In deciding between a non-degradable versus a degradable polymer for an implantable drug delivery system, what would you need to know before proceeding with the selection? List the questions you would have, including tests that would need to be carried out.

Before conducting any bench or pre-clinical testing, you should think about issues such as: (1) safety; (2) drug and polymer stability, toxicity, and efficacy; (3) control of delivery rate and duration of delivery; and (4) cost-effectiveness with a system that is as simple and practical as possible. Then list specific questions and issues as an initial guide before conducting any experiments.

ANSWER

1. How has this disease been treated before, if at all? What were the advantages and disadvantages of the current treatment and what disadvantages need to be overcome? Is there an unmet medical or technological component?

2. Does the therapy need to be acute or chronic?

3. Where is the site of the disease?

4. What type of implant is required to be as site-specific as possible?

5. Can this implant be designed so as to overcome all the potential disadvantages listed in Table II.5.16.D.3, while emphasizing the benefits highlighted in Table II.5.16.D.2?

6. What potential polymers could be used for the control of the release of drug and the scaffold if it is needed?

7. Among the potential polymers identified, would any of them elicit an adverse foreign-body reaction or local inflammatory response?

8. Review the stability of the drug and polymer in its anticipated environment. Are the degradation byproducts, if any, known and acceptable? What is the interaction between the drug and the polymer?

Obtain an understanding of the controlled release profile. Can the dose, rate, and delivery to the specific site be adequately controlled and reproduced? The drug release mechanism has to be understood.

If possible, once the drug has been selected, it is best to tune the polymer for the required drug diffusivity. Drug release is best controlled by permeation, where the drug first dissolves into the polymer and then diffuses through the polymer. This is best done by developing a phase diagram and understanding what polymer–drug concentrations are miscible.

Then fine-tune to obtain the desired drug release profile by varying the drug–polymer ratio, the glass transition, and possibly the crystallinity.

If the polymer cannot be tuned to dissolve the drug, the release has to be controlled by a porous mechanism or by the degradation kinetics of the polymer, if it is biodegradable. This mechanism is much more difficult to control, and is best for drugs which have a wide efficacious window. In some cases, the mechanism is even more complex, in that the release mechanism is a combination of more than one system.

After this paper exercise, it is best to start bench testing with a focus on drug release mechanism and stability. This may require several iterations, until the most advantageous stable release profile is obtained. This paper exercise is not comprehensive in that it can be more complex or simpler depending upon the implant type.