Supplementary material

A comparative study of two data-driven modeling approaches to predict drug release from ER matrix tablets

Sousa, A.S.[1,2], Serra, J.[2], Estevens, C.[2], Costa, R.[2], Ribeiro, A.J.[1,3]*

[1] Universidade de Coimbra, Faculdade de Farmácia, 3000-148 Coimbra, Portugal;

[2] Grupo Tecnimede, Quinta da Cerca, Caixaria, 2565-187 Dois Portos, Portugal;

[3] i3S, IBMC, Rua Alfredo Allen, 4200-135 Porto, Portugal.

Table S1
Experimental dataset of 84 formulations – composition and *in vitro* drug release.

Batch ID.	PEO N-750 (%)	PEO 1105 (%)	PEO N-60K (%)	PEO 303 (%)	Diluent type	Diluent (%)	Total Polymer (%)	15	30	60	120	180	240	300	360	420
F1	20	0	0	40	SMCC	19	60	2.37	3.65	5.73	9.49	13.24	17.09	20.96	24.84	28.69
F2	40	0	0	20	SMCC	19	60	2.59	4.68	7.69	13.12	18.43	23.68	28.91	34.02	39.10
F3	7.5	0	0	40	SMCC	31.5	47.5	2.59	3.84	5.91	9.63	13.25	16.96	20.65	24.30	28.01
F4	40	0	0	7.5	SMCC	31.5	47.5	3.26	5.95	10.61	20.04	29.49	38.62	47.14	54.85	61.86
F5	7.5	0	0	40	SMCC	31.5	47.5	2.30	3.57	5.68	9.48	13.30	17.15	21.02	24.88	28.75
F6	7.5	0	0	24.89	SMCC	46.61	32.39	3.82	5.70	8.35	13.09	17.53	21.85	26.04	30.15	34.11
F7	27	0	0	7.5	SMCC	44.5	34.5	4.63	7.22	11.70	20.06	28.42	36.40	44.43	51.59	58.24
F8	7.5	0	0	7.5	SMCC	64	15	21.25	25.66	32.39	41.49	50.32	57.79	64.63	70.56	76.07
F9	40	0	0	20	SMCC	19	60	2.67	4.32	6.96	11.93	16.98	22.53	27.85	32.97	38.02
F10	20	0	0	40	SMCC	19	60	2.39	3.83	6.16	10.16	13.92	17.73	21.49	25.28	29.01
F11	7.5	0	0	7.5	SMCC	64	15	20.45	26.89	33.27	41.16	48.50	55.27	61.90	67.79	73.40
F12	20.81	0	0	21.29	SMCC	36.9	42.1	3.29	5.09	7.96	13.20	18.10	22.83	27.49	32.07	36.43
F13	0	0	0	69	SMCC	10	69	1.82	2.82	4.51	7.55	10.48	13.41	16.42	19.44	22.47
F14	69	0	0	0	SMCC	10	69	2.48	4.85	10.84	25.67	40.47	56.49	70.52	81.97	88.74
F15	0	27.5	0	0	SMCC	51.5	27.5	10.62	14.20	20.32	33.72	48.44	60.55	70.71	79.20	85.57
F16	0	40	0	0	SMCC	39	40	4.04	6.52	11.83	24.71	38.15	50.09	60.32	69.55	77.46
F17	30.6	10.56	0	0	SMCC	37.84	41.16	4.01	7.17	14.63	30.08	43.30	55.95	67.20	77.85	86.22
F18	27.5	40	0	0	SMCC	11.5	67.5	2.31	4.17	8.24	17.96	29.21	41.17	53.29	64.99	75.59
F19	40	10	0	0	SMCC	29	50	2.88	5.40	11.27	24.86	38.60	51.95	64.81	76.28	84.81
F20	50	0	0	0	SMCC	29	50	5.31	9.45	19.17	39.94	57.87	74.10	86.23	93.65	95.97
F21	25	25	0	0	SMCC	29	50	2.82	5.06	18.75	21.82	34.05	45.99	57.20	67.94	77.93
F22	12.34	12	0	0	SMCC	54.66	24.34	16.64	22.19	31.14	48.55	62.36	72.69	81.99	90.52	95.73
F23	11.85	28	0	0	SMCC	39.15	39.85	4.18	6.79	12.60	25.94	39.42	51.21	61.50	71.11	80.05

F24	10	40	0	0	SMCC	29	50	2.94	5.18	10.35	22.53	35.67	47.70	58.78	69.09	78.44
F25	15	0	0	0	SMCC	64	15	92.81	96.85	97.89	99.20	99.24	100.01	100.02	100.06	100.12
F26	0	15	0	0	SMCC	64	15	93.18	97.98	98.85	99.45	99.67	100.02	100.03	100.13	100.32
F27	27.5	0	0	0	SMCC	51.5	27.5	10.25	15.50	25.21	44.21	61.87	75.57	88.06	95.64	97.93
F28	40	0	0	0	SMCC	39	40	4.24	7.95	16.88	36.62	56.07	72.55	84.60	93.85	97.09
F29	10.56	0	30.66	0	SMCC	37.78	41.22	3.14	4.94	7.94	14.17	21.14	28.62	36.16	43.38	50.59
F30	40	0	27.5	0	SMCC	11.5	67.5	2.47	4.27	7.51	14.17	21.70	29.82	38.66	47.59	56.56
F31	10	0	40	0	SMCC	29	50	2.67	4.34	7.16	12.94	19.10	25.58	32.46	39.38	46.15
F32	0	0	40	0	SMCC	39	40	3.27	4.95	7.94	13.81	19.86	26.07	32.29	38.53	44.62
F33	25	0	25	0	SMCC	29	50	3.13	5.21	8.75	16.13	23.86	31.78	39.69	47.40	54.68
F34	12	0	12.34	0	SMCC	54.66	24.34	10.49	13.87	19.24	29.76	41.33	52.66	62.02	70.14	77.57
F35	28	0	11.85	0	SMCC	39.15	39.85	4.01	6.49	11.30	21.97	32.85	43.48	53.29	62.00	69.68
F36	40	0	10	0	SMCC	29	50	3.02	5.40	10.34	21.70	33.84	45.47	56.17	65.39	73.69
F37	0	0	15	0	SMCC	64	15	47.51	58.51	67.32	75.15	81.00	85.71	89.41	90.74	95.18
F38	15	0	0	0	SMCC	64	15	91.47	94.62	96.46	98.10	98.81	99.26	99.18	99.18	99.53
F39	0	0	27.5	0	SMCC	51.5	27.5	5.87	8.31	11.94	18.60	25.79	33.43	41.22	48.90	56.16
F40	0	0	40	0	SMCC	39	40	2.39	3.84	6.42	11.55	17.04	22.73	28.49	34.22	39.93
F41	0	30.6	10.56	0	SMCC	37.84	41.16	3.57	5.68	9.54	17.88	27.13	36.54	45.36	53.94	61.67
F42	0	27.5	40	0	SMCC	11.5	67.5	2.38	4.01	6.98	12.82	19.10	25.56	32.06	38.61	45.12
F43	0	40	10	0	SMCC	29	50	2.72	4.66	8.30	16.39	25.39	34.46	43.34	52.10	60.57
F44	0	50	0	0	SMCC	29	50	3.79	6.19	11.20	22.94	35.43	46.56	56.05	64.44	72.55
F45	0	25	25	0	SMCC	29	50	2.52	4.20	7.04	12.72	19.08	25.90	33.03	40.10	47.44
F46	0	12.34	12	0	SMCC	54.66	24.34	10.33	13.77	18.76	27.65	37.13	46.51	54.83	62.09	68.87
F47	0	11.85	28	0	SMCC	39.15	39.85	3.64	5.46	8.76	15.13	22.14	29.67	37.08	44.17	51.16
F48	0	10	40	0	SMCC	29	50	2.93	4.68	7.82	13.86	20.16	26.72	33.42	40.07	46.57
F49	0	15	0	0	SMCC	64	15	81.98	90.77	95.35	97.03	97.12	97.21	98.01	97.60	98.17
F50	0	0	15	0	SMCC	64	15	70.22	85.23	95.59	98.31	97.47	97.87	98.79	98.41	99.01
F51	33.91	26.09	0	0	SMCC	19	60	2.37	4.13	7.88	16.82	26.94	37.27	48.23	58.83	68.71

F52	36.92	23.08	0	0	SMCC	19	60	2.46	4.36	8.36	17.21	27.20	37.88	48.34	58.15	67.68
F53	39.31	20.69	0	0	SMCC	19	60	2.24	3.84	7.57	16.72	26.94	37.38	47.88	58.33	68.44
F54	31.09	23.91	0	0	SMCC	24	55	2.75	4.85	9.52	20.67	32.73	44.74	56.00	66.23	75.51
F55	33.85	21.15	0	0	SMCC	24	55	2.35	3.92	7.48	16.04	25.92	36.09	46.10	56.15	66.22
F56	36.03	18.97	0	0	SMCC	24	55	2.73	4.66	9.18	19.66	31.21	41.85	51.79	62.68	72.73
F57	28.26	21.74	0	0	SMCC	29	50	2.93	4.93	9.46	20.12	31.14	42.31	53.08	63.58	73.41
F58	30.77	19.23	0	0	SMCC	29	50	2.98	5.04	9.62	20.73	32.14	42.95	52.98	62.94	72.90
F59	32.76	17.24	0	0	SMCC	29	50	2.89	5.27	10.72	23.82	37.07	49.50	60.99	70.95	79.68
F60	33.87	16.13	0	0	SMCC	29	50	2.67	4.68	9.41	20.14	32.00	43.92	56.02	67.24	77.24
F61	35.71	14.29	0	0	SMCC	29	50	2.74	4.85	9.62	21.00	32.57	43.76	54.86	66.60	77.73
F62	36.84	13.16	0	0	SMCC	29	50	2.81	4.97	9.79	21.12	33.05	45.59	57.45	68.45	77.99
F63	33.87	16.13	0	0	SMCC	29	50	2.71	4.72	9.04	19.29	30.11	40.99	52.26	63.48	72.99
F64	24.62	15.38	0	0	SMCC	39	40	3.51	5.96	11.30	24.25	37.20	49.14	60.95	71.67	81.07
F65	27.1	12.9	0	0	SMCC	39	40	3.48	5.85	11.60	25.43	39.17	52.57	64.55	74.95	84.24
F66	29.47	10.53	0	0	SMCC	39	40	3.61	6.16	11.86	25.23	38.09	50.92	63.26	74.49	83.08
F67	27.1	12.9	0	0	SMCC	39	40	2.98	5.30	10.65	23.34	36.73	49.56	61.67	73.26	82.46
F68	36.84	13.16	0	0	SMCC	29	50	2.26	4.00	7.93	17.59	27.71	38.28	48.68	59.36	70.42
F69	36.84	13.16	0	0	SMCC	29	50	2.61	4.82	9.83	22.04	34.10	47.11	59.31	70.72	81.99
F70	37.8	12.2	0	0	SMCC	29	50	2.67	4.69	9.43	20.86	33.47	45.71	57.51	68.27	78.25
F71	39.36	10.64	0	0	SMCC	29	50	3.05	5.48	11.14	24.91	39.42	53.37	67.06	78.06	86.62
F72	24	0	0	16	MD-IT12	39	40	3.35	5.64	10.02	18.91	27.93	37.60	46.92	56.90	67.21
F73	30	0	0	10	MD-IT12	39	40	3.03	6.06	11.87	25.58	38.75	52.81	66.92	78.17	86.17
F74	32.73	0	0	7.27	MD-IT12	39	40	3.17	5.95	12.05	25.56	39.68	54.01	69.59	84.10	94.20
F75	24	0	0	16	G721	39	40	3.68	6.21	10.99	20.34	30.51	41.38	52.74	64.13	74.10
F76	30	0	0	10	G721	39	40	3.36	5.89	11.32	20.46	35.45	49.72	65.03	78.98	90.64
F77	32.73	0	0	7.27	G721	39	40	3.33	5.90	11.82	26.29	41.78	59.29	77.46	91.14	96.68
F78	31.11	0	0	8.89	MD-IT12	39	40	2.43	4.63	9.96	21.29	32.88	44.87	58.28	70.03	79.98
F79	32	0	0	8	MD-IT12	39	40	2.84	5.19	10.48	22.22	34.25	47.07	60.06	72.89	84.18

F80	30	0	0	0	G721	49	30	2.84	5.21	9.88	19.90	30.20	40.74	51.92	63.73	76.88
F81	31.67	0	0	8.33	G721	39	40	2.71	5.17	10.74	23.59	37.02	50.22	66.70	83.67	95.22
F82	29.47	0	0	10.53	G721	39	40	3.47	6.32	12.65	26.24	41.32	57.16	70.77	80.63	87.44
F83	30	0	0	10	G721	39	40	3.02	5.65	10.53	20.92	32.56	44.52	58.57	70.36	83.18
F84	30.48	0	0	9.52	G721	39	40	3.26	5.96	11.08	22.61	35.11	46.99	59.74	71.89	84.22
F85	21	49	0	0	SMCC	11.8	70	1.99	3.66	6.95	15.21	24.64	33.92	42.88	51.60	59.95
F86	28	42	0	0	SMCC	11.8	70	2.08	3.60	7.17	15.89	25.90	36.20	46.43	56.51	65.86
F87	19.5	45.5	0	0	SMCC	16.8	65	2.30	4.06	7.72	15.93	25.15	34.75	44.72	54.88	65.11
F88	24	36	0	0	SMCC	21.8	60	2.18	3.92	7.92	17.91	28.05	38.00	48.00	58.06	67.59
F89	18	42	0	0	SMCC	21.8	60	2.29	3.94	7.46	16.06	25.22	34.32	43.62	52.93	61.74
F90	15	45	0	0	SMCC	21.8	60	2.32	4.13	7.82	17.11	26.98	36.84	46.32	55.39	63.89
F91	17.5	52.5	0	0	SMCC	11.8	70	2.36	4.05	7.49	15.36	24.37	34.30	44.34	54.56	64.19

Table S2

Model screening report for each continuous response – R^2 and RASE.

Response		Method										
		ANN	BF	BT	Fit Stepwise (Linear)	Fit Stepwise (2FI Quad)	KNN	Lasso (Linear)	Lasso (2FI Quad)	Least Squares (Linear)	Least Squares (2FI Quad)	SVM
15	R^2	0.873	0.425	0.367	0.583	0.631	0.525	0.640	0.716	0.582	0.216	0.356
	RASE	1.002	2.135	2.239	1.818	1.710	1.939	1.688	1.500	1.820	2.492	2.259
30	R^2	0.914	0.319	0.365	0.618	0.710	0.467	0.643	0.705	0.618	0.352	0.335
	RASE	1.057	2.967	2.864	2.221	1.935	2.624	2.149	1.952	2.221	2.895	2.931
60	R^2	0.909	0.316	0.355	0.650	0.478	0.428	0.651	0.677	0.650	0.478	0.270
	RASE	1.451	3.978	3.863	2.848	3.476	3.639	2.843	2.735	2.848	3.476	4.110
120	R^2	0.904	0.373	0.316	0.615	0.883	0.412	0.615	0.689	0.615	0.624	0.175
	RASE	2.295	5.854	6.115	4.589	2.534	5.670	4.589	4.120	4.589	4.535	6.715
180	R^2	0.921	0.265	0.349	0.523	0.852	0.375	0.518	0.667	0.518	0.651	0.172
	RASE	2.777	8.462	7.962	6.812	3.793	7.801	6.853	5.697	6.853	5.826	8.980
240	R^2	0.897	0.210	0.338	0.513	0.798	0.362	0.450	0.672	0.450	0.666	0.207
	RASE	3.629	10.049	9.193	7.888	5.081	9.027	8.379	6.474	8.379	6.531	10.068
300	R^2	0.876	0.128	0.311	0.414	0.773	0.346	0.401	0.683	0.401	0.684	0.257
	RASE	4.236	11.245	10.000	9.216	5.736	9.736	9.320	6.786	9.320	6.769	10.378
360	R^2	0.852	0.194	0.345	0.406	0.734	0.363	0.383	0.694	0.383	0.703	0.292
	RASE	4.583	10.704	9.644	9.187	6.151	9.515	9.363	6.592	9.363	6.501	10.031
420	R^2	0.832	0.219	0.375	0.411	0.748	0.386	0.379	0.714	0.379	0.717	0.382
	RASE	4.288	9.246	8.276	8.031	5.250	8.201	8.244	5.593	8.244	5.570	8.224

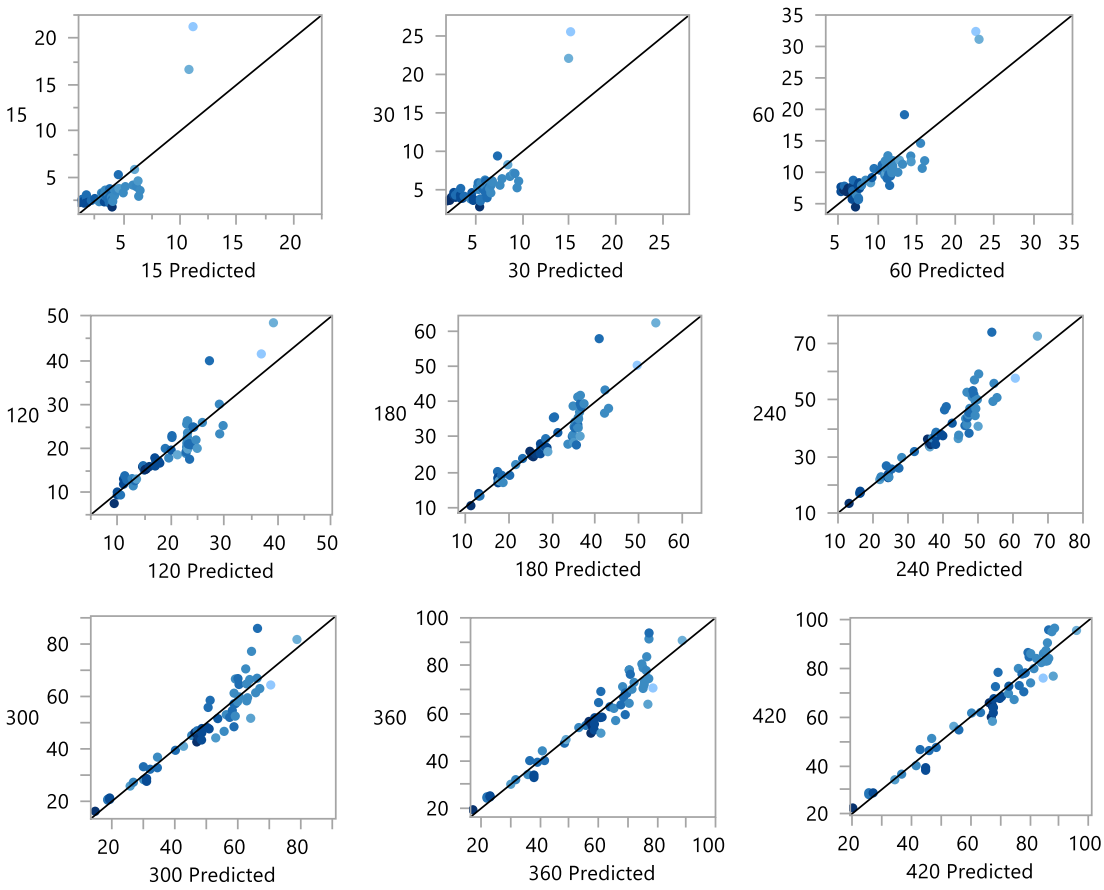

Fig. S1. Plots of Actual by predicted results for training dataset, for the nine dissolution time points. The gradient color represents the increase in total polymer percentage in the formulation.

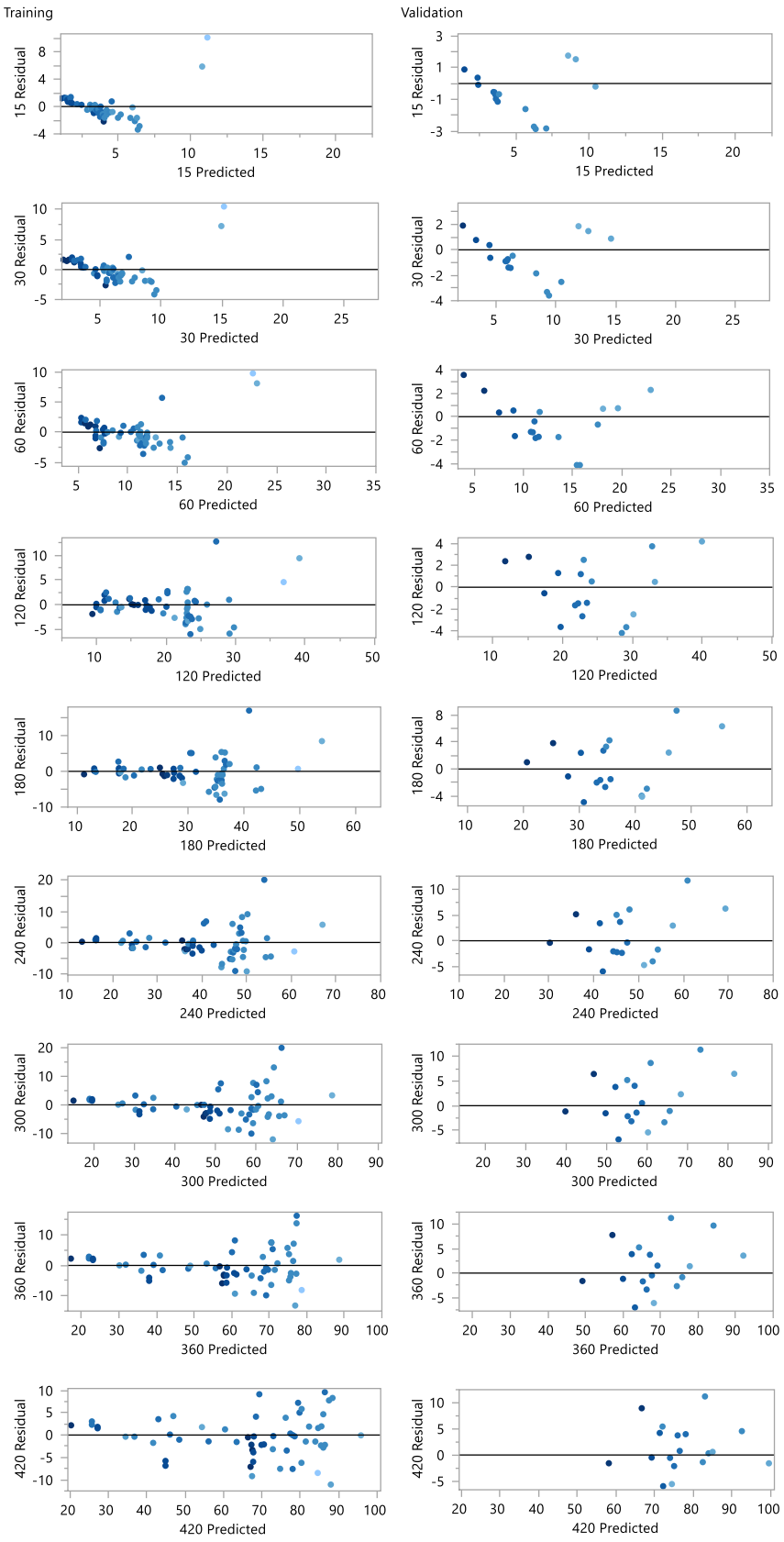

Fig. S2. Residual plots of predicted dissolution time points from the proposed ANN model.