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Supporting Information

Optimizing the selection of drug-polymer-water formulations for spray-dried solid dispersions in pharmaceutical manufacturing

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MOO formulation for designing drug-polymer-water blends

$$\max_{w,x,y} \quad w_{H2O} \tag{S1}$$

$$s.t. \quad \frac{w_{API}}{w_{p1}} \geq \varepsilon;\ \varepsilon = 0.2, 0.4, \dots, 1.8 \tag{S2}$$

$$\breve{T}_{g,mix} = \frac{\sum_{i\in I} K_i \breve{w}_i T_{g,i}}{\sum_{i\in I} K_i \breve{w}_i} \geq T_g^L \tag{S3}$$

$$K_i = \frac{\rho_{API} T_{g,API}}{\rho_i T_{g,i}};\ \ i = API, p_1, H_2O \tag{S4}$$

$$w_{API} \leq 0.95 \breve{w}_{API} \tag{S5}$$

$$ln\, \tilde{x}_{API}^{eq} + ln\, \gamma_{API}(T, P, \tilde{\boldsymbol{x}}^{eq}) = \frac{\Delta H_{fus,API}}{R}\left[\frac{1}{T_{m,API}} - \frac{1}{T}\right] \tag{S6}$$

$$\tilde{w}_i^{eq} = \frac{\tilde{x}_i^{eq} MW_i}{\sum_{j\in I} \tilde{x}_j^{eq} MW_j}; i = API, p1, H_2O \tag{S7}$$

$$\frac{\partial\, ln\, \hat{\gamma}_{i,j}((T,P,\hat{\boldsymbol{x}})}{\partial \hat{x}_{i,j}} + \frac{1}{\hat{x}_{i,j}} \geq 0; i = API, p1;\ j = p1, H_2O;\ i < j \tag{S8}$$

$$\hat{x}_{i,j} = \frac{x_i}{x_i + x_j}; i = API, p1;\ j = p1, H_2O;\ i < j \tag{S9}$$

$$\hat{w}_i = \frac{\hat{x}_i MW_i}{\sum_{j\in I} \hat{x}_j MW_j}; i = API, p1, H_2O \tag{S10}$$

$$\sum_{p=1}^{N_p} y_{p1,p} = 1 \tag{S11}$$

$$x \in [x^L, x^U] \subset \mathbb{R}^I;\ \ w \in [w^L, w^U] \subset \mathbb{R}^I;\ y \in \{0,1\}^q$$

Optimal solutions obtained with the MOO ternary model

Table S1: Optimal solutions obtained when solving the ternary MOO model. The results include the optimal API/polymer ratios; the mass fraction of API, polymer and water in the designed blends, and the phase boundary mass fraction ($\breve{w}_{API}$) for calculating the glass transition curve ($\breve{T}_{g,mix}$); the identity of the optimal polymers and the number of the repeated units (N_m) in each polymer.

$\frac{w_{API}}{w_{p1}}$	w_{H2O}	w_{p1}	w_{API}	$\breve{w}_{API}$	$\breve{T}_{g,mix}(\breve{w})$ [K]	Polymer	N_m
0.2	0.135	0.721	0.144	0.152	399.79	HPMC p55	10
0.4	0.105	0.639	0.256	0.269	387.73	HPMC p55	30
0.6	0.081	0.574	0.345	0.363	376.63	HPMC p55	15
0.8	0.062	0.521	0.417	0.439	367.06	HPMC p55	27
1	0.046	0.477	0.477	0.502	358.81	HPMC p55	61
1.2	0.032	0.440	0.528	0.556	338.15	HPMC p55	34
1.4	0.021	0.408	0.571	0.601	338.15	HPMC p55	34
1.6	0.010	0.381	0.609	0.641	338.15	HPMC p55	34