Investigation Into Intermolecular Interactions and Phase Behavior of Binary and Ternary Amorphous Solid Dispersions of Ketoconazole

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SUPPORTING INFORMATION

Figure S1. FTIR spectra of PAA and its sodium salt. The peaks $\sim 1549 \text{ cm}^{-1}$ and 1399 cm⁻¹ found in sodium salt of PAA are attributed to antisymmetric and symmetric stretching of the carboxylate group.

Figure S2. FTIR spectra of 50:50 KET:PAA system showing N+-H peak at 2490 cm-1 in spray dried dispersion but absent in the respective physical mixture. The peak \sim 2490 cm-1 is attributed to the protonation of the imidazole group of KET.

Figure S3. Comparison of FTIR spectrum of PAA, HPMC and their spray dried blends. In presence of HPMC, the intensity of dimer peak (~1695 cm⁻¹) decreases and moves to higher wavenumbers as the weight fraction of HPMC increases. Spectrum of 50:50 physical mixture of PAA and HPMC is shown as a reference.

Figure S4. Donor to acceptor molar ratio calculated for binary KET:PAA and ternary KET:PAA:HPMC as a function of weight percent of KET. The cross point on the curve represent the theoretical 1:1 molar ratio in each case.

Figure S5. ¹³C CP/MAS spectra of PAA and its sodium salt. The main peak in the carbonyl region of sodium salt resonated around ~186 ppm.

Figure S6. ¹³CP/MAS spectra of 50:50 KET:PAA binary dispersion (red) and 50:50 KET:PAA physical mixture (purple). The shoulder peak around 172 ppm is visible in dispersion sample but absent in physical mixture. Spectra of PAA and amorphous KET are included as a reference.

Figure S7. ¹³CP/MAS spectra of spray dried blends of PAA and HPMC at various ratios.

Figure S8. Deconvolution of the carbonyl region of (A) binary KET:PAA and (B) ternary KET:PAA:HPMC dispersions. The fitted peaks are shown in blue; the sum of the fit is shown in yellow; the residual is shown in red.

 Table S1. Proton relaxation times of as received and amorphous KET along with polymers PAA and HPMC.



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Proton Relaxation Time	Ketoconazole		Polymers	
	As received	Amorphous	PAA	НРМС
T ₁ (s)	13.88±0.11	5.32±0.24	1.45±0.04	1.35±0.02
$T_{1\rho}$ (ms)	52.71±0.76	4.30±0.07	8.58±0.07	12.53±0.10