

Supplementary material File S1

## **Inhibition of Liquid-Liquid Phase Separation for Overcoming Dissolution Barrier of Amorphous Solid Dispersions to Improve Oral Absorption of Naftopidil**

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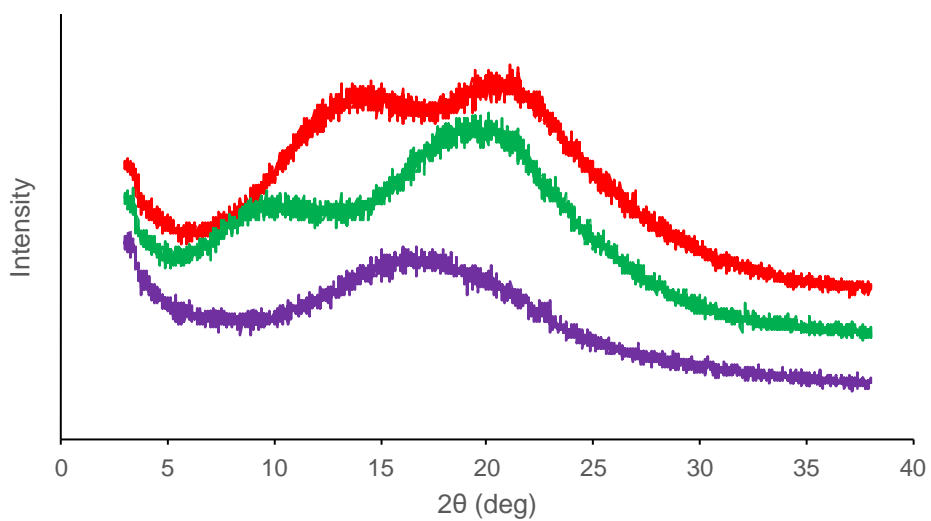
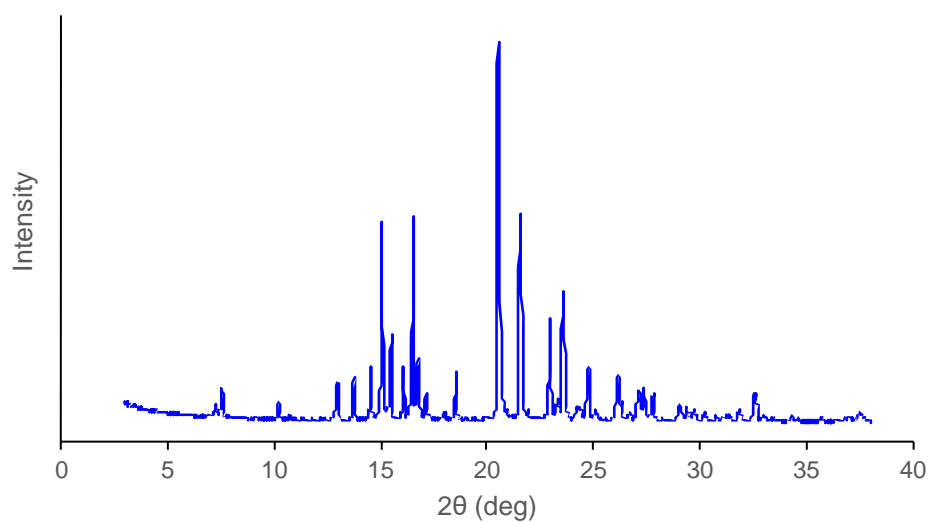
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## 1. Physical Characterization of ASDs

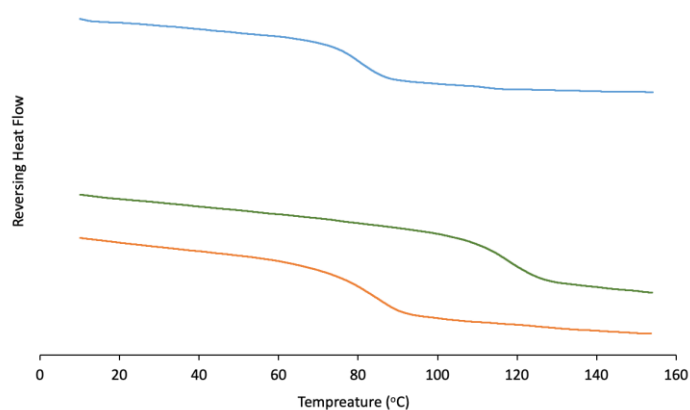
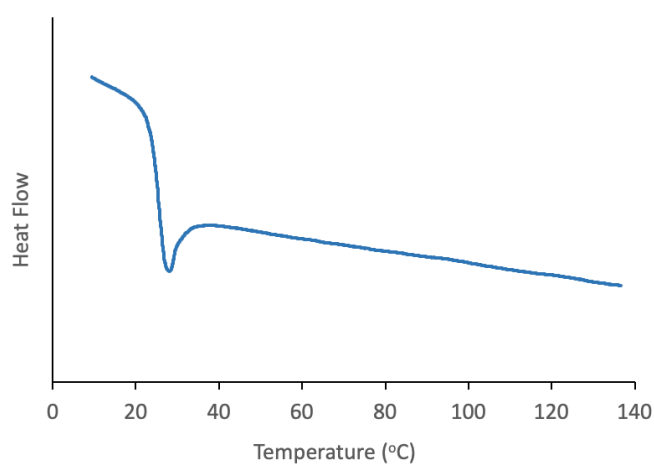
X-ray powder diffraction (XRPD) measurements of ASDs were performed on a SmartLab X-RAY diffractometer (Rigaku, Tokyo, Japan). The voltage and the current were 40 kV and 200 mA, respectively. Data were collected at intervals of  $0.02^\circ$  (2 theta) with a scan speed  $30^\circ/\text{min}$ .

XRPD measurements proved that absence of diffraction peaks for all ASDs.



Differential scanning calorimetry (DSC) and temperature-modulated DSC (TM-DSC) were performed on a Discovery DSC (TA Instruments, New Castle, DE, USA), which calibrated monthly using indium and sapphire. Dry nitrogen was used as the inert gas at a flow rate of 50 mL/min. Approximately 2 mg of samples were measured using crimped aluminum pans.

No melting peaks were observed for all the ASDs in the DSC measurements. Single glass transition temperature ( $T_g$ ) were observed in DSC curves at 82, 85, and 118 °C for PVPVA, HPMCAS, and Eudragit ASDs, respectively. These  $T_g$ s were much higher than that for neat NFT glass (25 °C) and in between of those of NFT and polymer, suggesting molecular mixing of NFT and the polymers.



2. Detailed numerical data for the D/P/ study.

	Dose/well (mg)	Apical Solution	Conc. ( $\mu$ g/mL)								Flux	Papp
			Apical		Apical free		Basal				$\mu$ g/cm <sup>2</sup> /s	cm/s
			15 min	120 min	15 min	120 min	30 min	60min	90min	120min		
PM	3.6	TM	0.77	0.89	0.77	0.89	0.08	0.19	0.29	0.39	1.78E-04	2.01E-04
HPMCAS ASD	0.1	TM	4.33	3.11	4.33	3.11	0.50	1.08	1.65	2.09	9.23E-04	2.96E-04
	0.4	TM	19.20	16.25	19.20	16.25	2.69	5.27	7.85	9.89	4.18E-03	2.57E-04
	1.2	TM	26.85	25.05	26.85	25.05	3.93	7.64	11.00	14.12	5.86E-03	2.34E-04
	3.6	TM	34.20	34.25	34.20	34.25	4.44	8.12	11.39	15.64	6.37E-03	1.86E-04
Eudragit ASD	0.1	TM	2.04	1.33	2.04	1.33	0.34	0.74	1.12	1.40	6.10E-04	4.61E-04
	0.4	TM	7.65	9.95	7.65	9.95	0.93	1.89	2.96	4.27	1.91E-03	1.92E-04
	1.2	TM	5.00	8.00	5.00	8.00	0.64	1.29	2.06	2.84	1.27E-03	1.59E-04
	3.6	TM	1.94	2.44	1.94	2.44	0.28	0.54	0.79	1.01	4.26E-04	1.75E-04
PM	3.6	SIF	23.31	24.66	1.47	1.56	0.26	0.55	0.84	1.13	5.00E-04	2.03E-05
HPMCAS ASD	0.1	SIF	7.19	7.99	0.45	0.50	0.08	0.22	0.36	0.49	2.34E-04	2.94E-05
	0.4	SIF	34.35	40.25	2.17	2.54	0.32	0.73	1.20	1.61	7.45E-04	1.85E-05
	1.2	SIF	105.60	119.55	6.66	7.54	0.87	1.61	2.90	3.97	1.83E-03	1.53E-05
	3.6	SIF	425.70	443.70	26.86	27.99	1.83	4.61	7.53	9.88	4.67E-03	1.05E-05
Eudragit ASD	0.1	SIF	7.24	7.75	0.46	0.49	0.10	0.24	0.36	0.48	2.18E-04	2.82E-05
	0.4	SIF	29.55	34.95	1.86	2.20	0.29	0.71	0.99	1.40	6.22E-04	1.78E-05
	1.2	SIF	73.35	101.85	4.63	6.43	0.43	1.01	1.55	2.40	1.11E-03	1.09E-05
	3.6	SIF	48.15	58.50	3.04	3.69	0.26	0.58	0.80	1.02	4.29E-04	7.34E-06