

Name: _____

UFID #: _____

PHA 5127

Second Exam

Fall 2012

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

Name

Put all answers on the bubble sheet

TOTAL _____/150 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. 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, and dissolves in the GI tract. When given to Patient A, it has a f_u of 0.9, and an intrinsic clearance of 300,000 L/h. Patient B has a fraction unbound of 0.99; the only difference to Patient A.

1. T F The oral bioavailability of this drug is higher in Patient B.

2. T F The AUC of plasma concentration vs time curve in Patient B after iv bolus injection is higher than when the same dose is given as iv bolus to Patient A.

3. T F The C_{max} after iv bolus injection is lower in patient A when the same dose is given as iv bolus injection.

4. T F Decrease in tissue binding will affect the AUC_{0-inf} in both Patient A and B.

5. T F Increase in liver blood flow will affect the half-life of the drug in both patients.

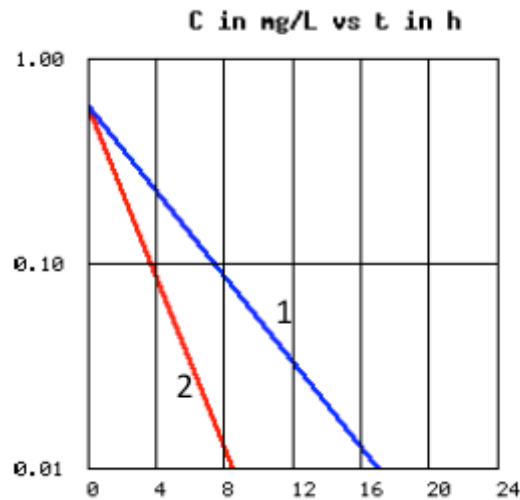
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Question Set II

(16 points)

A patient participated in a clinical study. The patient receives first 100mg IV bolus dose of Alprazolam (Scenario 1) The patient then receives 100mg IV bolus Alprazolam+50mg IV bolus Carbamazepine (Scenario 2). The plasma concentration time profiles of Alprazolam in scenario 1 and scenario 2 are shown in the figure below.



Please provide a qualitative comparison (A: greater than , B: lesser than B; or C equal to) of following parameters

- 6) Clearance of the patient in scenario 1 is that of the patient in scenario 2
- 7) Volume of Distribution of the patient in scenario 1 is that of the patient in scenario 2
- 8) Initial drug concentration (C_{max}) of the patient in scenario 1 is that of the patient in scenario 2
- 9) If the drug regimens are given orally,
the oral bioavailability of alprazolam given alone (Scenario 1) is that of alprazolam+50 mg carbamazepine (scenario 2)

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Question Set III

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

(24 points)

A new analysis technique has enabled you to measure the drug concentration before and after the blood passes through the liver. The plasma concentrations before and after the liver was passed were 1.0 and 0.95 mg/mL, respectively. Consider that differences should be clinically significant.

- 10) T F The drug is a low extraction drug
- 11) T F The oral bioavailability will be low
- 12) T F The oral bioavailability will depend on the liver blood flow
- 13) T F Clearance will depend on tissue protein binding

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. Assume a drug which is eliminated through hepatic metabolism only.

- 14) T F A change in the intrinsic clearance will affect the volume of distribution
- 15) T F Intrinsic clearance and volume of distribution are independent of each other
- 16) T F If the drug is a high extraction drug, enzyme induction of the relevant enzyme will affect the hepatic clearance.
- 17) T F For a low extraction drug, changes in plasma protein binding will affect either volume of distribution or hepatic clearance, as Vd and CL are independent parameters.

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Question Set IV

(10 points)

18) A 59 year-old white male patient is hospitalized for a ruptured duodenal diverticulum. Before surgery you are asked to begin this patient on aminoglycosides. Other pertinent patient data are: height 5ft, 1in; weight 65kg, serum creatinine 1.3mg/dl. Please estimate the clearance of this patient.

- A) 56.3 mL/min
- B) 39.3 mL/min
- C) 3 L/h
- D) 3 mL/min
- E) 3.8 L/h

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Question Set V

(15 point)

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

Mark false if there is not sufficient information provided to answer the question.

The lipophilic drug A, neither an acid nor base, is completely dissolved in the GI tract, crosses membranes easily, and is cleared only via the kidneys, and is not subject to transporter-mediated processes.

- 19) T F The oral bioavailability of drug A is likely to be large.
- 20) T F Plasma protein binding will affect the oral bioavailability of this drug.
- 21) T F It is unlikely that the renal clearance of this drug is affected by drug-drug-interactions.
- 22) T F Changes in liver blood flow will significantly alter the clearance of drug A.
- 23) T F The renal clearance of this drug is close to renal blood flow.

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Question Set V

(30 points)

A lipophilic acidic drug ($pK_a = 13.9$) is only renally eliminated, is 75% plasma protein bound, and crosses membranes easily in its unionized form. The patient taking this drug has a normal glomerular filtration rate and a urine flow of 1.8mL/min. The pH of the urine is similar to that in blood. The drug's volume of distribution was determined as 50L.

24) Which of the following values describes best the clearance of this drug? (15 pts)

- A) 130mL/min
- B) 32.5mL/min
- C) 0.45mL/min
- D) 16.25mL/min
- E) 0.23mL/min

25. The same drug is given at the same dose to two patients as a single intravenous bolus. These patients only differ in their ability to eliminate the drug from the system (Cl_{ren} differs). Select the answer that lists all the pharmacokinetic parameters that differ between these two patients? (15 pts)

- A) Peak concentrations and clearance
- B) Half-life
- C) AUC
- D) Half-life and AUC
- E) Half-life and volume of distribution

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Question Set VI (20 points)

You receive a call from your emergency room physician saying he has a number of patients in the ER that overdosed on the following five drugs (1-5). Which of the methods A-E would you recommend to your physician to help his patients?

Please select the single best choice for detoxification for drugs 1-5 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 works
- E) None of the above

- 26. Drug 1 is eliminated primarily via the liver (high extraction drug) _____
- 27. Drug 2 is lipophilic (nor acid or base) and is only eliminated via the kidneys _____
- 28. Drug 3, a lipophilic acid ($pK_a = 7.4$), is solely eliminated via the kidneys _____
- 29. Drug 4, a lipophilic unionized drug is solely eliminated via the kidneys _____
- 30. Drug 5 is eliminated primarily via the liver (low extraction drug) _____

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Question Set VII

(20 points)

Assume GFR is 130mL/min, urine flow is 1.8mL/min. For the following situation, indicate whether the drug is:

- A) Only filtered
- B) Passively reabsorbed
- C) Actively secreted
- D) Actively reabsorbed

Question 31: A drug with $f_u = 0.3$ and $Cl_{ren} = 0.54$ mL/min

Question 32: A drug with $f_u = 0.6$ and $Cl_{ren} = 0.2$ mL/min

Question 33: A drug with $f_u = 0.25$ and $Cl_{ren} = 32.5$ mL/min

Question 34: A drug with $f_u = 0.2$ and $Cl_{ren} = 32.5$ mL/min