UNIVERSITY OF TORONTO

FACULTY OF APPLIED SCIENCE AND ENGINEERING

FINAL EXAMINATIONS, APRIL, 1999

Fourth Year - Program 5bme

MMS452S - BIOMATERIALS & BIOCOMPATIBILITY

Examiners - R.M. Pilliar, J.P. Santerre, J.E. Davies, C. Holy

Answer all 12 questions. All questions are of equal value (10 marks each). Where appropriate, you may use point-form answers.

Question 1

Acute inflammation is a natural defense mechanism in the body.

a. (6 marks) Give three examples of how this mechanism works to defend the body against the effects of injury.

b. (4 marks) Give two examples of how the acute inflammatory response can alter the surface of an implanted biomaterial.

Question 2

The developers of a new suture (product used to sew cardiovascular products to native cardiovascular tissues) have selected a polyamide to produce the product?

a. (2 marks) Knowing the application, give at least two reasons to support the rationale for the selection of this polymer.

b. (4 marks) The developers have recently acquired some technology that would permit the coupling of thrombomodulin directly to the surface of the polyamide through a condensation reaction with the amide groups on the surface of the material. Provide a rationale for the attachment of this specific molecule.

c. (4 marks) In preliminary quality control testing of the final packaged product, it was found that the thrombomodulin coating was denatured and no longer active, yet post-modification analysis showed that the coupling of the molecule to the polyamide was successful and the activity was very high. As a consultant for the company you have been asked to assess and identify possible processing step(s) that may have contributed to the loss of the product's activity. Provide one possible explanation for the loss of function associated with processing, along with a brief rationale for your selection.

Question 3

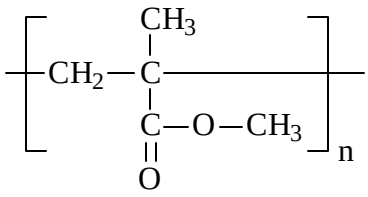
Functional adaptation of tissues next to implants is observed in some cases with orthopaedic, cardiovascular, and dental implants.

a. (1 mark) What is meant by 'functional adaptation'?

b. (9 marks) For each of these three application areas, provide one example each of 'functional adaptation'. Explain whether or not it is beneficial or harmful for the intended application. If it is beneficial, explain why. If it is harmful, explain why and suggest an approach for moderating the effect.

Question 4

Polymethyl methacrylate (chemical structure is shown below) is a polymer that is used in the biomedical field because of its light transparency properties and relatively good weathering properties.



a. (2 marks) Is this a crystalline or amorphous polymer? Briefly explain.

b. (3marks) This polymer is hydrophobic and tends to readily adhere proteins which can lead to fouling. Provide a strategy that may be used to resolve this problem.

c. (3 marks) Comment on how you anticipate the changes introduced in question 4 b) will alter the physical characteristics of the material.

d. (2marks) The hydrophilicity of this material can be increased by hydrolyzing the carbonyl group to release methanol and form a carboxylic acid on the side chain or by reacting the latter carboxylic acid with 1,2 ethylene diol ($HOCH_2CH_2OH$). Which of these two approaches would potentially lead to a more platelet reactive surface.

Question 5

A 45-year old male suffering from osteoarthritis is presented with two options for total hip replacement namely the implantation of a metal-on-metal bearing prosthesis consisting of 1) a cementable femoral component (forged, high-C, CoCrMo) and a cementless porous-coated cast CoCrMo acetabular component, or 2) an implant in which both the forged femoral component (same type) and a non-porous-coated acetabular component are cemented.

a. (3 marks) For this relatively young and active patient which option would you recommend and why?

b. (4 marks) What is the rationale for the selection of a metal-on-metal bearing system rather than the more conventional metal-on-polymer bearing implant and what special recommendation would you advise for the fabrication of the implants to ensure acceptable performance?

c. (3 marks) List 3 necessary requirements (design- and/or treatment-related) for successful bone ingrowth with the porous-coated component.

Question 6

Polyurethanes are extensively used in the biomedical field for various applications from cosmetic surgery to wound healing dressings and cardiovascular applications. However, the potential ability of these materials to undergo degradation has raised many questions in regards to their long term applications.

a. (2 marks) Why does this family of materials possess such versatile function?

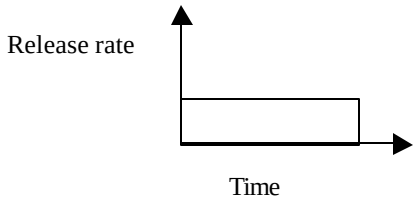
b. (3 marks) Briefly describe three mechanisms of degradation that could alter the physical character of polyether-urethanes.

c. (2 marks) If a polymer undergoes degradation mediated by macrophages, what changes might you anticipate in the polydispersity values of the material. Briefly explain your answer.

d. (3 marks) A new type of vascular implant graft, made of polyurethanes, has recently been introduced with metallic stents (i.e. metallic reinforcing cages) within the polymeric graft. What two principle concerns might you have regarding the longterm stability of these products?

Question 7

You are working on a project to develop a controlled drug release device. You wish your device to release drug at an ideal zero-order release rate (shown below).

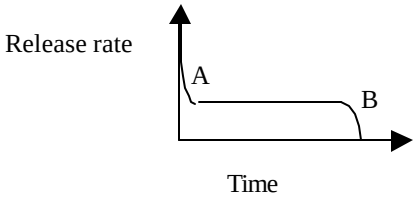


Explain briefly;

a. (2 marks) the type of device (a reservoir or monolithic structure) that you would recommend for achieving the zero-order release rate,

b. (6 marks) how it could be prepared.

After preparing your drug delivery device, you decide to measure its drug release rate. Your experimental data indicates that the release rate is somewhat different from the ideal zero-order rate shown above and looks like the following.



c. (2 marks) Provide an explanation for the occurrence of the non-linear regions A and B?

Question 8

a. (2 marks) Draw a schematic diagram of a graft polymer chain.

b. (2 marks). Draw a schematic diagram of a polymeric material composed of graft polymeric chains.

c. (2 marks). Assuming that the polymeric chains in b) are composed solely of carbon and hydrogen atoms (i.e. polyolefin chains), what specific type of intermolecular interactions do you expect to dominate in this system?

d. (2 marks) How would you chemically alter the terminal ends of the grafts in order to generate a hydrogel? Briefly explain the rationale for your choice.

e. (2 marks) What chemical group would you incorporate into the backbone of the polymer chain described in b) in order to endow the material with flexibility?

Question 9

a. (4 marks) Define 'bioactivity index' (I_B) and describe a method for its determination for candidate bone-interfacing biomaterials.

b. (4 marks) Particulate materials are to be used for mandibular ridge augmentation as a prerequisite to endosseous dental implant placement. Two silicate-based granular materials are available. Both are very similar in terms of particle size and shape. Material 'A' is characterized by a bioactivity index, $I_B = 10 days^{-1}$ while for material 'B', $I_B = 3 days^{-1}$. Which material would you predict has the higher ratio of network formers to modifiers? Which material would you recommend for the treatment and why?

c. (2 marks) Subsequent to this treatment, when would you consider it suitable to proceed with the implant installation (i.e. first-stage surgery assuming a 2-stage implantation procedure)? (State the criterion upon which you base this recommendation).

Question 10

In a recent publication, which was discussed in the course, bamboo was reported as a potential biomaterial for bone repair. Explain;

a. (4 marks) the rationale for using bamboo as a bone repair biomaterial,

b. (6 marks) the initial tests performed to determine bamboo's suitability as a biomaterial; two different kinds of tests were performed one dealing strictly with the material's properties and the other dealing with the material's biological compatibility. Explain both test procedures in your answer.

Question 11

a. (4 marks) Describe the process of bone fracture healing indicating how the use of internal fracture fixation using stainless steel plates and screws may affect this process.

b. (2 marks) Assuming that a metallic plate and metallic screws are to be used, is stainless steel your metal of choice or would you recommend another alloy? Justify your answer.

c. (3 marks) Describe the properties of an ideal biodegradable fracture fixation implant system that would overcome any major concerns that may arise with the use of metallic implants.

d. (1 mark) What material(s) would you suggest for fabricating this biodegradable implant?

Question 12

Fractal 3-D structures have been used in the past for tissue engineering applications. Explain briefly;

a. (2 marks) what a fractal structure is,

b. (3 marks) the processing strategy used to create it,

c. (2 marks) the rationale for using such a structure,

d. (3 marks) the main disadvantage of fractal structures.