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

Max. Marks: 60 **Open Book** **Duration: 120 Minutes**

Q1. You have been appointed to lead a research group at Scaffold Biologicals, a prominent manufacturer of biologically active scaffolds based on collagen-GAG copolymers used in regenerative medicine. You now have your first assignment. You have been asked to spend a budget of approximately $500K to equip a new laboratory that will support both research activities and manufacturing. Your first task is to buy some necessary instruments/equipment (I/E) to measure important properties of scaffolds. You also need to justify to management the basis of what logic (or data) you have used in making your selection.

a) Pore size of active scaffolds: Describe very briefly a study that you will set up to optimize the pore size in order to maximize the biological activity of scaffolds, based on the selection of a range of desirable pore sizes. **[5]**

b) Propose a mechanism that explains the existence of an optimal range in pore size. **[5]**

c) The existence of an optimal range in regenerative activity requires that the activity drop both at pore sizes below and those that are above the optimal range. Provide a molecular explanation for the existence of an optimal range in regenerative activity in terms of a specific molecular property of a collagen-GAG scaffold. **[5]**

d) Crosslink density of active scaffold: Propose a mechanism based on the scale of a cell or organ that explains the existence of an optimal range in crosslink density. **[5]**

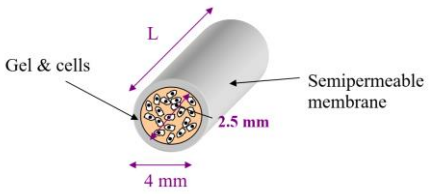
Q2. You are working under a very tight budget due to your company's efforts to survive the recession. You are asked to develop a device for regenerating skin in patients who have scars in their skin of size about 10X10 cm^2. Each scar will be removed surgically, and your new device will be grafted on the freshly generated skin wound.

a) Select an animal species with which you will conduct model studies of your candidate device(s). The animal species you select should have approximately the same scar-forming ability as humans. **[2]**

b) Describe the wound model that you will generate in order to test the ability of your device to replace scars. Explain briefly why you are selecting this wound model. **[3]**

c) Describe your "best" design for making a regenerating skin graft, which is supposed to prevent scarring. **[5]**

Q3. In conventional cell culture studies, Hamster-BHK cells transfected with the gene for CNTF, showed promisingly high secretion rates of 1 ng/10^6cells/day. In prototype devices prepared by your company (**Fig 1**), cells were seeded in a polyethylene oxide (PEO) hydrogel within the membrane and cultured in nutrient-rich media to test for CNTF release. To your dismay, the release rate was found to be much lower than anticipated from studies of the same cells seeded on conventional culture plates. Moreover, survival of the cells was seen to decrease monotonically over several days in culture. Provide two likely explanations for these observations. **[5]**



Q4. Why is hydration important in keeping protein soluble? Why is the structure of water very important in the formation of protein secondary structures and protein-protein interaction? **[5]**

Q5. Discuss in detail the interlink between inflammation and granulation tissue formation, putting emphasis on the role played by macrophages. **[5]**

Q6. Discuss in detail modification strategies in biomaterials to reduce immune recognition and activation. **[5]**

Q7. Discuss about different mechanotransduction pathways and their influence on cellular behavior. **[5]**

Q8. Discuss about the interplay of different TGFβ isoforms and scar tissue formation. How it can be modulated to inhibit scar formation? **[5]**