Study the kinetics of drug after single intravenous dose
One compartment open model

Compartment model

الحجرة هي مجموعة النسج التي لها تروية دموية واحدة ونفس الألفة تجاه الدواء.

Compartment is group of tissues having the same blood flow and the same affinity to drug.

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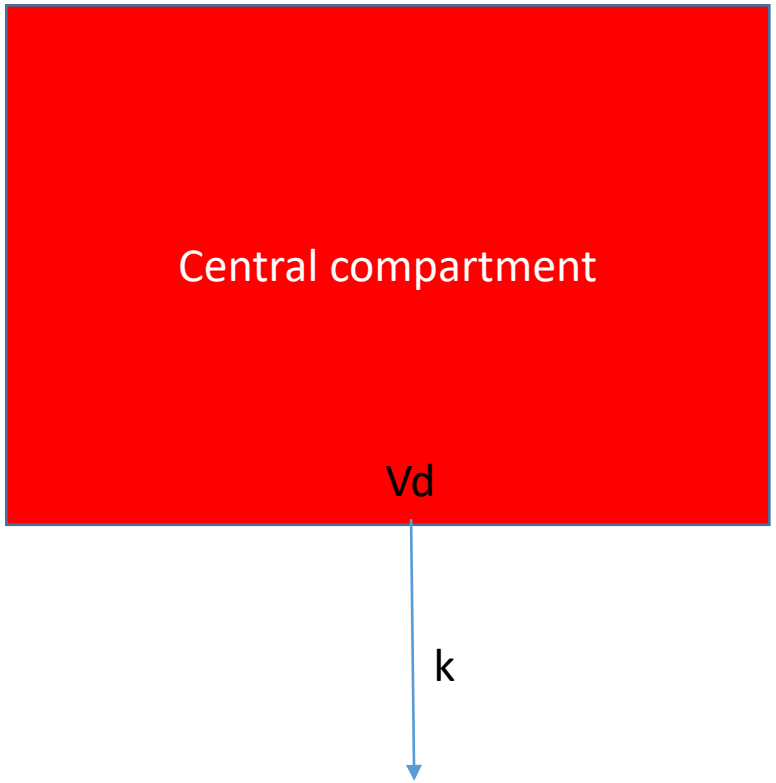
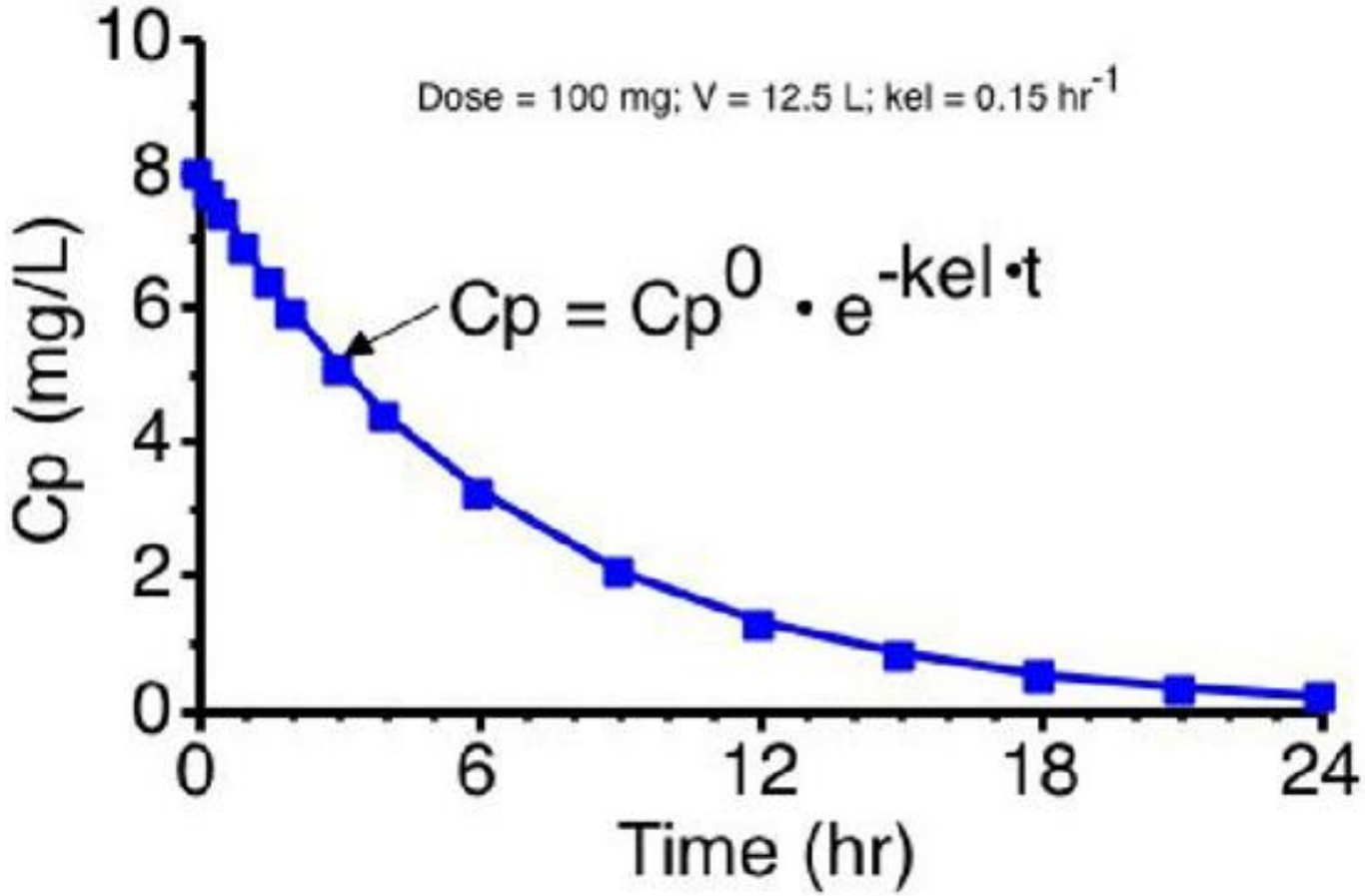
One compartment open model



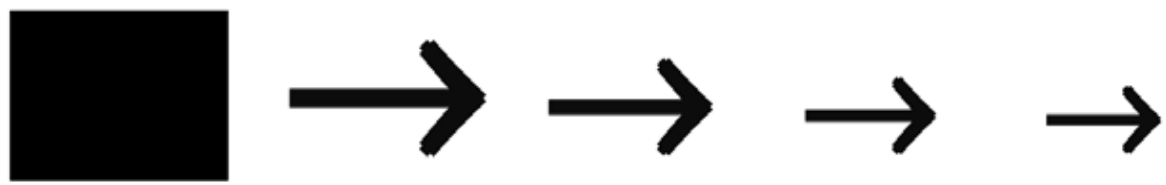
K: elimination rate constant
Vd: apparent volume of distribution


Dose = 100 mg; V = 12.5 L; kel = 0.15 hr-1
Cp = Cp0 • e-kel•t
Cp (mg/L)
Time (hr)
0
2
4
6
8
10
0
6
12
18
24

Zero-order

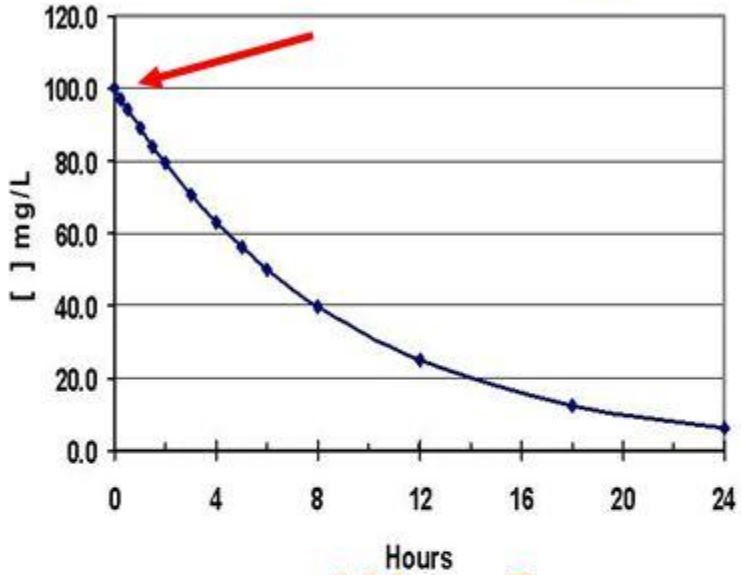
100% 80% 60% 40% 20%

First-order

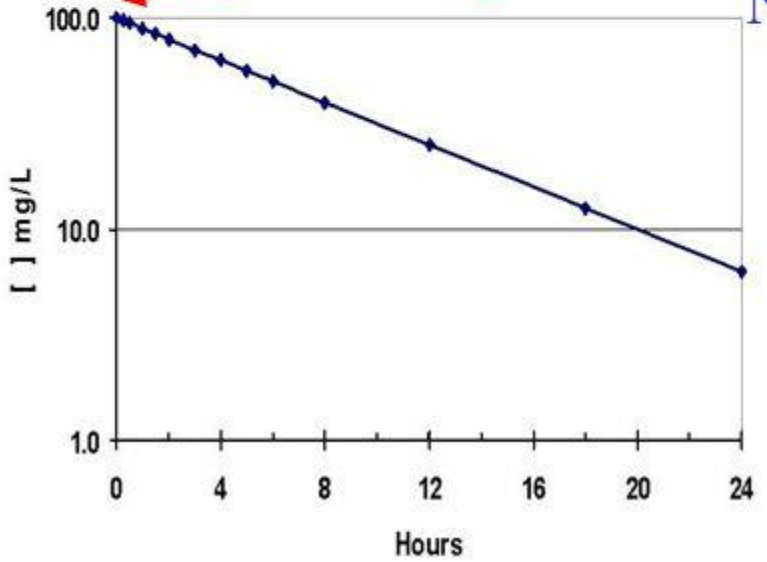


100% 90% 81% 72% 64%

Determining Elimination Rate Constant



100 mg/L



So why did we use logarithms?

If a patient with a volume of 10 L is administered a bolus dose of 1000 mg, a plot of concentration vs. time would produce this graph.

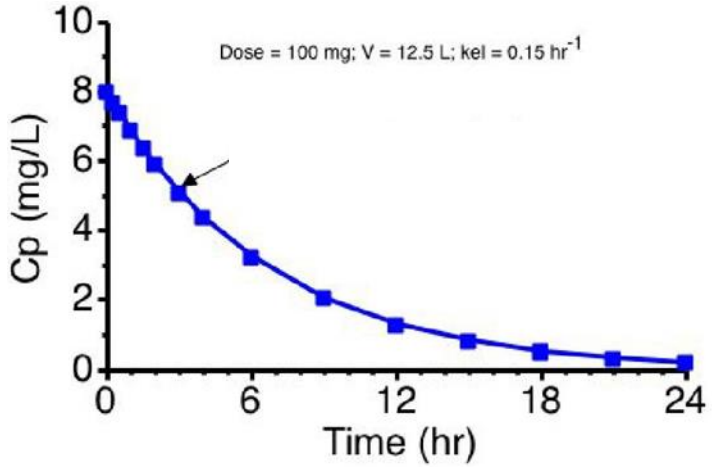
$$C = C_0 e^{-Kt}$$

Note: The initial concentration is 100 mg/L.

However, if we convert each concentration to a common logarithm, the same concentration-time plot would now look like linear.

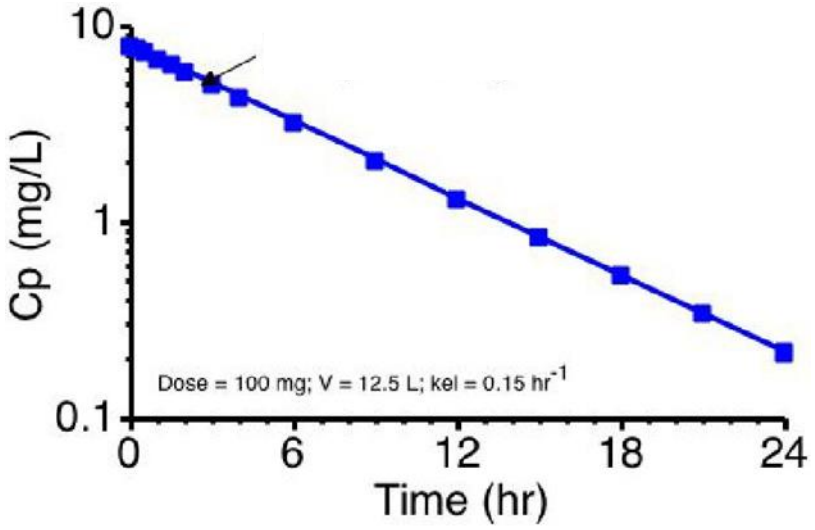
- $\frac{-dC}{dt} = kC$
- By integration
- $\int_0^t \frac{-dC}{dt}$

$$C = Coe^{-kt}$$



lnC = lnCo - Kt

- Concentration of drug at time tmg/L:C
- Concentration of drug at time 0 mg/L :Co
- elimination rat constant :K
- time t : t



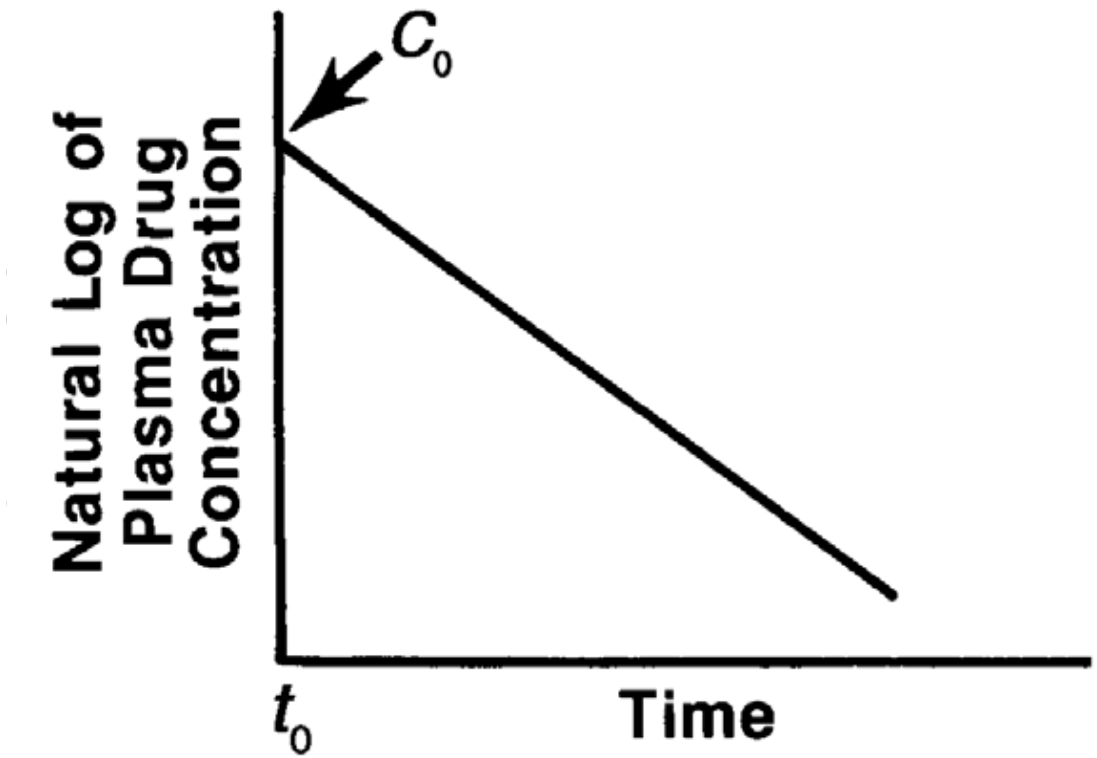
وتحول المعادلة إلى اللوغاريتم العشري

$$\text{Log C} = \log Co - \frac{K}{2.3} t$$

A straight line equation

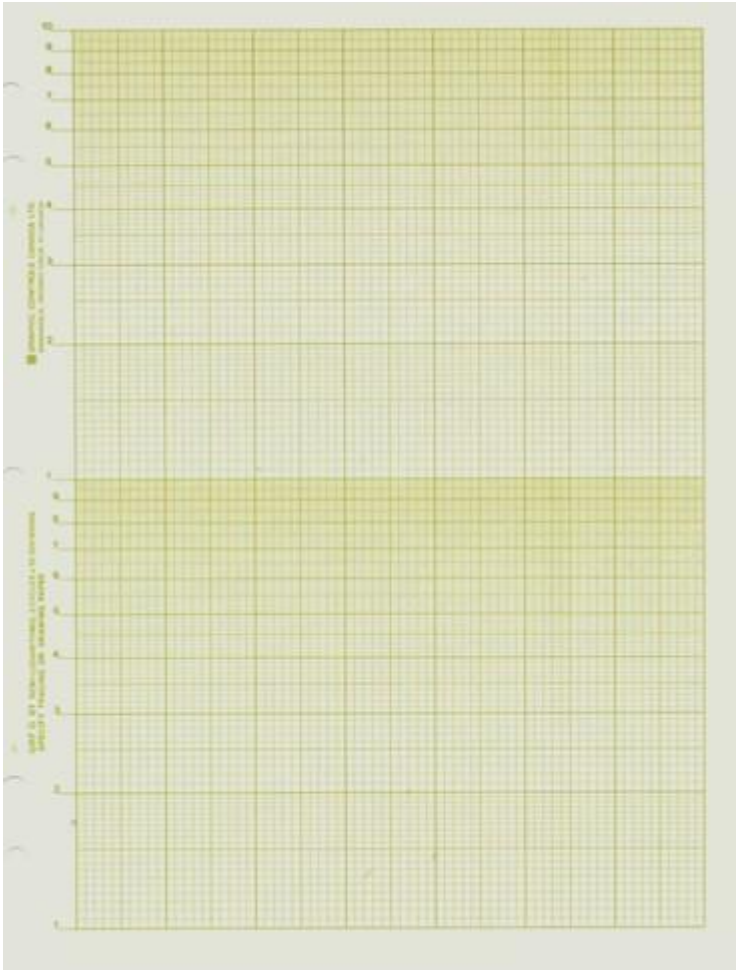
From the slope u can calculate K

$$slope = \frac{\log C_2 - log \;\; C_1}{t_2 - \; t_1}$$



تحديد Co برسم البيانات البلازمية على ورق نصف لوغاريتمي

Semilog paper



العمر النصفي للدواء Biological half life

$$t_{1/2} = \frac{0.693}{K}$$

ومنه نجد أن واحدة k هي (زمن)$^{-1}$

Biological half life العمر النصفي للدواء

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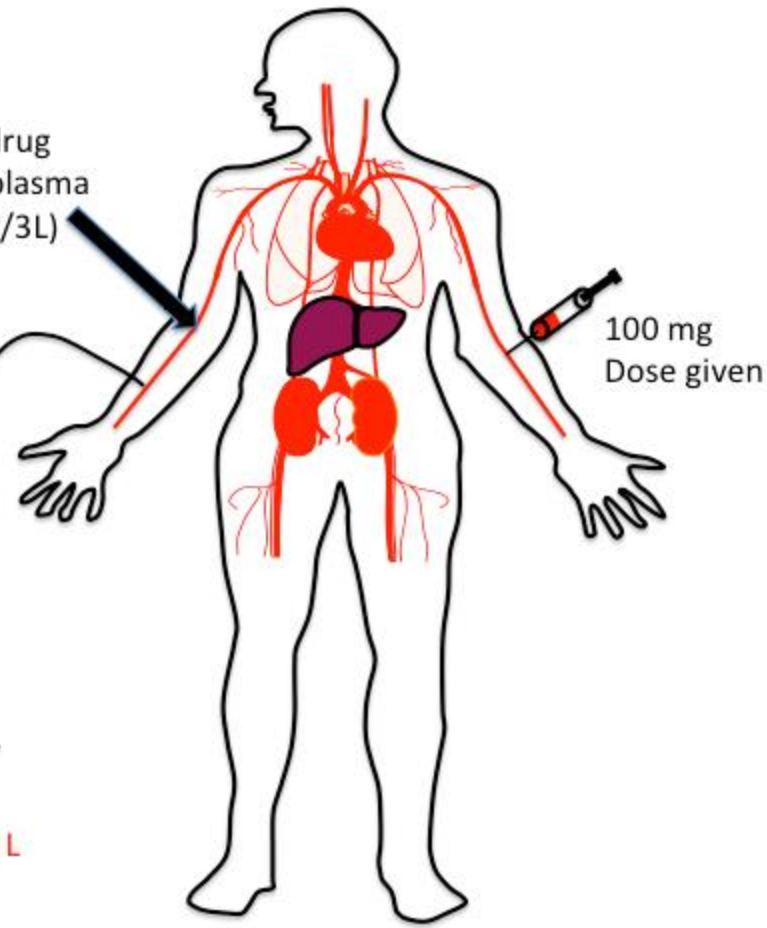
Apparent volume of distribution حجم التوزيع الظاهري

$$V_d = \frac{Do}{Co}$$

يقدر بواحدة الحجوم ل أو مل

Vd Limited to Central Compartment



"Apparent" Vd:

$$Vd\ (L) = \frac{\text{Dose (g)}}{\text{[Drug] (g/L)}}$$

$$Vd = \frac{100\ mg}{33 mg/L} = 3.0\ L$$

Total Body Clearance

Drugs can be cleared from the body by many different mechanisms, pathways, or organs, including hepatic biotransformation and renal and biliary excretion. Total body clearance of a drug is the sum of all the clearances by various mechanisms.

التصفية الكلية للدواء Cl_T Total Body Clearance

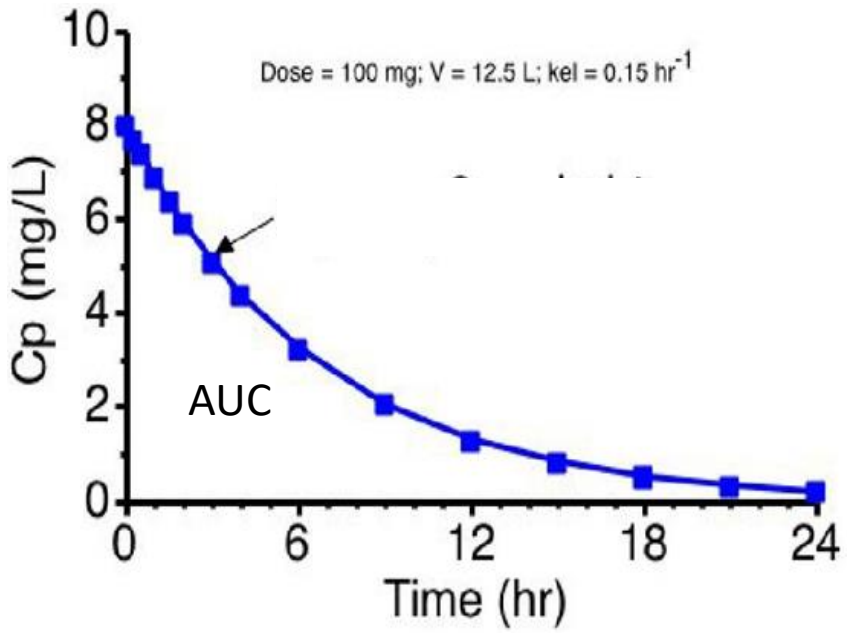
هي قياس لمعدل اختفاء الدواء من الجسم بكل طرق الإطراح

$$Cl_T = K.V_d$$ لتر / سا

Area Under the Curve AUC المساحة تحت منحني التراكيز البلازمية

$$AUC_o^{\infty} = \frac{Co}{K}$$ ملغ.سا/ل

أو مكغ.سا/مل



The following data obtained after giving 300 mg intravenously to patient :

18	12	6	3	1	0.5	0.25	Time hr
0.4	1.11	3.09	5.15	7.23	7.87	8.21	Conc (Mg/L

Calcuate K?

Calculating K:

- $slope = \frac{\log C_2 - log\ C_1}{t_2 - t_1}$

$$slope = \frac{\log 0.4 - log\ 1.11}{18 - 12}$$

$$slope = \frac{-K}{2.3}$$

K=0.173 $^{1-}$سا

Calculating apparent volume of distribution ?Vd

$$\text{Log } 7.23 = \log Co - \frac{0.173}{2.3} \text{ X1}$$

$C0$=8.4 mg/L

$$V_d = \frac{300}{8.4} \text{=35.7 L}$$

Biological half life?

$$t_{1/2} = \frac{0.693}{K}$$

$$K = 0.173\ \text{سا}^{-1}$$

$$t_{1/2} = 4\ \text{سا}$$

If this antibiotic losing its activity at concentration 2Ug/ml so calculate the duration of activity

$$log2 = log8.4 - \frac{0.173}{2.3}\ t$$

t= 8.29 سا

How long it takes for 99.9% of the drug eliminated?

لكي ينطرح 99.9 % أي يبقى 0.1% من الدواء في الجسم

$$log0{\cdot}0084 = log8{\cdot}4 - \frac{0{\cdot}173}{2{\cdot}3}\,t$$

t= 39.9 سا

What about the duration of activity if the dose doubled?

إذا ضاعفنا الجرعة تتضاعف قيمة Coأي تصبح

16.8 = 2 × 8.4 ملغ/ل وعليه

نحسب فترة الفاعلية الجديدة

$$log2 = log16.8 - \frac{0.173}{2.3} \times t$$

t= 12.3 سا

Is it possible to use Urine dataK?

نعم يمكن إذا

1. Significant amount of unchanged drug is excreted in urine
2. Specific analytical method for the drug
3. Frequent sampling
4. 7 t1/2 should be waited

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Calculation of K from Urinary Excretion Data

- The elimination rate constant *k* may be calculated from urinary excretion data.

- In this calculation the excretion rate of the drug is assumed to be first order.

$$\frac{dD_u}{dt} = k_e D_B$$

$$\frac{dD_u}{dt} = k_e D_B^0 e^{-kt}$$

$$\log \frac{dD_u}{dt} = \frac{-kt}{2.3} + \log k_e D_B^0$$

Where:
k_e is the renal excretion rate constant.
D_u is the amount of drug excreted in the urine.

لأجل استخدام البيانات البولية لا بد من تحديد Ke

Ke هي ثابتة سرعة الإفراغ (الانطراح) الكلوي

Du هي كمية الدواء المنطرح في البول

$\frac{dDu}{dt}$ = معدل الإفراغ الكلوي للبول

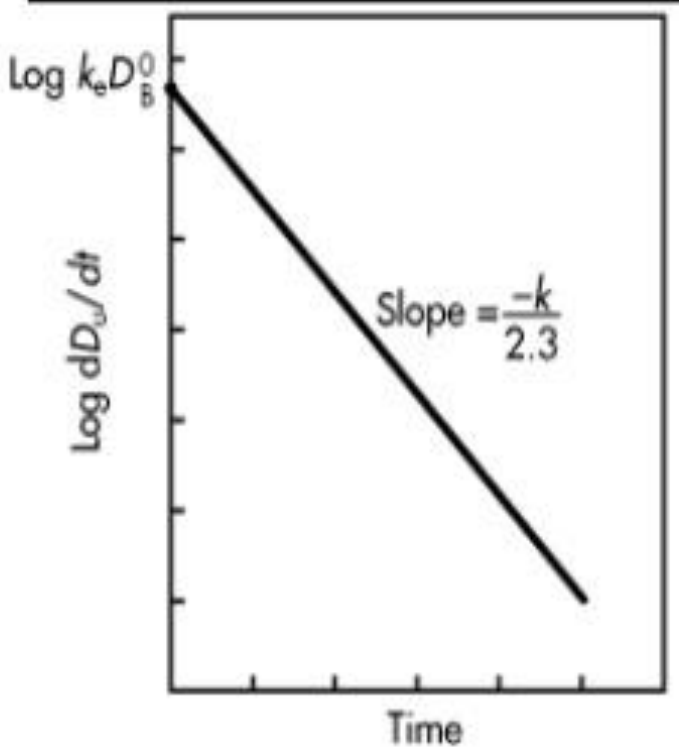
$$\frac{dDu}{dt} = K_{e}D$$

D هي كمية الدواء في الجسم

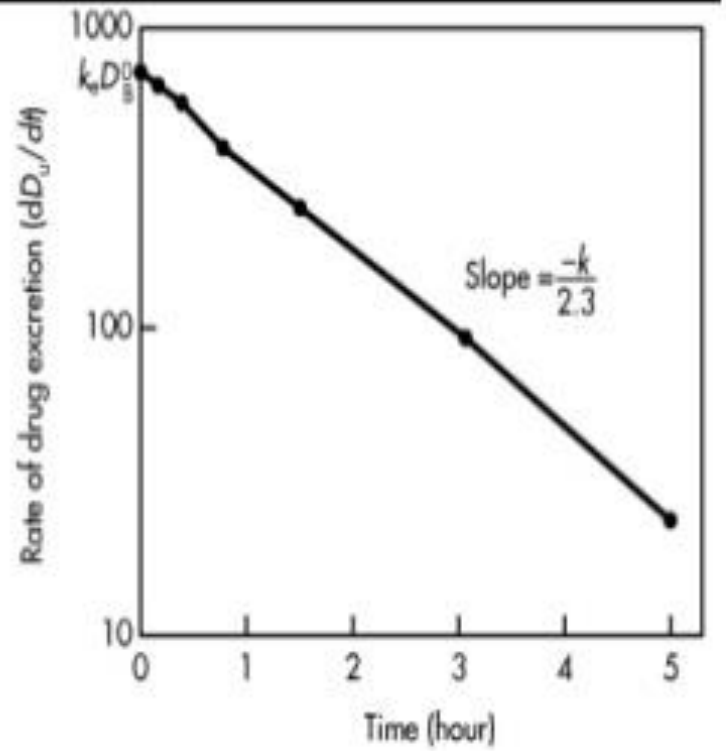
$$log\frac{dDu}{dt} = log^{K_{e}D} - \frac{K}{2{\cdot}3}t$$

معادلة خط مستقيم يمكن من خلال حساب ميل هذا الخط حساب قيمة K.

Calculation of K from Urinary Excretion Data



log rate of drug excretion versus *t* on regular paper.



Semilog graph of rate of drug excretion versus time

Example

- A single IV dose of an antibiotic was given to a 50-kg woman at a dose level of 20 mg/kg. Urine and blood samples were removed periodically and assayed for parent drug. The following data were obtained:

Time (hours)	C_p (μg/mL)	D_u (mg)
0.25	4.2	160
0.50	3.5	140
1.0	2.5	200
2.0	1.25	250
4.0	0.31	188
6.0	0.08	46

Caculate k and $t_{1/2}$?

Solution

Solution

Set up the following table:

Time (hours)	D_u (mg)	D_u/t	mg/h	t^* (hours)
0.25	160	160/0.25	640	0.125
0.50	140	140/0.25	560	0.375
1.0	200	200/0.5	400	0.750
2.0	250	250/1	250	1.50
4.0	188	188/2	94	3.0
6.0	46	46/2	23	5.0

Here t^* = midpoint of collection period and t = time interval for collection of urine sample.

Solution

- Slope = -k/2.303
- K = o,68 hr^{-1}
- $t_{1/2}$ = 0.693/k
  = 1.01 hr