Answer the following questions:

1. Explain and describe the procedures to determine the concentration of a weak acid with pKa = 4.5 and MW = 358 in 10 ml plasma using high performance liquid chromatography (HPLC). (10%)

2. Fluocinonide solutions of different concentration are prepared by mixing a 500 μg/ml solution of fluocinonide in cosolvent 1 (ethanol:propylene glycol=1:1) with different ratios of cosolvent 2 (water-glycerol=1:1) to cosolvent 1.

Solution	Concentration (μg/ml)
A	100
B	150
C	200
D	250

Calculate the ratio of cosolvent 2/cosolvent 1 required to prepare each solution and the final solvent composition for each solution. (10%)

3. Explain, from the point of dosage form design, why some of the oral dosage forms should not be broken in half for administration. (10%)

4. Describe the theory for skin permeability. From the theory, discuss the properties of a compound that influence its skin permeability. (10%)

5. Describe the approaches to improve oral drug absorption? (10%)

6. What is therapeutic drug monitoring? Describe factors that should be considered when initiating and interpreting the therapeutic drug monitoring. (10%)

7. Describe the dissolution apparatuses and techniques. (10%)

(背面仍有題目,請繼續作答)

8. Misoprostol (Cytotec) is a synthetic prostaglandin E1 analog. It is extensively absorbed and undergo rapid de-esterification to its active metabolite misoprostol acid. According to the manufacturer, the following kinetic data of misoprostol acid were obtained when misoprostol was taken with an antacid or high-fat breakfast.

Mean ± SD	C_{max} (pg/mL)	$AUC_{0\text{-}4hr}$(pg·hr/mL)	t_{max} (min)
Fasting	811±317	417±135	14±8
With antacid	689±315	349±108*	20±14
With high-fat breakfast	303±176*	373±111	64±79*

* Comparisons with fasting results statistically significant, $p<0.05$.

What is the effect of *antacid* and *high-fat breakfast* on the bioavailability of misoprostol? Comment on how *these factors* affect the rate and extent of systemic drug absorption. (10%)

9. The inactive ingredients of Cytotec oral tablets are hydrogenated castor oil, hydroxypropyl methylcellulose, microcrystalline cellulose, and sodium starch glycolate. Describe the usage(s) of these excipients in the formulation. (8%).

10. The hepatic clearance of two drugs are as follows:

    Drug A: 1200 mL/min

    Drug B: 25 mL/min

    Which drug is likely to show the greatest increase in hepatic clearance when hepatic blood flow is increased from 1 L/min to 1.5 L/min? Which drug will likely be blood-flow limited? (4%)

11. An industrial pharmacist would like to design a controlled-release drug product to be given every 12 hours. The active ingredient has a molecular weight of 350, an apparent volume of distribution of 10 L, an elimination half-life of 3.5 hours, and a desired therapeutic concentration of 20 mg/L. It is highly bound to plasma proteins (unbound fraction 0.02) and is mainly eliminated by hepatic excretion. Calculate the zero-order release rate of the controlled-release drug product and the total amount of drug needed, assuming no loading dose is required. (8%)