للوصول الى guidance الفارما و تفاريغ المادة كاملة :

كل اعمال الفريق العلمي تنشر على قناة التيليغرام

تجدون في guidance مادة الفارما على موقع النادي :

قبل ما نبلش المحاضرة... عشان أنا كتير منيحة الله يرضى عني😇😂
قررت أخليكم تكسبو أجر كبير بكل سهولة... شفتو محسني😌😂
طب شو هو الأجر وكيف يا لانا المتواضعة؟🤦🏻‍♀️😁
الأجر يا حلوين أنه تتبرعو برصيد الطباعة تبعكم اذا ما بتحتاجوه لطلاب بحاجته (قلتلكم اجر بسهولة)🤍💜
طيب شو لازم نعمل؟
أول شي لازم تفوتو ع بوابتكم ومن عند خدمات أخرى __ رصيد الطباعة
هلأ من هي الخطوة بس بدي تتأكدو انو رصيدكم موجود ولا خالص لو اعطاك (لا يوجد اي حركات طباعة حاليا) معناها الرصيد موجود وفيكم تتبرعو فيه
طيب تمام وكيف نتبرع؟
من بوبابتكم ومن عند خدمات أخرى __ الدخول لشبكة الانترنت (المختبرات واللاسلكية) بتاخدوا اسم المستخدم (والي هو رقمكم الجامعي) وبتنسخوا كلمة السر
واخر شي بتدخلو على QR code الي تحت👇 بتعبو فورم التبرع بالرصيد وبس.
سهلة القصة والله وفيها اجر كبير (اجر ع كل نقطة وحرف وكلمة انطبعت من رصيدك لشخص محتاج واجر بكل حرف اندرس من الورق الي انطبع برصيدك الي انت اصلا ما بتستخدمه).

Function of kidney:

1) filtration
2) secretion
3) reabsorption

Elimination = (filtration + secretion) - reabsorption

GFR = 120 ml/minute

لو كان ال elimination قيمته قريبة من قيمة GFR معناها العملية معتمدة على ال filtration

لو كان ال elimination قيمته أكبر من قيمة GFR معناها العملية معتمدة على ال filtration and secretion

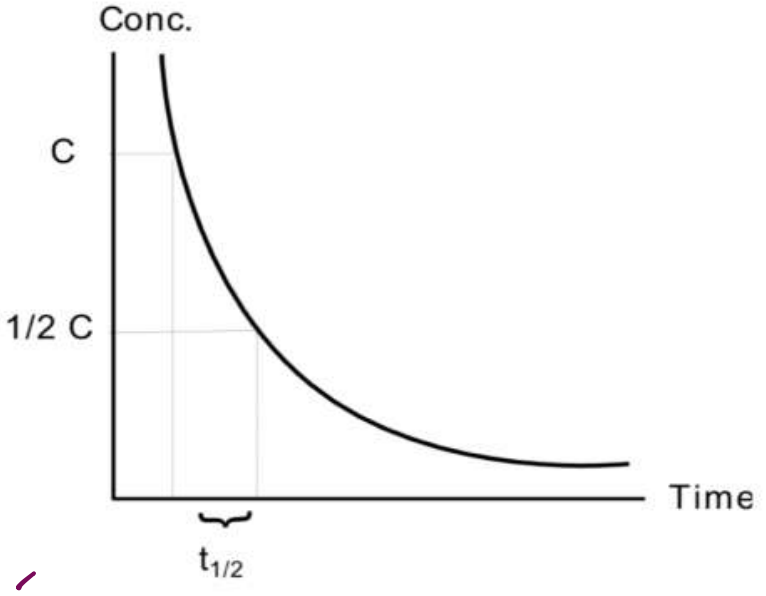
لو كان ال elimination قيمته أقل من قيمة GFR معناها العملية معتمدة على ال reabsorption

2. Plasma (elimination) half life ($t_{½}$)

Definition

- It is the time required to eliminate 50% of drug from plasma.

الوقت الي بحتاجه لحتى تركيز الدواء ينزل للنصف



Calculation:

- It depends on: Clearance & V_d
- The larger the V_d, the longer the $t_{½}$ (it takes longer to remove drug from deep within tissue). The larger the Cl, the shorter the $t_{½}$

$$t_{½} = \frac{0.693 \times V_d}{Cl_s}$$

0.7

تناسب طردي

تناسب عكسي

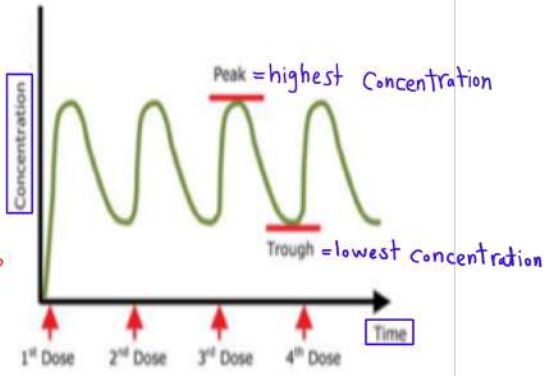
Value of elimination t½

1. It determines the **dosage interval (τ or T_m)**. → زي لما الدكاترة يحكوا خد هاي الحبة كل س ساعات

important

- If τ = t½ → this is an accepted choice to avoid wide fluctuations of the **peak** (highest pl.conc. of the drug) and **trough** (lowest pl.conc.).
- If τ < t½ → more drug accumulation occurs. ← Toxicity
- If τ > t½ → decrease in drug concentration occurs between doses.

الأصل كل مريض بلتزم بالدواء لحتى الـ Curve تبعه يكون هيك ت وسأمين التزم →

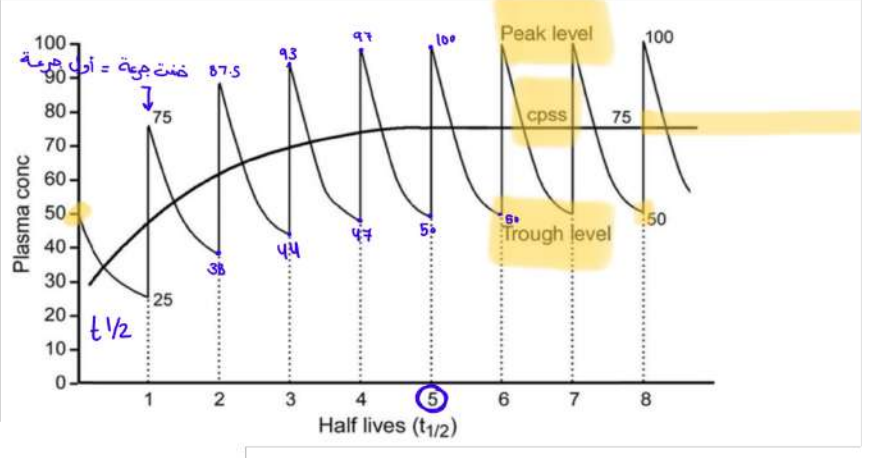


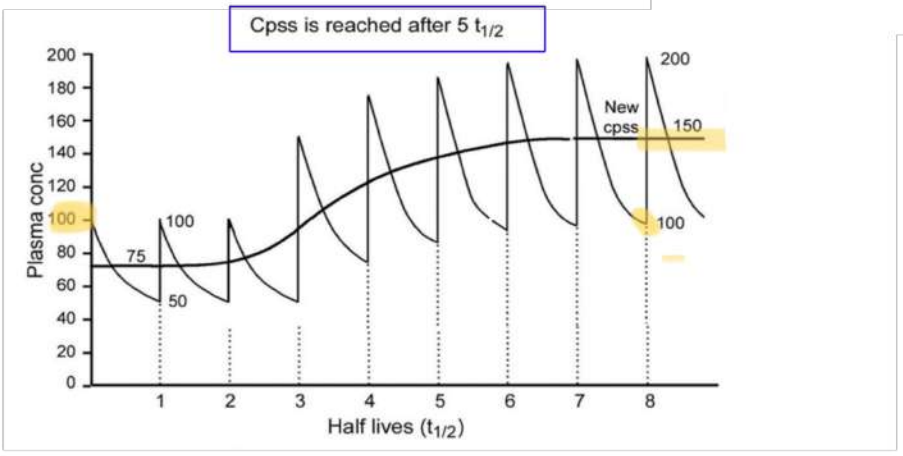
الهدف اني بدي أخلي الدواء موجود بجسمي بالكمية المطلوبة لهيك انا كطبيب لازم اعرف كم و متى لازم يوخد المريض جرعة ليضل الدواء بالكيمة المطلوبة بالدم، و ما يصير في سمية (اعلى من الpeak) و هاد الشي بنحكيله accumulation + و ما نفقد فعالية الدواء (اقل من trough)
هسا كم و متى عن طريق انا نحسب t1/2

2. It indicates **T_{ss} (time required to attain Css)**: it is equal to 5 t½ (after 4 t½ ; > 95% of the Css is attained)
3. It indicates the **time** needed for **complete elimination**: occure after 5 t½
4. Drugs having long t½ are given once/day

We reach the steady state after 5 t1/2

The drug is expired after 5 t1/2





Factors affecting elimination t½

فلو فيهم disease حيصير عندي تأخير بال elimination فال t1/2 حتزيد

1. The state of the eliminating organs i.e. liver & kidney functions
2. The delivery of the drug to the eliminating organs e.g.:
   a. Plasma protein binding limits renal filtration and increase t½
   b. Drugs with very high V_d may escape from elimination in the tissues and increase t½ → اكيد في حالات شاذة +Such as hydrophilic drugs
   plasma 1/2 of hydrophilic بتكون أقل من plasma1/2 of lipophilic ال
   metabolism in liver بصيرلها lipophilic لانه
   c. Blood flow (decrease renal bl.flow in HF may increase t½)

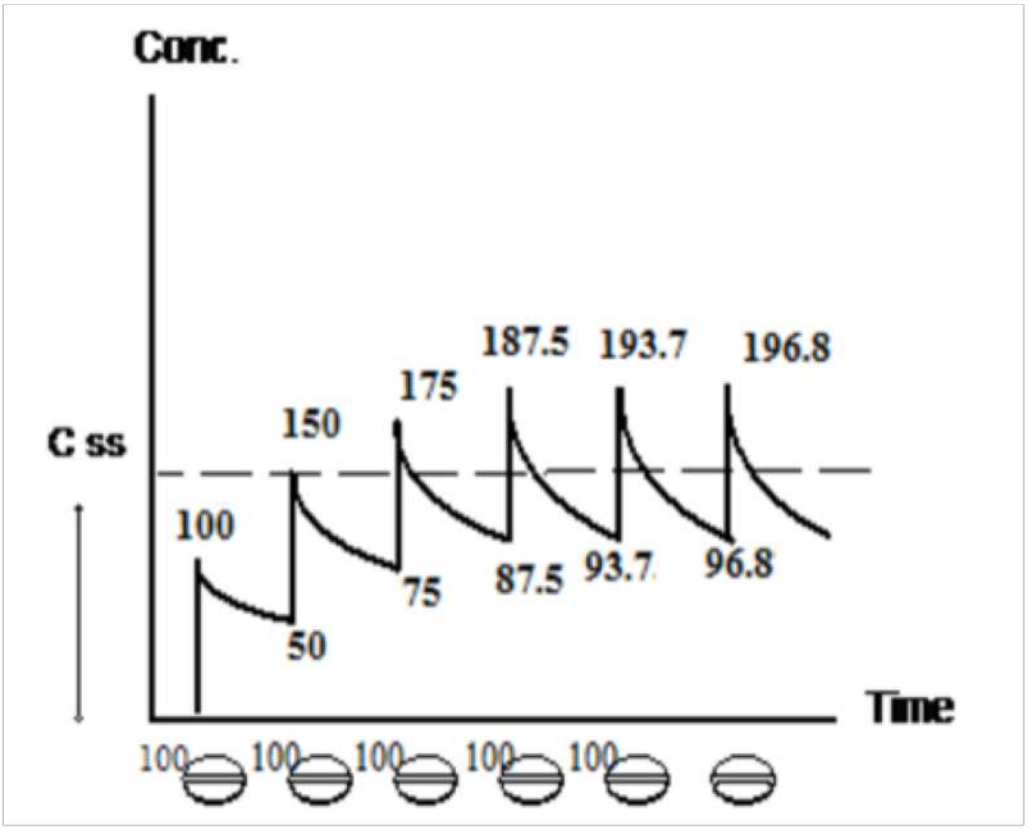
3. Steady state concentration (Css)

Definition: the steady level of drug in plasma achieved when the rate of administration equals the rate of elimination. Rate of administration = Rate of elimination

The rule of (5):

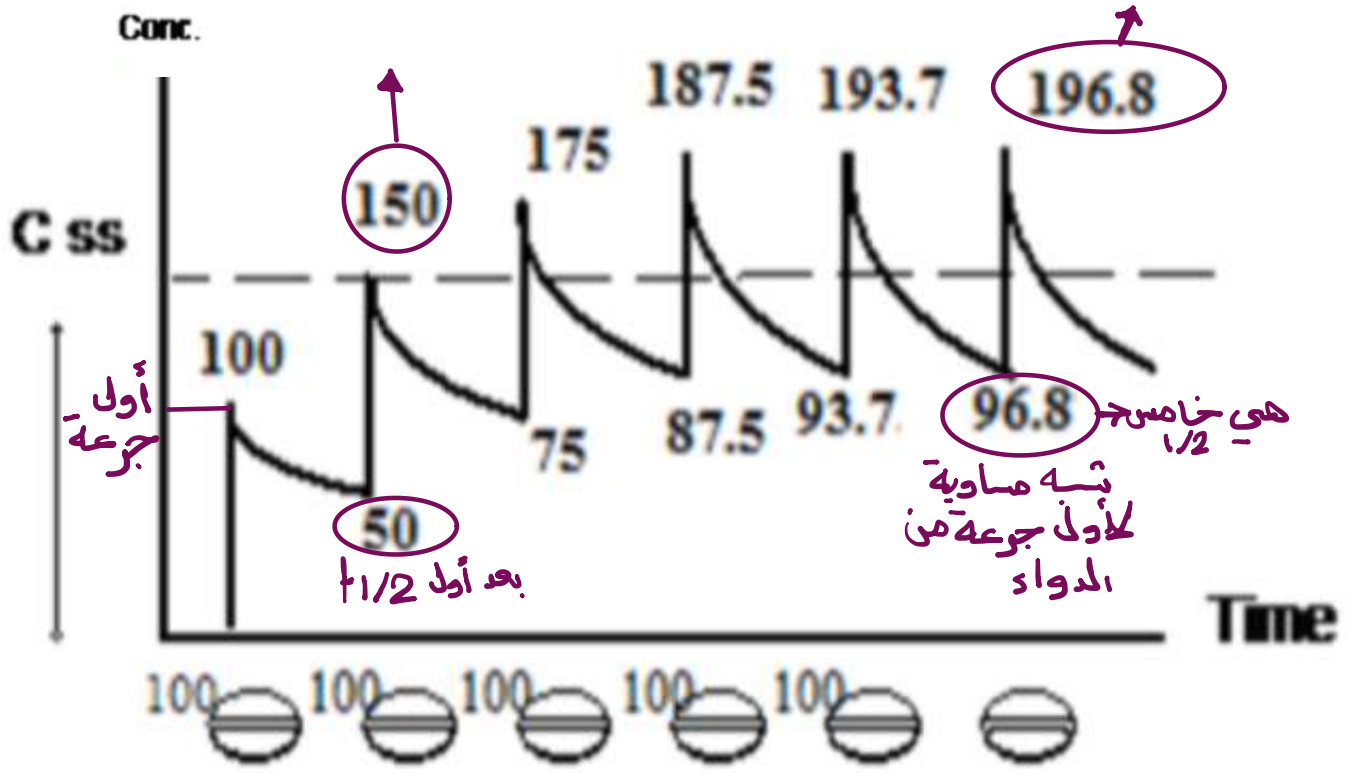
- The Cpss is reached after 5 t½ بشرط طبعاً اني لما اوصل للt1/2 ارجع اعطيه جرعة
- If we change the dose, the new Cpss is reached after 5 t½
- If dosing stop, complete elimination of drug occurs after 5 t½

**Plasma concentration (CSS) is directly proportional to the dose and inversely proportional to the clearance.



بعد ما يروح نخبرها رح يضل تقريبا (100) وبعدين رح أضيف جرعة الدواء والي هي 100 فهون وصلنا Css

هون جرعة الدواء الي لازم ياخوها المريض (100 ml) بس لسا في بالجسم 50 ml من الجرعة السابقة فصار التركيز بالجسم (150 ml)



عند 1/2 t 1 فقدنا 50 % من الدواء
عند 1/2 t 2 فقدنا 75 % من الدواء
عند 1/2 t 3 فقدنا 87.5 % من الدواء
عند 1/2 t 4 فقدنا 93.7 % من الدواء
عند 1/2 t 5 فقدنا ~ 100 % من الدواء

ممكن يجي سؤال عند أي 1/2 t يفقد 95 % من الدواء ؟ بين 1/2 t 4 و 1/2 t 5
أو سؤال كم فقدنا عند 1/2 t 3 ؟ 87.5 %

4. Loading dose (LD)

- **Loading dose (LD):** the dose given at the onset of therapy to achieve a rapid increase in plasma drug concentration to reach Cpss without toxicity.

important

$$LD_{IV} = V_d \times Css \text{ (target } C_P)$$

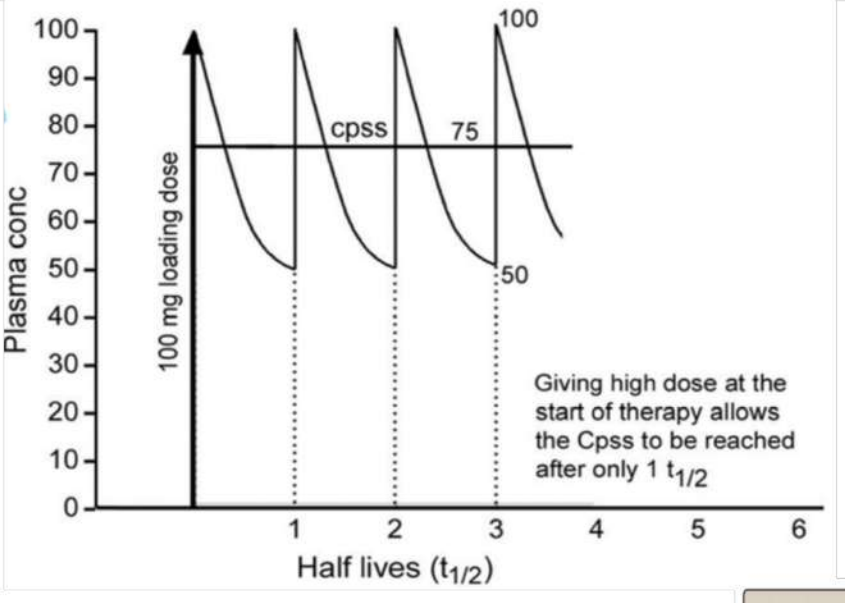
$$LD_{Oral} = \frac{LD_{IV} = Vd * Css}{F \text{ (fraction of oral bioavailability)}}$$

- Used for:
  1. drugs with **Long $t_{1/2}$** (e.g. amiodaron) or
  2. in an **Emergency**

**

↳ t1/2 = 90 day → لهيك بعطيه كمية كبيرة لتقل الـ t1/2

↳ مثلاً طفل حرارته مرتفعة



From the book :

Sometimes rapid obtainment of desired plasma levels is needed (for example, in serious infections or arrhythmias).

Therefore, a "loading dose" of drug is administered to achieve the desired plasma level rapidly, followed by a maintenance dose to maintain the steady state .

In general, the Disadvantages of loading doses include increased risk of drug tox- icity and a longer time for the plasma concentration to fall if excess levels occur.

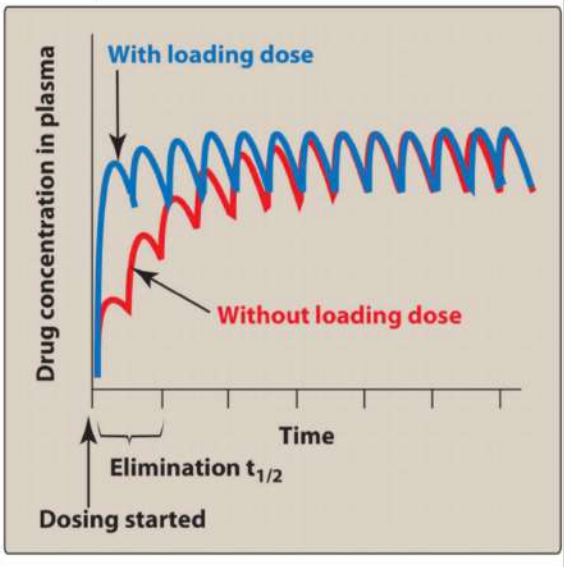


Figure 1.25
Accumulation of drug administered orally without a loading dose and with a single oral loading dose administered at t = 0.

5. Maintenance dose (MD) → Maintain Steady State.

- **Maintenance dose (MD):** the dose needed to keep the plasma drug concentration constant at Css (the dose needed to compensate the amount eliminated).

  - Dosing rate (rate of administration) = rate of elimination = Cl X Css (حسب بوصة الزين)
  - If drug taken by *continuous IV infusion*:

    معدل الحقن الوريدي **Infusion rate = CLs X Css**

  - If drug taken in *repetitive doses*:

    الفترة بين كل جرعة والثانية فلو كانت x ساعات بضرب بـ x

$$\mathbf{MD_{IV}} = \mathbf{CLs\ X\ Css\ X\ Tm}\ (\text{dosing interval})$$

$$\mathbf{MD_{Oral}} = \frac{\mathbf{CLs\ X\ Css\ X\ Tm}}{\mathbf{F}\ (\text{fraction of oral bioavailability})}$$

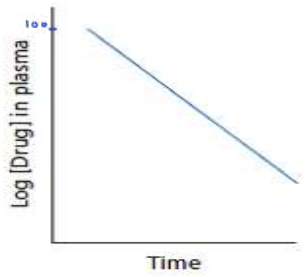
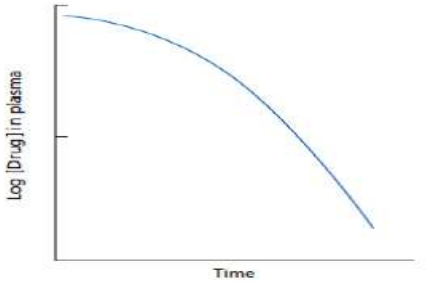
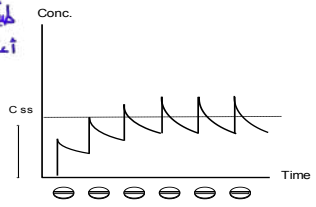
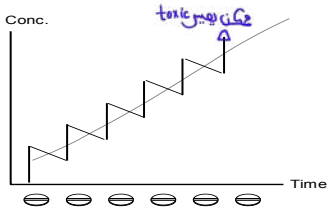
Drugs are generally administered to maintain a Css within the therapeutic window. It takes 4 to 5 half-lives for a drug to achieve Css.

To achieve a given concentration, the rate of administration and the rate of elimination of the drug are important.

The dosing rate can be determined by knowing the target concentration in plasma (Cp), clearance (CL) of the drug from the systemic circulation, and the fraction (F) absorbed (bioavailability)

Cls * Css = تبع الدوا elimination أحسب الـ بالجسم لربك بدي Cpss * بدي أحافظ على

6. Kinetic orders

A. First order kinetics	B. Zero order (saturation) Kinetics
• A constant **fraction** of drug is eliminated per unit time.	• A constant **amount** of drug is eliminated per unit time.
• Rate of elimination is **proportional** to the concentration of drug	• Rate of elimination is **constant** (limited capacity of kinetics due to saturation of involved enzymes and/or carriers
• It has a **linear** elimination kinetics i.e. plasma concentration can be expected at any time *(using log conc.-time disappearance curve)* 	• It has a **non-linear** elimination kinetics i.e. plasma concentration can NOT be expected at any time *(using log conc.-time disappearance curve)* 
• **Constant** t½.	• t½ is **not constant**
• A steady-state concentration **(Css) is reached** on repeated dosing after 5 $t_{1/2}$. 	• **NO Css** is reached; repeated dosing → overshooting of drug concentration. 
• Modest changes in dose → are usually **tolerated** because when drug conc. ↑→ elimination ↑ by the same ratio.	• Modest changes in dose → **toxicity** due to drug cumulation
• Drug metabolites do **Not vary** with dose.	• Drug metabolites **may vary** with dose
• Examples: Most drugs.	Example: **Large dose of Aspirin, Alcohol, Phenytoin** (they follow 1st order kinetics at small doses)

First-Order Elimination Rate يعني انا بفقد هالقد نسبة بالوقت الفلاني ، مثال : بفقد 50% من الدواء كل ثلاث ساعات

With first-order elimination rate, a constant fraction of the drug is eliminated per unit time (t1/2 is a constant). Graphically, first-order elimination follows an exponential decay versus time. If 80 mg of a drug is administered and its elimination half-life = 4 h, the time course of its elimination is:

	4 h		4 h		4 h		4 h	
80 mg	→	40 mg	→	20 mg	→	10 mg	→	5 mg

The rate of elimination is directly proportional to plasma level (or the amount present), i.e., the higher the amount, the more rapid the elimination.

*Most drugs follow first-order elimination rates

*t1/2 is a constant

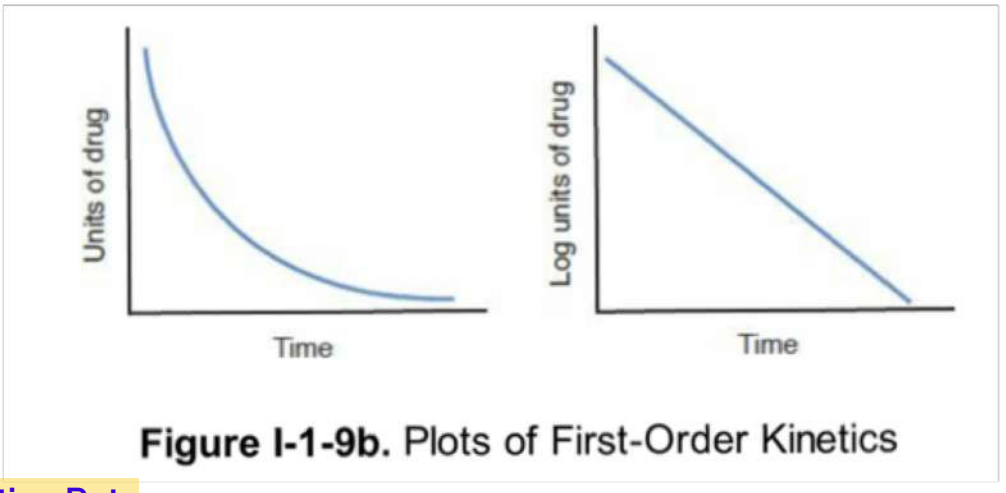


Figure I-1-9b. Plots of First-Order Kinetics

Zero-Order Elimination Rate يعني انا بفقد هالقد كمية كل فقترة ، مثال : بفقد 5 ml من الدواء كل 4 ساعات

With zero-order elimination rate, a constant amount of drug is eliminated per unit time. If 80 mg is administered and 10 mg is eliminated every 4 h, the time course of drug elimination is:

	4 h		4 h		4 h		4 h	
80 mg	→	70 mg	→	60 mg	→	50 mg	→	40 mg

The rate of elimination is independent of plasma concentration (or amount in the body).

*Drugs with zero-order elimination have no fixed half-life (t1/2 is a variable)

*Drugs with zero-order elimination include ethanol (except low blood levels), phenytoin (high therapeutic doses), and salicylates (toxic doses)

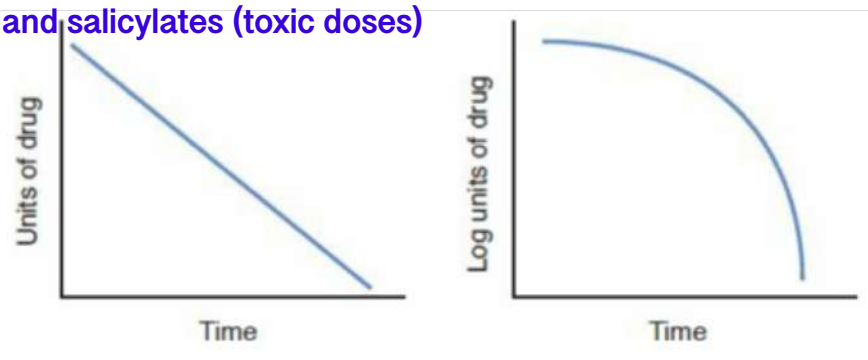


Figure I-1-9a. Plots of Zero-Order Kinetics

تجميعة القوانين (1)

- Bioavailability = $\frac{\text{AUC of adminstration}}{\text{AUC}} \times 100$
- Vd = $\frac{\text{Amount of drug in the body}}{\text{Plasma concentration (Cp)}}$
- Total amount of drug = Vd x C_p
- Loading $dose_{IV}$ = Vd x Css
- Loading $dose_{oral}$ = $\frac{Vd \times Css}{F \text{ (fraction of oral bioavailability)}}$
- infusion rate = Clearance x Css
- Clearance = $\frac{.7 \times Vd}{t1/2}$
- Dosage rate = Clearance x Css
- MD_{IV} = Cls x Css x Timing
- MD_{oral} = $\frac{Cls \times Css \times Timing}{F}$

Quiz Time ⏰

1) A 74-year-old man was admitted to the hospital for treat- ment of heart failure. He received 160 meg of digoxin intravenously, and the plasma digoxin level was 0.4 ng/ mL. If the desired plasma concentration of digoxin for optimal therapeutic activity in heart failure is 1.2 nglml, and the patient has an estimated Vd of 400 L, calculate the additional dose of digoxin needed for this patient to achieve the desired plasma concentration.

A. 128 meg B. 160 meg C. 320 meg. D. 480 meg E. 640 meg

2) A pharmacokinetic study of a new antihypertensive drug is being conducted in healthy human volunteers. The half-life of the drug after administration by continu- ous intravenous infusion is 12 hours. Which of the fol- lowing best approximates the time for the drug to reach steady state?

A. 24 hours B. 48 hours C. 72 hours. D. 120 hours E. 240 hours

3) A 64-year-old female patient (60 kg) is treated with experimental Drug A for type 2 diabetes. Drug A is available as tablets with an oral bioavailability of 90%. If the vd is 2 L1kg and the desired steady-state plasma concentration is 3.0 mg/L, which of the following is the most appropriate oral loading dose of Drug A?

A. 6mg. B. 6.66mg C. 108 mg D. 360 mg E. 400 mg

4) A 55-year-old woman is brought to the emergency department because of seizures. She has a history of renal disease and currently undergoes dialysis. She receives an intravenous infusion of antiseizure Drug X. Which of the following is likely to be observed with use of Drug X in this patient?

	Half-life	Dosage
A.	↑	↑
B.	↓	↓
C.	↑	↔
D.	↑	↓
E.	↔	↔

5) An IV infusion of a drug is started 400 mg/h. If C1 = 50 L/h, what is the anticipated plasma level at steady state?

A. 2mg/L B. 4mg/L C. 8mg/L D. 16mg/L E. 32mg/L

6) At 6 h after IV administration of bolus dose, the plasma level of a drug is 5 mg/L. If the Vd = 10 L and the elimination half-life = 3 h, what was the dose administered?

A. 100mg

B. 150mg

C. 180mg

D. 200mg

E. 540mg

Quiz Time ⏰👏

1) Which statement is accurate for the drug shown in the example below?

100 mg 2hr → 50 mg 2hr → 25 mg 2hr → 12.5 mg

A. The rate of elimination is constant

B. The elimination half-life varies with the dose

C. The volume of distribution varies with the dose

D. The clearance varies with the dose

E. The rate of elimination varies directly with the dose

2) All the following statements are true for zero-order kinetics EXCEPT:

A. Elimination rate is independent of the dose

B. Elimination depends on saturable enzyme system

C. Plasma concentration of the drug cannot be expected at any time

D. Thet1/2ofthedrugisnotconstant

E. There is no fear from drug cumulation or interactions