

Understanding the Role of Particle Size of Poloxamer P407 on Properties of Tablet Prepared by Direct Compression Process

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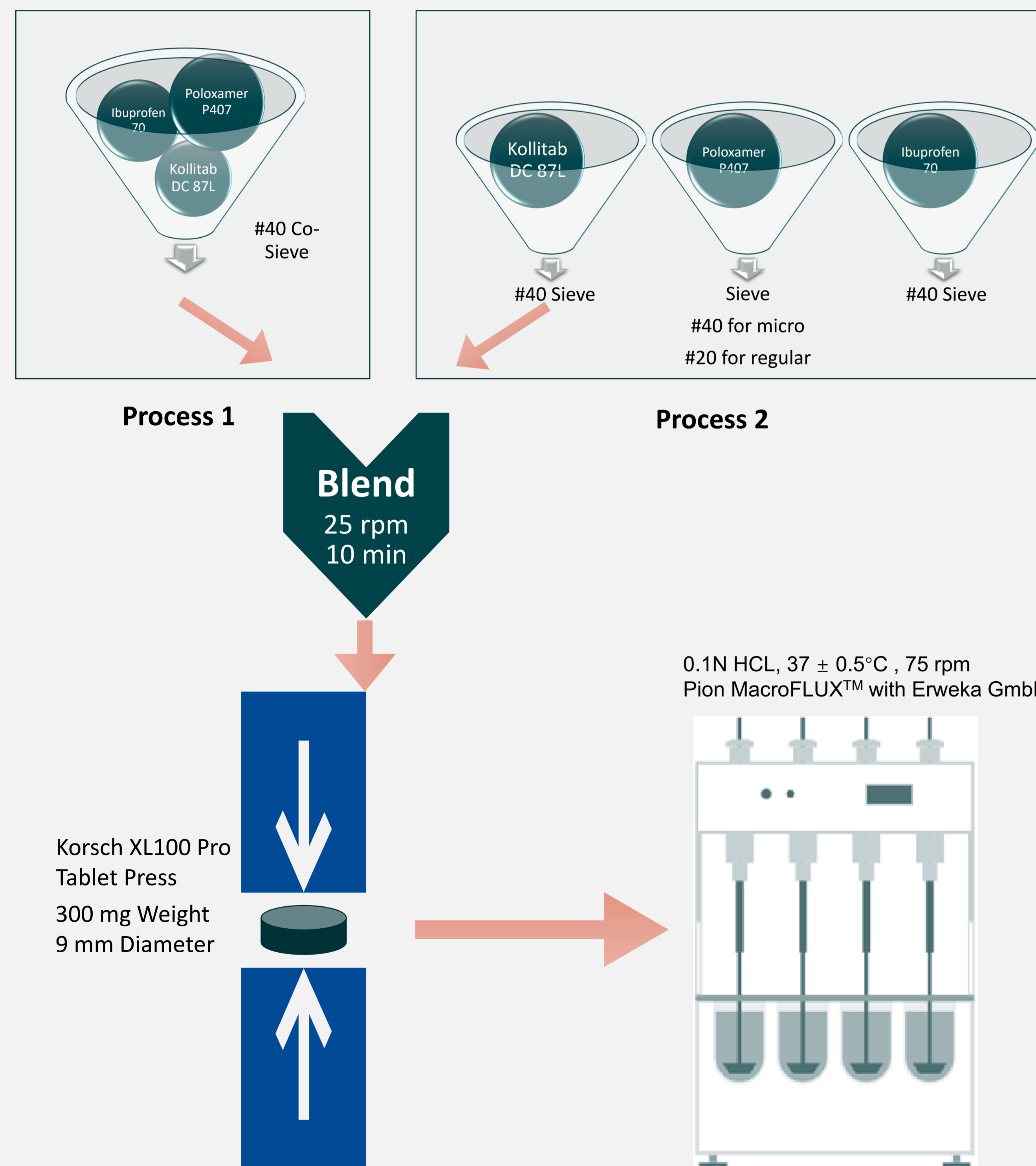


PURPOSE

Poloxamer P407 has been used as a surfactant to increase the solubility of poorly soluble active pharmaceutical ingredients (API) because of the micelle formation property in the aqueous environment at concentration above critical micelle concentrations (CMC).

This study aims to investigate the effect of particle size of Poloxamer P407 on tablet properties and dissolution of a model drug (ibuprofen, IBU), using the "all-in-one" co-processed direct compression excipient (Kollitab™ DC 87L).

METHOD(S)



RESULT(S)

A blend of 15% IBU 70 (mean particle size, D50 of ~70 μm) with 5% poloxamer P407 and 80% of the co-processed excipient shows good/ passable flowability based on HR and CI (Table 1)¹. IBU/regular P407 (mean particle size, D50 of ~500 μm) blend has better flowability compared to the blend with P407 micro (mean particle size, D50 of ~50 μm). The blend with better flowability had good tabletability but demonstrated segregation problems (Figure 1, red circled). Meanwhile, tablet picking was observed when simple blending (non co-sieving) was used during compression (Figure 2 A). Tablets prepared by mixing of the drug and excipients followed by sieving procedure did not show any picking issue during the tablet manufacturing over the entire compression cycle (Figure 2 B). The thermogram of blends tested by differential scanning calorimetry confirmed no chemical or eutectic mixture forming between IBU-poloxamer (Figure 3). Therefore, uniform distribution of P407 micro particle in IBU and the co-processed excipient blend was achieved by mixing/ sieving of the excipient followed by blending to avoid tablet picking issue.

Table 1 Tapped density testing results of IBU/poloxamer P407/ the co-processed excipient blend

Sample	Type of poloxamer P407	Sieving method	Hausner ratio (HR)	Carr's index (CI)	Flow properties
A*	No P407	Sieve separately	1.19	15.8 ± 0.60	Good/fair, no segregation observed
B*	P407 (regular)	Sieve separately	1.20	16.5 ± 0.00	Fair, but segregation observed
C*	P407 (micro)	Sieve separately	1.24	19.6 ± 0.60	Fair, no segregation observed
D*	P407 (micro)	Co-sieved	1.25	19.7 ± 0.60	Fair, no segregation observed

*Note:
A: 15% Ibuprofen 70 + 85% the co-processed excipient;
B: 15% Ibuprofen 70 + 5% poloxamer P407 (regular) + 80% the co-processed excipient;
C: 15% Ibuprofen 70 + 5% poloxamer P407 (micro) + 80% the co-processed excipient ;
D: 15% Ibuprofen 70 + 5% poloxamer P407 (micro) + 80% the co-processed excipient, co-processed sieving.

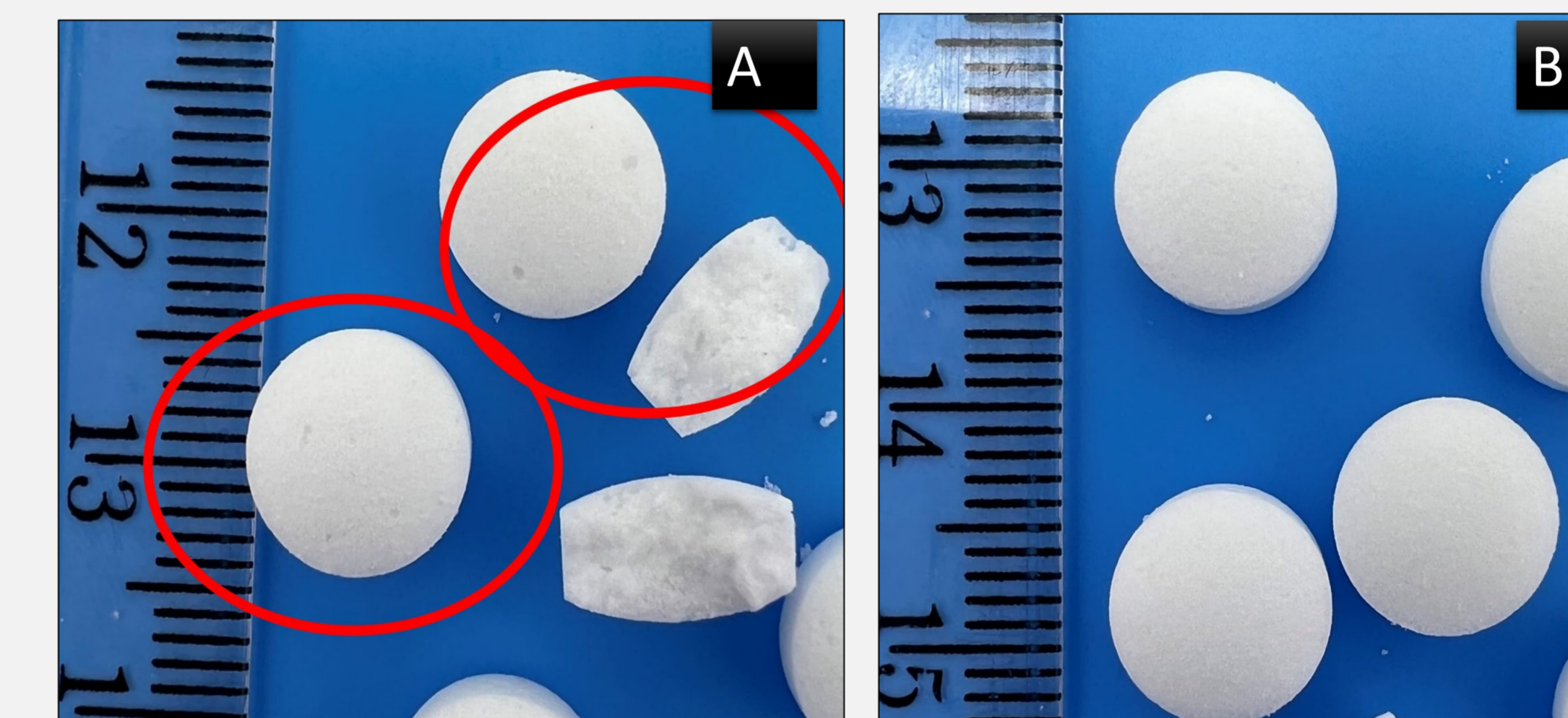


Figure 1 IBU tablet with poloxamer P407 stored at 60 °C for 72 hours. A) IBU tablets with regular P407. B) IBU tablets with micro P407. Red circle shows the segregation of regular P407

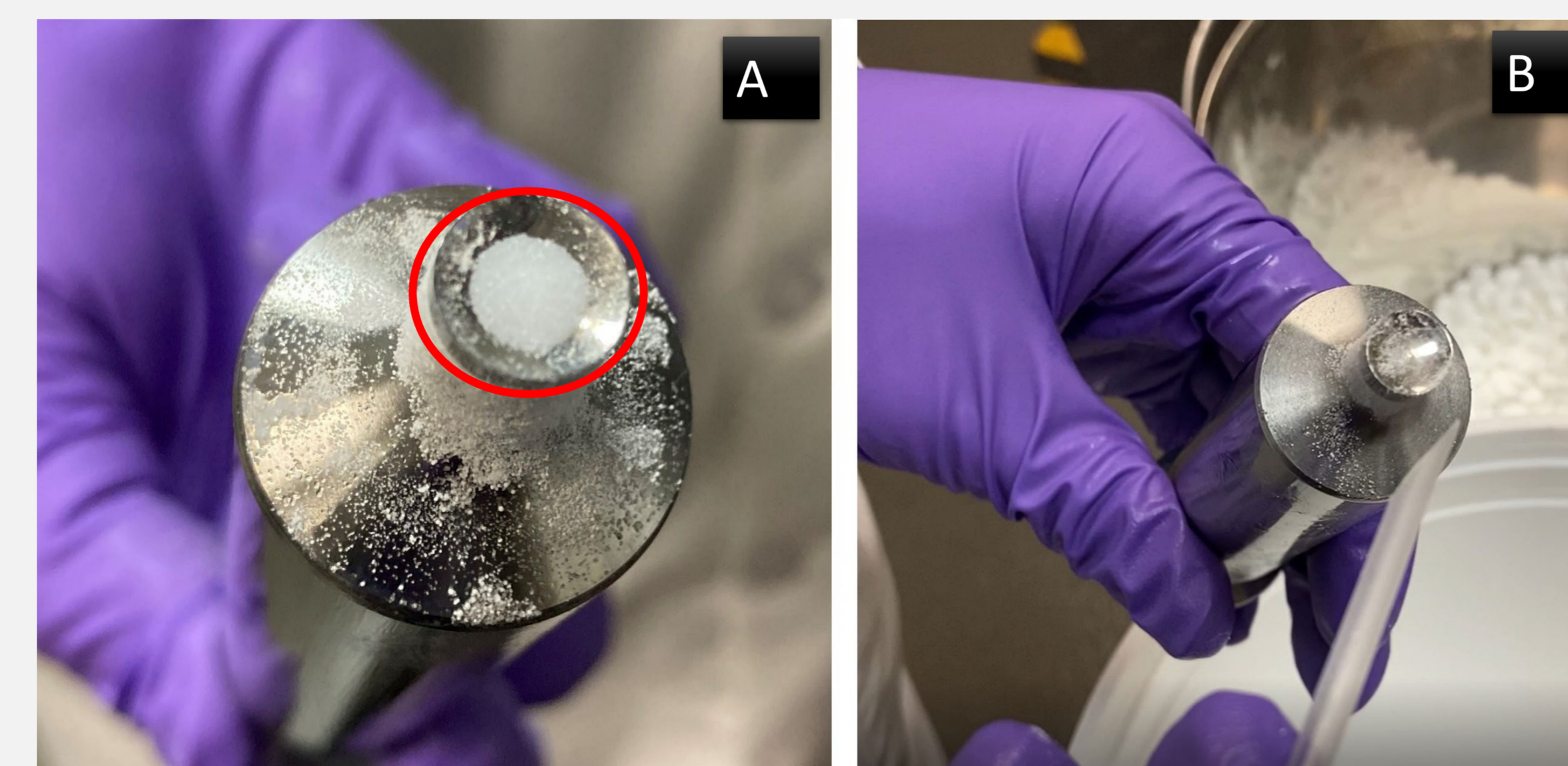


Figure 2 IBU tablet compression with poloxamer P407 after ~5 minutes compression A) simple blending (non co-sieving process); B) co-sieving process. Red circle showed the picking issue

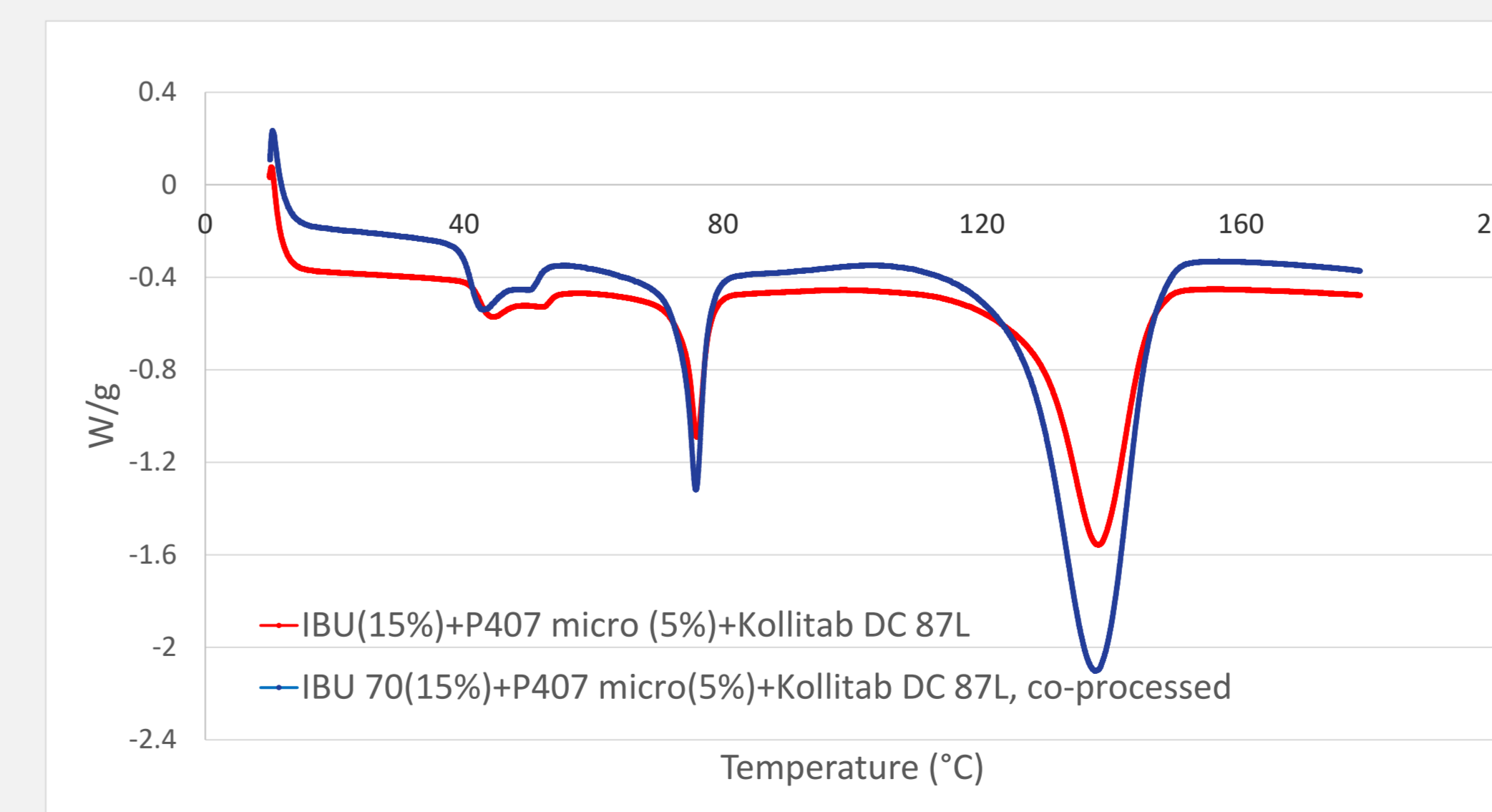


Figure 3 DSC results of IBU-poloxamer-Kollitab blends with different processing procedures

Dissolution of the IBU tablets were tested with/without poloxamer P407 in 0.1N HCl (Figure 4). The saturation concentration of IBU in 0.1N HCl was found to be ~63 mg/mL after 6 hours and presence of 5% P407 regular or micro in the formulation significantly improved the solubilization of API (~84 mg/mL and ~80mg/mL, respectively).

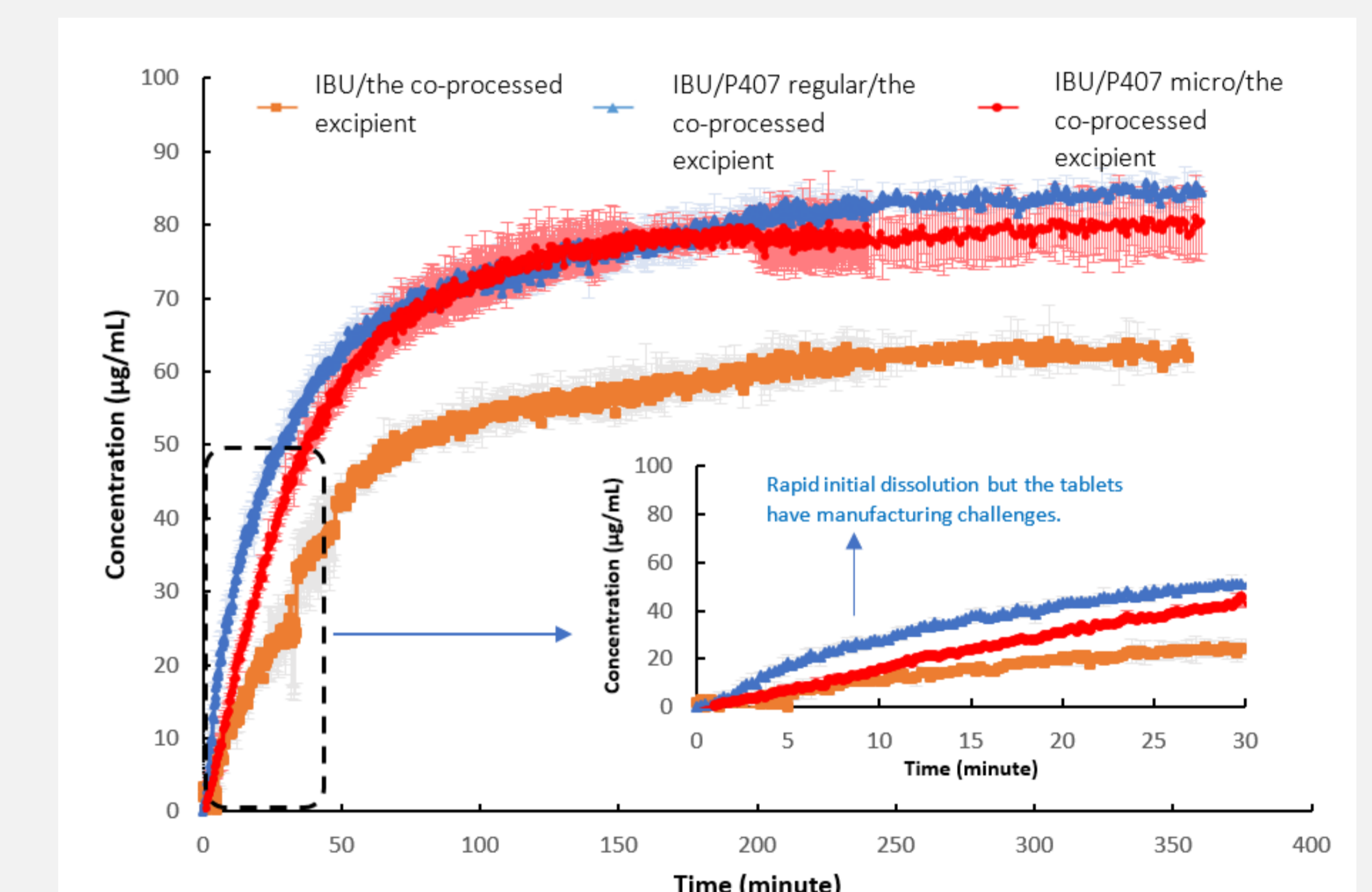


Figure 4 Dissolution profile of IBU tablets in 0.1N HCl media maintaining at 37°C and stirring at 75 rpm (each data point showed as average ± SD; n=3).

CONCLUSION(S)

- Use of poloxamer P407 micro with IBU resulted in robust tablet manufacturing process (no segregation/ sticking problem).
- P407 micro helps in uniform distribution leading to better performance during tableting, unlike P407 regular.
- P 407 micro and P407 regular provided similar solubility enhancement in IBU formulation.
- P407 micro should be a better choice for manufacturing of tablet containing poorly soluble API as compared to P407 regular.

REFERENCE

[1] C. Turchiuli, M. Fuchs, M. Bohin, M.E. Cuvelier, C. Ordonnaud, M.N. Peyrat-Maillard, E. Dumoulin, Innovative Food Sci. Emerg. Technol. 2005, 6: 29–35.