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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	Solver
0.2	0.135	0.721	0.144	0.177	339.15	HPMC p55	10	SCIP
0.4	0.105	0.639	0.256	0.269	387.73	HPMC p55	30	SBB
0.6	0.081	0.574	0.345	0.363	376.63	HPMC p55	15	SBB
0.8	0.062	0.521	0.417	0.495	349.15	HPMC p55	10	SCIP
1	0.046	0.477	0.477	0.541	344.37	HPMC p55	21	SCIP
1.2	0.032	0.440	0.528	0.581	338.15	HPMC p55	10	SCIP
1.4	0.021	0.408	0.571	0.601	338.15	HPMC p55	34	SBB
1.6	0.010	0.381	0.609	0.643	338.39	HPMC p55	14	SCIP