Birla Institute of Technology and Science, Pilani (Rajasthan)

First semester 2023-24

PHA G 542: Advanced Physical Pharmaceutics

Comprehensive Examination

Max. Marks: 35 **Closed Book**

Date: 18-12-2023 **Duration: 3h**

Instruction: Write clear and legible answers. Avoid overwriting.

Q1. (a) What are primary requirement for generic product development? What are the information one can get from the innovator product for the development of generic product? Write different storage condition recommended for product stability testing for general case. [3M]

(b) A drug has 3 polymorphs A, B and C having solubility 0.20 mg/ml, 2 mg/ml, and 20 mg/ml respectively. The dose of drug X is 50 mg thrice a day. Give the following answer with proper justification: (i) You have to suggest the most suitable polymorph of drug X for tablet production. (ii) If you want to improve the onset of action of drug 'X' then which polymorphic form is the most suitable. (iii) If you want to make fast dispersible tablet then which polymorphic form is the most suitable. (iv) If you want to make sustained release tablet then which polymorphic form is the most suitable. [2M]

Q2. (a) In what situations Similarity and Dissimilarity (Difference) factor plays an important role? Why one should perform in-vitro release testing in simulated fast and fed small intestine conditions during product development? [4M]

(b) Suggest Universal Tests and Specific Tests name for emulsion formulation as per ICH Q-6A [2M]

Q3. (a) Discuss the significance of Biopharmaceutical classification system and IVIVC for drug product development and approval. [3 M]

(b) A company has approval of sustained release tablet product which consist of HPMC K15M (50 mg) in each tablet (500 mg). Later, based on some trials and to make product cost effective, scientist proposed for different vendor of HPMC K15M and increase the HMPC K15M amount to 80 mg. Suggest the documentations required for the approval as per SUPAC guidelines. [2 M]

Q4. (a) A BCS class I drug formulated in different dosage form as given. Draw in-vitro drug release profiles of these formulations in single figure for: (i) Delayed release tablet; (ii) Zero order controlled release tablet; (iii) Enteric coated tablet; (iv) Rapid dissolving tablets. Assume the test was performed first 2 hrs in 0.1 N HCl medium followed by pH 6.8 phosphate buffer for 10 hrs. [2M]

(b) Two drugs A (max dose = 10 mg) and B (max. dose= 50 mg) are having aqueous solubility 100 and 10 mg/100 ml respectively. The mean dissolution time and mean absorption time of Drug A were found to be twice and half of drug B respectively. The mean absorption time and mean dissolution time for drug B was found to be 3 hr 20 min and 8 hr respectively. Suggest the BCS class of above drugs with complete justification. (Assume Mean Residence time in GI is 180 min). [3M]

Q5. (a) The measured contact angle of water on the surface of compact powder of compound 'X' and 'Y' are θ=120°and 45°, respectively. Their surface tensions (against air) are 72.3 and 71.6 dynes/cm, respectively. (i) Compute the interfacial tension between water and powders. (ii) Compute the spreading of water on solid surfaces. Water surface tension (against air) is 72.8 dyne/sec. [2M]

(b) The drug release data for three tablet batches (F1, F2 and F3) of drug X are given below:

Release model	**Zero order**		**Fist order**		**Higuchi model**	
Formulation	K_0	R^2	K_1	R^2	K_H	R^2
F1	4.16	0.971	0.23	0.938	23.53	0.878
F2	3.78	0.822	0.23	0.886	21.88	0.982
F3	3.35	0.697	0.22	0.997	20.367	0.901

K is dissolution rate constant; R^2 is regression coefficient for different models. Calculate the time for 50% drug release from formulation F1, F2 and F3. [3M]

Q6. (a) For preparation of o/w emulsion, 30% oil phase (density=1.2g/cm^3) dispersed in water. Oil phase contain 40% castor oil, 30% mineral oil and 30% cottonseed oil which RHLB values are 14, 10 and 7 respectively. Calculate the require quantity of surfactant mixture (density=0.90 g/cm^3) and require quantity of each surfactant for this emulsion. Surfactant mixture contain X (HLB=15) and Y (HLB=5) surfactants. [3M]

(b) You have 1000 ml of '1 in 200' drug solution. From this solution, how will you make 60 ml of '1 in 4000' drug solution? [2M]

Q7 The solubility of two drugs A and B were evaluated in various proportion of solvent X in water at 27°C as given in below table. Solubilization Power of stronger solvent for drug A is 4.49 and for B is not reported. Dielectric Constant of solvent X and water are 25 and 78.36 respectively. Calculate the solubility of drug A and B in 35% v/v and 70% v/v of solvent X solutions. [4M]

Volume fraction solvent X	**Drug A Solubility mg/ml**	**Drug B Solubility mg/ml**
0	0.007	0.014
0.10	0.010	0.062
0.20	0.015	0.101
0.50	2.50	0.35
0.90	48.65	3.56
1	63.35	3.32