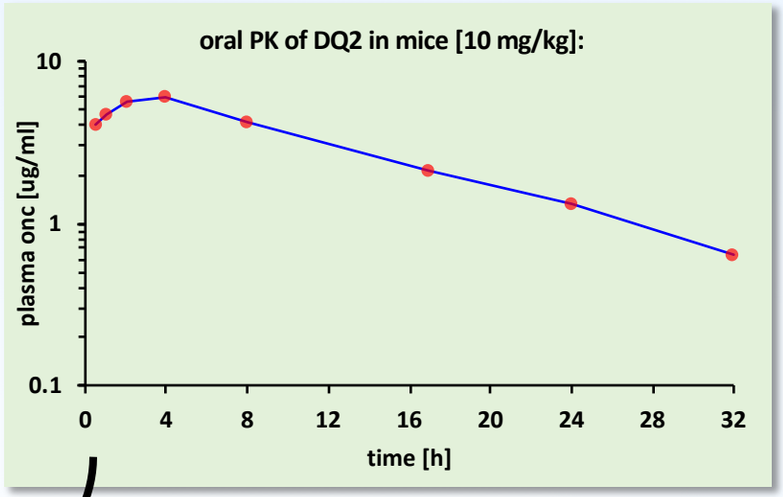
Graphical Estimation of Oral Pharmacokinetic Parameters

Ramesh Jayaraman, DoseQuantics Consulting

Dose Quantics

As a part of a PK/PD study, DQ2 was dosed orally to mice at a dose of 10 mg/kg. The mean plasma concentration time are tabulated. PK parameters were estimated graphically using the method of residuals and non-compartmental analysis.

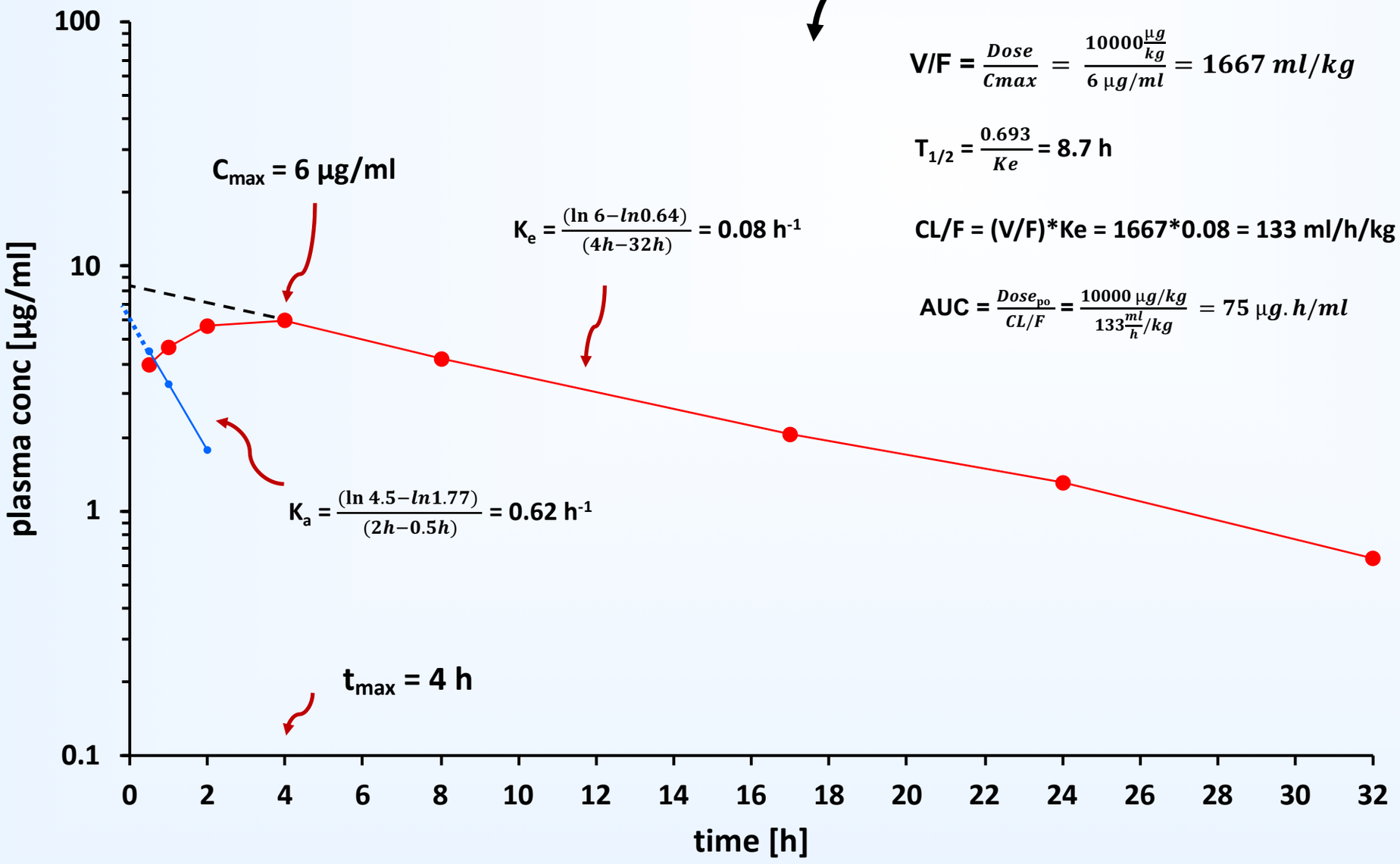
Time (h)	Plasma conc. (µg/ml)
0.5	4.00
1	4.68
2	5.73
4	6.00
8	4.20
17	2.08
24	1.31
32	0.64



- First order absorption
- First order elimination
- One compartment elimination post peak

$$C = \frac{K_a * F * Dpo}{V(ka - Ke)} \left[e^{-Ke*t} - e^{-Ka*t}\right]$$

Graphical estimate of PK parameters of DQ2 in mice



$$V/F = \frac{Dose}{Cmax} = \frac{10000 \frac{\mu g}{kg}}{6\ \mu g/ml} = 1667\ ml/kg$$

$$T_{1/2} = \frac{0.693}{Ke} = 8.7\ h$$

$$CL/F = (V/F) * Ke = 1667 * 0.08 = 133\ ml/h/kg$$

$$AUC = \frac{Dose_{po}}{CL/F} = \frac{10000\ \mu g/kg}{133 \frac{ml}{h}/kg} = 75\ \mu g.h/ml$$

Method of residuals for estimation of Ka

Time (h)	Plasma conc. (µg/ml)	Residuals for Ka (µg/ml)
0.5	4.0	4.5
1	4.68	3.32
2	5.73	1.77
4	6.0	
8	4.2	
17	2.08	
24	1.31	
32	0.64	

Graphical estimates of PK parameters of DQ2 in mice

Parameter	Estimate
K_e (h^{-1})	0.080
K_a (h^{-1})	0.622
V/F (ml/kg)	1667
Cl/F (ml/h/kg)	133
$AUC_{0-\infty}$ (µg.h/ml)	75
C_{max} (µg/ml)	6.0
T_{max} (h)	4.0
$T_{1/2}$ (h)	8.7

Parameter estimates can be used as input parameters for PK and PK/PD modelling & simulation