BPS 4131: Mid Term Test, January 29, 2013

Instructor: Dr. Krishnan Tirunellai, Time 60 min., closed book exam, marks 15% of total

Q 1-17: Multiple choice questions (1 mark each) should be answered on the scantron sheet provided using HB pencil. Answers to the short-answer questions should be written in point form legibly in the space provided.

1. Arrange the following dosage forms in decreasing order of bioavailability for an orally administered drug (> means faster than):

a. Solution>suspension>solid

b. Suspension>solid>solution

c. Solid>suspension>solution

d. Solution = suspension > solid

e. Solution = suspension = solid

2. For a patient suffering from angina the most suitable dosage form to deliver nitroglycerin would be:

a. oral tablet

b. trasdermal patch

c. buccal tablet

d. ointment

e. cream

3. As per BCS classification furosemide is a class IV drug, which means it is a drug that has:

a. low solubility and low permeability

b. low solubility and high permeability

c. high solubility and low permeability

d. high solubility and high permeability

4. Among the routes of administration listed below for an antihypertensive drug, the route that would give the highest bioavailability is:

a. Oral

b. Sublingual

c. Transdermal

d. Intramuscular

e. Intranasal

5. The bioavilability of drug X (an acid) was found to be low due to its poor solubility in the physiological pH. Its bioavailability could be improved by:

I. Using its sodium salt

II. Using micronized drug substance

III. Making an orally disintegrating tablet.

a. I only

b. III only

c. I and II only

d. II and III only

e. I, II and III

6. Bioavailability of an oral dosage form is determined by measuring the:

a. relative amount of the administered drug that reaches the systemic circulation intact.
b. rate of the administered drug that reaches the systemic circulation intact.
c. rate and relative amount of the administered drug that reaches the systemic circulation intact.
d. rate and relative amount of the administered drug that is absorbed from the GI tract.
e. Cmax and Tmax of the administered drug that reaches the systemic circulation intact.

7. A drug following first-order kinetics has a half-life of 3 hours. This would mean:

10 half lives
5 ½

a. In 3 hours 95% of the drug would be eliminated.
b. In 30 hours 95% of the drug would be eliminated
c. In 15 hours 99.9% of the drug would be eliminated.
d. In 30 hours 99.9% of the drug would be eliminated.

8. Based on FMECA (failure mode effect and control analysis) technique for the evaluation of risk and criticality, use of improved technology would help in:

I. Reducing severity of the problem should it occur
II. Improving the detectability of the failure
III. Reducing the probability of occurrence of the failure

a. I only
b. III only
c. I and II only
d. II and III only
e. I, II and III

* ASK

9. As a general rule, a generic tablet will be considered to be bioequivalent to the innovator's tablet if:

I. the confidence interval (CI) for the statistical evaluation is 90% or above ✓

II. the ratios of the mean response for AUC and Cmax are within the limits of 0.8 to 1.25. ✓

III. the number of subjects chosen for the study is at least 12. 4 Depend on Narrow therapeutic drug.

a. I only

b. III only

c. I and II only

d. II and III only

e. I, II and III

10. For a drug substance that has low permeability, its oral bioavailability can be improved by:

I. Making a more lipid soluble prodrug ✓

II. By administering the drug with food ✓

III. By giving the drug on an empty stomach

a. I only

b. III only

c. I and II only

d. II and III only

e. I, II and III .

11. To ensure tablets in a batch containing a small dose the drug substance (e.g., 1 mg/tablet) meet Content Uniformity, the drug-excipient mixture should be:

I. subjected to direct compression process.

II. granulated using wet granulation process.

III. granulated using dry granulation process.

a. I only

b. III only

c. I and II only

d. II and III only

e. I, II and III

12. Use of excess lubricant (e.g., magnesium stearate) or prolonged lubrication time of granules would:

a. Increase the dissolution time

b. Reduce the dissolution time

c. Improve the flow property of the granules

d. Increase tablet hardness

e. Reduce tablet hardness

13. Drug X is hygroscopic with a melting point of 50°C. Tablets containing 50 mg of X should be manufactured using:

I. direct compression process

II. dry granulation process

III. wet granulation process

a. I only

b. III only

c. I and II only

d. II and III only

e. I, II and III

14. Tablets of drug X from a lot were tested using the standard friability test, and the weight loss was 5%. This would mean the tablets from this lot will most likely:

a. be able to stand the rigors of packaging operation and transport.

b. not be able to stand the rigors packaging operation and transport.

c. have poor dissolution property.

d. have very high hardness.

e. meet all the tests for an immediate release tablet.

15. Performing in-process tests during the manufacturing of a large batch of tablets will help in:

I. monitoring the quality of the entire batch. ← said directly in notes

II. reducing variability in quality.

III. making timely correction to maintain important quality attributes.

a. I only

b. III only

c. I and II only

d. II and III only

e. I, II and III

16. Donepezil is used to treat dementia in Alzheimer patients. The most suitable way to deliver the medication would be formulate it as:

a. Immediate release tablet to be swallowed

b. Modified release tablet

c. Effervescent tablet

d. Orally disintegrating tablet

e. Sustained release tablet

17. Drug X is poorly soluble. Its recommended dose is 2 mg. The formulator decided to manufacture its immediate release tablet by wet granulation process using the fluid bed drier (FBD). This manufacturing method would:

I. Yield more dense granules that would take longer to dissolve.

II. Ensure Content Uniformity is achieved in the batch.

III. Yield porous granules that would take less time to dissolve.

a. I only

b. III only

c. I and II only

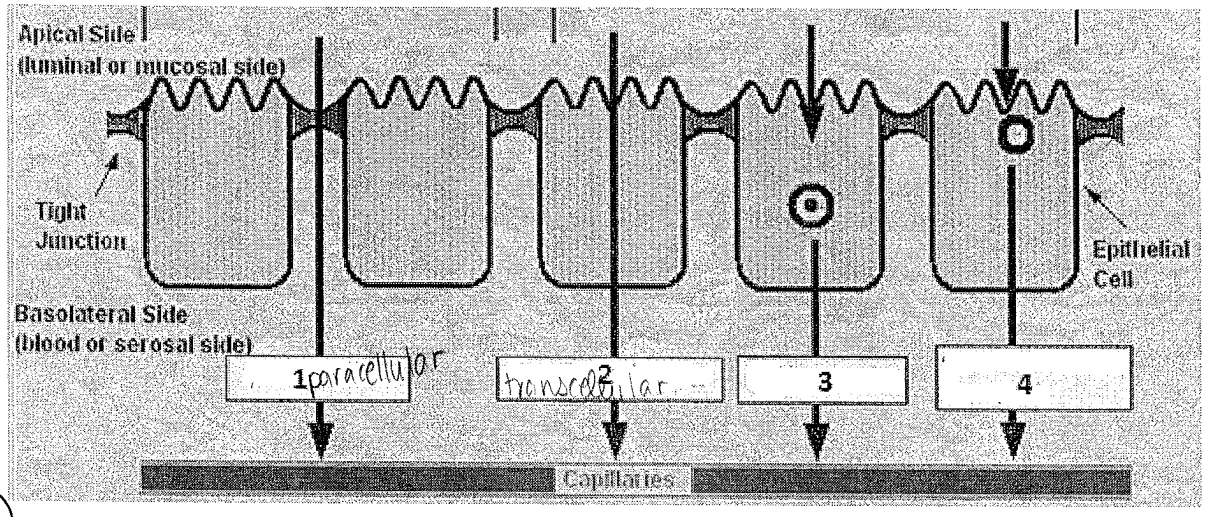
d. II and III only

e. I, II and III

6/10 8/13

Short Answer Questions (answer the questions in the space provided)

18. List the different transport pathways (mechanisms), for drug transport through the gastrointestinal tract (2 marks)



1/2

1. paracellular ✓
2. transcellular Passive diffusion
3. Carrier mediated transport (facilitated diffusion - 3. Endocytosis via a protein assuming that the circle is a protein that contains the drug)
4. Passive diffusion (assuming that the circle represents the drug passing through the cell)

Transcellular

2/3

Partly

19. Using the principles of product development list the different steps expected for developing a drug product (3 marks). (If you need additional space to write use the back side of this page).

Steps for developing a drug product

1) Pre formulation → choosing excipients based on quality target product profile & dosage form (QTPP → CQA → composition → Mfg. Process → Controls)
2) formulation → choosing API, excipients & choosing appropriate dosage form & manufacturing process
3) Determining manufacturing process (and packaging) & Determining Quality control
4) Performing Clinical trials for Drug product & getting approval from Health Canada for the drug product based on the results of the clinical trial
5) Scale up batch size of drug for commercial manufacturing
6) validation for market consumption.
7) Distribution of drug product to the market.

hygroscopic = abs moisture

20. In a study conducted in human volunteers the AUCs of an antihypertensive were which are given below. (2 marks)

Drug product to reduce blood pressure	AUC (mg/L) x hr
a) Intravenous injection	100
b) Company A`s tablet	60
c) Company B`s tablet	50

0

Determine:

a) The absolute bioavailability (F) of the antihypertensive drug : F = 0.6 or 60% $F = \frac{100\%}{\text{for IV}} = 1$

b) The relative bioavailability (F) of Company B`s tablet: F = 0.83̄ or 83% $\frac{50}{100} = 0.5$

5/6

21. On administering 2 g of an antibiotic by IV the following plasma drug concentration – time data were obtained. The drug follows first order elimination process.

Time (hours)	Plasma concentration (mg/L)
0	200
0.3	170
0.5	150
1.0	110
1.7	75
2.0	58
4.0	19
5.0	10

-30, -20, -40, -35

$\ln C_T =$ 2mg

$\ln(170) = \ln(200) - kel(0.3)$

$kel(0.3) = \ln(200) - \ln(170)$

$kel = 0.5$

0.575364

$\frac{mg}{L \cdot hours}$

Determine the following pharmacokinetic terms (*answers should have appropriate units*) (6 marks)

a. Half life 200 to 100 (1.278 hours)

1.5

$t_{1/2} = \frac{0.693}{kel} = \frac{0.693}{0.542} = 1.3$ hours ✓

↑ from value in back page

b. Elimination rate constant

1 $\frac{Kel(0.3)}{2.303} = \log(200) - \log(170)$

$Kel = [\log(200) - \log(170)](2.303)$

$= 0.542 \frac{0.3}{hours}$ $0.54\ hr^{-1}$

c. Clearance

1 $CL = ke\ Vd$

$= (0.542)(10L)$

$= 5.42\ L/hr$ ✓

1.5 **d. Apparent volume of distribution**

$Vd = \frac{Dose}{C_0} = \frac{2000mg \cdot L}{200mg} = 10L$ ✓

Useful equations

$ke = Cl_T / Vd$

$AUC_{0-\infty} = \frac{Dose}{V_d k_{el}} = \frac{c_p^0}{k_{el}} = \frac{Dose}{clearance}$

$V_d = Dose/C_0$

$\frac{K_{el}t}{2.303} = Log\ C_p^0 - Log\ C_p = \frac{Log\ C_p^0}{C_p}$

$\frac{Kel(0.5)}{2.303} \log(200) - \log(150)$

$Kel = 0.575466$

$t_{1/2} = \frac{2.303\ Log\ 2}{K_{el}}$ $t1/2 = \frac{C_0}{2\,K_0}$

$\frac{kel\ (0.3)}{2.303} = \log(200) - \log(170$

$= 0.541825.$

$\frac{kel\ (1)}{2.303} = \log(200) - \log(110)$