National Exams December 2017

04-Bio-A1, Biomaterials and Biocompatability

3 hours duration

NOTES:

1. If doubt exists as to the interpretation of any question, the candidate is urged to submit with the answer paper, a clear statement of any assumptions made.

2. This is an OPEN BOOK EXAM.
   Any non-communicating calculator is permitted.

3. FIVE (5) questions constitute a complete exam paper.
   The first five questions as they appear in the answer book will be marked.

4. Each question is of equal value.

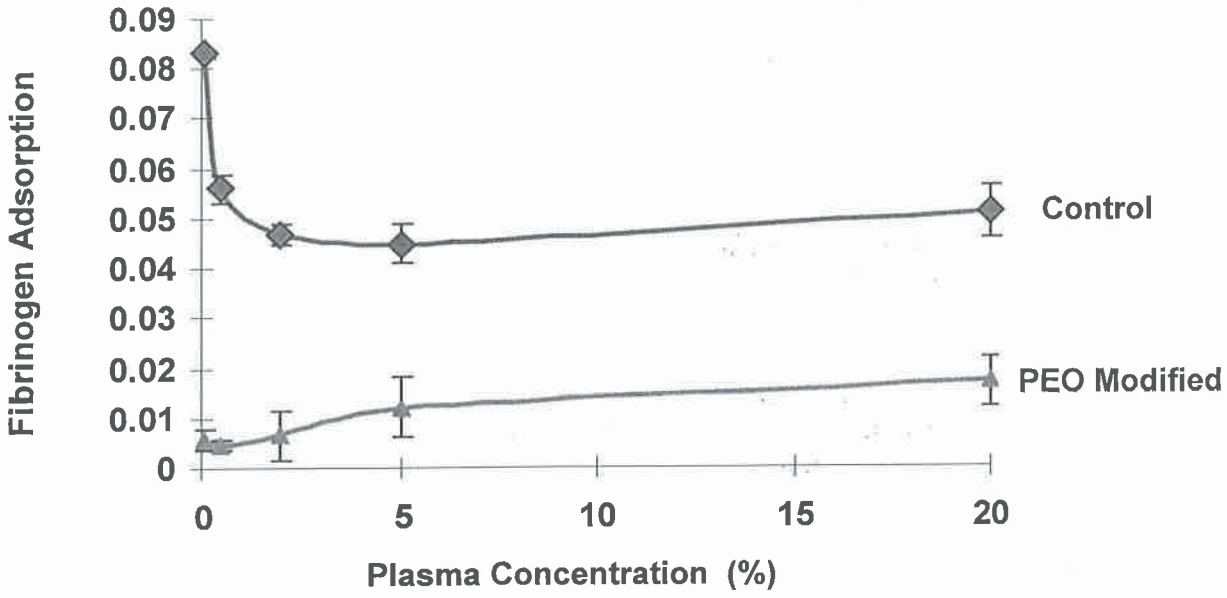
5. Most questions require an answer in essay format. Clarity and organization of the answer are important.

Question 1:

a) Large diameter (>6 mm) vascular grafts made from Dacron or poly (tetrafluoroethylene) (PTFE) have enjoyed significant success for the replacement of diseased or damaged vessels. However, in cases where the vessel to be replaced has a diameter 5 mm or less, the only option for replacement is a patient's native veins. Explain in detail why this is the case, what the challenges are in terms of developing a successful small diameter vascular prosthesis and why you think this goal has yet to be achieved.

b) The following results were obtained for the adsorption of fibrinogen from plasma to two different surfaces, a control and a surface modified with polyethylene oxide. Explain the curves and their significance in terms of developing materials with improved blood compatibility.

c) It has recently been reported that phospholipids, molecules that mimic the membranes of cells, including red blood cells, can be put onto surfaces with high density and that these surfaces show low levels of protein adsorption. Explain why these surfaces may ultimately show promise in developing more blood compatible biomaterials.

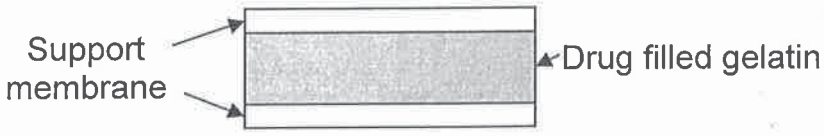


Question 2:

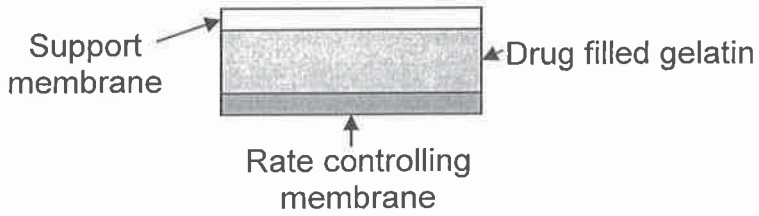
a) Your company holds a patent on a novel and very useful drug. The drug, with a molecular weight of 355, has been dubbed "healitall" and is useful for the treatment of glaucoma, gastrointestinal disorders and surprisingly has been shown to be a useful medication for reducing blood pressure. All of these indications are covered by existing patents. However, these patents will expire within the next one to three years and your company has exhausted all avenues attempting to find other disorders that can be treated by this drug. It has therefore been suggested that you look at the development of a delivery system for healitall in order that the company can continue to dominate these fields and make loads of money (i.e. your job potentially depends on the success of the delivery system). Someone else has been assigned the

gastronintestinal and eye problems – it is the job of your group to come up with an appropriate delivery systems for treating high blood pressure. You have shown that the skin is actually quite permeable to this drug and that therefore a transdermal system, similar to the nicotine patches, is likely the best method of delivery in the case of the blood pressure treatment. Two models are proposed by two different members of your team. Given that you require a system that can be applied daily (i.e. every 24 hours), but accounting for patient compliance, should be able to provide a release rate at 28 hours of at least 200 μg/day, and that the device should be a disk with a diameter of approximately 3 cm which of the methods do you select? You can assume that the patches will be applied to a skin region where there is very high vascularization meaning that the concentration of the drug is virtually zero in the skin and tissue beneath the patch. Explicitly state any other assumptions that you make.

Method 1: It is proposed that the drug be dissolved in a thin (0.1-1 cm thick) gelatin film. The film containing the drug is then sandwiched between two thin polymeric membranes – the outer membrane is virtually impermeable to healitall, while the inner membrane offers negligible resistance to the passage of the drug. The diffusivity of the drug in the gelatin is 3 x 10^{-7} cm^2/s and its solubility is 1.2 mg/mL. You can vary the thickness of the gelatin film



Method 2: The drug is dispersed in a gelatin matrix for support at a concentration of 1000 mg/mL. This drug containing gelatin is then placed between two membranes. As above, the outer membrane is virtually impermeable to healitall. The inner membrane, which has a thickness of 0.2 mm is designed to act as a rate controlling membrane. The diffusion coefficient of the drug in this membrane has been determined to be $2x10^{-8}$ cm^2/s and the solubility of the drug in this membrane is 0.4 mg/mL.



b) Suggest an alternative method that could be used and justify your answer.

Question 3:
Cell interactions with a surfaces can be experimentally manipulated through either chemical or topographical signals.

a) Describe two different methods that have been used to control cell interactions with surfaces.
b) Despite many years of research, in vivo results never match performance in vivo. Discuss why this is the case and describe how the methods for testing performance may be altered to improve predictability.

Question 4:
The order of events following implantation of a material has been suggested to be:

1. Injury
2. Blood material interactions
3. Provisional matrix formation
4. Acute inflammation
5. Chronic inflammation
6. Granulation tissue formation
7. Foreign body reaction
8. Fibrosis / Capsule formation.

In this context discuss the following figure, providing specific examples of each interaction.

Question 5:
Various indications require the replacement or regeneration of bone.

a) Discuss the materials that have been used in the field of bone repair and regeneration.
b) Based on the structure of native bone, discuss what methods have the most promise in the development of new bone.
c) What are the limitations of current osteoinductive materials.

Question 6:
Artificial heart valves can either be made with synthetic materials or natural materials.

a) Discuss the pros and cons of each of the materials.
b) Two patients, a 50 year old male and an 80 year old female are scheduled for valve replacement surgery. Which type of valve would you recommend for each of these patients?