Kinetics of drug after single oral dose
One compartment open model

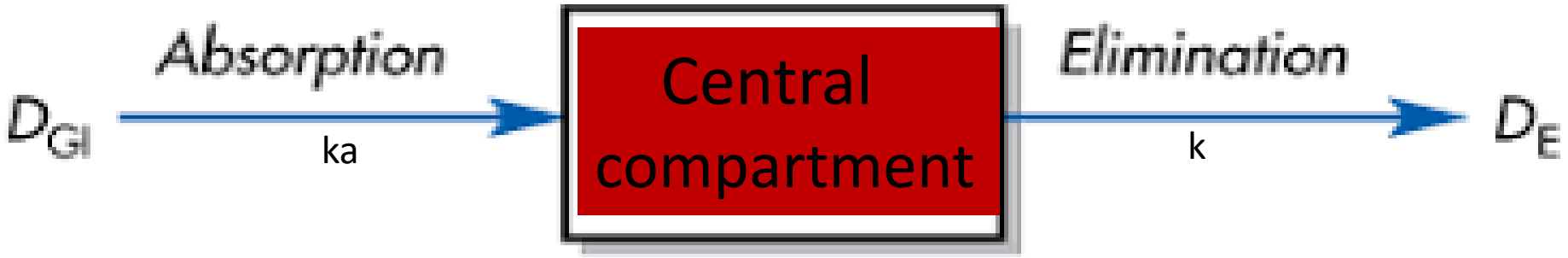
First-Order Absorption Model

- The maximum plasma concentration after oral dosing is C_{max}, and the time needed to reach maximum concentration is t_{max}.

- The t_{max} is independent of dose and is dependent on the rate constants for absorption (k_a) and elimination (k).

- At C_{max}, sometimes called *peak concentration*, the rate of drug absorbed is equal to the rate of drug eliminated.

D_{GI} تمثل جرعة الدواء في الجهاز الهضمي



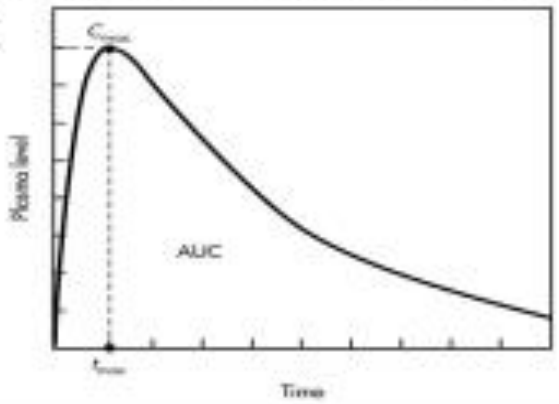
Source: Shargel L, Wu-Pong S, Yu ABC: *Applied Biopharmaceutics & Pharmacokinetics, 6th Edition*: www.accesspharmacy.com

Cmax التركيز الأعظمي

Tmaxزمن الوصول للتركيز الأعظمي

First-Order Absorption Model

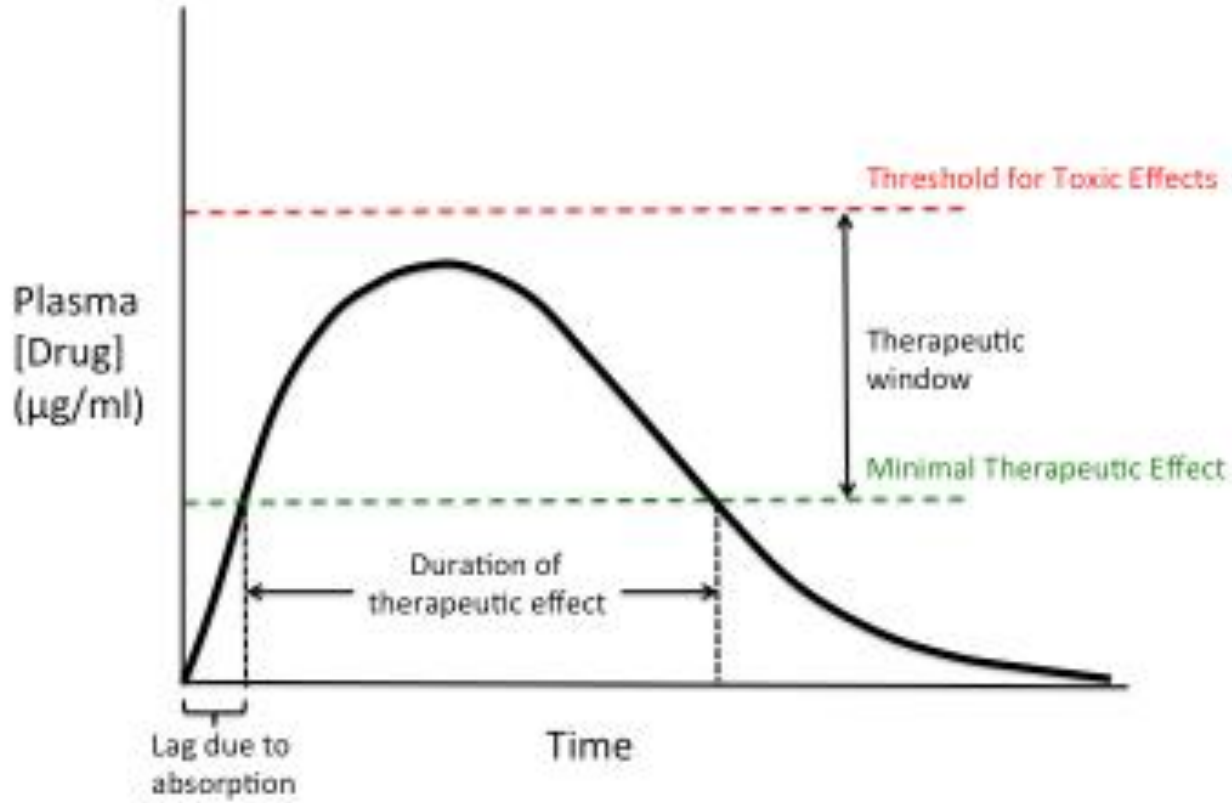
- A typical plot of the concentration of drug in the body after a single oral dose is present

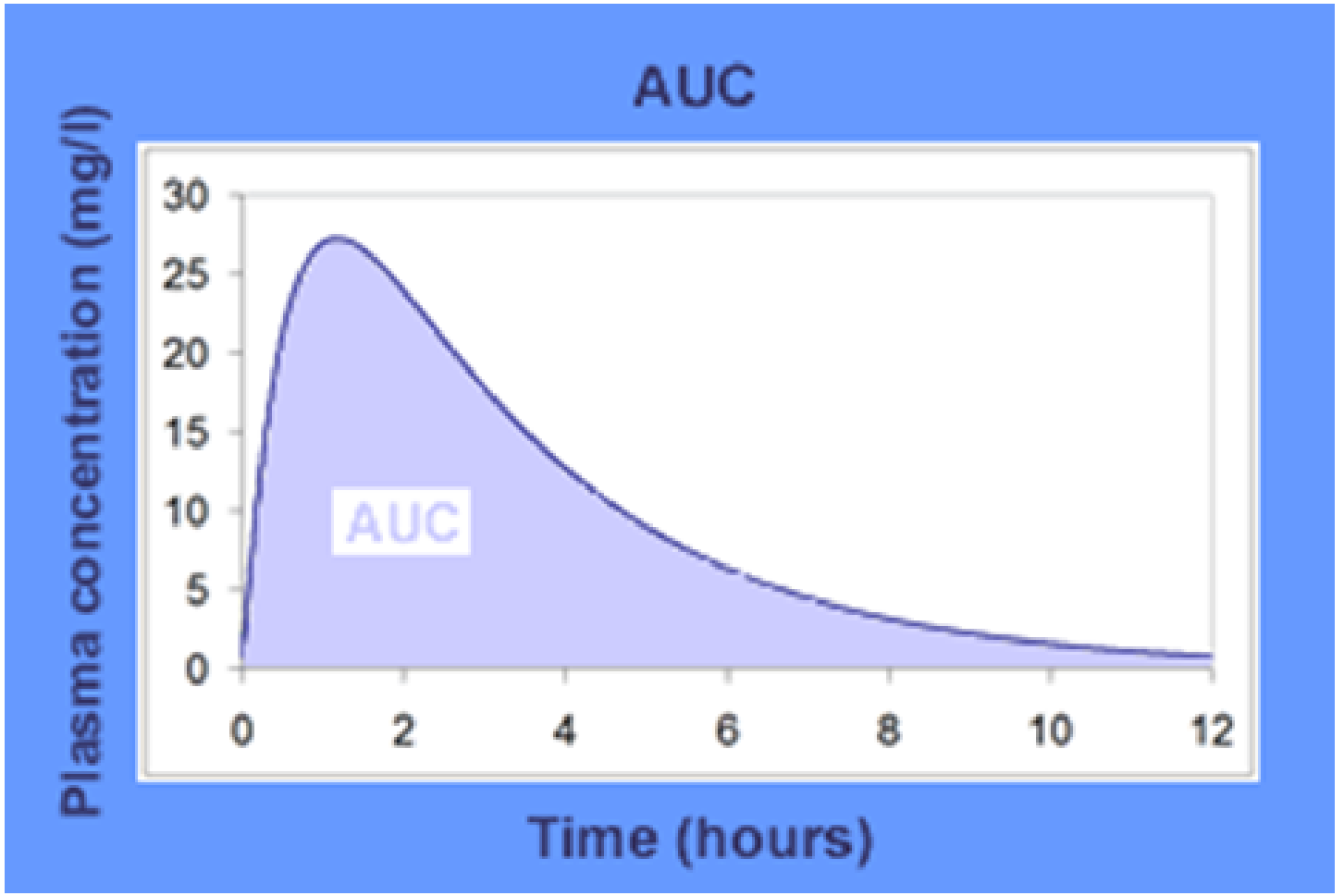


Typical plasma level–time curve for a drug given in a single oral

يمثل المنحني تركيز الدواء في البلازما
بعد جرعة فموية وحيدة

Time Course of Drug Action (Oral)





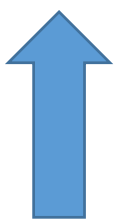
المساحة تحت منحني التراكيز البلازمية Area Under The Curve

First-Order Absorption Model

- The value of *F* may vary from 1 for a fully absorbed drug to 0 for a drug that is completely unabsorbed.

- This equation can be integrated to give the general oral absorption equation for calculation of the drug concentration (C_p) in the plasma at any tim

$$C_P = \frac{Fk_aD_0}{V_D(k_a - k)}\left(e^{-kt} - e^{-k_at}\right)$$



يمكن حساب تركيز الدواء في الجسم وفق المعادلة اعلاه حيث تمثل F الجزء الممتص من الجرعة وتتراوح قيمته من 0 الى 1

First-Order Absorption Model

- At C_{max}, the rate of concentration change can be obtained by:

معادلة حساب زمن الوصول الى التركيز الأعظمي

$$t_{\max} = \frac{\ln k_a - \ln k}{k_a - k} = \frac{\ln\left(k_a / k\right)}{k_a - k}$$

$$t_{\max} = \frac{2.3\log\left(k_a / k\right)}{k_a - k}$$

First-Order Absorption Model

- The first-order elimination rate constant may be determined from the elimination phase of the plasma level–time curve.
- At later time intervals, when drug absorption has been completed, ie, $e^{-kat} \approx 0$, Equation

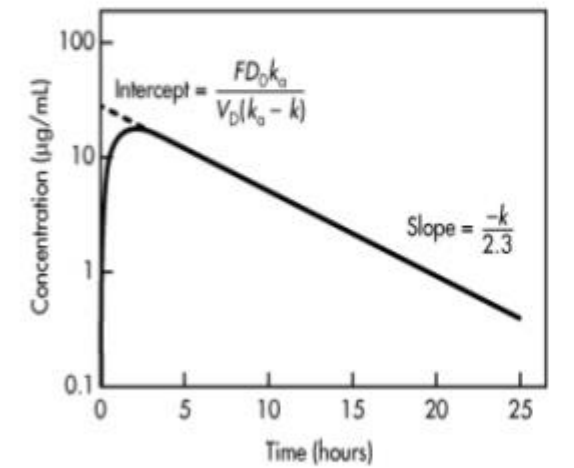
$$C_P = \frac{Fk_aD_0}{V_D(k_a - k)}e^{-kt}$$

$$\log C_P = \log \frac{Fk_aD_0}{V_D(k_a - k)} - \frac{kt}{2.3}$$

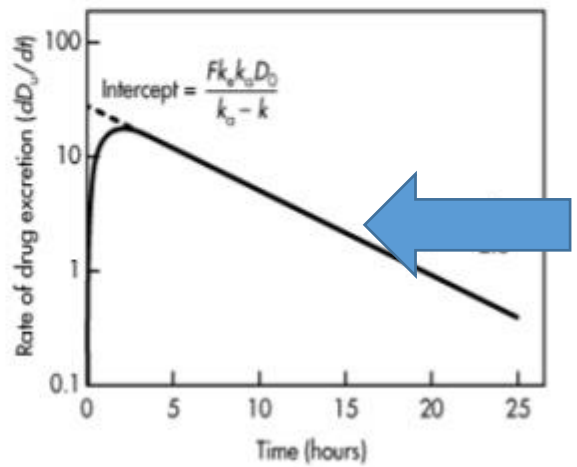
لأجل حساب k نستخدم البيانات البلازمية التابعة الى طور الاطراح
حيث بعد مرور وقت طويل تتوقف عملية الامتصاص وتبقى عملية الاطراح فقط فيصبح شكل المعادلة:

First-Order Absorption Model

- plotting log C_p versus time will yield a straight line with a slope of $-k/2.3$



Plasma drug concentration versus time

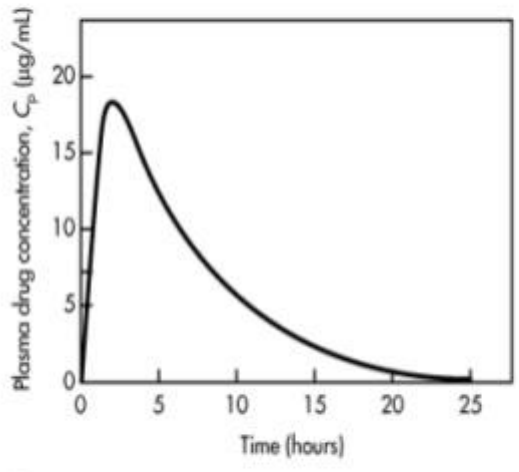


Rate of urinary drug excretion versus time

طور الاطراح

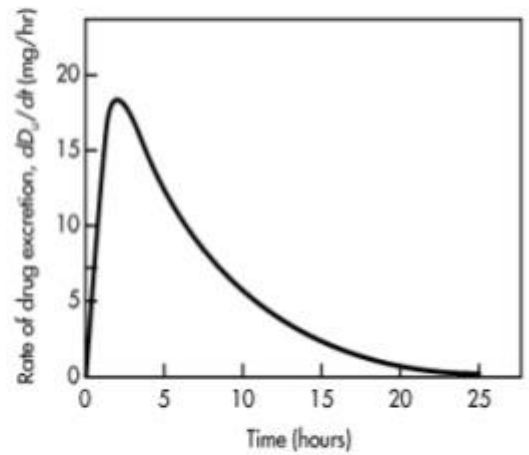
نلاحظ خطية العلاقة بين لوغاريتم التركيز والزمن في طور الاطراح

First-Order Absorption Model



Plasma drug concentration versus time

single oral dose.



Rate of urinary drug excretion versus time

single oral dose.

First-Order Absorption Model

- urinary drug excretion data may also be used for calculation of the first-order elimination rate constant.

معدل انطراح الدواء في البول dDu/dt

- The rate of drug excretion after a single oral dose of drug is given $\frac{dD_u}{dt} = \frac{Fk_a k_e D_0}{k_a - k}\left(e^{-kt} - e^{-k_a t}\right)$

الجرعة (ملغ) D0

- After drug absorption is virtually complete, $-e^{-k_a t}$ approaches zero, and the equation reduces to $\frac{dD_u}{dt} = \frac{Fk_a k_e D_0}{k_a - k} e^{-kt}$

First-Order Absorption Model

- Taking the natural logarithm of previous eq.

$$\log \frac{dD_u}{dt} = \log \frac{Fk_a k_e D_0}{k_a - k} - \frac{kt}{2.3}$$

- When log (dD_u/dt) is plotted against time, a graph of a straight line is obtained with a slope of $-k/2.3$.

- Because the rate of urinary drug excretion, dD_u/dt, cannot be determined directly for any given time point, an average rate of urinary drug excretion is obtained, and this value is plotted against the midpoint of the collection period for each urine

dDu/dt معدل انطراح الدواء في البول

D0 الجرعة (ملغ)

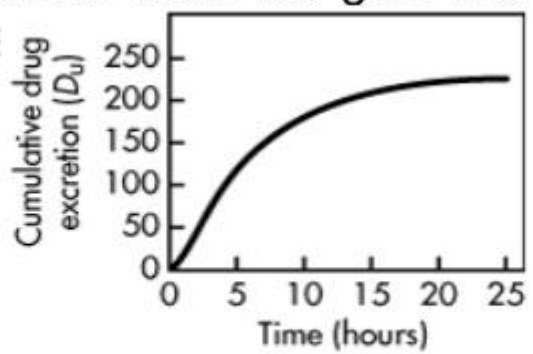
First-Order Absorption Model

- To obtain the cumulative drug excretion in the urine

$$D_u = \frac{Fk_a k_e D_0}{k_a - k}\left(\frac{e^{-k_a t}}{k_a} - \frac{e^{-kt}}{k}\right) + \frac{Fk_e D_0}{k}$$

Du كمية الدواء المنطرحة في البول (ملغ) في اللحظة t

- A plot of D_u versus time will give the urinary drug excretion curve



Cumulative urinary drug excretion versus time single oral dose.

First-Order Absorption Model

- When all of the drug has been excreted, at $t = \infty$. Equ. reduces to:

$$D_u^\infty = \frac{Fk_eD_0}{k}$$

where: D^∞_u is the maximum amount of active or parent drug excreted.

D_u^∞ كمية الدواء الأعظمية المنطرحة في البول (ملغ)