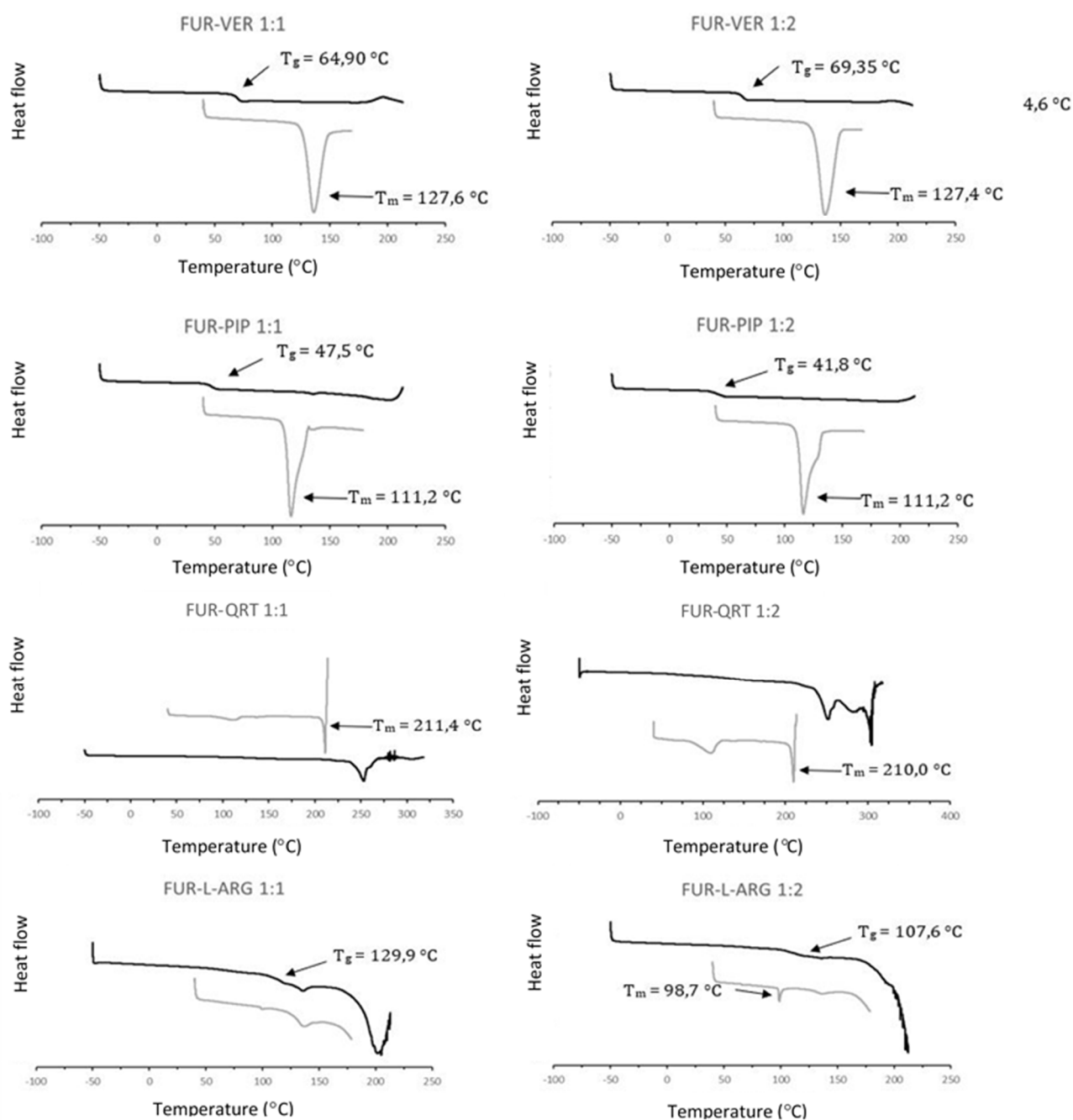


# Supplementary Materials: Co-Amorphous Formulations of Furosemide with Arginine and P-Glycoprotein Inhibitor Drugs

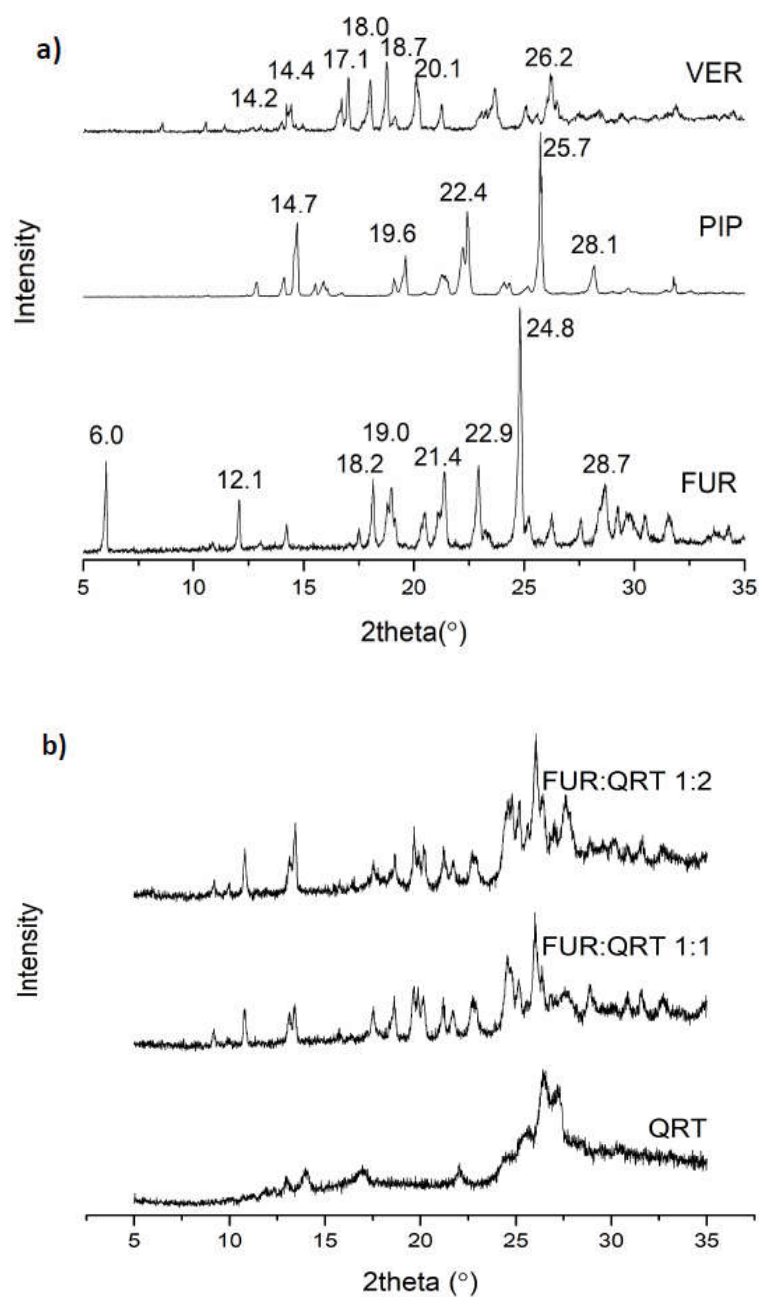
Marika Ruponen, Konsta Kettunen, Monica Santiago Pires and Riikka Laitinen

**Table S1.** Outlet temperatures, inlet temperatures, pump rates and flow rates for the co-amorphous mixtures prepared by spray drying.

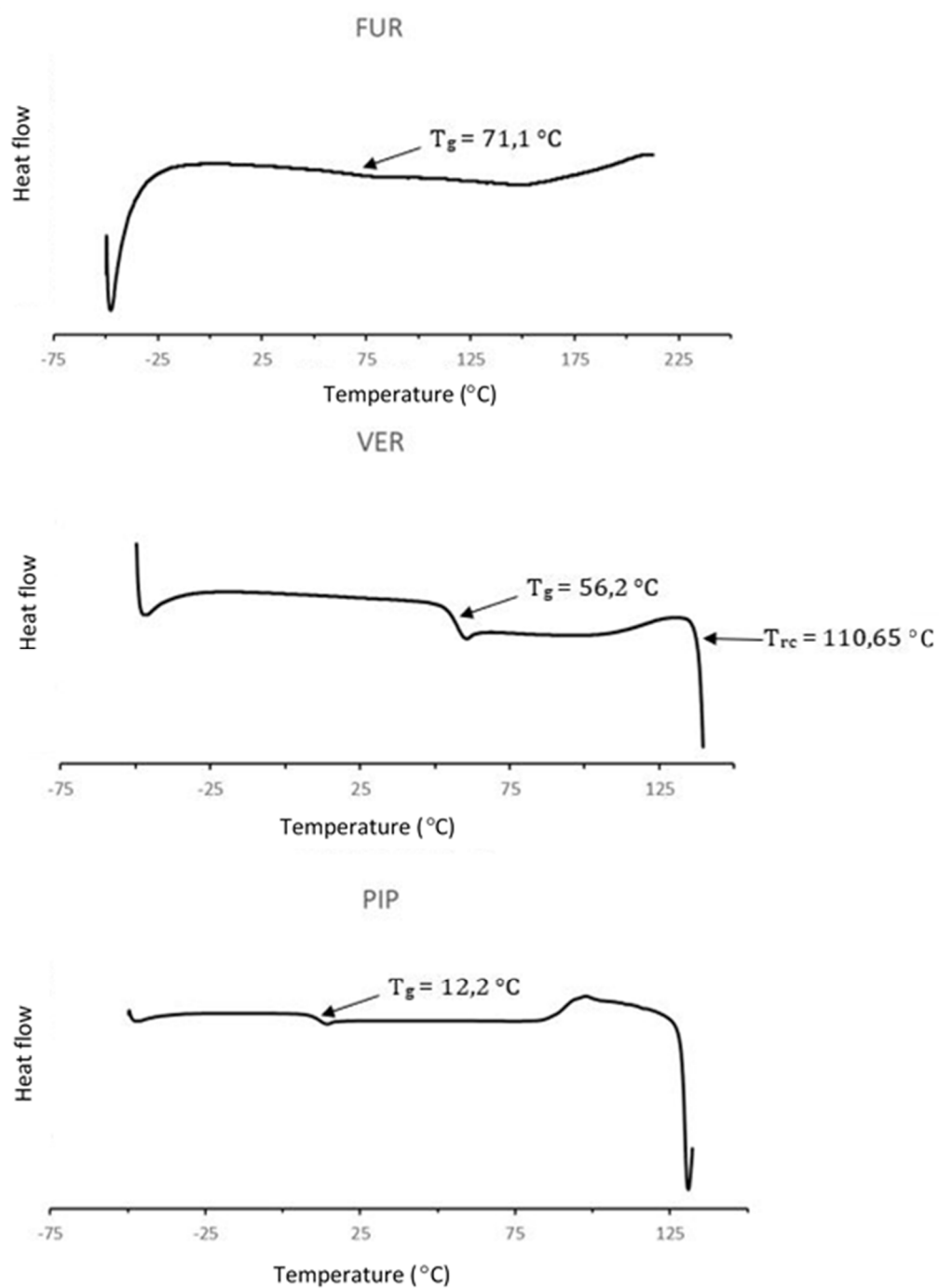
Mixture	Outlet temperature (°C)	Inlet temperature (°C) (min-max)	Pump rate (%) (min-max)	Flow rate (ml/min) (min-max)
FUR + L-ARG 1:1	160	91-94	27-30	2.94-5.87
FUR + L-ARG 1:2	160	82-86	10-30	2.13-6.17



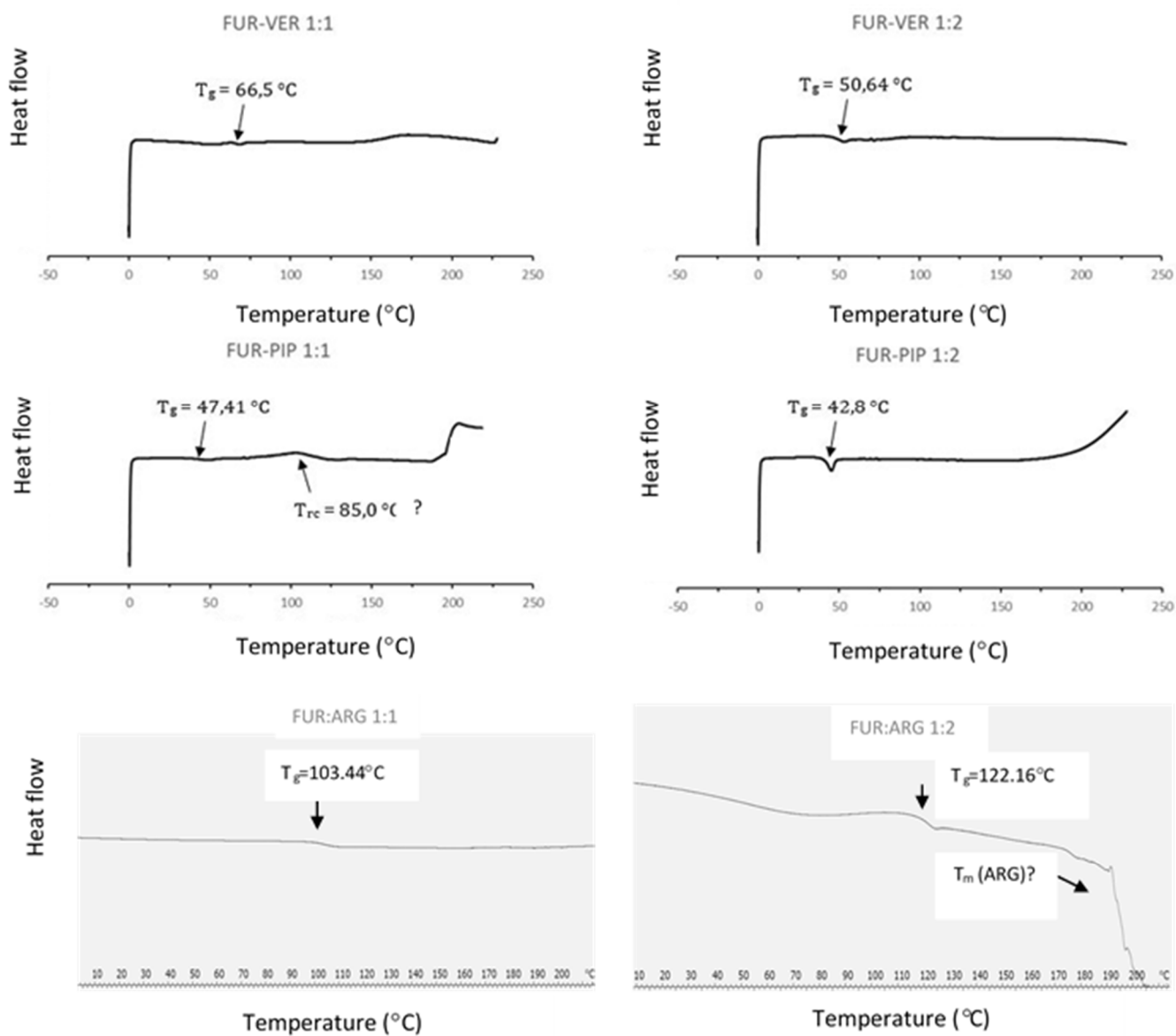
**Figure S1.** Example thermograms of furosemide:verapamil HCl (FUR:VER), furosemide:piperine (FUR:PIP), furosemide:quercetin (FUR:QRT) mixtures and furosemide:arginine (FUR:L-ARG) at 1:1 and 1:2 molar ratios.



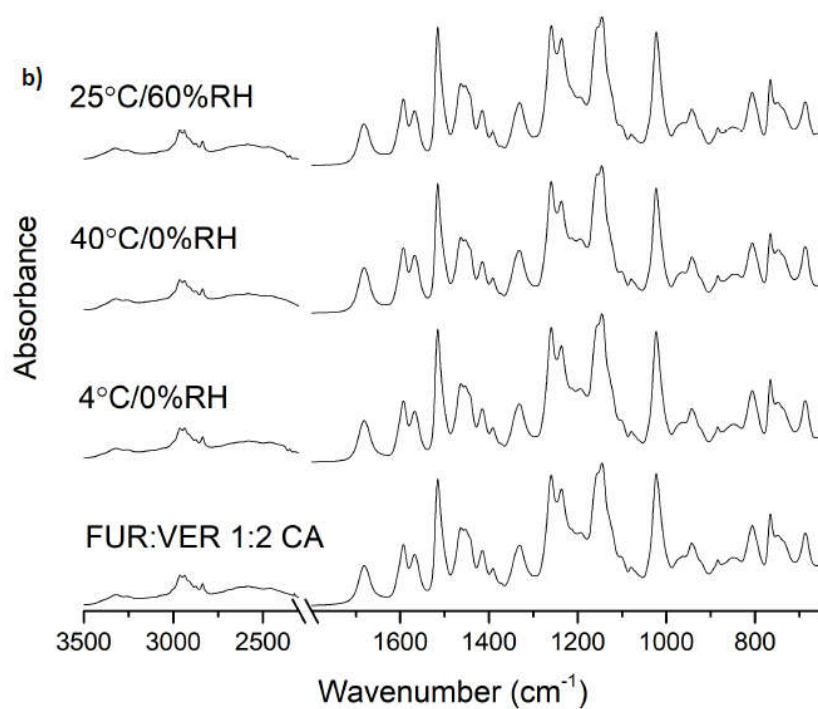
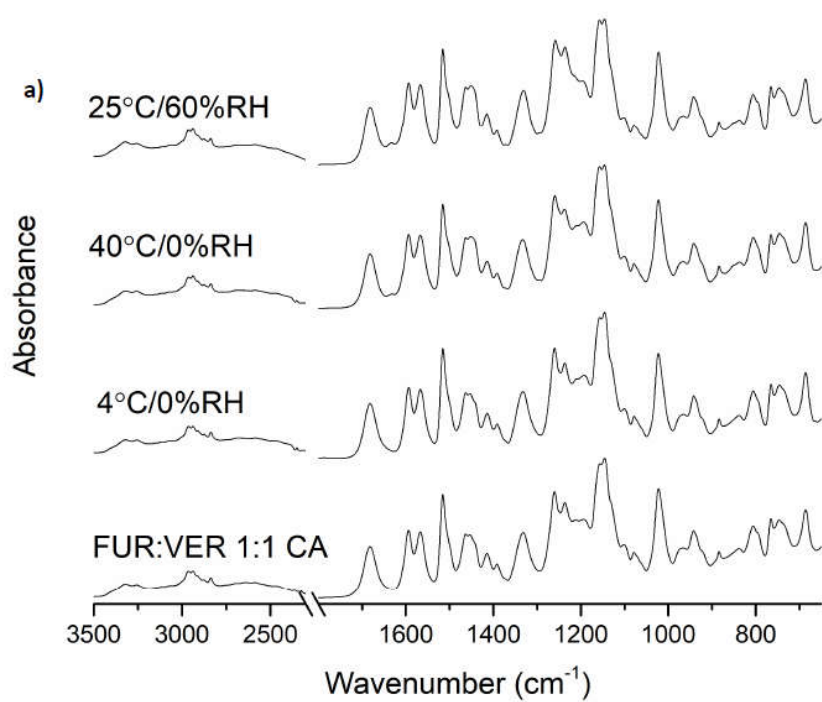
**Figure S2.** X-ray diffractograms of a) the crystalline starting materials furosemide (FUR), piperine (PIP) and verapamil hydrochloride (VER). Diffractogram of ARG has been published previously by Ruponen et al., 2018 and 2020; b) crystalline quercetin (QRT) and FUR:QRT 1:1 and 1:2 molar mixtures prepared by the evaporation method.

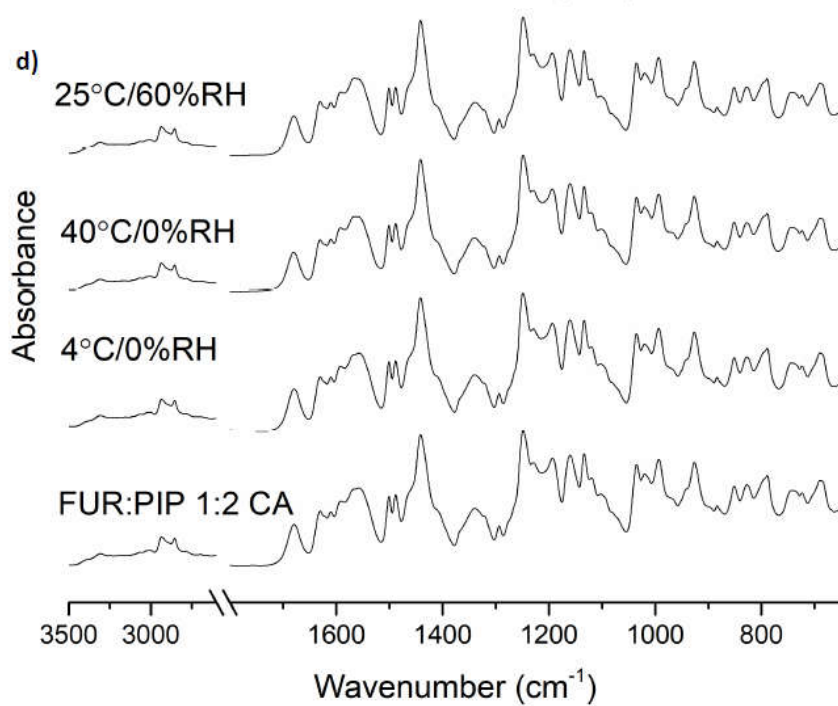
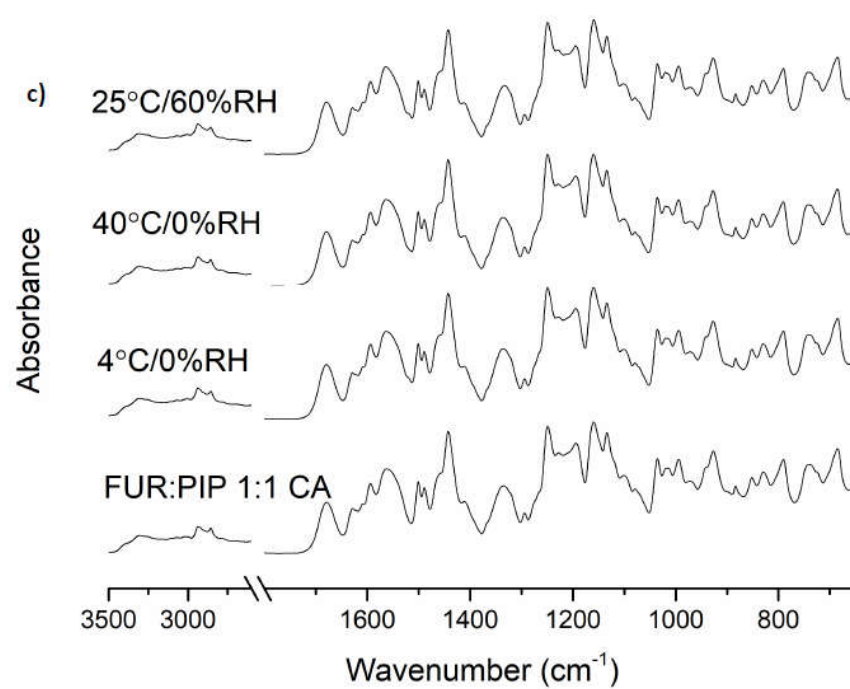


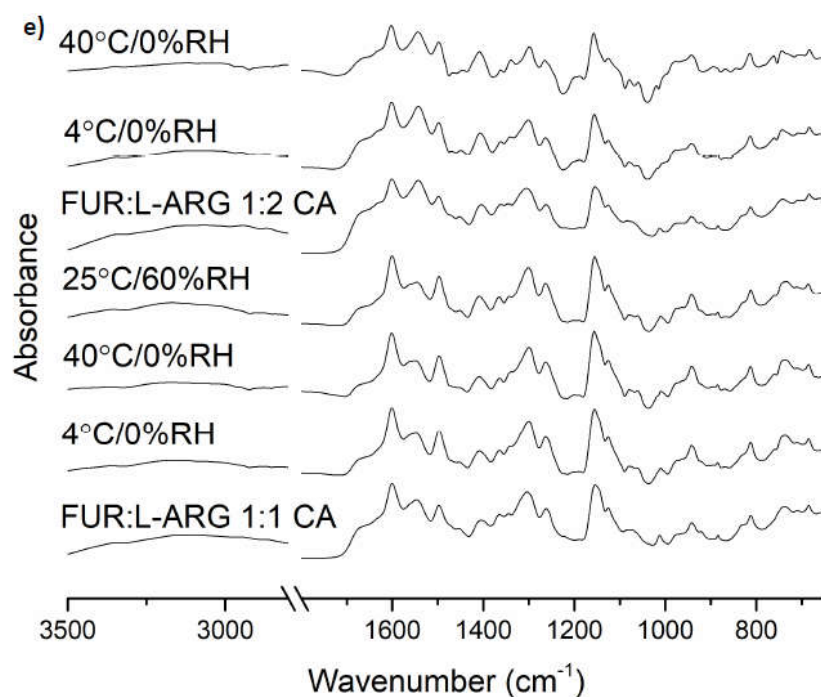
**Figure S3.** Example thermograms (second heating cycle) of the crystalline starting materials furosemide (FUR), verapamil hydrochloride (VER) and piperine (PIP) showing glass transitions ( $T_g$ , midpoint).



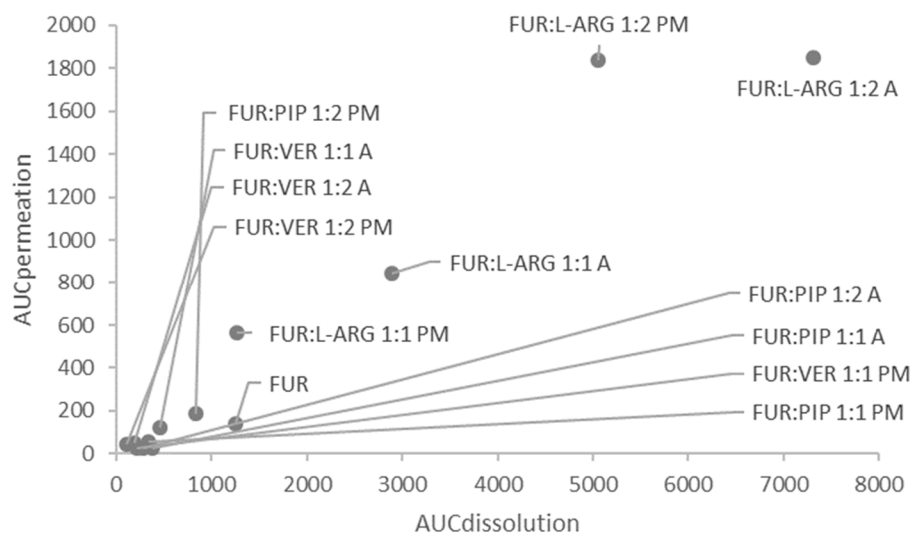
**Figure S4.** Example thermograms of the co-amorphous mixtures of furosemide (FUR), verapamil hydrochloride (VER), piperine (PIP) and arginine (ARG) at 1:1 and 1:2 molar ratios.







**Figure S5.** Fourier-transform infrared (FTIR) spectra of the co-amorphous materials after storage at 4°C/0% RH, 40°C/0% RH and 25°C/60% RH a) furosemide:verapamil hydrochloride (FUR:VER) 1:1 molar ratio at eight weeks; b) FUR:VER 1:2 molar ratio at eight weeks; c) furosemide:piperine (FUR:PIP) 1:1 molar ratio at eight weeks; d) FUR:PIP 1:2 molar ratio at eight weeks; e) furosemide:arginine FUR:ARG) 1:1 and 1:2 molar ratios at nine weeks.



**Figure S6.** The correlation between the AUC values for dissolution and permeation.