Birla Institute of Technology and Science, Pilani
First Semester 2022-23
Pharmaceutical Applications of Polymers and Biopolymers (PHA G623)
Mid-Sem Examination

Max. Marks: 40 **Open Book** **Duration: 90 Minutes**

Q1. Materials used *in-vivo* can be placed into one of three classes, based on the ultimate fate of the material. What are these 3 classes, and what is the characteristic fate in vivo of materials of each type? **[4]**

Q2. Draw the chemical structure and name 3 examples of bonds typically sensitive to hydrolysis under physiologic conditions; show the chemical structure of the immediately resulting products that are created by hydrolysis of each. **[4]**

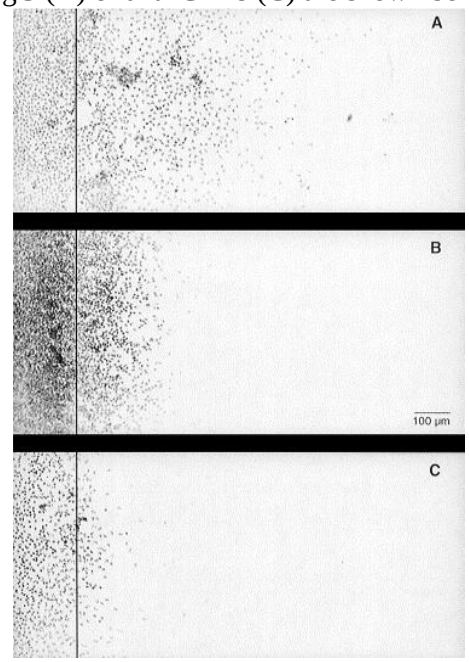
Q3. Why are physical hydrogels most commonly formed by block copolymers (copolymers where two chemically different repeat units occur in strings, e.g., AAAABBBBAAAABBBB), rather than random copolymers (random monomer sequences, e.g., ABAABBABBBAAAB)? **[4]**

Q4. Your research group decides to test encapsulation of a therapeutic protein in poly(lactide-co-glycolide) (PLGA) matrices formed as implantable scaffold. Explain what your biggest concern would be with the use of PLGA encapsulation for delivery of the polypeptide and why. **[4]**

Q5. Expanded polytetrafluoroethylene (ePTFE) is a commonly used material for synthetic vascular grafts. One mode of failure of such devices is via bacterial infection initiated during implantation. Upon the introduction of a foreign material into the body, a competition for the surface ensues between bacteria and leukocytes that serve to fight infection. One hypothesis for elevated infection rates for PTFE graft implantations is that leukocyte migration is impeded on ePTFE surfaces, allowing bacteria to become established in the early stages following implantation.

(a) Describe the process by which leukocytes are attracted and migrate to the site of a vascular graft implantation. **[3]**

(b) To investigate which integrin subunits play a significant role in leukocyte migration on ePTFE, Chang and coworkers performed random migration studies on populations of fluorescently labeled polymorphonuclear leukoocytes (PMN's or neutrophils) exposed to antibodies for different integrin subunits. Confocal microscopy images depicting PMN migration on ePTFE after 3 h of incubation with IgG (A) or anti-CD18 (C) are shown below.



Confocal micrograph of population level PMN migration on ePTFE in the presence of uniform concentration of fMLP (10−8 m) and after 3 h incubation with specific antibody: (a) control IgG, (b) anti-CD11abc (cocktail), and (c) anti-CD18. The vertical line to the left indicates the periphery of cell well from which cell migration occurs outwards to the right.

Provide a molecular level explanation for the observed differences in migration between PMN's exposed to anti-CD18 vs. those exposed to IgG. **[3]**

Q6. Consider the following 6 protocols that have been suggested for inducing skin regeneration in your animal model at lowest cost. For each candidate protocol provide a prediction of its efficacy and explain your answer briefly. **[6×3=18]**

a. Keratinocytes (KC) + dermis regeneration template (DRT) [*in-vitro*]. It is proposed that new skin will hypothetically be formed in vitro using these two reactants, followed by grafting on this hypothetical skin onto the model wound. DRT is formed by coprecipitating collagen and a glycosaminoglycan in acetic acid solution, followed by freeze drying to form a scaffold with average pore size of 100 μm and is crosslinked to give a degradation half-life *in-vivo* of about 14 days.

b. KC in cell culture medium will be pipetted onto the wound [*in-vivo*].

c. KC + FB will be pipetted into the wound, each cell type to be pipetted in its own cell culture medium [in vivo].

d. TGFb1 solution will be pipetted on to the skin wound, followed by grafting the wound with KC + DRT [in vivo].

e. KC + dermis regeneration template (DRT) [*in-vivo*]. KC will be seeded into DRT before grafting onto the model skin wound.

f. Fibroblasts (FB) + KC + DRT [*in-vivo*]. FB and KC will both be seeded into DRT, before grafting onto the model skin wound.