

PHA 5127
Homework #3

1. Drug A is administered as a 250 mg IV bolus dose. 2 hours after administration the concentration in plasma is 4 mg/L and 10 hours after administration the concentration in plasma is 1 mg/L. This lipophilic drug is cleared by the liver and this patient has a liver blood flow of 80 L/hr. The tissue protein binding is 0.6.

A. Calculate C_0 (2 pts)

B. Calculate V_d (1 pts)

C. Calculate f_u (1 pts)

D. Is this a high extraction drug or low extraction drug? (1 pt)

E. If this drug were coadministered with Drug B, which is known to cause enzyme induction for the enzymes responsible for the metabolism of Drug A, would you expect to see a change in clearance? (1 pt)

2. How will the following parameters change for a drug that is a high extraction drug eliminated by hepatic clearance only if the free fraction in plasma is changed from 0.8 to 0.2. Indicate increase, decrease, or remain the same (half point each).

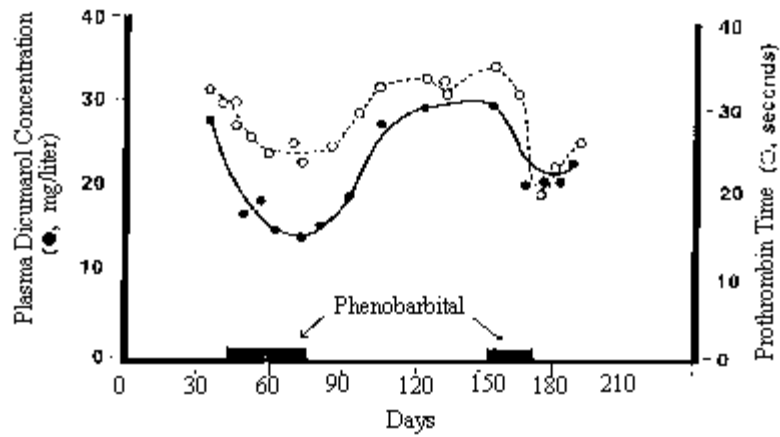
A. V_d

B. E_H

D. Cl

E. K_e

3. Administration of phenobarbital (60 mg daily) to a patient receiving dicumarol (75 mg daily) chronically, reduces the plasma concentration of the anticoagulant (black circle) and the prothrombin (open circle) time, a measure of its effect on the concentration of the vitamin k_1 -dependent clotting factors. (2pts)



What kind of pharmacokinetic interaction is responsible for the observed pharmacodynamic interaction? Explain your answer.

Note:

- 1) Dicumarol is an anticoagulant
- 2) Prothrombin time is a measure of its effect