23CGP077

Drug Delivery and Targeting

Semester 1 2023/24 In-Person Exam paper

This examination is to take place in-person at a central University venue under exam conditions. The standard length of time for this paper is **2 hours**.

You will not be able to leave the exam hall for the first 30 or final 15 minutes of your exam. Your invigilator will collect your exam paper when you have finished.

Help during the exam

Invigilators are not able to answer queries about the content of your exam paper. Instead, please make a note of your query in your answer script to be considered during the marking process.

If you feel unwell, please raise your hand so that an invigilator can assist you.

You may use a calculator for this exam. It must comply with the University's Calculator Policy for In-Person exams, in particular that it must not be able to transmit or receive information (e.g. mobile devices and smart watches are **not** allowed).

Part A carries 20 marks and Part B carries 30 marks.

All questions in **Part A** and **Part B** are **compulsory**.

Candidates should show full working for calculations and derivations.

Part A

This question is compulsory

1. (a) With the aid of a schematic diagram, explain how liposomes may be used for non-viral gene transfection. [3 marks]

   (b) Using the diagram shown in Figure Q1(b), explain how the solubility of a polymer in a solvent can be predicted based on solubility parameters. Also, write down the equation for R_a and explain the meanings of δ_d, δ_h and δ_p. [3 marks]

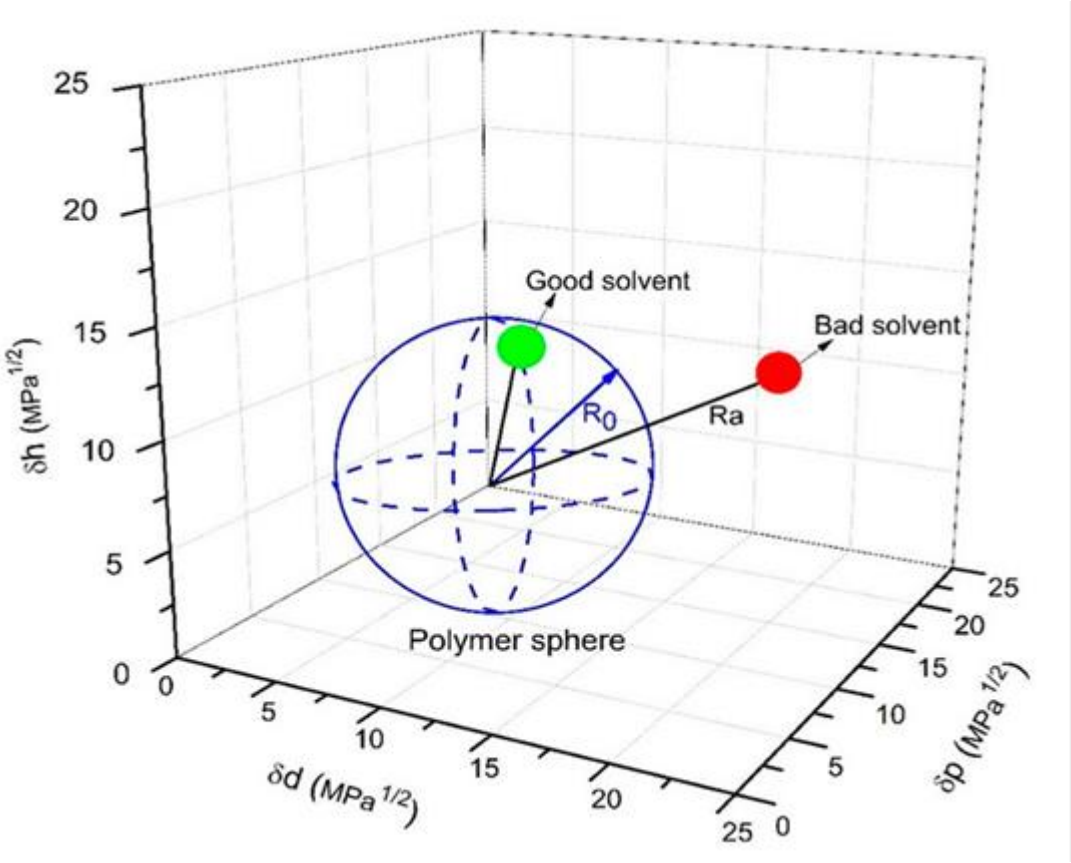

Figure Q1(b). Hansen solubility space for a typical biodegradable polymer. The position of a good and bad polymer solvent is indicated.

   (c) Stating the number of tablets involved, describe the British Pharmacopoeia uniformity of content test and the conditions that give a pass. [3 marks]

Continued/…

(d) A patient has been prescribed a medication for migraine relief called amitriptyline. It is to be taken orally in the evening and is expected to be absorbed via the stomach or upper small intestine. The patient regularly takes antacids for acid reflux (these neutralise stomach acid).

(i) In general, why is it important that a patient mentions any other medication they are taking to their doctor and/or pharmacist (both prescribed and over the counter)? [1 mark]

(ii) Will taking antacids at the same time as amitriptyline impact on how much amitriptyline is absorbed? Justify your answer and/or highlight what additional information you might need about amitriptyline to make a decision. [5 marks]

(e) The bioavailability of orally administered amitriptyline is typically 33-62% in patients taking no other medications.

(i) Define bioavailability. [1 mark]

(ii) Aside from poor absorption, what might cause the bioavailability of orally administered amitriptyline to be low? [2 marks]

(iii) Discuss why bioavailability might vary between patients taking amitriptyline. [2 marks]

Part B

Answer **ALL** questions

2. A hydrophobic drug is encapsulated within propene glycol diacetate (PGDA) microspheres with a diameter of 100 μm. The drug loading in microspheres is 20% and the drug diffusion coefficient in PGDA is 5×10^{-13} m^2 s^{-1}. If 100 mg of drug-loaded particles are placed in a large volume of the release medium, calculate:

   (a) The amount of drug (in mg) that will be released after 30 days. [3 marks]

   (b) The percentage reduction in the amount of drug that will be released after 30 days if the particle diameter is increased to 25 μm. [4 marks]

   (c) The drug diffusion coefficient if it is found that 70% of the drug is released in 2 weeks from drug-loaded microspheres with a diameter of 10 μm. [3 marks]

   Data

   The fraction of drug remaining in microspheres can be calculated using the equation:

$$\frac{M_1-M_t}{M_1}=\frac{6}{\pi^2}\sum_{n=1}^{\infty}\frac{1}{n^2}exp(-Dn^2\pi^2t/a^2) \quad \text{(Eq. Q2)}$$

   Where M_t is the total mass of drug removed from the microspheres after time t, M_1 is the initial mass of drug encapsulated in the microspheres, D is the drug diffusion coefficient, and a is the microcapsule radius. For convenience, the equation Q2 is plotted in Figure Q2 overleaf. You are advised to use the graph to answer the question.

Continued/…

Q2 Continued/…

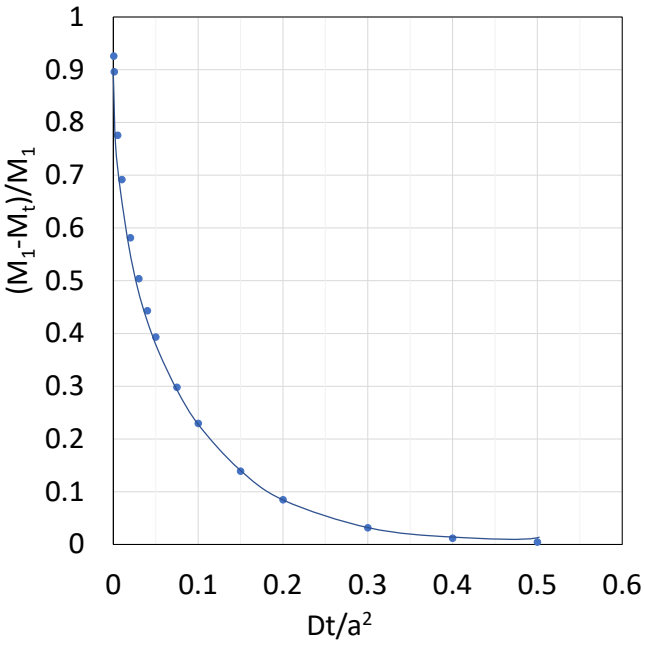

Figure Q2. The fraction of drug remaining in microspheres as a function of dimensionless time.

3. (a) State seven possible causes of capping and lamination during tablet manufacture and their remedy. [7 marks]

   (b) A dosage form consists of size 3 hard gelatine capsules containing 0.3 g of a powder formulation, which have 10% active ingredient. State the Quality Target Product Profile (QTPP), Critical Quality Attributes (CQA) and Critical Process Parameters (CPP) of this dosage form. [3 marks]

4. A pharmaceutical company aims to develop a transdermal patch for fentanyl delivery. To help develop the patch, the company aims to carry out an *in silico* modelling study to determine the effects of different parameters on fentanyl concentration in skin and blood assuming a two-compartment body pharmacokinetic model.

   (a) With the help of a schematic diagram, identify the most salient mechanisms that are likely to govern the drug's concentration in the skin and blood. [4 marks]

   (b) Identify two general classifications of pharmacodynamic model that the company may use in their *in silico* modelling. [2 marks]

   (c) With the help of a schematic diagram, briefly describe an experimental approach which the company may adopt to obtain skin permeation data to help the *in silico* modelling study for the transdermal patch. [4 marks]

END OF PAPER

Dr DB Das, Prof K Coopman, Dr MC Leaper, Dr G Vladisavljevic