# **Supporting information**

# Effect of Polymeric Excipients on Nucleation and Crystal Growth

# **Kinetics of Amorphous Fluconazole**

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### References

# **Experimental details**

#### Methods:

**Preparation of FCZ Form II.** According to the literature<sup>1</sup>, the FCZ Form II was prepared by dissolving an excess of fluconazole powder in propan-2-ol at 313K. The solution was then filtered into a preheated conical flask and left to cool for 5 days at room temperature (RT).

#### Thermogravimetric analysis (TGA)

TGA was performed using a TA Q500 thermogravimetric analysis instrument under 60 mL /min  $N_2$  purge. The sample was analyzed from room temperature to 523K at a heating rate of 20 K/min.

#### Viscosity measurement.

The viscosities were measured using a HAAKE MARS 60 rheometer (Thermo Fisher scientific, USA). Measurements were conducted using two 20mm diameter parallel plates with a 0.3mm gap between the upper and lower plates. Briefly, the sample was melted between the two parallel plates, and was held at 428K for 5min to ensure melting of any nuclei or crystalline materials formed during the viscosity measurement. After that, the samples were cooled to the desired temperature for measurements. Upon equilibration, a shear deformation at a rate of 1 s<sup>-1</sup> was applied to the sample, and the shear viscosity of the material was recorded when a steady-state reading was observed.

#### Density measurement.

True density of amorphous FCZ was measured using a AccuPyc 1340 helium pycnometer (Micormetrics, Norcross, GA). About 0.5 g sample was loaded into a cell volume of 1.338 cm<sup>3</sup> for each measurement, and the results are reported as average from five measurements.

# **Results:**

Table S1.The	properties	of the	materials	used.
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Material	M <sub>W</sub> (g/mol)	<i>Т<sub>g</sub></i> (К)	Density (g/cm <sup>3</sup> )
FCZ	306.27	305 <sup>a</sup>	1.39ª
PEO	100K	226 <sup>b</sup>	1.30 <sup>d</sup>
РУРК30	44-54K	440 <sup>c</sup>	1.18 <sup>d</sup>
HPMCAS	55 K–93 K	387 <sup>c</sup>	1.30 <sup>d</sup>

<sup>a</sup> T<sub>g</sub> and density of amorphous FCZ was determined in this study; <sup>b</sup> ref2;<sup>c</sup> ref 3;<sup>d</sup> ref 4



Figure S1. (a) TGA of FCZ and (b) DSC traces of amorphous FCZ and two polymorphs of FCZ.



**Figure S2.**The crystal growth rates of FCZ Form I in the presence of absence of 10% w/w polymers as a function of temperature (n=3).

<b>T</b> o mark and (17)	Log η(Pa·s)			
Temperature(K)	Pure FCZ	10% w/w PEO	10%w/w PVP K30	10%w/w HPMCAS
413	-0.96	-	-0.04	-0.83
403	-0.83	-	0.27	-0.68
393	-0.46	-	0.68	-0.15
383	-0.04	-	1.12	0.28
373	0.44	-	1.68	0.81
363	1.07	-	2.33	1.41
353	1.82	-	3.07	2.16
343	2.73	2.57	3.91	3.05
333	3.85	2.91	4.95	4.12
323	-	3.89	-	-
313	-	5.00	-	-
303	-	6.43	-	-

Table S2. The viscosity of pure FCZ and mixtures of FCZ with 10% w/w PEO, PVP K30, HPMCAS <sup>a</sup>

<sup>a</sup> The viscosity of pure FCZ, 10% PVP K30-FCZ and 10% HPMCAS-FCZ at 303, 313 and 323 K was too high to obtain reliable measurements. The viscosity of 10% PEO-FCZ above 353 K could not be obtained because of the quick crystallization during the measurement.

### VFT equation fitting.

The viscosity of amorphous FCZ and FCZ doped with polymers were found to follow the VFT equation,

$$\eta = A \exp\left(\frac{B}{T - T_0}\right) \tag{S1}$$

A ,B and  $T_0$  are all constants, take the log of both sides,

$$\lg \eta = A + \frac{B}{T - T_0} \tag{S2}$$



**Figure S3.** The viscosity of FCZ with or without 10% w/w polymers. (The dashed line is a VFT fit of the viscosity data.)

Table S3. The VFT equation fit of different systems.

System	Fitting equation	R <sup>2</sup>
Pure FCZ	lgη=-5.62+698.8/(T-258.81)	0.999
10% w/w PVP K30-FCZ	lgη=-5.96+1020.52/(T-239.58)	1.000
10% w/w HPMCAS-FCZ	lgη=-6.25+878.77/(T-248.34)	0.999
10% w/w PEO-FCZ	lgη=-2.19+404.03/(T-256.25)	0.996



**Figure S4.**DSC thermograms of pure FCZ Form II and FCZ Form II in the presence of 10% w/w PEO, PVP K30 and HPMCAS.

System	<i>Т<sub>т</sub></i> (К)	ΔH (J/mol)
FCZ	409	36630
10% w/w PEO-FCZ	411	31141
10% w/w PVP K30-FCZ	402	27598
10% w/w HPMCAS-FCZ	402	30225

**Table S4.** Thermal properties of FCZ Form II and FCZ Form II in the presence of 10% w/w PEO, PVP K30 and HPMCAS.

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