Case Study 2 (Fall 2008) Solution

Q1) A 80 kg male patient was given a single i.v. dose of 45 mg cocaine which is known to have a half-life of 0.693 hr and a volume distribution of 2 L/kg.

(1) What is the clearance of cocaine? Is it solely metabolized by liver? Why?
(2) Predict $AUC_{0-\infty,}$

(1)

ke =0.693 / t1/2 =1 hr -1 Vd =2∗80 =160 L
Cl=ke •Vd =1∗160=**160 L/hr>90 L.hr**
There exists non-hepatic metabolism .

(2)
$AUC_{0-\infty,}$ = *Dose/ Cl* =45/160 **= 0.28 *mg. hr/ L***

Q2) A patient is to be started on two medications (A and B) administered by IV bolus injections. Blood samples were taken at 1 and 4 hours following the first injections of drug A or B alone in order to determine whether concentrations were in an appropriate range for each drug. See table below for these levels and additional information.

Drug	**Dose (mg)**	**Cp at 1h (mg/L)**	**Cp at 4h (mg/L)**	**E_H**	**fu**
A	400	1.22	0.76	0.8	0.1
B	1200	0.92	0.51	0.1	0.3

Assume liver blood flow of 90 L/h, where E_H is the extraction ratio and fu is the fraction unbound. Both drugs are metabolized by CYP 3A4.
Is it possible to calculate the $AUC_{0-\infty,}$ for drug B, if yes how much is it ? if no , why not ?

Ke = ln C2 – ln C1/(t2-t1) = 0.20 /hr
T1/2 = 0.693/ 0.2 = 3.45 hr

C_0 = Ct / exp(-ke * t)
C_0 = 1.13 mg/L

$Vd = dose / C_0$
$Vd = 1200 / 1.13 = 1062$ L

$CL = Vd * Ke = 1062 * 0.20 = 212.4$ L/ hr
$AUC_{0-\infty} = dose / Cl = 1200 / 212.4 = 5.65$ mg.hr/L

Q3) Say True or False

T **F** For a drug with high tissue binding, the volume of distribution will be very low.

T **F** Volume of distribution is not important to determine what loading dose is required.

T **F** Drug A has 98% protein binding and has a narrow therapeutic index. Any change in the protein binding is not of significant consequence since already 98% drug is bound and very less is available for receptors

T **F** If volume of distribution changes, this will affect the drug clearance as well since this means less volume of drug to be cleared.

T F If Drug A and Drug B are being administered at the same time then dose adjustment may be needed if there are drug interactions between A and B

T F Clearance and Volume of distribution are independent parameters.

T **F** If the drug clearance changes then the volume of distribution changes since ke= Cl /Vd

T F If Drug A is cleared only by hepatic metabolism only, then the clearance of drug A cannot be greater than liver blood flow.

T F If Drug A and Drug B are being administered at the same time then dose adjustment may be needed if there are drug interactions between A and B

T F For a low extraction drug, the lower the protein binding the higher will be the clearance