Pharmacokinetics of Drug Absorption

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1. One compartment open model, Oral route.
2. Determination of absorption rate constant (Plasma data, Urine data).
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One compartment open model, Oral route

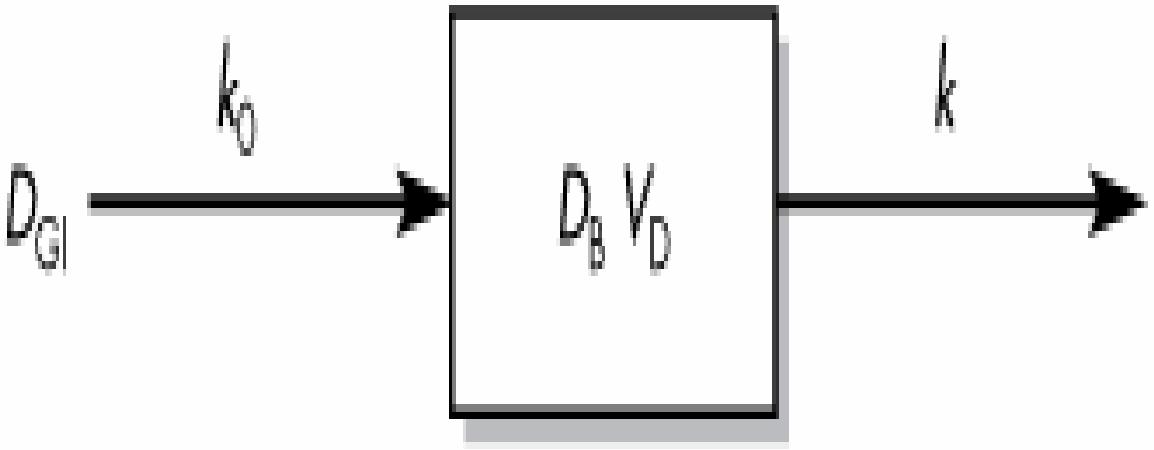
- Although this chapter will focus primarily on oral dosing.
- In pharmacokinetics, the overall rate of drug absorption may be described as either a **first-order** or **zero-order** input process.
- Most pharmacokinetic models assume first-order absorption unless an assumption of zero-order absorption improves the model significantly or has been verified experimentally

Drug absorption

- **Zero order process** can be defined as the one whose rate is independent of concentration of drug undergoing reaction that is the rate of reaction cannot be increased by further increase in concentration of reactants.

- **First Order process** is the one whose rate is directly proportional to concentration of the drug undergoing reaction that is greater the concentration faster the reaction.

Zero-order absorption model

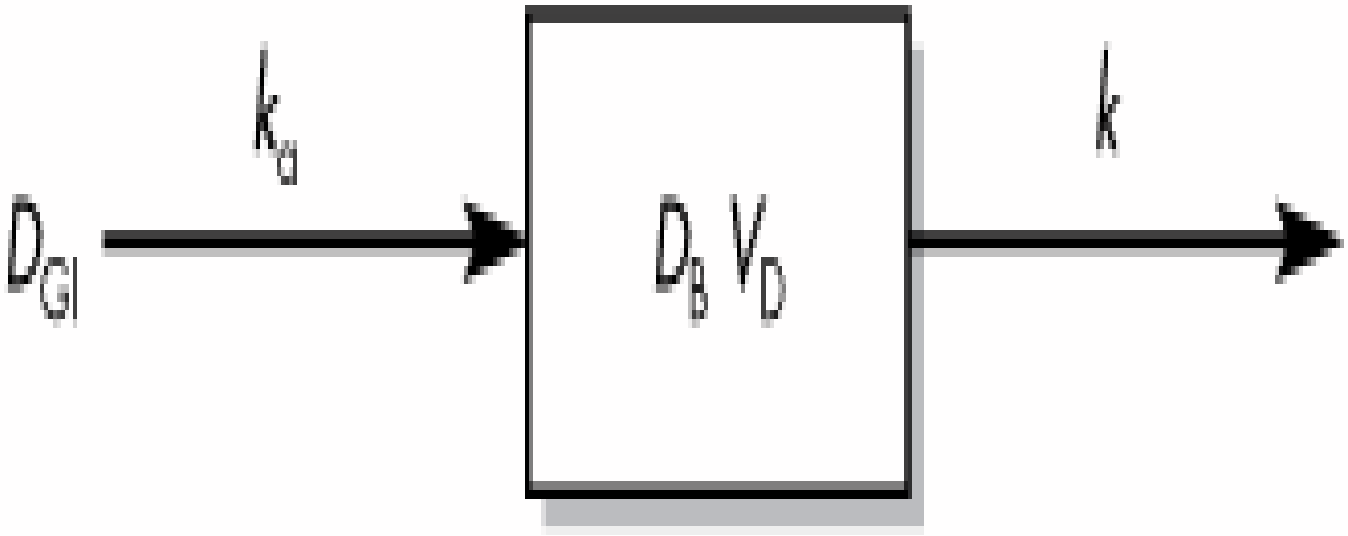


One-compartment pharmacokinetic model for zero-order drug absorption and first-order drug elimination.

Zero-order absorption model

- Zero-order drug absorption from the dosing site into the plasma usually occurs when either the drug is absorbed by a saturable process or a zero-order controlled-release delivery system is used.
- The pharmacokinetic model assuming zero-order absorption is described in this model, drug in the gastrointestinal tract, D_{GI}, is absorbed systemically at a constant rate, k_0.
- Drug is simultaneously and immediately eliminated from the body by a first-order rate process defined by a first-order rate constant, k.

First-order absorption model

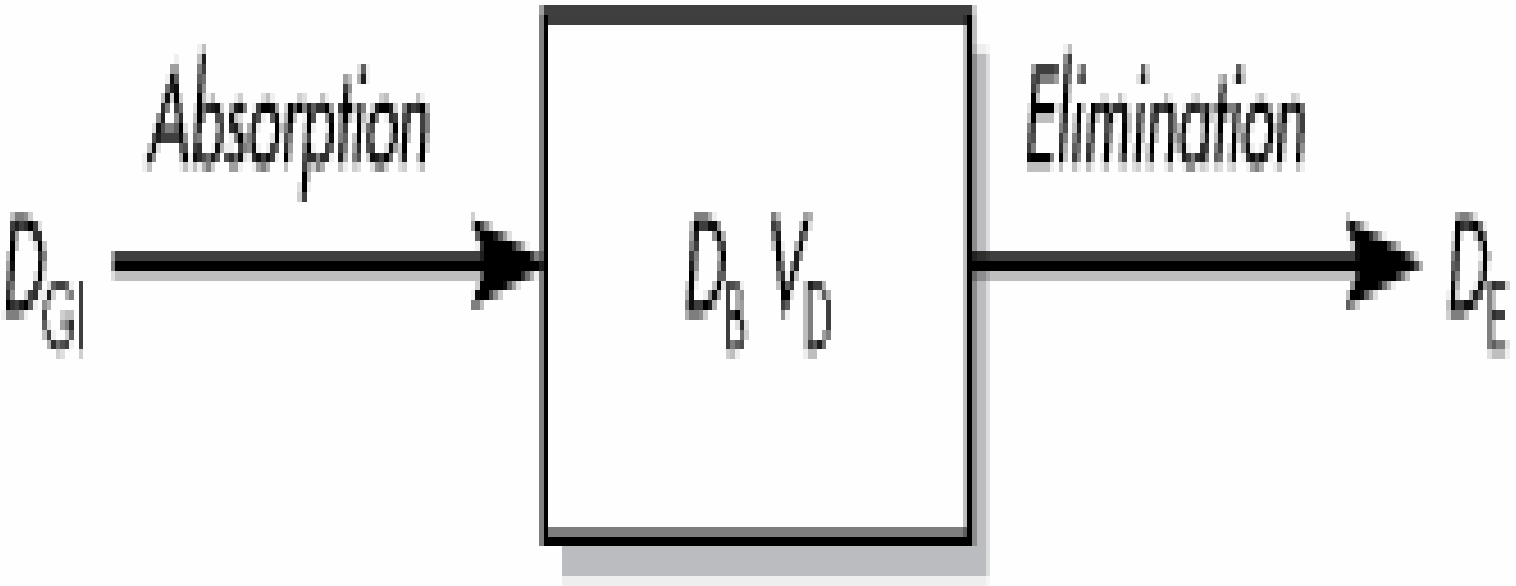


One-compartment pharmacokinetic model for first-order drug absorption and first-order elimination.

First-order absorption model

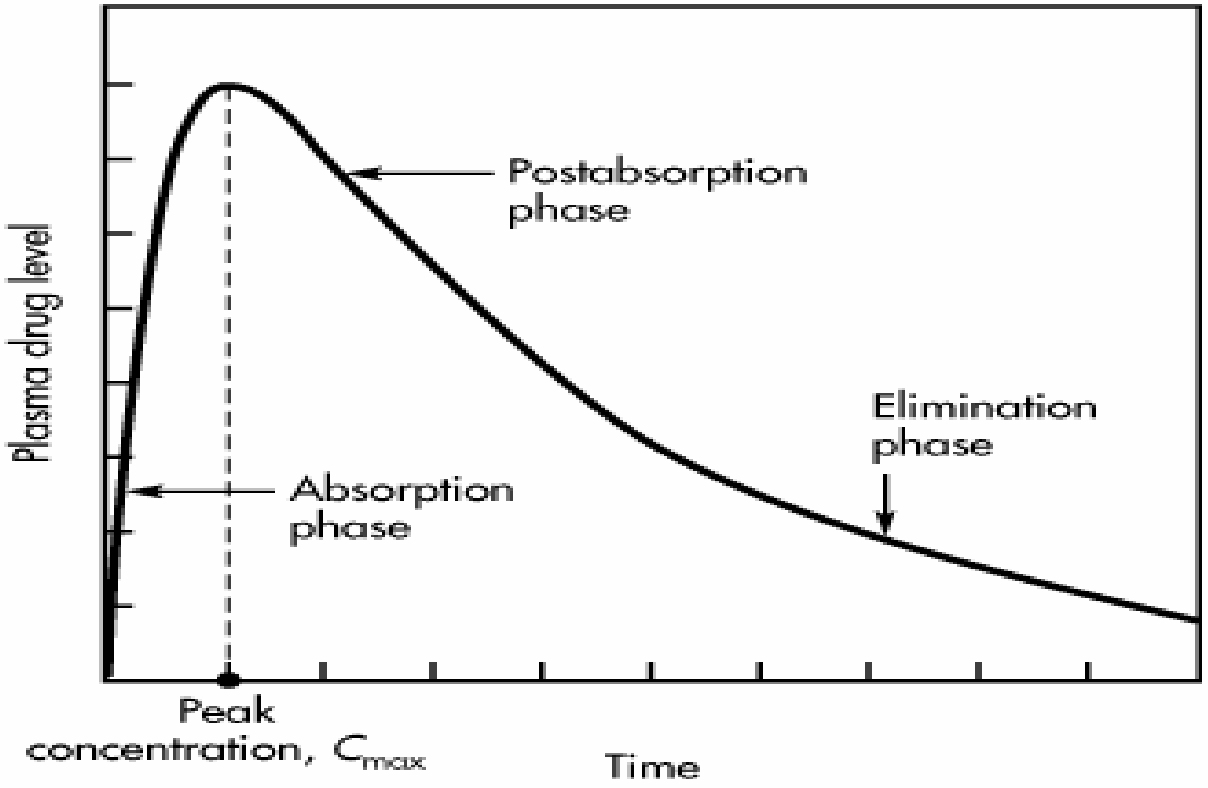
- Although zero-order absorption can occur, absorption is usually assumed to be a first-order process.
- This model assumes a first-order input across the gut wall and first-order elimination from the body.
- This model applies mostly to the oral absorption of drugs in solution or rapidly dissolving dosage (immediate release) forms such as tablets, capsules, and suppositories.

Absorption and elimination



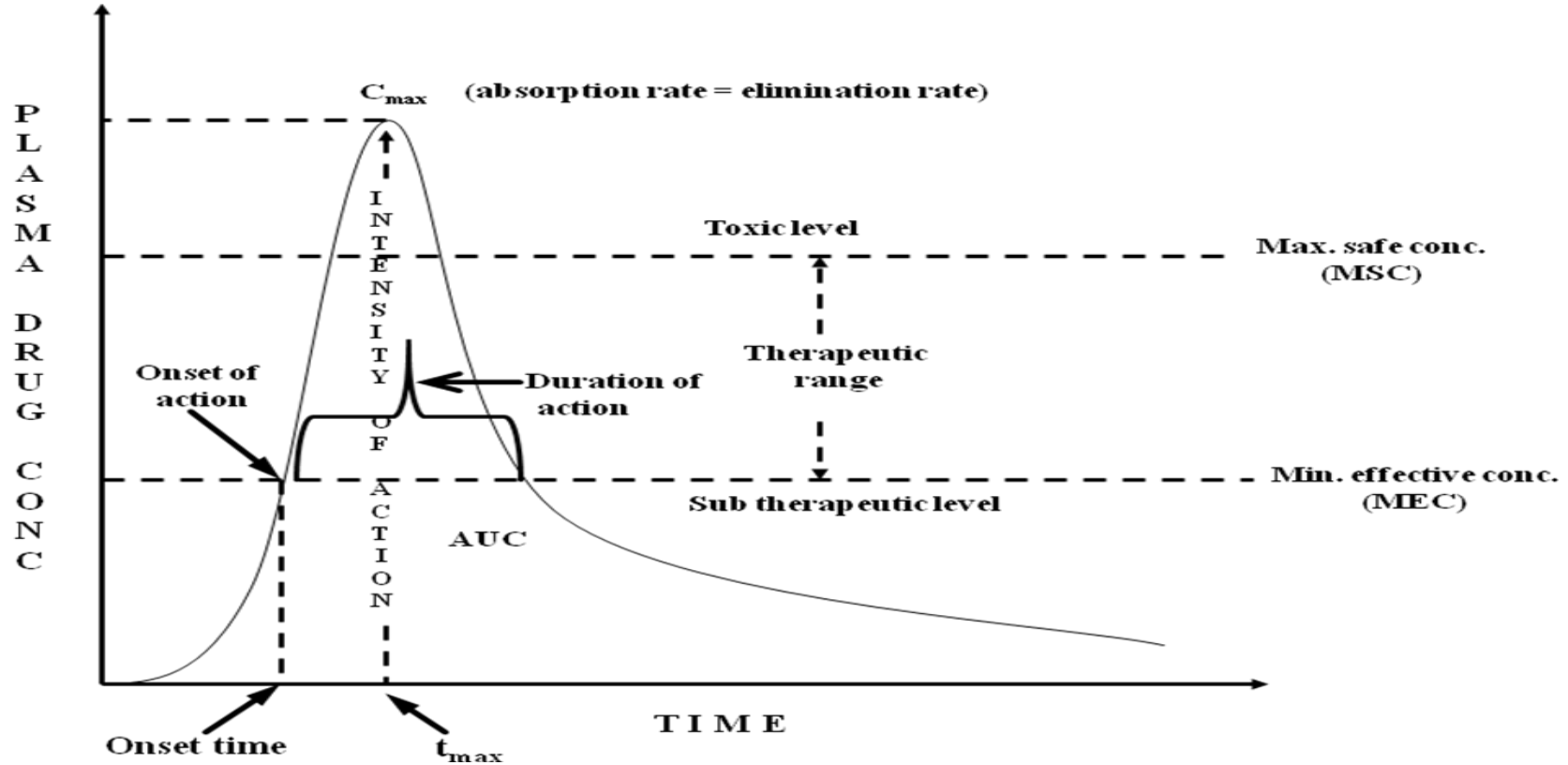
Model of drug absorption and elimination
D_B =drug in body; V_D = apparent volume of distribution

Single oral dose



Plasma level–time curve for a drug given in a single oral dose. The drug absorption and elimination phases of the curve are shown.

Pharmacokinetic and Pharmacodynamic



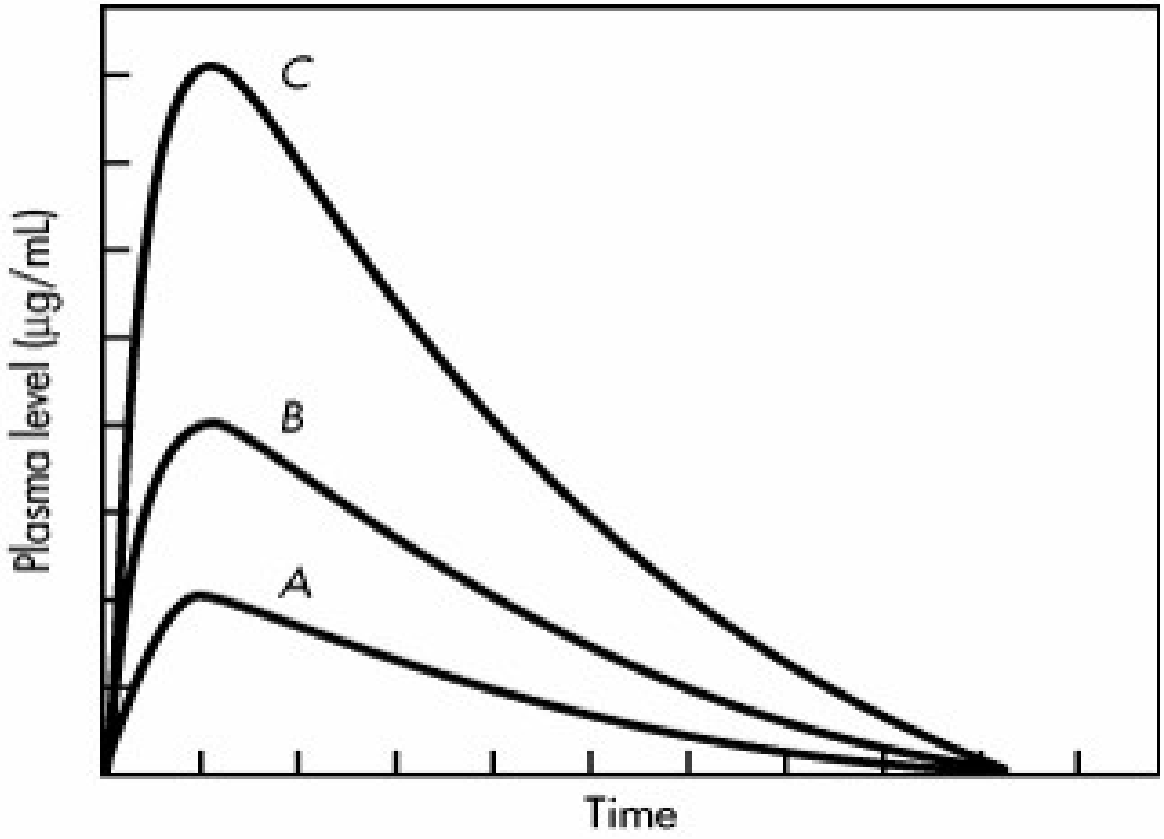
A typical plasma concentration-time profile showing pharmacokinetic and pharmacodynamic parameters obtained after oral administration of single dose of drug.

Determination of absorption rate constant (plasma data, Urine data)

- The absorption rate constant is determined by a method known as “feathering,” “method of residuals,” or “curve stripping.”

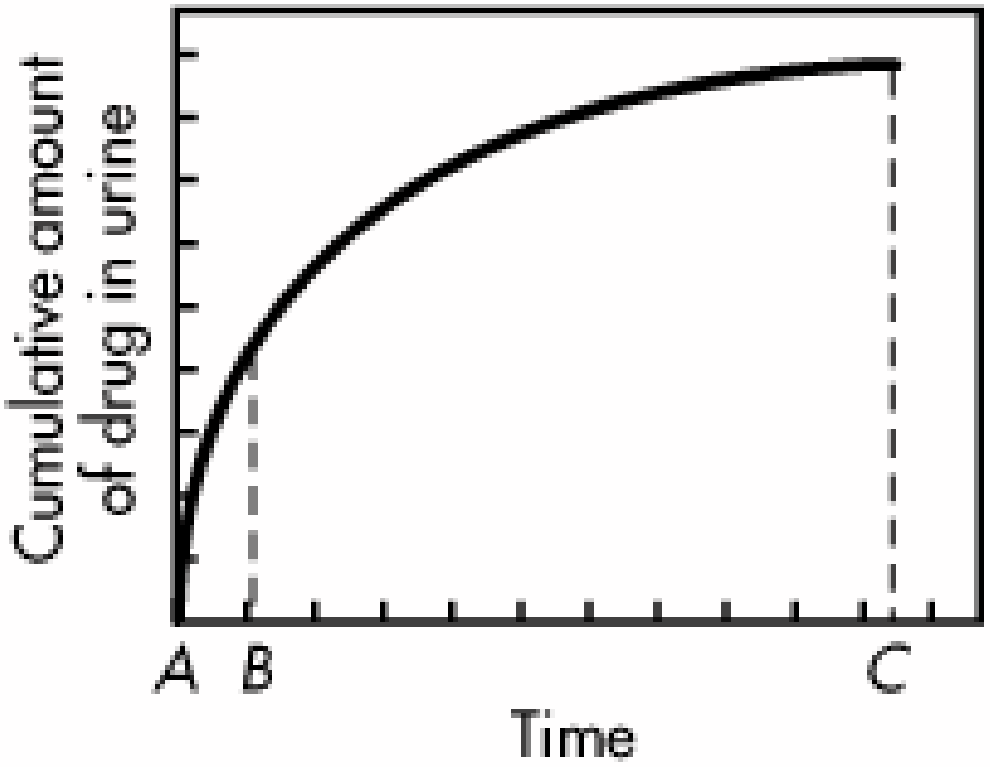
- From the plasma concentration versus time data obtained or provided to you and the plot of the data

Plasma data



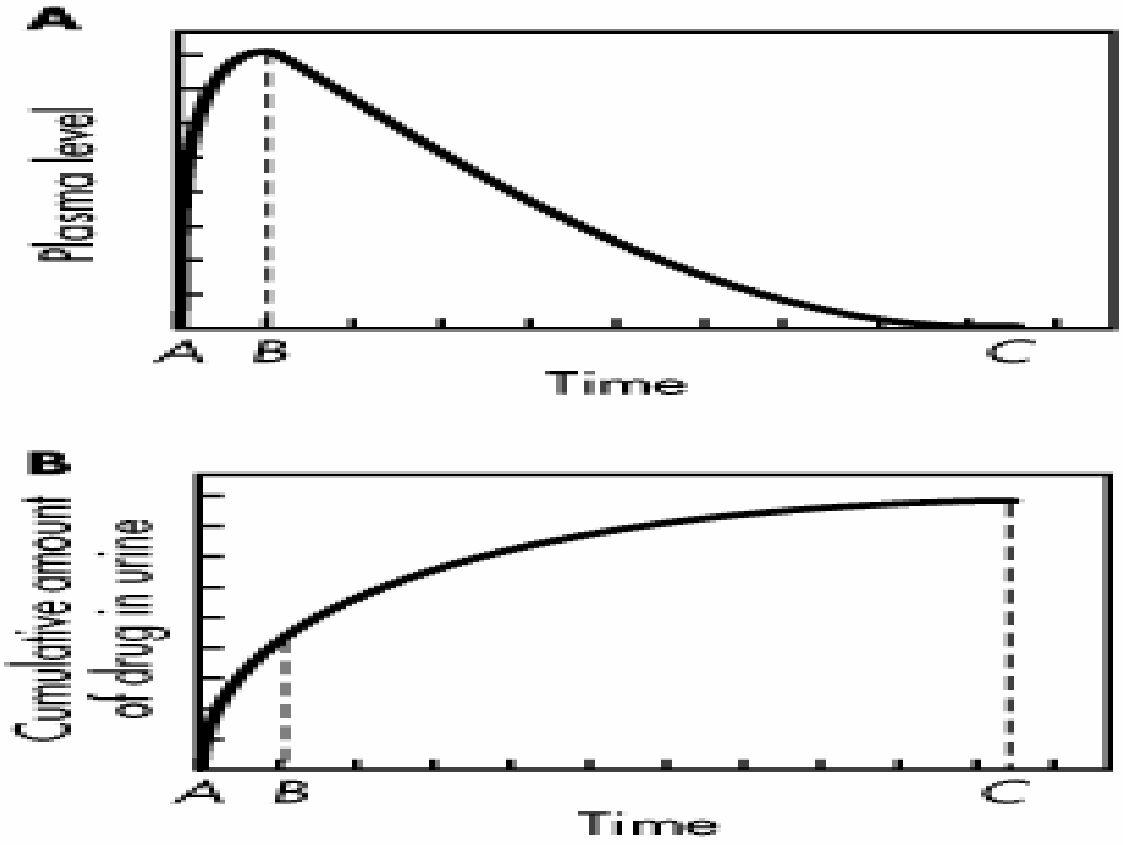
Plasma level–time curve following administration of single doses of **(A)** 250 mg, **(B)** 500 mg, and **(C)** 1000 mg of drug.

Urine data



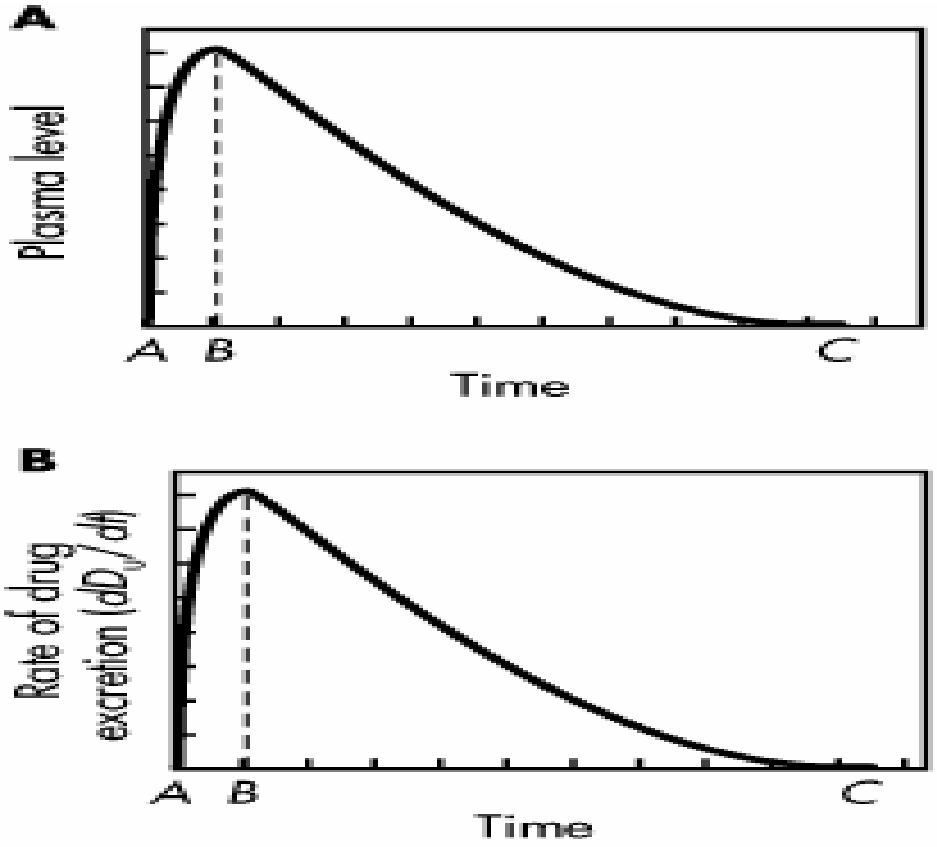
Corresponding plots relating the plasma level–time curve and the cumulative urinary drug excretion

Plasma and Urine data



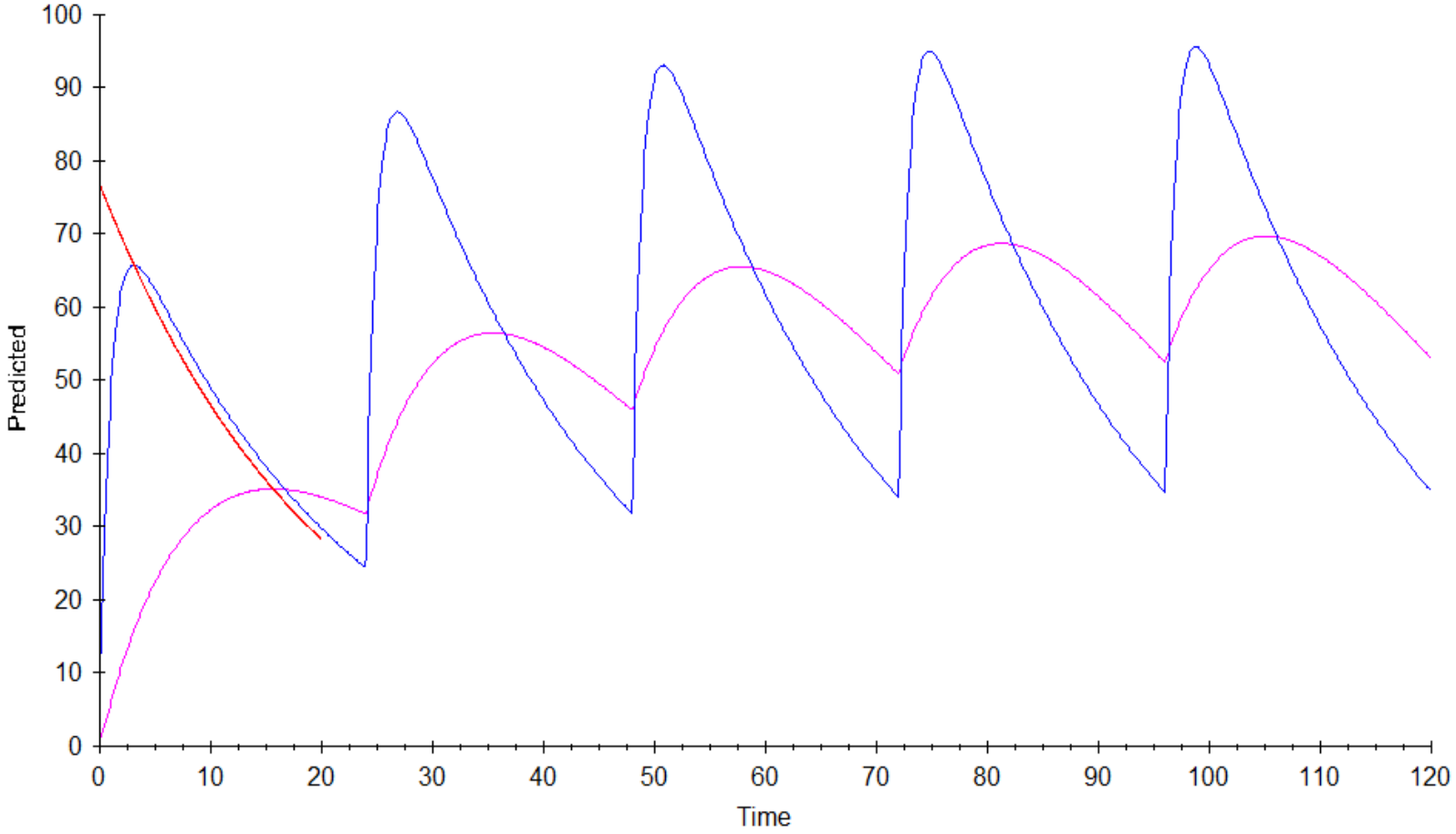
Corresponding plots relating the plasma level–time curve and the cumulative urinary drug excretion.

Plasma and Urine data

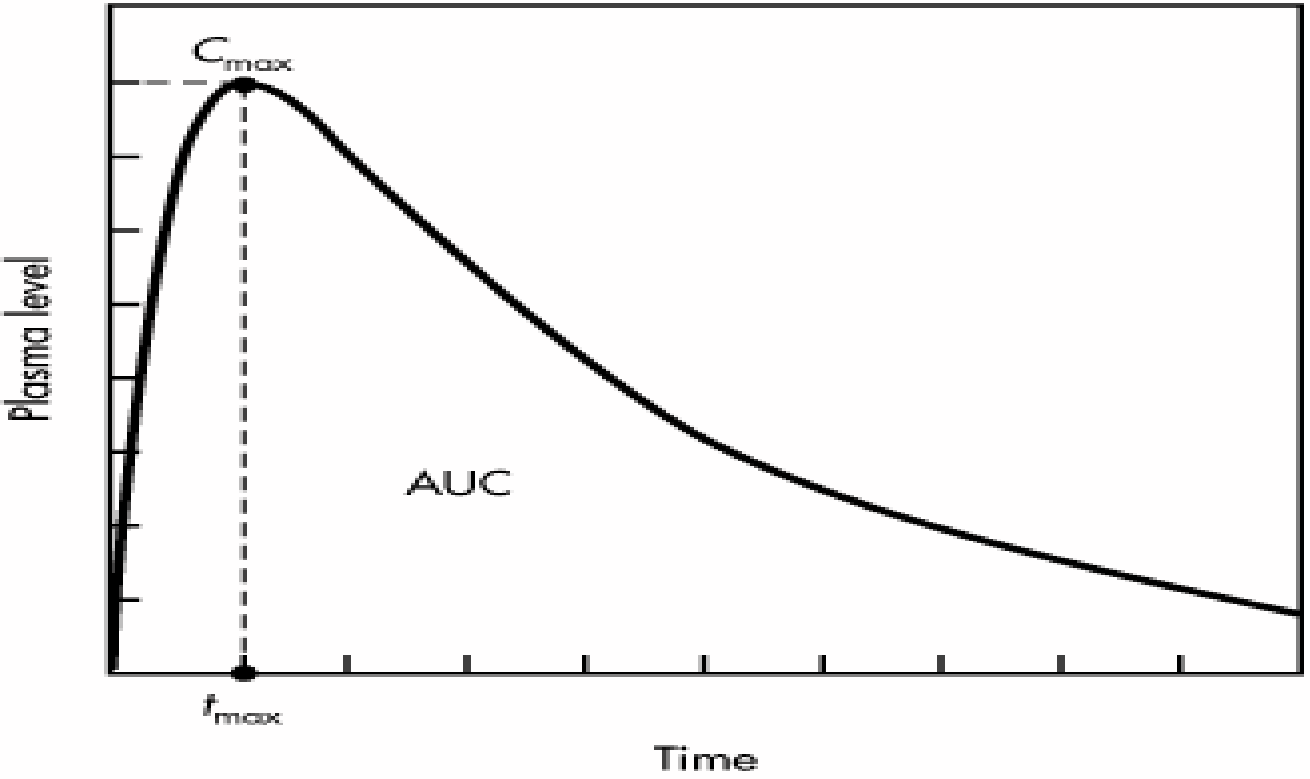


Corresponding plots relating the plasma level–time curve and the rate of urinary drug excretion.

Extravascular multiple dose administration



Extravascular single dose administration



Typical plasma level–time curve for a drug given in a single oral close


THANK YOU
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