

Supporting Information

Tablet formulation of 2-((3-(chloromethyl)benzoyl)oxy)benzoic acid by linear and quadratic models

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Chapter S1. Tablet Dosage Calculation

Data on 3CH₂Cl based on pharmacokinetic experiments on rats were plasma drug concentration (C_p) = 0.57 g/mL; volume of distribution (V_d) = 7200 mL; elimination constant (K_{el}) = 0.0003/hour; and bioavailability (F) = 0.8.

$$\text{Amount of drug in the body (A)} = C_p \times V_d = 0.57 \text{ g/mL} \times 7200 \text{ mL} = 4104 \text{ g} = 4.104 \text{ mg}$$

$$\text{Rate out} = K_{el} \times A = 0.0003 \text{ hours}^{-1} \times 4.104 \text{ mg} = 0.0012 \text{ mg/hour}$$

$$\text{Release rate} = \text{Rate out} / F = 0.0012 \text{ mg/hour} / 0.8 = 0.0015 \text{ mg/hour}$$

The drug preparation is designed to release the drug for 8 hours

$$\text{Maintenance dose (DM)} = \text{Release rate} \times 8 \text{ hours} = 0.0015 \text{ mg/hour} \times 8 \text{ hours} = 0.0123 \text{ mg}$$

$$\text{Load dose (LD)} = A/F = 4.104 \text{ mg} / 0.8 = 5.13 \text{ mg}$$

$$\text{Total dose} = \text{DM} + \text{LD} = 0.0123 \text{ mg} + 5.13 \text{ mg} = 5.1423 \text{ mg (rat dose 200 g)}$$

$$\text{Human dose (DH)} = \text{Rat dose} \times \text{conversion factor} = 5.1423 \text{ mg} \times 56 = 287.9695 \text{ mg} \approx 300 \text{ mg}$$

Table S1. Statistical analysis of 3CH₂Cl tablets

ANOVA	Flow time	Carr index	Hardness	Friability	Disintegrating time	Drug release
R-Squared	0.9897	0.9868	0.9857	0.9932	0.9908	0.9896
Adj R-Squared	0.9795	0.9737	0.9715	0.9865	0.9817	0.9792
Pred R-Squared	0.8613	0.8224	0.8075	0.9088	0.8761	0.8597
Adeq Precision	17.0000	15.0000	14.4000	21.0000	18.0000	16.9000

The coefficient of the polynomial equation of the linear model is accepted if the difference between R-Square and Pred R-Square is less than 0.2 and Adeq Precision is more than 4.

Table S2. The release of 3CH₂Cl from the tablets

t [min.]	TA		TB		TC		T Opt.	
	[%]	SD	[%]	[%]	[%]	SD	[%]	SD
0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
10	26.54	1.12	28.74	1.93	39.18	1.06	34.29	0.97
20	41.29	0.88	42.34	1.39	56.24	1.80	51.51	0.82
30	50.40	0.22	51.53	1.57	67.64	1.81	63.73	1.01
45	54.74	1.07	60.62	1.50	76.25	1.25	73.31	0.82
60	59.41	0.95	69.95	1.00	85.04	1.05	81.53	0.86

The release of 3CH₂Cl from tablets contains SLS [%] and CS [%]: TA (0.50:4.00), TB (0.75:3.00), TC (1.00:2.00), and and T Opt. (0.92:2.33).

The release kinetics of 3CH₂Cl from tablets for each formula was based on the similarity of the observed point profile to the predicted line profile using DDSolver software (Figure S1-S4).

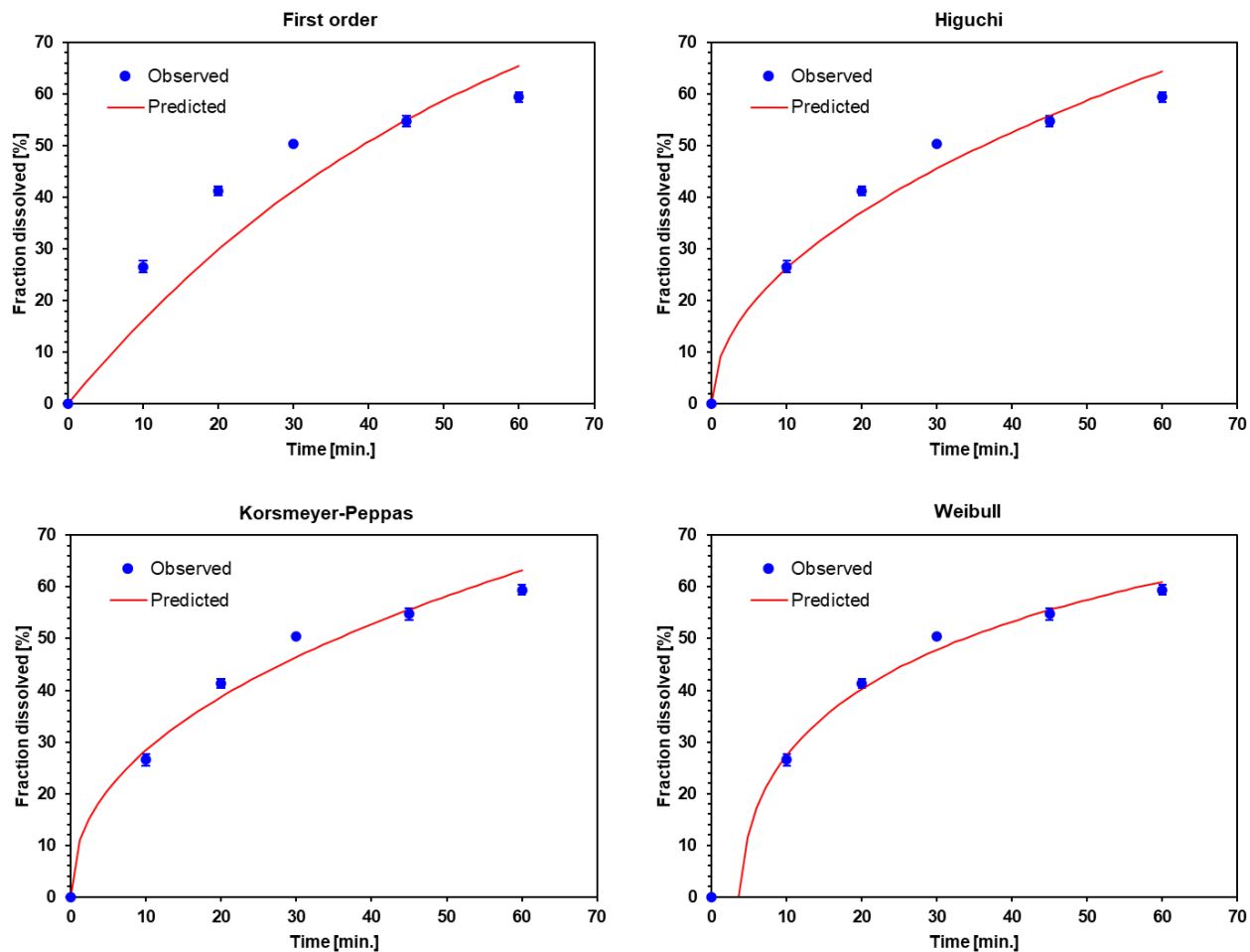


Figure S1. The kinetics profile of the release of 3CH₂Cl from TA tablets with various model kinetic. Based on the profile, the observation point is most similar to the Weibull model prediction line with a value of Rsqr_adj 0.9907; MSE_root 2.0408; and AIC 20.5635.

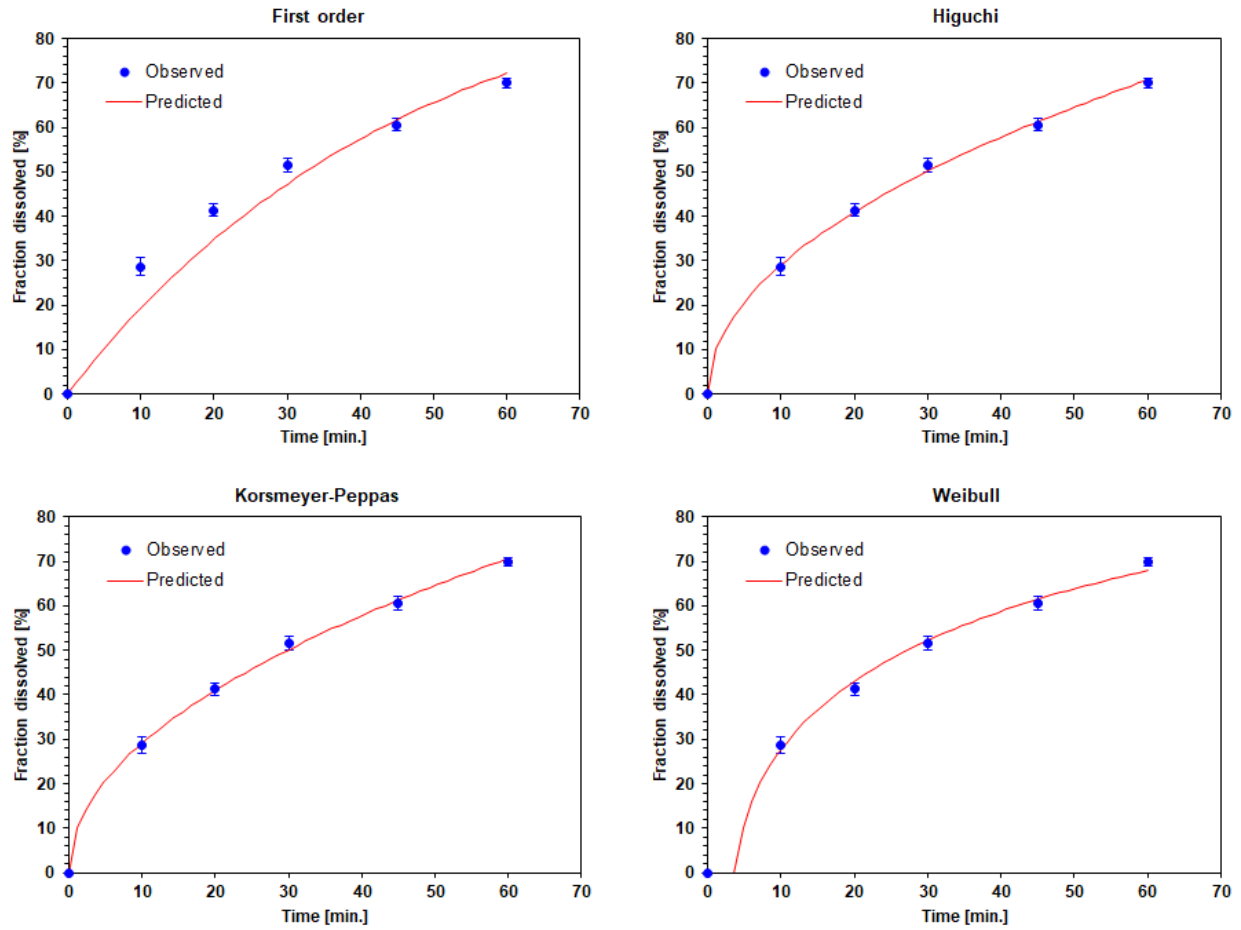


Figure S2. The kinetics profile of the release of 3CH₂Cl from TB tablets with various model kinetic. Based on the profile, the point of observation is most similar to the Higuchi model prediction line with a value of Rsqr_adj 0.9966; MSE_root 1.4227; and AIC 15.3644.

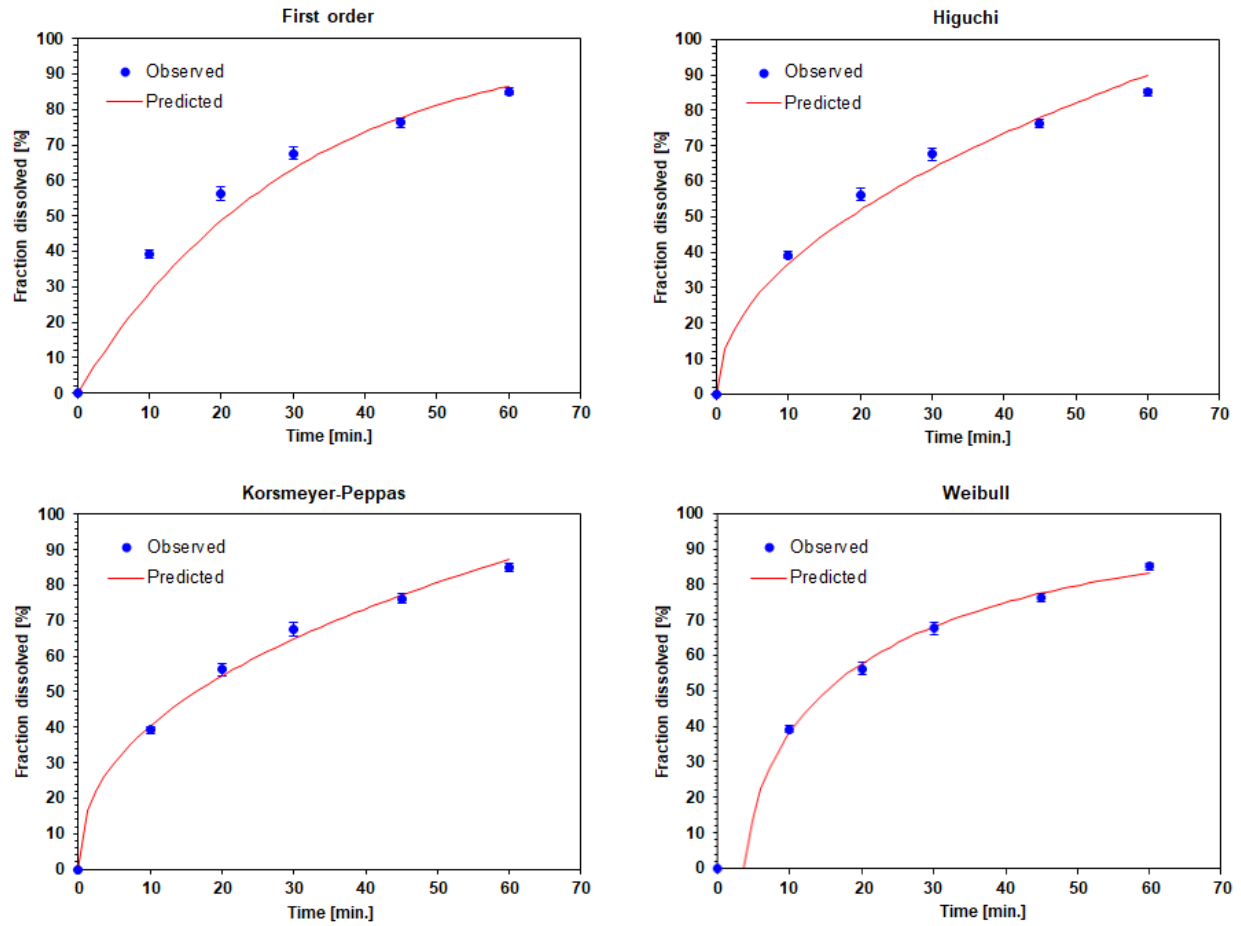


Figure S3. The kinetics profile of the release of 3CH₂Cl from TC tablets with various model kinetic. Based on the profile, the point of observation is most similar to the Weibull model prediction line with a value of Rsqr_adj 0.9963; MSE_root 1.8553; and AIC 19.9178.

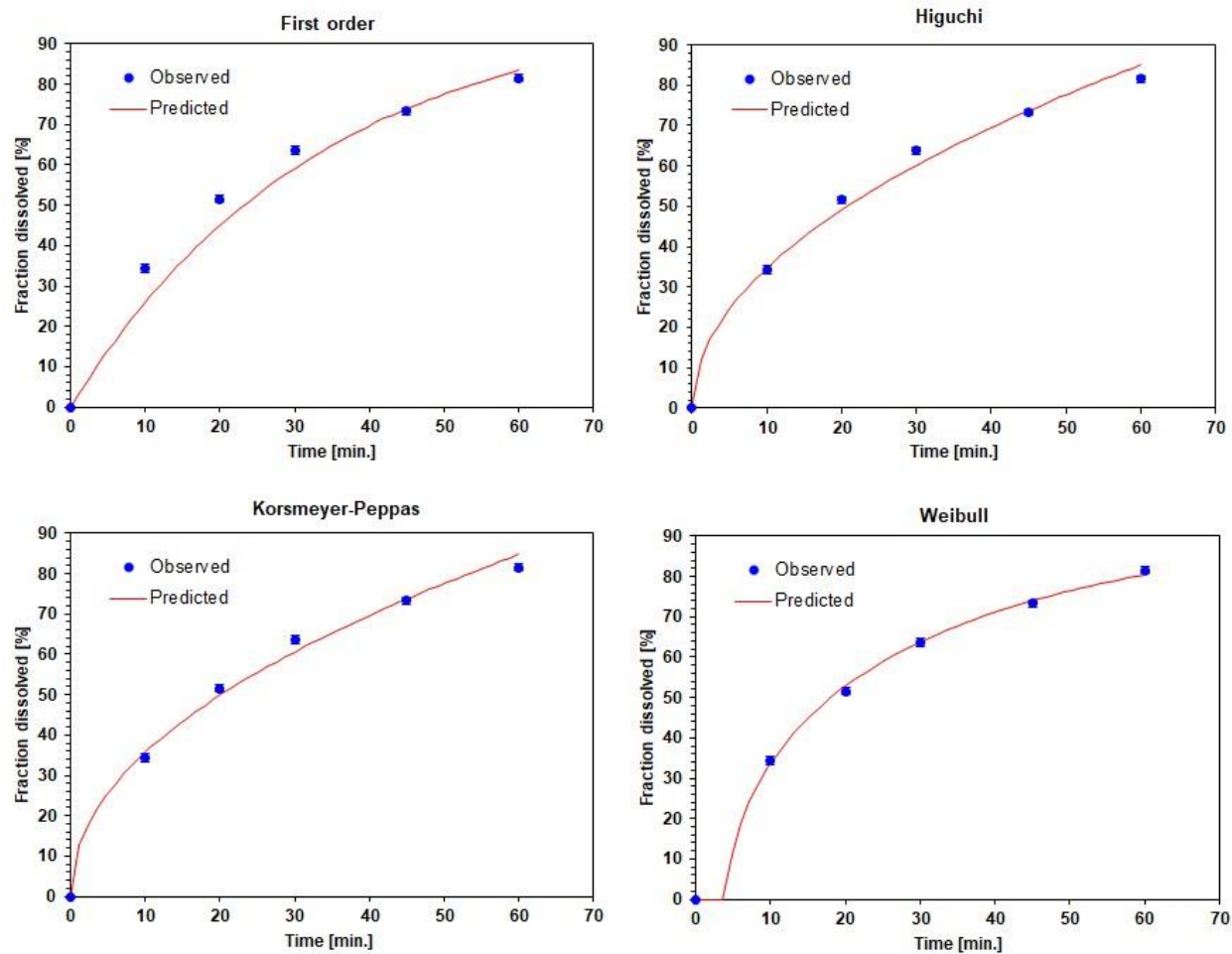


Figure S4. The kinetics profile of the release of 3CH₂Cl from T Opt. tablets with various model kinetic. Based on the profile, the point of observation is most similar to the Higuchi model prediction line with a value of Rsqr_adj 0.9979; MSE_root 1.2986; and AIC 14.8858.