
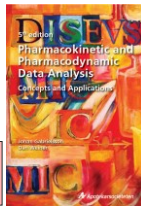


PML School: PK40
Enterohepatic Recirculation





Note: The exercise is based on exercise PK40 in the text: Gabrielsson, J. & Weiner, D.L. (5th ed., 2016). *Pharmacokinetic and Pharmacodynamic Data Analysis: Concepts and Applications*. Swedish Pharmaceutical Press, Stockholm.

PK40: Objective

- Model enterohepatic recirculation after intravenous administration
- Find estimates for
 - Cl – plasma clearance
 - V_c – central volume
 - Cl_g – inter-compartmental distribution
 - V_t – peripheral volume
 - K_a – absorption rate constant
 - K_{1g} – bile excretion rate constant
 - τ – bile emptying interval

Gabrielsson & Weiner, Pharmacokinetic and Pharmacodynamic Data Analysis - Concepts and Applications, 5th Edition, Swedish Pharmacology Press (2016)

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PK40: Problem specification

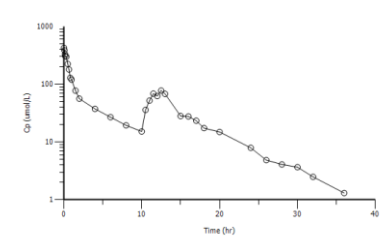
- 1 subject received an intravenous bolus dose of 5,617.3 µg
- Plasma concentrations were measured over a period of 36 hours

Gabrielsson & Weiner, Pharmacokinetic and Pharmacodynamic Data Analysis - Concepts and Applications, 5th Edition, Swedish Pharmacology Press (2016)

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PK40: Exploratory Data Analysis

- Semilog plot of concentration versus time



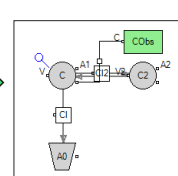
Gabrielsson & Weiner, Pharmacokinetic and Pharmacodynamic Data Analysis - Concepts and Applications, 5th Edition, Swedish Pharmacology Press (2016)

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PK40: From Built-In to Graphical Model

Population?	Structure	Parameters	Input Options	Initial Estimates	Run Options	Model Test	Plot
Type: [PK]	Parameterization: Absorption: [Intravenous]	Num. Compartments: [2]	Parameters: V, V2, Q, C1, C2	Statements: deriv(A1 + Q * C2 * (C - C2)), deriv(A2 + Q2 * (C - C2)), C = A1 / V, C2 = A2 / V2	Residual Error: C [CObs] [Eps] [Multivariate]	BOL? []	Stdev: [] [Freeze]

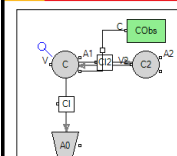
↘



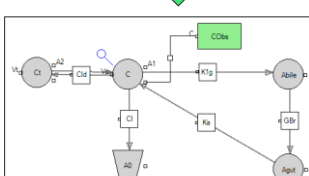
Need to add compartments and flows for bile and gut through graphical model

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PK40: Graphical Model



↘



Need to add bile emptying event in textual model

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Coming up...

Accessing Grid Computing from Your Desktop for NLME

Speakers: Fred Sotanshahi, Michael Tomashevsky, Serge Guzy
Date: January 25, 2017
Time: 11 am EST
Duration: 1 hour



One-compartment 1st and 0-order Input

Fit and discriminate between first and zero-order absorption models
 February 2, 2017 | 10am EST
Presenter: Chris Mehl

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