請依題號順序作答

一、 Theophylline 300 mg 藥品靜脈注射給藥後於體內的濃度變化與時間的關係，可用下列數學方程式表示：$C_p = 35\ e^{-5.8t} + 15\ e^{-0.16t}$

(C_p 表示藥品 plasma concentration (μg/mL)，t 表示給藥後之時間 (hr^{-1}))。(每小題各五分)

1. 依據上述公式，該藥品於體內的變化可以下列哪一藥動模式描述？(單選)
   (a) one-compartment model
   (b) two-compartment model
   (c) three-compartment model
   (d) non-compartment model
2. 請問在時間為零時，假設所有藥品都在 central compartment，其該藥品之濃度為何?
3. 該藥品於 central compartment 的分布體積為何?
4. 該藥品在六小時後，其排除半衰期(elimination half-life)為何?

二、 某一抗病毒藥品，研發出口服錠劑之新劑型，另原有之劑型包括針劑及口服液劑，在 BA/BE 的研究結果如下表:

Drug product	Dose (mg)	AUC (μg hr/mL)
IV bolus injection	100	40
Oral solution	400	120
Oral tablet	500	90

請以本例子，解釋何謂「relative bioavailability」及「absolute bioavailability」並分別計算出其百分比。(本題共二十分)

三、 王先生 45 歲，60 公斤，正常腎功能，在服用下列二個藥品過量劑量時，身體血液至血液透析機的流速為 50 mL/min，經血液透析可移除之藥品的情況如下表。

Drug	V_D (L) 分布體積	Cl_T (mL/min) 生體總廓清率	$C_{entering}$ 藥品進入透析機之濃度	$C_{leaving}$ 藥品離開透析機之濃度
A	60	100	200 μg/mL	20 μg/mL
B	600	100	10 ng/mL	9 ng/mL

假設該二種藥品於體內的濃度變化與時間的是線性關係且為一室模式(one-compartment model)，請回答下列問題（每小題各十分）

1. 請問該血液透析機對於 A 藥及 B 藥之廓清率(clearance)分別為何?
2. 請問正在使用血液透析機時，A 藥及 B 藥於王先生體內之半衰期(half-life)，分別為何?
3. 你認為血液透析機可有效率地移除哪一藥品，並說明理由。

見背面

四、 A drug is eliminated by first-order renal excretion and hepatic metabolism. The drug follows a one-compartment model and is 90% systemically available when it is given orally. The elimination half-life for this drug is about 3.3 hours and its apparent volume of distribution is 60 L. Following a single oral dose (100 mg), the total amount of unchanged drug recovered in the urine is 60 mg, and the total amount of metabolite recovered in the urine is 30 mg (expressed as milligram equivalents to the parent drug). （每小題各五分）請詳述解題過程

1. Find the renal clearance.
2. Please explain whether there is apparent renal reabsorption or secretion.

五、 It is known that drug-A is metabolized by CYP2C19. The AUC and AUMC values of drug-A following an I.V. bolus of 5 mg are 278 μg-hr/L and 1390 μg-hr^2/L, respectively. Assuming this drug follow one-compartment model, （每小題各五分）請詳述解題過程

1. Calculate the volume of distribution at steady-state (Vd_{ss}) of this drug.
2. Is there a decrease in hepatic clearance of drug-A in a patient who is a CYP2C19 poor metabolizer? Why?

六、 Valproic acid is an anticonvulsant agent. The oral bioavailability of valproic acid is about 0.9. The plasma protein binding of valproic acid is high but could decrease at high concentration. The fe value of valproic acid is about 0.7 to 0.8. Warfarin is known to be a low extraction ratio drug and its protein binding degree is high (about 99%). Please predict possible effects of warfarin on AUC and F of valproic acid based on pharmacokinetic equations. （本題十分）請詳述解題過程

試題隨卷繳回