1. The first-order degradation rate constant of a pharmaceutical product was found to be 7.7 × 10^{-3} day^{-1} at 25℃. The activation energy for the degradation process has been determined to be 12 kcal/mol.
   (1) Determine the shelf-life of the product if the product is manufactured as 100% labeled content. The specification of active ingredient in the product is from 90 to 115%. (4%)
   (2) Describe two different ways to extend the shelf-life of the product. And what will be its extended shelf-life? (16%)

2. Describe the apparatuses and techniques to determine the *in vitro* release of transdermal or topical delivery systems. Explain the purposes of such a test. (10%)

3. A drug is selected to develop a 3-day transdermal patch. The candidate has a MW of 336, apparent volume of distribution of 6 L/kg, an elimination half-life of 8 hours, and a desired therapeutic concentration of 10 ng/ml. Determine the zero-order skin delivery rate of the transdermal patch. (10%)

4. Describe the procedures to prepare a 50 ng/ml solution of a compound in water. The compound is only slightly soluble in water and freely soluble in methanol. An analytical balance with a sensitivity of 1 mg, 50-ml volumetric flasks, and a 1-ml adjustable pipet are available in the laboratory for use. (10%)

(背面仍有題目,請繼續作答)

5. Describe and explain the following equations. (18%)

(1). Arrhenius equation

(2). Henderson-Hasselbalch equation

(3.) Noyes-Whitney equation

6. The pharmacokinetic parameters of a drug X following intravenous (i.v.) and oral administration as immediate-release (IR) and slow-release (SR) tablets are listed in Table 1.

Route	Dose (mg)	Half-Life (hr)	AUC (mg/L*hr)	Amount excreted (0-48 hr) (mg)
i.v.	500	2.7	13.1	333
IR	1000	3.0	20.8	588
SR	1000	3.1	19.8	555

(1). Estimate both absolute bioavailability and relative bioavailability of SR tablet from both plasma and urine data. What are the assumptions made in your calculations? (10%)

(2). Was the urine collected over a long enough time interval to obtain a good estimated of the cumulative amount excreted at infinite time? (5%)

(3). Does renal clearance of drug X vary much among the three treatments? (5%)

7. Describe the important issues that should be considered in the evaluation of modified-release drug products. (12%)