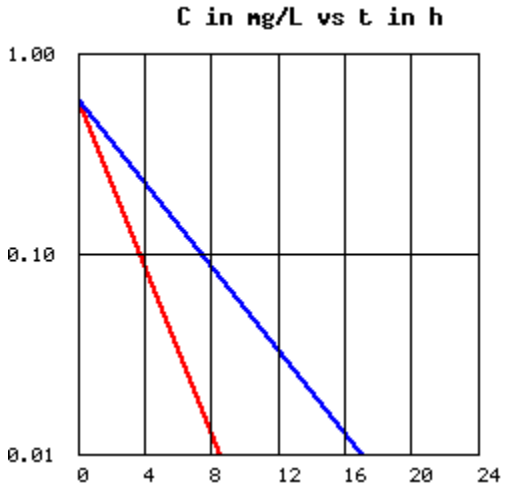
PHA 5127 Homework – 3 (Due – Sep 20) 10 points

Question 1 Drug-Drug Interaction

Lipophilic and unionized drug Phenytoin (Vp= 3L, VT = 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 (fu* 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)