

## **Supplementary material**

### **3D printed **spherical mini-tablets**: Geometry versus composition effects in controlling dissolution from personalised solid dosage forms**

**Sejad Ayyoubi<sup>a,b</sup>, Jose R. Cerda<sup>a</sup>, Raquel Fernández-García<sup>a</sup>, Peter Knief<sup>c</sup>, Aikaterini Lalatsa<sup>c</sup>, Anne Marie Healy<sup>d</sup>, Dolores R. Serrano<sup>a,e\*</sup>**

<sup>a</sup> Department of Pharmaceutics and Food Science, Facultad de Farmacia, Universidad Complutense de Madrid, 28040, Madrid, Spain.

<sup>b</sup> School of Pharmacy, Utrecht University, Universiteitsweg 99, 3584 CG Utrecht, The Netherlands.

<sup>c</sup> UCD Centre for Precision Surgery, Catherine McAuley Education and Research Centre, Dublin 7, Ireland.

<sup>d</sup> Biomaterials, Bio-engineering and Nanomedicine (BioN) Lab, Institute of Biomedical and Biomolecular Sciences, School of Pharmacy and Biomedical Sciences, University of Portsmouth, White Swan Road, Portsmouth PO1 2 DT, U.K.

<sup>e</sup> SSPC The SFI Research Centre for Pharmaceuticals, School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin, Dublin 2, Ireland

<sup>f</sup> Instituto de Farmacia Industrial y Galénica, School of Pharmacy, Universidad Complutense de Madrid, 28040, Madrid, Spain.

Corresponding author:

Dolores R. Serrano  
Department of Pharmaceutics and Food Science  
School of Pharmacy  
Universidad Complutense de Madrid  
Email: [drserran@ucm.es](mailto:drserran@ucm.es)  
Tel: +34 91 394 1620

**Table S1. Characteristics of the in-house manufactured filaments and mini-tablets.**

Formulations	Average mini-tablet weight (mg)	SD	Average filament diameter (mm)	SD	Drug-release in 24 hours (%)
PD	386.20	8.76	1.75	0.05	100
EC30	64.65	1.34	1.51	0.02	47.97
EC40	63.75	0.21	1.45	0.02	40.80
EC50	64.30	1.84	1.46	0.06	61.08
<sub>CP</sub> EC50	69.533	2.81	1.46	0.06	48.53
EC60	86.70	1.99	1.45	0.03	18.14
<sub>CP</sub> KVA150	81.90	1.27	1.53	0.03	108.93
KVA250	110.20	0.28	1.57	0.02	74.85

**Table S2. The fraction of crystalline NFD within the mini-tablets derived from the heat of fusion taking into account the amount of NFD within the formulation. BQL: below the quantification limit.**

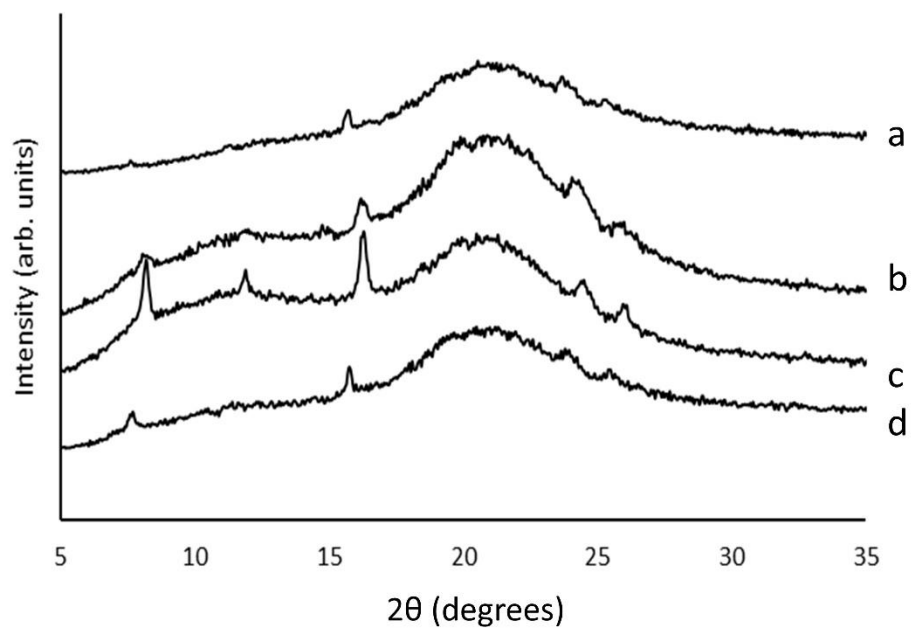
Raw NFD and mini-tablet formulations	Heat fusion (J/g)	Amount of NFD in the formulation (%)	Fraction of crystalline NFD (%)
Raw NFD	112.5	100	100
<sub>CP</sub> KVA150	13.57	50	24.1
KVA250	5.00	50	8.8
EC30	21.34	30	63.2
EC40	22.12	40	49.2
EC50	32.16	50	57.17
EC60	37.54	60	55.5
PD	-	4	BQL

**Table S3. Glass transition temperatures for raw KV64, raw EC and 3D printed mini-tablets calculated from the reversed heat flow DSC thermograms.**

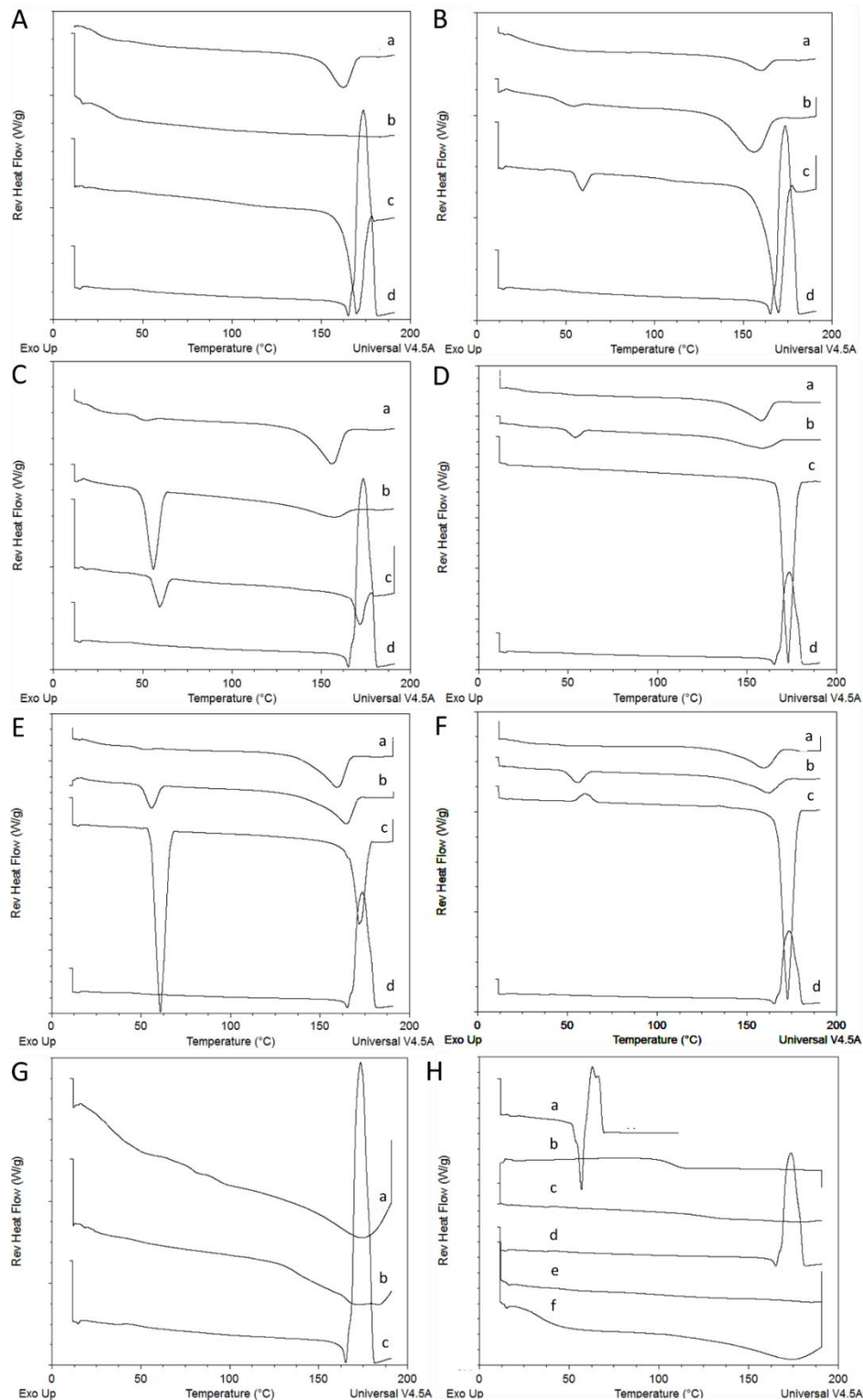
<b>Formulation (mini-tablets)</b>	<b>T<sub>g</sub> (°C)</b>
Raw KVA64	101.90 ± 1.2
Raw EC	122.64 ± 2.3
<sup>CP</sup> KVA150	47.23 ± 0.8
KVA250	43.98 ± 0.7
EC30	47.6 ± 1.2
EC40	49.46 ± 1.1
EC50	48.54 ± 0.9
EC60	46.79 ± 0.8
PD	43.98 ± 0.8

**Table S4. Dissolution modelling data**

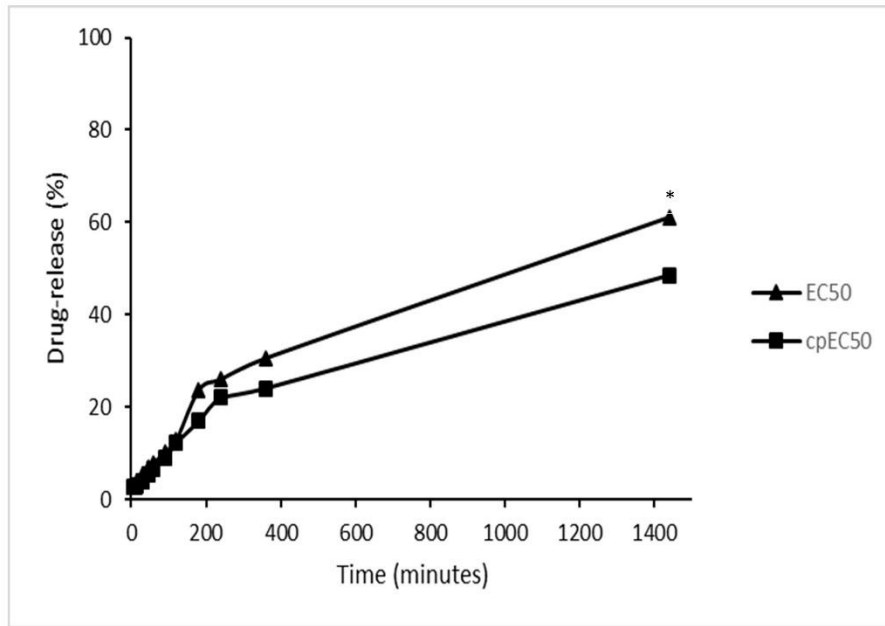
	Formulation	First order (R <sup>2</sup> )	Zero order (R <sup>2</sup> )	Hixson–Crowell (R <sup>2</sup> )	Korsmeyer–Peppas (R <sup>2</sup> )	Higuchi (R <sup>2</sup> )
<i>HME</i>	<b>EC30</b>	0.9287	<b>0.9954 (0-120 min)</b> <b>0.9943 (180-1440 min)</b>	0.9160	0.9840	0.9840
	<b>EC40</b>	0.9439	<b>0.9698 (0-120 min)</b> <b>0.9993 (180-1440 min)</b>	0.9333	0.9869	0.9867
	<b>EC50</b>	0.9851	<b>0.9938 (0-120 min)</b> <b>0.9982 (180-1440 min)</b>	0.9843	0.9790	0.9669
	<b>EC60</b>	0.9592	<b>0.9913 (0-120 min)</b> <b>0.9663 (180-1440 min)</b>	0.9400	0.9854	0.9827
	cp <b>EC50</b>	-2,2255	<b>0,9926 (0-120 min)</b> <b>0,9895 (180-1440 min)</b>	0,9797	0,9819	0,9752
	cp <b>KVA150</b>	-1.015	<b>0,9925 (0-180 min)</b> <b>0,9973 (240-1440 min)</b>	0.9511	0.4445	0.9221
	<b>KVA250</b>	0.9855	<b>0,9935 (0-180 min)</b> <b>0,9989 (240-1440 min)</b>	0.9536	-0.0786	0.9056
<i>PD</i>	<b>6 mm mini-tablets</b>	0.9595	0.9653	0.9806	<b>0.9878</b>	0.8856
<i>Commercialised formulations</i>	<b>STADA</b>	0.8588	0.1845	0.7621	0.8659	<b>0.8859</b>
	<b>ADALAT OROS</b>	0.8913	<b>0.9874</b>	0.9307	0.7646	0.7000



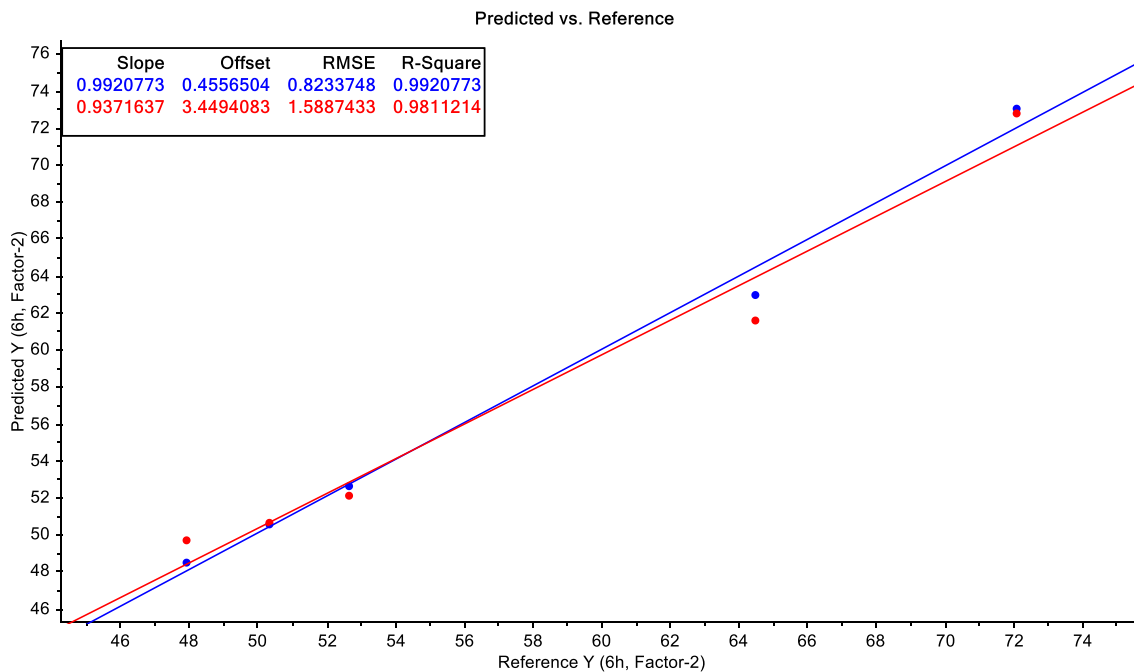
***Figure S1. PXRD analysis of the surface of the EC-based mini-tablets: EC60 (a), EC50 (b), EC40 (c) and EC30 (d).***



**Figure S2.** DSC reverse heat flow thermograms of the raw materials, physical mixtures, filaments and 3D printed mini-tablets. Key: *cpKVA150* (A), *KVA250* (B), *EC30* (C), *EC40* (D), *EC50* (E), *NC60* (F), *PD* (G) and for all raw material (H). Within the graphs (A-F): mini-tablet (a), filament (b), PM (c) and raw NFD (d). For graph (G); mini-tablet (a), loaded HS filament (b) and raw NFD (c). For graph (H); PEG4000 (a), KVA64 (b), EC (c), NFD (d), HPC (e) and HS (f).



**Figure S3. Drug-release profiles for the EC50 and cpEC50 formulations. Key: statistically significant differences are depicted with \* $p < 0.05$ .**



**Figure S4. PLS prediction model of NFD release.**