Loughborough University

23MPC231

Biomaterials 2 (Biomaterials for Drug Delivery)

Semester 2 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).

Answer **THREE** questions.

1. (a) Describe what is meant by extended-release dosage of a drug and outline some advantages of extended-release dosages over conventional ones. [5 marks]

   (b) Sketch a graph of the typical concentration of a drug in the body plasma resulting from a single oral administration of the drug, against the time after administration. On your graph, mark the onset time, minimum effective concentration, minimum toxic concentration, therapeutic range, and duration of action. [7 marks]

   (c) Consider a pill taken orally containing a drug which exerts its action in the colon. Outline the chemical barriers which the drug and its delivery system will have to overcome to be effective. [8 marks]

2. (a) Briefly explain the difference between zero-order and first-order kinetics of drug release. [2 marks]

   (b) Define a reservoir system and explain how reservoir systems can act as sources for both zero-order and first-order kinetics of drug release. [8 marks]

   (c) Consider spherical particles acting as a reservoir device loaded with a particular drug. The particles are coated with a copolymer of uniform thickness. The mass M_t of drug released by time t is given by

$$\frac{M_t}{M_\infty} = 1 - \exp\left(-\frac{3R_o DK}{R_i^2 R_o - R_i^3} t\right)$$

   where M_∞ is the mass of the drug released after infinite time, R_o is the radius of the particle and coating, D is the diffusion constant of the drug in the coating, K is the partition coefficient and R_i is the radius of the uncoated particle.

   (i) Without doing any calculation, state whether the kinetics in this system are zero-order or first-order, and explain why. [2 marks]

   (ii) The radius of the uncoated particle is $0.5\ mm$, and the diffusion coefficient of the drug in the coating is $3.0 \times 10^{-8}\ cm^2/s$. Assuming that the partition coefficient is 1, calculate the thickness of the coating needed to ensure 75% release of the drug in 3 hours. [8 marks]

3. (a) You work for a company that specialises in drug delivery, and you have been asked to investigate the use of a novel acrylic polymer for the delivery of a drug. The polymer is an amphiphilic diblock copolymer that can assemble in aqueous conditions to form higher order structures.

(i) Describe the self-assembly process, explaining the main thermodynamic driving forces governing this. [4 marks]

(ii) Discuss what effect changing the block length ratio of an amphiphilic block copolymer will have on the morphology of the particles formed by self-assembly. Use labelled sketches if required. [3 marks]

(iii) You have been approached by a customer who would like know which self-assembly method will be most appropriate to prepare suitable polymer particles for the delivery of the drug. List 3 questions that you would need to ask to help you to select the correct process, explaining how the answers would help your selection.

[6 marks]

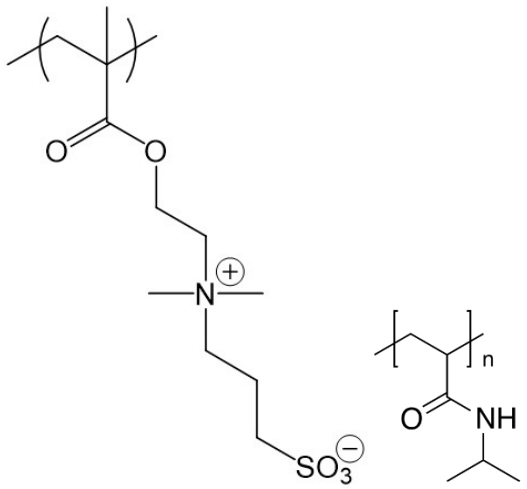
(b) The biophysicochemical characteristics of particles can affect their applications, with polymer nanoparticles between 10-100nm typically used in vivo.

(i) Discuss how particle size can affect excretion from the body. [2 marks]

(ii) PEGylation is a method commonly used in the preparation of nanoparticles to introduce stealth behaviour. It involves attaching polyethylene glycol to the surface of the particles. State the main advantages that this can provide in a drug delivery system, when compared to a charged polymer particle. [2 marks]

(iii) Describe (using sketches) how nanoparticles can be internalised into cells by pinocytosis. [3 marks]

4. (a) Stimuli-responsive polymers have the potential to be used in smart drug delivery systems.



Left – Polybetaine, Right – Poly *N*-Isopropylacrylamide

Explain which of the polymers shown above display the following phenomena in aqueous solution, describing them in terms of interactions between the chains and stating the main thermodynamic driving forces that govern these.

(i) UCST [3 marks]

(ii) LCST [3 marks]

(b) Biodegradable polymers such as PCL and PLA are typically made using ring-opening polymerisation (ROP).

(i) Draw the molecular mechanism for the anionic ring opening polymerisation (ROP) of the monomer valerolactone, shown below, using the anionic initiator $RO^{\ominus}$. Include the final polymer structure. [3 marks]

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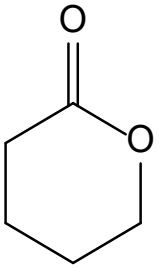

Molecular structure of valerolactone monomer.

(ii) Explain how the molecular structure of PVL means it is more easily degraded than an acrylic polymer? [1 mark]

(iii) Discuss the advantages and disadvantages of ROP compared to radical polymerisation. [4 marks]

(c) It has been noted that the number of journal publications on formulations for drug delivery continues to rise, but this has not been accompanied by a similar increase in therapeutic advances. Discuss 3 possible reasons for this and for each suggest how the situation can be improved. [6 marks]

END OF PAPER

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