Loughborough University

24CGP077
Drug Delivery and Targeting

Semester 1 2024/25 | 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).

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

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

Candidates should show full working for calculations and derivations.

A list of equations is included on the final page of the exam paper.

Part A: This question is compulsory

1. (a) Look at the following plot, Fig. Q1.

   (i) Why do you think that to achieve approximately the same plasma concentration, a higher dose (50 mg kg^{-1}) had to be administered orally compared to an intravenous injection (10 mg kg^{-1})? [2 marks]

   (ii) Why does the plasma concentration in both scenarios decrease over time? [2 marks]

   (iii) Draw a rough sketch of what you predict the profile of blood plasma concentration for this drug would be in mice if 10 mg kg^{-1} were administered via intravenous injection every 4 hours over 24 hours. Briefly justify your answer. [4 marks]

   (iv) The drug being tested in Fig. Q1 was designed for the treatment of idiopathic pulmonary fibrosis, a condition in which the lungs become scarred and breathing, therefore, becomes increasingly difficult. Asthma is also a condition, which makes breathing more difficult, and it is caused by inflammation and a tightening of the muscles in the airways. Why do you think that we administer salbutamol, a drug which relaxes the muscles in the airways during an asthma attack via an inhaler, but the researchers did not consider an inhaled method of drug delivery in the pulmonary fibrosis condition? [3 marks]

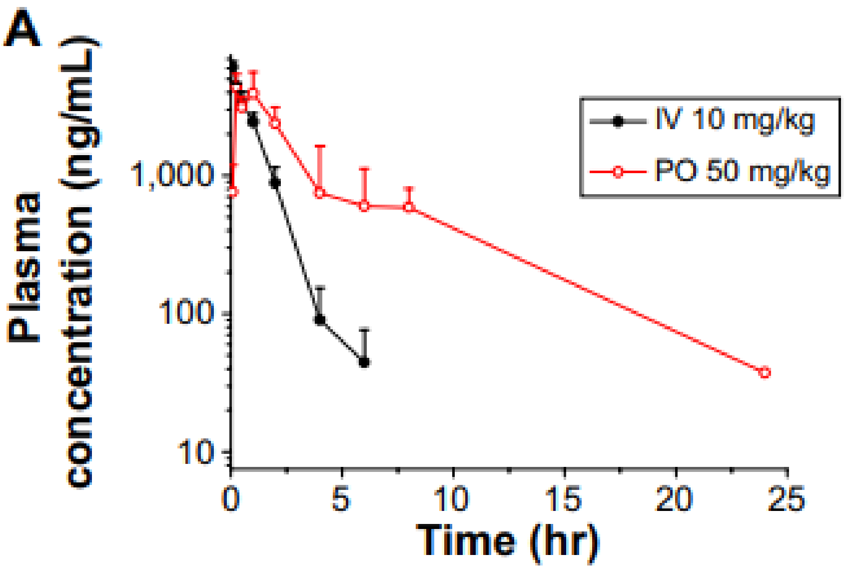

Fig. Q1: Mean plasma concentration versus time profile after intravenous injection (IV) or oral administration (PO) in mice of a drug in pre-clinical testing. Taken from Fig. 2 in DOI:10.2147/DDDT.S83055.

Continued/…

Q1 Continued/…

(b) Briefly explain three ways computational simulations can help optimise a gene gun to effectively deliver genetic material into target cells without causing excessive cell damage or triggering adverse immune responses. [3 marks]

(c) 2 g of PLGA microcapsules containing 44 wt% drug is incubated in a release medium. 60 wt% of the initial drug loading is released over 2 days following the zero-order release kinetics. Calculate the zero-order rate constant, K_0 (g day^{-1}). [3 marks]

(d) State the fundamental differences between hard gelatine capsules (HGC) and soft gelatine capsules (SGC). [3 marks]

Part B: All questions are compulsory

2. (a) With the help of a suitable diagram, explain how the rate of dissolution in a microneedle is controlled to ensure effective delivery of an active substance without compromising skin integrity or causing premature or delayed degradation of the microneedle.

[5 marks]

(b) With the help of a diagram, discuss how NASA's bioreactor can provide predictable and accurate drug toxicity test results compared to conventional 2D culture models.

[5 marks]

3. 100 mg of PLGA microcapsules with 30 wt% drug loading are incubated in a release medium. 60 wt% of the initial drug loading is released over 2 days in accordance with the first-order release kinetics and, an additional 30 wt % of the initial drug loading is released by following zero-order release kinetics over the next 3 days.

Determine:

(a) The amount of drug (in mg) released from microcapsules each day over 5 days.

[2 marks]

(b) The amount of drug (in mg) remaining in microcapsules after each day over 5 days.

[2 marks]

(c) The cumulative amount of drug (in mg) released after each day over 5 days. [2 marks]

(d) The time needed for 100% drug release if the initial release rate could be sustained until the end of the release process. [2 marks]

Continued/…

Q3 Continued/…

(e) Sketch a plot representing the amount of drug remaining in microcapsules and the cumulative amount of drug released from microcapsules as a function of time.

[2 marks]

Input the results for parts (a), (b) and (c) using Table Q3:

Table Q3. Kinetics of drug release from PLGA microparticles over 5 days. Please add here the results obtained for parts (a), (b) and (c).

Time, t (day)	Mass of drug released on each day (mg)	Mass of drug remaining after each day (mg)	Cumulative mass of drug released (mg)
0			
1			
2			
3			
4			
5			

4. Describe the difference between the behaviour of a typical tablet and a hard gelatine capsule in the gastrointestinal tract, including delivery of the active pharmaceutical ingredient (API) delivery. [10 marks]

END OF PAPER

Dr DB Das, Professor K Coopman, Dr G Vladisavljevic, Dr M Leaper

List of equations

Maxwell's equations, $\nabla \cdot \mathbf{E} = \frac{\rho}{\varepsilon_0}$, $\nabla \cdot \mathbf{B} = 0$, $\nabla \times \mathbf{E} = -\frac{\partial \mathbf{B}}{\partial t}$, $\nabla \times \mathbf{B} = \mu_0 \left(\mathbf{J} + \varepsilon_0 \frac{\partial \mathbf{E}}{\partial t} \right)$

Second Law of Thermodynamics, $dS \geq 0$

Mass-energy equivalence, $E = mc^2$

Schrodinger's equation, $i\hbar \frac{d}{dt} |\Psi(t)\rangle = \hat{H} |\Psi(t)\rangle$

Entropy in information theory, $\mathrm{H}(X) = -\sum_{x \in \chi} p(x) \log p(x)$

Logistic map, $x_{n+1} = r x_n (1 - x_n)$

Zero-order drug release kinetics, $Release\ rate = -\frac{dC_t}{dt} = const$

First-order drug release kinetics, $Release\ rate = -\frac{dC_t}{dt} = K_1 C_t$

Mass concentration of encapsulated drug in a particle at time t: $C_t = m_t / V_p$