Supplemental Material

Transmission Raman Spectroscopic Quantification of Active Pharmaceutical Ingredient in Coated Tablets of Hot-Melt Extruded Amorphous Solid Dispersion

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Figure S1. The extrudate, placebo extrudate and the filler amount in the samples

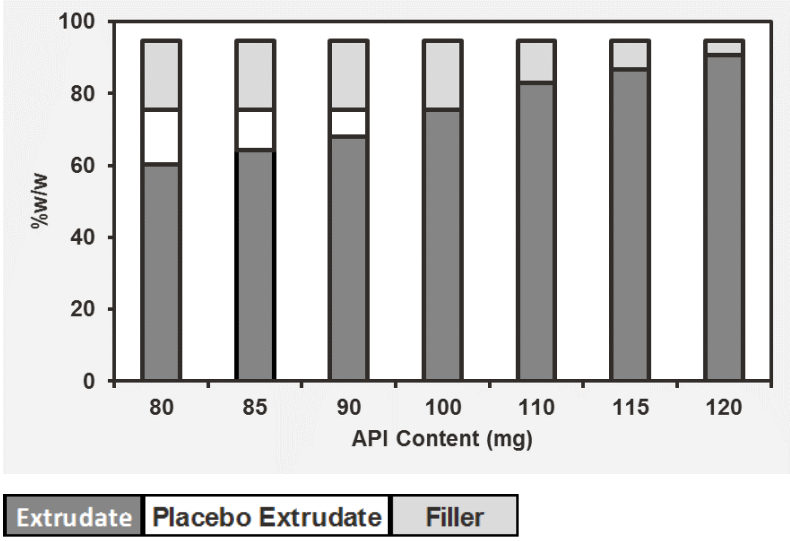

Figure S2. (a) Raw transmission Raman spectra. (b) Pre-processed spectra with a second SG derivative with a fifteen-point window, and a second order polynomial followed by SNV. (c) Pre-processed spectra with first SG derivative with a fifteen-point window and a second order polynomial followed by SNV.

Table S1. The design parameter nominal values and variation ranges used in the study design.

Design parameters	Nominal	Variation
Potency (mg per tablet)	100	80 ~ 120
Extrudate[a] (%w/w)	75.5	60.4 ~ 90.6
Filler (%w/w)	19.2	4.1 ~ 21.0
Coating (%w/w)	3.85	2.85 ~ 4.85
Key degradant (%w/w)	~ 0.15	0.15 ~ 0.43
Water content (%w/w)	2.7 ~ 3.2	3.4 ~ 3.9
Extrudate D50[b] (μm)	~ 100	70 ~ 100
Tablet hardness (kP)	~ 20	20 ~ 28

a. 12% API loading. b. Particle size of milled extrudate

Figure S3. (a) X-loading weight plot. (b) Regression coefficients plot.

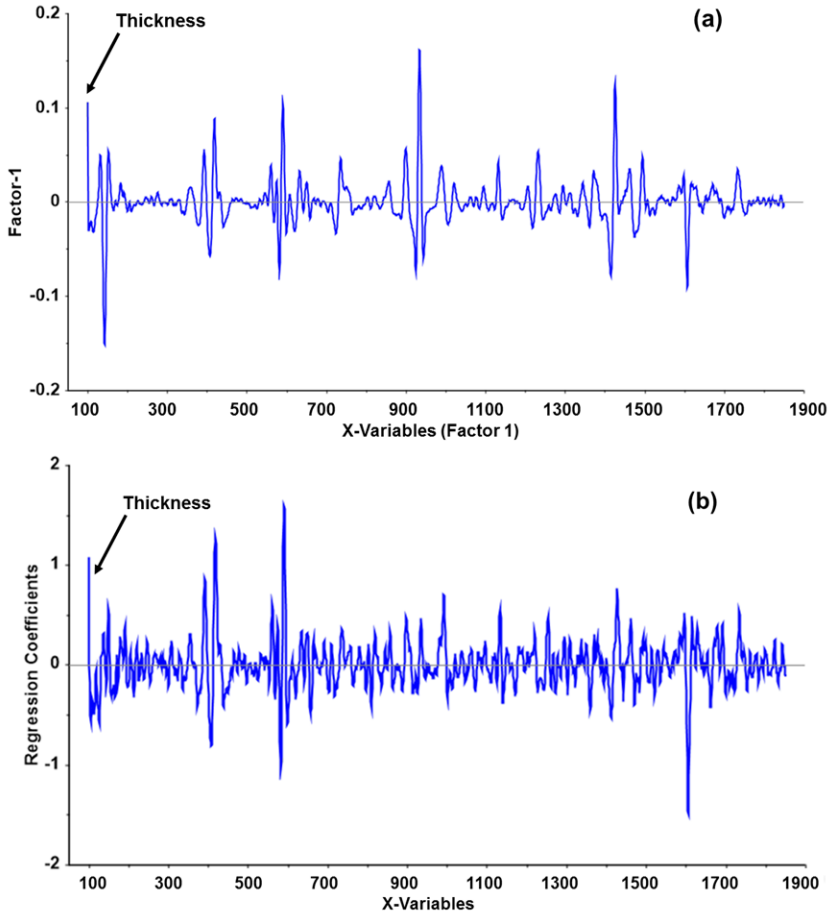

Table S2. RMSEP generated by different PLSR regression models.

Factors	RMSEP%	PLSR	
		Regions 1 and 2[a]	100 to 1850 cm^{-1}
2	Test set	8.03	4.06
	Clinical batch	14.70	12.10
4	Test set	4.56	2.08
	Clinical batch	1.89	4.10
6	Test set	3.58	1.86
	Clinical batch	4.68	1.15
7	Test set	3.23	2.17
	Clinical batch	4.54	1.01

a. Region 1: 1550 to 1650 cm^{-1}. Region 2: 100 to 200 cm^{-1}.

Figure S4. Hotelling's T2 statistics of clinical samples and test set samples.