymer concentration enhanced gel strength, viscoelastic recovery, and printability. F3 demonstrated optimal printability with straight filaments and well-shaped tablets with defined boundaries, while F1 failed to form viable filaments. These results underline the necessity of rheological pre-screening as a rational tool for ink formulation development in pharmaceutical SSE 3D printing.

Acknowledgment

The authors would like to acknowledge the support of the 3DOSE-IT project (No. 15-6171/41, dated 07.08.2025), funded by the Ministry of Education and Science of North Macedonia. Additionally, the authors would like to express their gratitude to Alkaloid AD Skopje, North Macedonia, for their generous donation of cefixime.

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