

Name: KEY

UFID #: XXXX-XXXX

PHA 5127

Second Exam

Fall 2010

On my honor, I have neither given nor received unauthorized aid in doing this assignment.



Name _____

Put all answers on the bubble sheet

Please select only one choice for each question

There are a total of XII question sets and 37 questions

TOTAL X /200 pts

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Question Set I (True or False)

(15 points)

True (A) or False (B). On the bubble sheet mark A for true or B for false

Mark whether the following statements are true (A) or false (B). Mark false if there is not sufficient information given to provide answer. Increases and decreases, differences should be of clinical significance, otherwise state "F".

The lipophilic drug A (neither an acid nor a base) is cleared only by hepatic metabolism, crosses membranes quite easily, dissolves in the GI tract. When given to Patient A, it has a f_u of 0.1, a f_{ut} of 0.3 and an intrinsic clearance of 30000 L/h. Patient B shows a tissue protein binding of 80%; the only difference to Patient A.

- 1: T F The oral bioavailability of this drug is high (>80%).
- 2: T F Changes in plasma protein binding will affect the AUC of this drug when given as an iv bolus to Patient A and B.
- 3: T F Patient B's clearance will differ from that of patient A.
- 4: T F Increase in tissue binding will affect the half-life of the drug.
- 5: T F Increase in f_u will affect the half-life of the drug.

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Question Set II

(15 Points)

6) Consider a hydrophilic unionized drug, eliminated only through renal elimination. How will an increase in both tissue binding (50% increase) and a change in creatinine clearance (50% increase) affect the initial concentration (C_0), clearance (CL), AUC, and half-life ($t_{1/2}$) when given as an iv bolus, bioavailability (F) when given as tablet of a low-extraction drug? (Please note that \leftrightarrow means no clinically relevant change, \downarrow and \uparrow clinically relevant changes)

A: $\downarrow C_0$, $\uparrow CL$, $\downarrow F$, $AUC \downarrow$, $\downarrow t_{1/2}$

B: $\leftrightarrow C_0$, $\leftrightarrow CL$, $\uparrow F$, $AUC \uparrow$, $\leftrightarrow t_{1/2}$

C: $\downarrow C_0$, $\leftrightarrow CL$, $\leftrightarrow F$, $AUC \leftrightarrow$, $\uparrow t_{1/2}$

D: $\uparrow C_0$, $\downarrow CL$, $\leftrightarrow F$, $AUC \uparrow$, $\uparrow t_{1/2}$

E: none of above combinations.

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Question Set III (Matching)

(20 points)

For the physiological changes listed below, select the induced changes on the pharmacokinetic parameters for a **lipophilic, protein bound acidic drug (pKa=13.8) that is only eliminated through renal elimination**. Some answers may be used more than once. However, only one answer per "physiological change"

Select the clinically relevant effect on pharmacokinetic parameters

(A) $Cl \uparrow$ (B) $Cl \downarrow$ (C) $V_D \downarrow$ (D) $F \downarrow$ (E) *nothing happens or effect is not listed*

Physiological change

7: Decrease in plasma protein binding

A

8: Increase in tissue binding

E

9: pH adjustment of urine from 7.4 to 6.3

E

10: Increase in GFR

F

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Question set IV (20point)

A drug (not an acid, not a base) is cleared through renal clearance ($Cl_{ren}=1$ ml/min;), only. Plasma protein binding suddenly doubles.

Indicate for this situation whether the following parameters increase (A), decrease (B), stay about the same (C) or not sufficient information is provided (D).

11: volume of distribution **B**

12: oral bioavailability **C**

13: renal clearance **B**

14: k_e **C**

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Question Set V

(20 points)

The following drugs have been given at toxic doses. What methods could be used to treat the patient if:

15) Drug is eliminated mainly through hepatic metabolism (high extraction drug) D

16) Drug is eliminated mainly through hepatic metabolism (low extraction drug) C

17) Lipophilic, neutral drug (not an acid, not a base) is eliminated through kidney. B

18) Lipophilic base, $pK_a=11$, is eliminated solely through the kidney. A or E

19) Lipophilic base, $pK_a=7.4$, eliminated solely through the kidney. A

Select for above drugs (the best single choice from the list below):

A: Adjust urine pH

B: Increase urine flow

C: Give drug that induces liver enzymes

D: Perform dialysis, as nothing else will work.

E: It is worthwhile to check whether the drug is actively reabsorbed. If yes transporters could be blocked

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Question Set VI (10 points)

- 20) A new hydrophilic drug is eliminated through renal and hepatic processes. Plasma protein binding is 50%. Urine flow is 2 ml. GFR is 120 ml/min. Liver blood flow is 60 L/h. E is 0.026, due to first pass metabolism in the liver.

What value best describes the total clearance? You might have to round. (15 points)

- A: 15 ml/min
- B: 20 ml/min
- C: 25 ml/min
- D: 30 ml/min
- E: none of the above

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Question Set VII

(15 points)

21) Robert is very sick and needs treatment with an aminoglycoside. In order to start him on the aminoglycoside you have to estimate Robert's creatinine clearance. Robert is 5 ft 10 inches tall, 34 years old, male, and weights 140 kg. His serum creatinine is 1.5 mg/dl. What is Robert's creatinine clearance ? You might have to round.

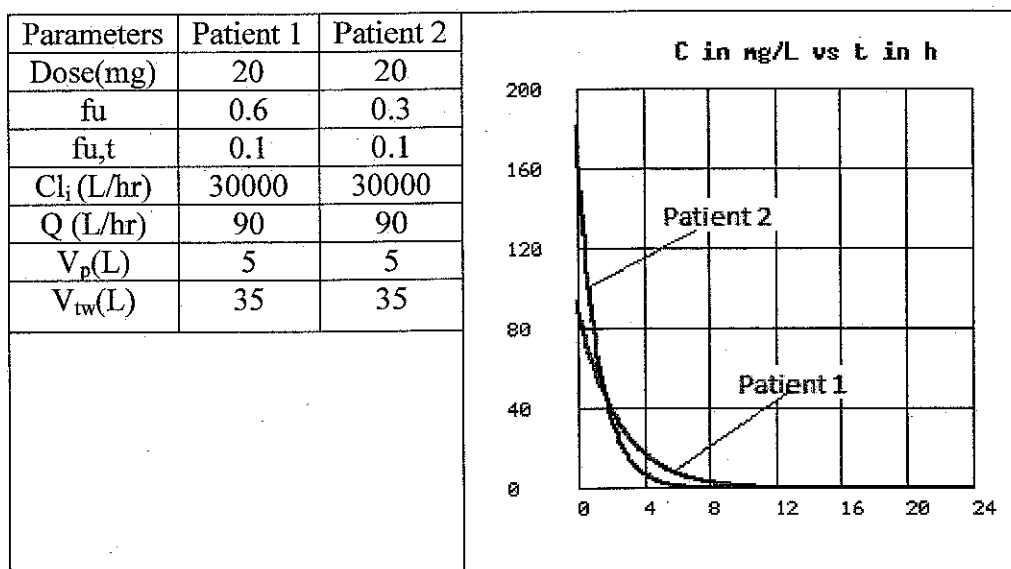
- A 60 ml/min
- B 80 ml/min
- C 100 ml/min
- D 120 ml/min
- E 140 ml/min

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Question Set VIII (30 points)

A lipophilic drug A cleared only through liver metabolism was administered to two patients 1 and 2. The values of some of the physiological parameters of the two patients (f_u – Fraction unbound in plasma; $f_{u,t}$ – Fraction unbound in tissue; Cl_i – Intrinsic Clearance ; Q – Liver blood flow; V_p – Plasma Volume; V_{tw} – Tissue Water volume) are given in the table along with the observed plasma concentration time profiles. Based on the information given in the table and the figure, answer whether the statement is true (A) or false (B).



- 22) T F Drug A is a low extraction drug?
- 23) T F The clearance of the drug in patient 2 is higher than that in patient 1?
- 24) T F The Extraction ratio of the drug in patient 1 is twice that in patient 2?
- 25) T F The AUC of patient 2 is greater than that of the patient 1?
- 26) T F Oral bioavailability of patient 1 is more pronounced.
- 27) T F The Volume of distribution in patient 1 is higher to that in patient 2?

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Question Set IX (True or False)

(15 points)

True (A) or False (B). On the bubble sheet mark A for true or B for false

Mark whether the following statements are true (A) or False (B) for a drug given as iv bolus when the concentration time profile is described by $C=C_p \cdot e^{-k_e \cdot t}$

- 28: T F It is assumed that membranes do not represent significant barriers.
- 29: T F The elimination rate depends on plasma concentration.
- 30: T F Drug metabolism is not saturable at doses used.
- 31: T F Renal transporters are not saturable at doses used.
- 32: T F Volume of Distribution depends on plasma concentration.

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Question Set X

(15 points)

True (A) or False (B). On the bubble sheet mark A for true or B for false

Patient A receives 100 mg of drug A. Patient B 200 mg of drug B. Evaluate the following statements. (Assume IV-bolus administration and linear pharmacokinetics).

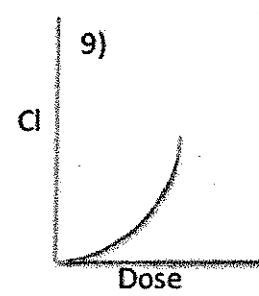
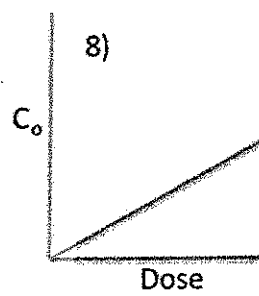
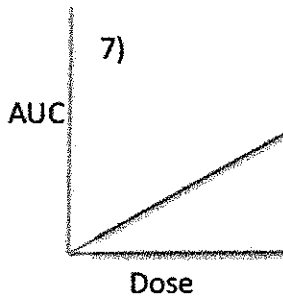
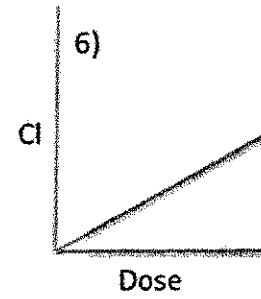
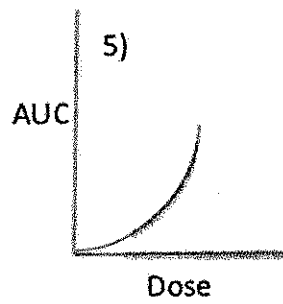
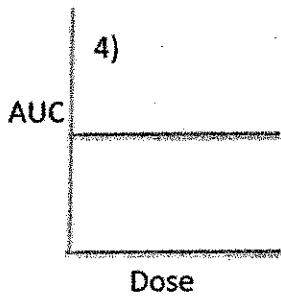
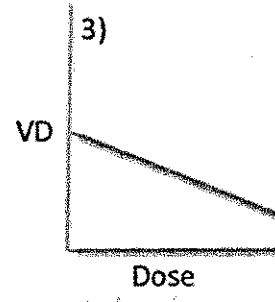
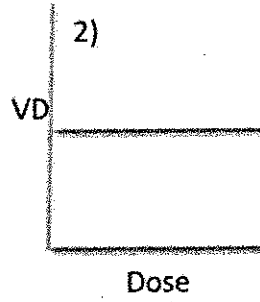
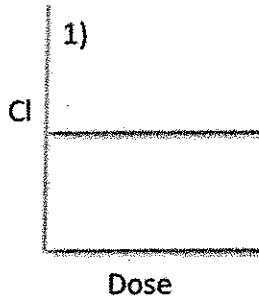
- 33: T F C_0 in patient A will be 100 mg.
- 34: T F At any given time after injection, the elimination rate in patient B will be twice that of patient A. **True was accepted as well**
- 35: T F If patient B received 400 mg of drug B instead of 200 mg, the volume of distribution of patient B is likely to be twice as high.

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Question Set XI (15 points)

36. Select the diagram(s) that clearly show non-linear pharmacokinetics with respect to clearance and/or volume of distribution?



- A) 5, 9
- B) 3, 8
- C) 3, 4, 6
- D) 3, 4, 5, 6, 9
- E) 1, 2, 4

D

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Question Set XII (10 points)

37. The pharmacokinetics of 4 new drugs (nothing is known about the acid/base character degree of ionization) were measured first time in man. Consider liver blood flow of 80 L/h, creatinine clearance of 120 ml/min, kidney blood flow 1.1 L/h, urine flow 1.5 ml/min. Oral bioavailability is determined by hepatic first pass metabolism. Clearance mechanism of the drugs is not known (Assume clearance is due to hepatic and/or renal processes)

The following results were obtained:

- A) Drug A $f_u=0.5$, Cl_{tot} 1.1 L/h, oral bioavailability 100%
- B) Drug B $f_u=0.5$, Cl_{tot} 1.1L/h, oral bioavailability 1%
- C) Drug C $f_u=0.5$, Cl_{tot} 0.75 ml/min, oral bioavailability 100%
- D) Drug D $f_u=0.5$ Cl_{tot} , 60 ml/min, oral bioavailability 100%

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The results for one drug cannot be true. Select the one.