Nano vs. Micro: Impact of Drug Particle Size in Extrusion-based 3D Printing on Tablet Performance

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INTRODUCTION

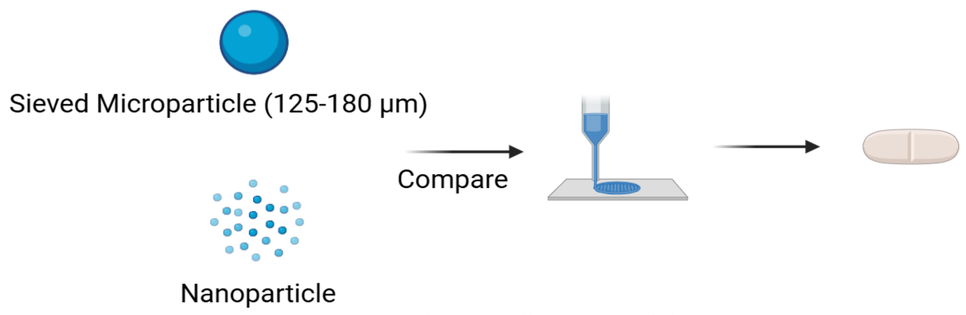

Figure 1. Schematic illustration of the project.

Semi-solid extrusion (SSE) 3D printing has emerged as a promising technique for the fabrication of personalized pharmaceutical dosage forms [1]. Despite its potential, the influence of ink properties, particularly the incorporation of solid drug particles, on the quality of printed tablets has not been thoroughly studied. This research aims to evaluate the effect of solid drug particle size within the ink formulations on the printing fidelity and structural integrity of porous 3D-printed tablets (Fig. 1).

METHOD

Preparation

- Sorafenib tosylate nanoparticles (ST-NP) were prepared via the nanoprecipitation method.
- An extrusion-based 3D printer was used to fabricate HPMC-based blank and sorafenib-loaded tablets.

Characterization

- Morphology: Dynamic Light Scattering (DLS), Scanning Electron Microscope (SEM), Transmission Electron Microscope (TEM).
- Solid-state properties: Fourier Transform Infrared spectroscopy (FTIR) and Powder X-ray Diffraction (PXRD).
- Dimensional fidelity (Dimensions of dried printed / CAD model) and Rheology studies.

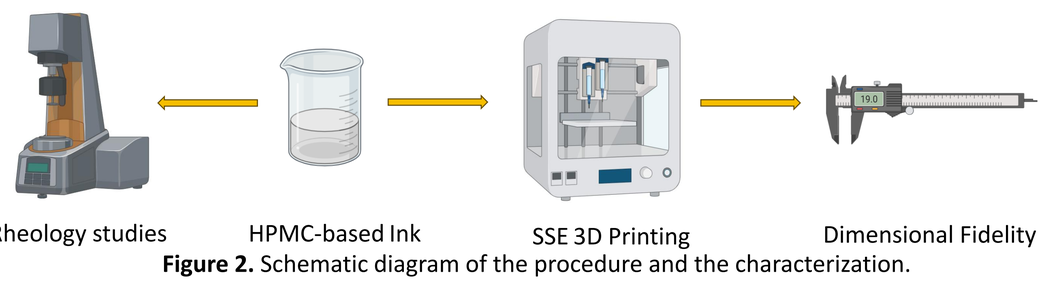

Figure 2. Schematic diagram of the procedure and the characterization.

RESULTS

1. Preparation of Sorafenib Tosylate Nanoparticles (ST-NP)

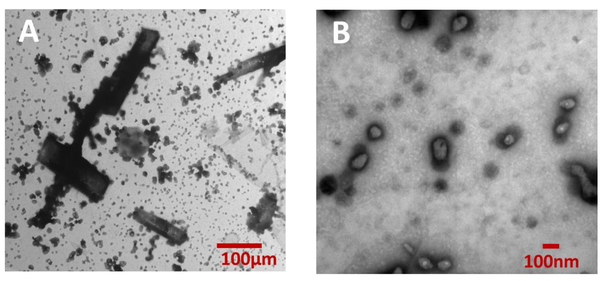

Figure 3. TEM image of (A) sieved raw drug (125-180 μm) (B) ST nanoparticles prepared via nanoprecipitation (214±4 nm with a PDI value of 0.219±0.02).

- Upon optimizing the antisolvent-to-solvent volume ratio and the drug-to-additive weight ratio, ST-NPs with an average size of 214 ± 4 nm and a Polydispersity Index (PDI) of 0.219 ± 0.02 were obtained (Fig. 3).

2. Optimization of Ink Formulation

- By optimizing the printing shape, internal pattern, infill density, and the concentrations of Hydroxypropyl methylcellulose (HPMC), Polyvinylpyrrolidone (PVP K30), and Croscarmellose sodium (CMS)—based on dimensional fidelity including thickness, length, and width—the optimal formulation was identified, as shown in the table below (Table 1).

Table 1. Composition of the optimal ink.

Composition	HPMC w/v (%)	PVP K30 w/v (%)	CMS w/v (%)
Optimal ink	1.2	18	16

3. Nano vs. Micro—Dimensional Fidelity and Morphology

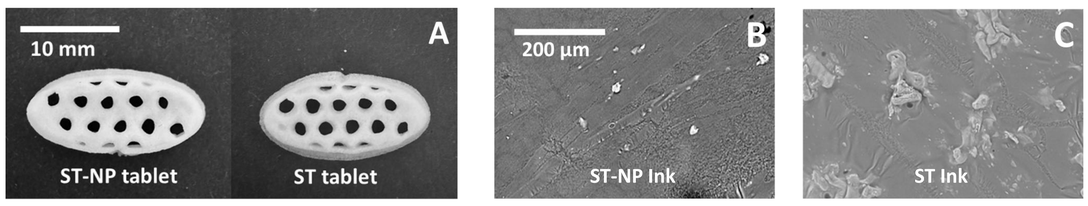

Figure 4. (A) image of tablets printed with ST-NP and sieved ST. (B) SEM micrograph illustrating the surface morphology of the ST-NP ink and (C) sieved ST ink.

The nanoparticle-based ink displayed reduced surface roughness compared to the sieved powder formulation, attributable to the finer particle size and improved dispersion (Fig. 4).

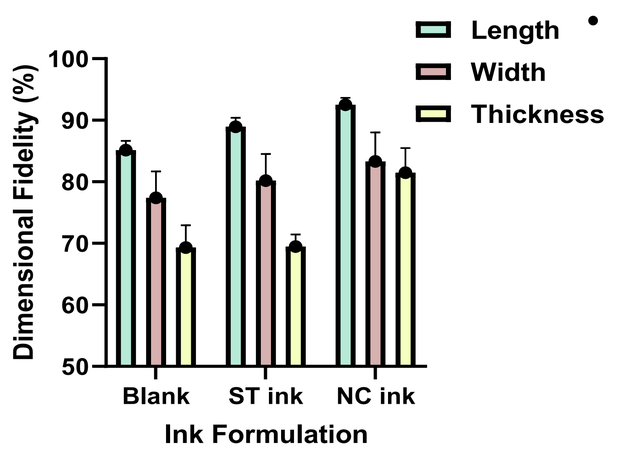

Figure 5. Dimensional fidelity of blank ink, ST ink and ST-NP ink. (One-way ANOVA, $p<0.05$)

- Tablets with ST-NPs showed improved dimensional fidelity due to better particle dispersion, higher packing density, and more efficient solvent evaporation. In contrast, sieved ST and blank tablets exhibited poorer fidelity, highlighting the importance of particle size and solid content in 3D printing quality (Fig. 5)

4. Solid-state Properties

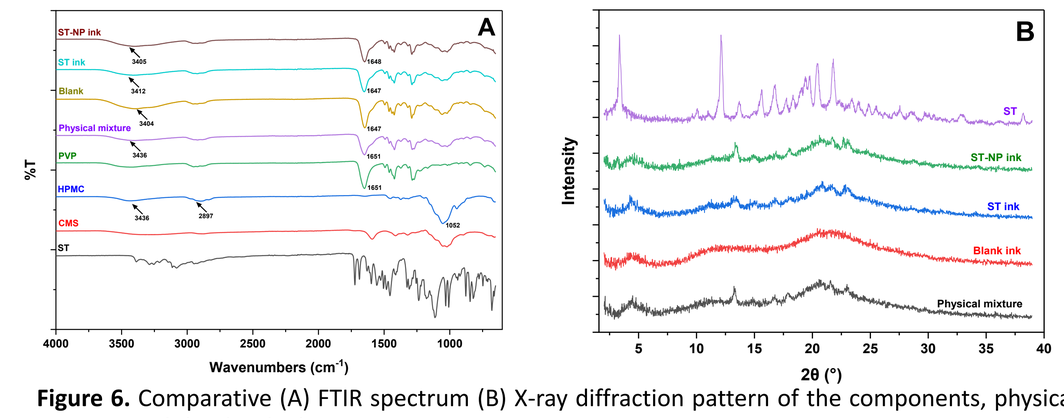

Figure 6. Comparative (A) FTIR spectrum (B) X-ray diffraction pattern of the components, physical mixture, and the dried inks.

- FTIR analysis showed shifts in both -OH and C=O stretching peaks, indicating hydrogen bonding between HPMC and PVP K30. PXRD data revealed residual crystalline peaks of the drug, suggesting partial crystallinity is retained within the amorphous polymer matrix (Fig. 6).

5. Rheological Studies

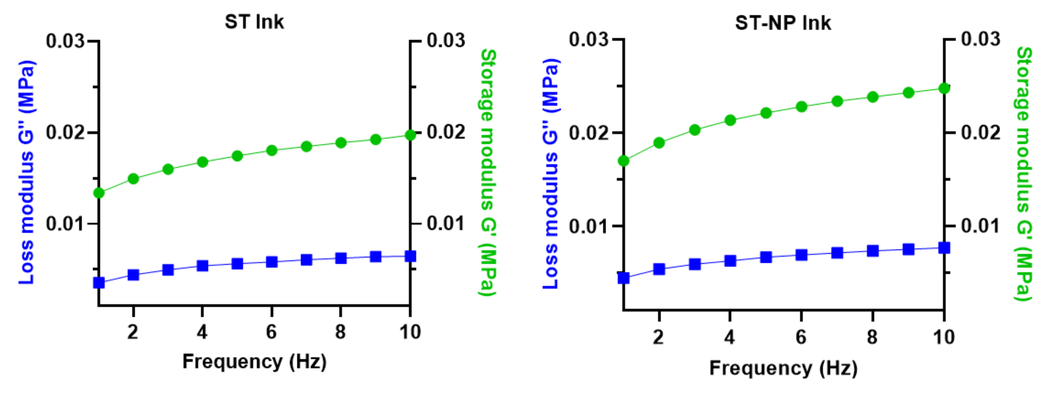

Figure 7. Oscillatory rheology curve of (A) ST ink; (B) ST-NP ink.

- The ST-NP ink exhibited the highest storage modulus (G’), loss modulus (G’’), and viscosity—reaching 3745 Pa·s at a shear rate of 0.01 s^{-1}—attributable to the small size and high surface area of the nanocrystals. This enhanced particle–polymer interaction and network formation, leading to improved elasticity, flow resistance, and dimensional fidelity (Fig. 7).

CONCLUSION

Nanoparticle-loaded ink exhibited improved viscosity, viscoelastic properties and higher quality of prints compared to the sieved-raw-drug-loaded ink. These findings suggest that reducing particle size within inks can enhance the printing quality of SSE 3D printing technology.

References

[1] https://doi.org/10.1016/j.ijpharm.2024.123902

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