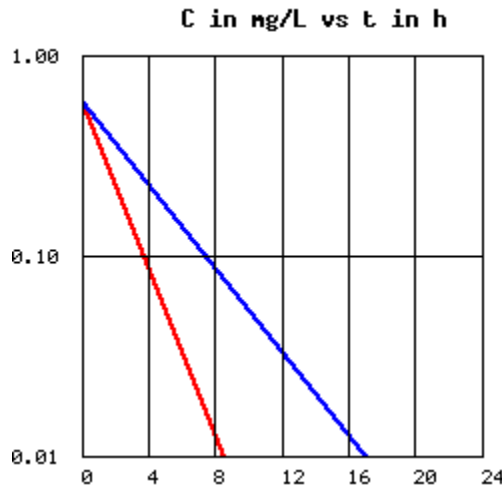


Question 1 Drug-Drug Interaction

Lipophilic and unionized drug Phenytoin ($V_p = 3L$, $V_T = 38L$) has a volume of distribution of 100L. Valproic acid displaces phenytoin from albumin binding sites (plasma) making a two-fold increase in the fraction unbound in plasma. Predict the change in volume of distribution of phenytoin when co-administered with valproic acid. (5)

Question 2 Drug-Drug Interactions (Enzyme Induction)

2 patients red and blue participated in a clinical study. Blue patient received 100mg IV bolus dose of Alprazolam, while the red patient received 100mg IV bolus Alprazolam+50mg IV bolus Carbamezapine. The plasma concentration time profiles of **Alprazolam** in red patient and the blue patient are shown in the figure below.



Please provide a qualitative comparison (greater than, lesser than or equal to) of parameters

- a) Clearance (1)
- b) Volume of Distribution, (1)
- c) Initial concentration (C_0) and free initial concentration ($f_u * C_0$) in the red patient and the blue patient for Alprazolam (1)

True or False (2)

- 1) The maximum value hepatic clearance can approach is the liver blood flow. (T/F)
- 2) For drugs with a hepatic extraction ratio of 1, the hepatocyte does not represent a strong diffusion barrier? (T/F)