Loughborough University

22CGP077
Drug Delivery and Targeting

Semester 1 2022/23 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 a schematic diagram, discuss a method by which a drug toxicity test can be determined under microgravity conditions. [3 marks]

   (b) Using Hansen Solubility parameter (HSP) sphere theory, show that dichloromethane (DCM) is a good solvent for poly(lactic-co-glycolic acid) (PLGA). For PLGA with the ratio of lactic acid (LA) to glycolic acid (GA) units of 65:35, the solubility parameters are: d_d = 16.69 $Pa^{1/2}$, d_p = 8.17 $Pa^{1/2}$, d_h = 10.49 $Pa^{1/2}$, and the interaction radius is: R_0 = 5.5 $Pa^{1/2}$. The solubility parameters for DCM are: d_d = 17 $Pa^{1/2}$, d_p = 7.3 $Pa^{1/2}$, and d_h = 7.1 $Pa^{1/2}$. All symbols have their usual meanings. [3 marks]

   (c) Describe the British Pharmacopeia test for the disintegration of standard, coated and soluble tablets. You should include a schematic diagram in your answer. [3 marks]

   (d) Research has shown that *Pseudomonas aeruginosa* and *Staphylococcus aureus* are two of the most common bacterial species found in infected wounds. The R&D team you work for has developed a bacteriophage mix targeting the most common strains of these bacteria and is now exploring the most effective ways to deliver this bacteriophage mix to patients. Which method would you propose to your team and what would be your justification? State any assumptions you are making and identify any additional information you might need to support your proposal. [11 marks]

Note: Bacteriophages are virus particles that infect and replicate only in bacterial cells. They can be diverse in size and morphology, but they consist of a core of genetic material surrounded by a protein capsid.

Part B: All questions are compulsory

2. (a) You have been asked by a pharmaceutical company to repurpose a transdermal drug delivery system (transdermal patch) into a polymeric microneedle-based transdermal drug delivery system. The initial plan is to carry out a mathematical modelling study to identify the best possible scenarios so that any effects of human growth hormone (a high molecular weight drug) delivery can be identified. Discuss the features of the modelling framework you will develop to achieve this purpose. [5 marks]

   (b) Explain the principles that can be adopted for gene therapy. For a gas-powered ballistic system for gene therapy, what key mechanisms can you exploit to achieve gene therapy? [2 + 3 marks]

3. Small unilamellar POPC (1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine) vesicles with an outer diameter of 20 nm are used for encapsulation of a hydrophilic drug. Calculate:

   (a) The number of POPC molecules on the inner and outer bilayer leaflet per vesicle and the total number of POPC molecules per vesicle. [1+1+1 marks]

   (b) The internal volume of POPC vesicles in μL/μmole of lipid. [4 marks]

   (c) The maximum content of drug (in mg) that can be entrapped in the liposomal formulation if the drug concentration in aqueous compartments within the vesicles is 20 mg/mL and the content of POPC in the formulation is 100 mg. [3 marks]

Data

The head group area of POPC molecule = 0.72 nm^2

The bilayer thickness of POPC molecule = 3.7 nm

The Avogadro number = 6.022×10^{17} μmol^{-1}

The molar mass of POPC = 760 g/mol

4. (a) Some granules were manufactured using the wet granulation process and made into tablets. It was found that the tablets formed were soft and friable and showed capping and lamination. The tablet punches were inspected and found to be in good order. Discuss two likeliest causes of the problems and how they could be remedied. [4 marks]

(b) A formulation of a known particle size distribution is mixed for 10 minutes and dried at 80°C for 5 minutes before being made into tablets of dosage 200 mg. Identify the Quality Target Product Profile (QTPP), Critical Quality Attributes (CQA) and Critical Process Parameters (CPP) within this manufacturing sequence. [6 marks]

END OF PAPER

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