Radiation Polymerization

Radiation Bioengineering

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Use made of radiation-induced polymerization, crosslinking and grafting reactions, to produce

- Biocompatible materials
- Immobilized bioactive materials

Biocompatible Materials

- Biological systems (e.g. humans) react adversely to many synthetic polymers
  - Important to modify polymer surfaces to make them biocompatible
- Thromboresistant materials (blood-compatible materials) have been successfully made, e.g., by
  - Radiation-grafting of N,N-dimethylacrylamide onto Aflon (polytetraethylene and ethylene-tetrafluoroethylene copolymers)
  - Radiation-grafting of N-vinyl-2-pyrrolidone onto silicone or polyethylene tubes

Woods and Pikaev (1994)

Biocompatible Products

- Soft contact lenses
  - Crosslinked hydrogels by radiation polymerization of 2-hydroxyethyl methacrylate + ethylene glycol dimethacrylate
  - Grafting of N-vinyl-pyrrolidone onto silicone rubber
- Contact lenses
  - Low temperature (~ -80°C) radiation polymerization of 2-hydroxymethyl methacrylate (radiation casting)
  - Other plastic lenses also made by radiation casting
- Heat-shrinkable connectors for severed blood vessels
  - Radiation crosslinking of trans-1,4-polyisoprene (electron irradiation in air, 100-200 kGy at 300 kGy/h)

Woods and Pikaev (1994)

Immobilized Bioactive Materials

- **Benefits of immobilization**
  - Controlled slow release of biologically active components, e.g., drugs
  - Anchoring the bioactive component for repeated use, e.g., enzymes
  - Shaping the material to a desired form, e.g., artificial organs, blood-compatible surfaces

- **Two widely used methods for immobilization**
  - Chemical bonding of bioactive material and a benign inactive support
  - Trapping bioactive material in a polymer matrix

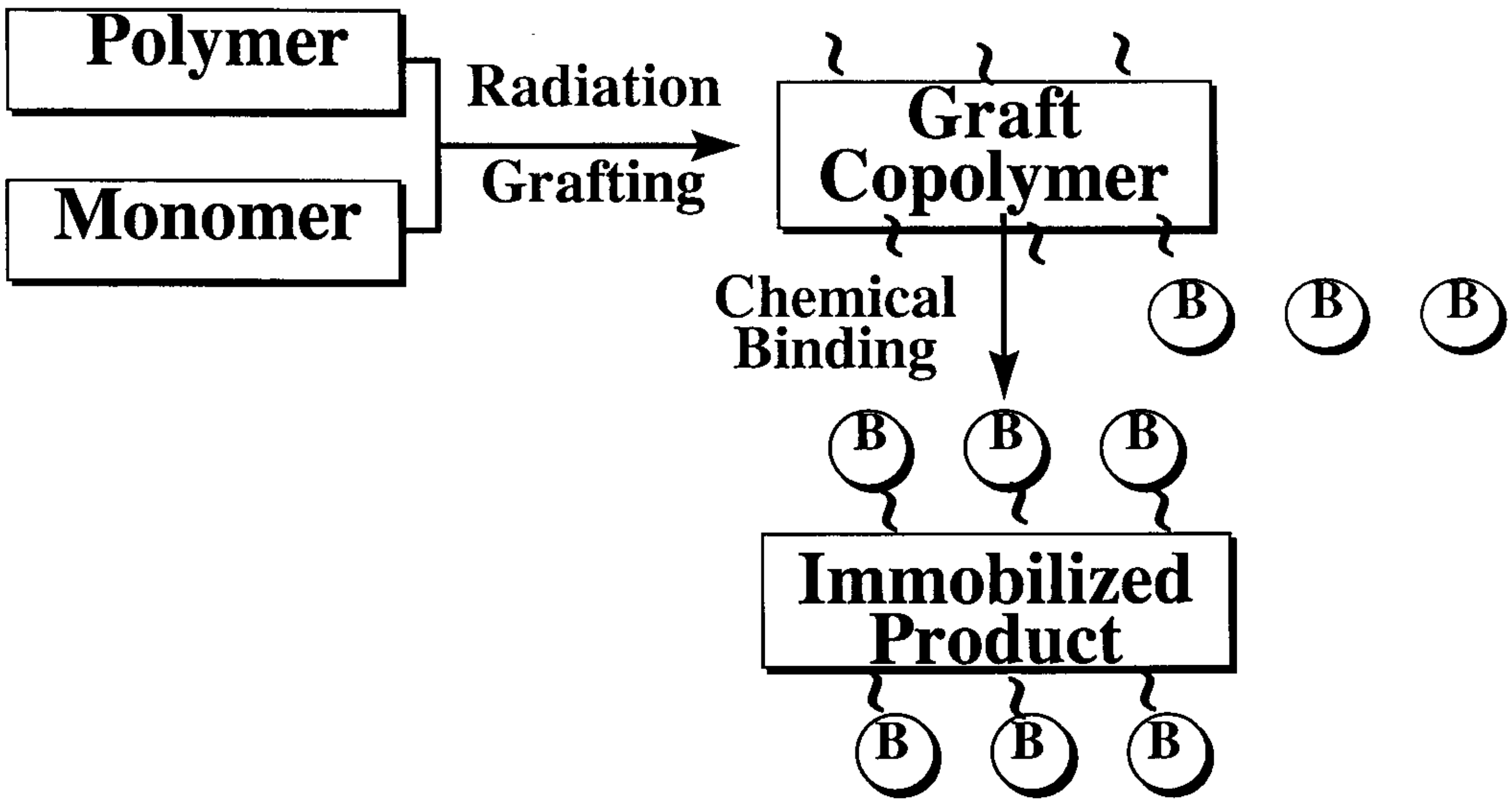
Immobilized Bioactive Materials

- Many applications, the most well known being slow-release drugs

Immobilized Species	Applications
Enzymes	Artifical organs, bioreactors, biosensors, separations, therapeutic agents
Antibodies and antigens	Biosensors, diagnostics, drug-delivery systems, immunoassays, separations
Antithrombogenic agents	Blood-compatible surfaces
Drugs	Drug-delivery systems, drug mechanism studies
Neurotransmitters, hormones	Biosensors
Cells and organella	Artifical organs, bioreactors, biosensors

Woods and Pikaev (1994)

Immobilization of Bioactive Materials



- Immobilization of a bioactive component by chemical bonding to a graft copolymer formed by irradiation

Immobilization of Bioactive Materials

- *Entrapment*

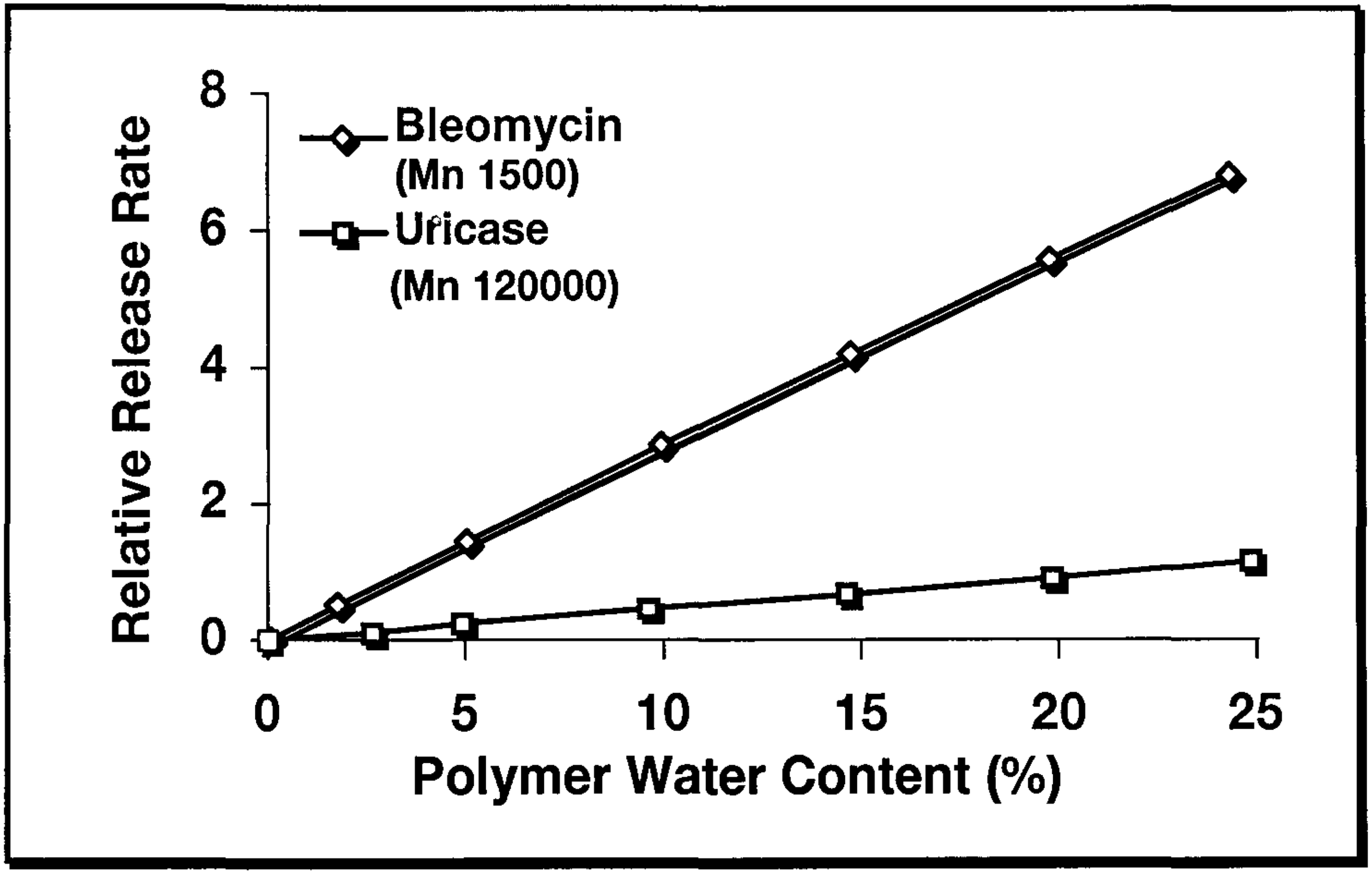
← a →

Water, Monomer Crosslinking agent, Additives Biocomponent ⇒ Irradiation at ambient temperature ⇒ Crosslinked gel with biocomponent entrapped

← b →

Homogeneous aqueous solution of biocomponent and monomer ⇒ Cooling formation of voids, ice and monomer phases ⇒ Irradiation at low temperature ⇒ Polymer matrix, bio-component in pores

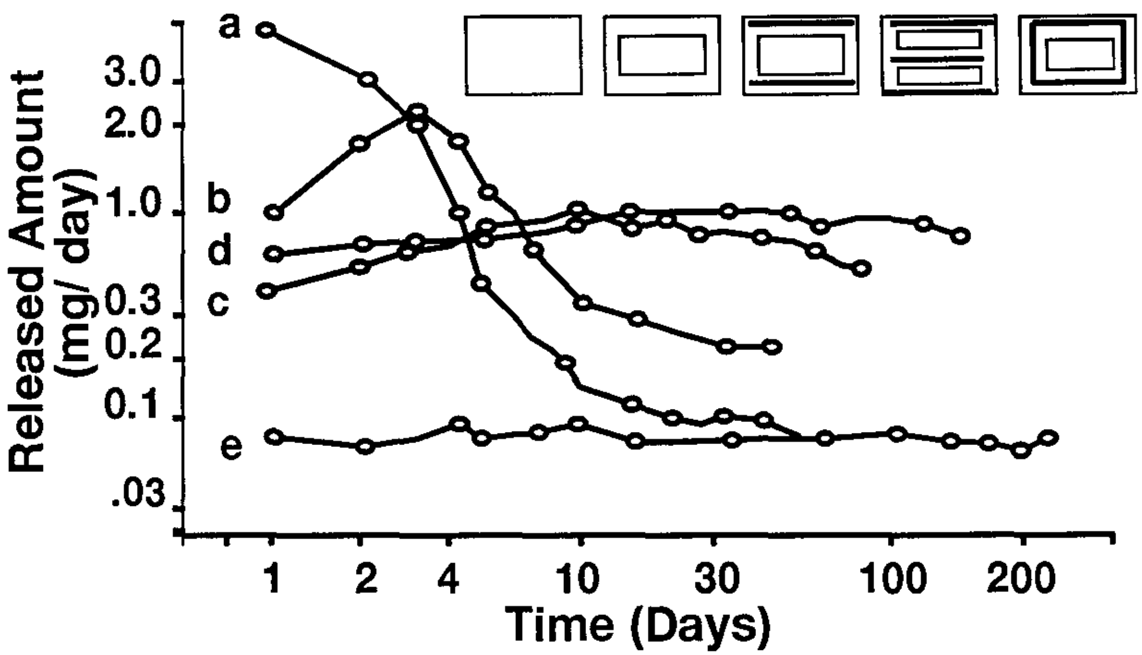
Variation of Drug Release Rate With Hydrophilicity and Molecular Weight



Variation of Drug Release Rate With Hydrophilicity and Molecular Weight
(contd)

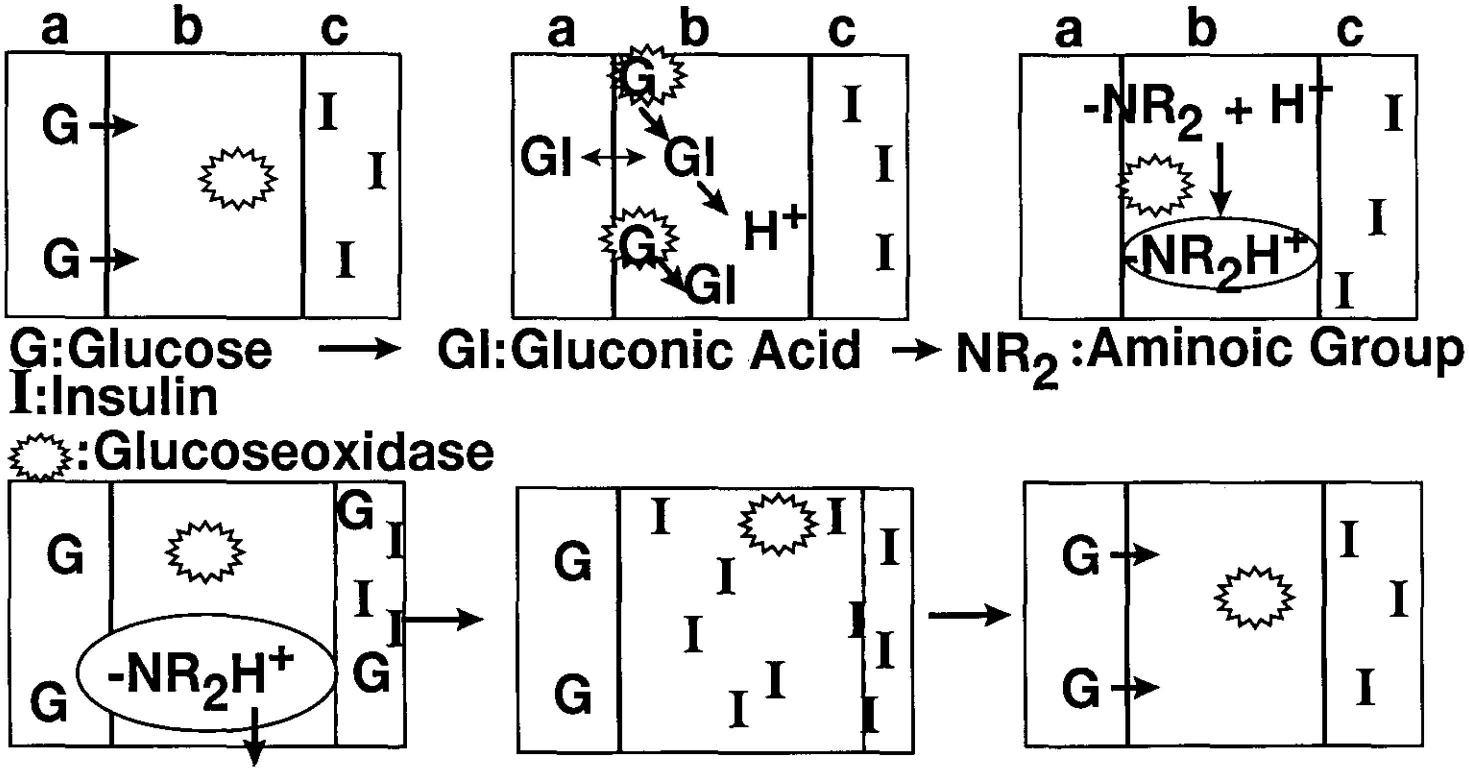
- Gamma-radiation-induced polymerization of monomers containing drugs at -78 °C
- Hydrophilicity changed by choosing polymers of different contents (2-hydroxyethyl methacrylate, ethylene glycol dimethacrylate, hydroxypropyl acrylate, tetraethylene glycol dimethacrylate, diethylene glycol dimethacrylate, and trimethylpropane triacrylate
- Release rates measured at 32°C

Variation of Release Rates of a Hormone at 32°C With Type of Polymer Entrapment (Kaetsu, 1992)



a. Homogeneously distributed; b. Inside one polymer layer
c. Inside a polymer layer and two polymer films
d. Two layers of hormone, several polymer layers
e. Inside one polymer film and one polymer layer

The Insulin Pump



$-NR_2H^+$ groups expand membrane allowing I to migrate from c to a and b

Release of Insulin

pH equilibration restores membrane structure in b, stopping migration of I

Enzyme Immobilization

- L-Aspartamine, an enzyme
  - Used to treat lymphatic leukemia
  - Shows undesirable side effects
  - Immobilized product better
- Steps in immobilization
  - Radiation grafting of methacrylic acid onto polypropylene, PP-COOH
  - Treatment with carbodiimide to give acylisourea derivative
  - Treatment with N-hydroxysuccinimide
  - Reaction with the enzyme

    PP-C(=O)-NH-enzyme

  - Has also been immobilized on cellulose

Woods and Pikaev (1994)

Tissue - Compatible Materials

- Skin covering
  - Radiation crosslinked polyacrylamide and polyvinyl pyrrolidone used as wound dressing
  - Radiation grafted cotton gauge/acrylamide/ provital; used as burn dressing which releases provital slowly
- Ocular disks/contact lenses
  - Radiation polymerized disks from a solution of N-vinylpyrrolidone, 2-hydroxyethyl methacrylate and pilocarpin hydrochloride, used to treat glaucoma

Kaetsu (1992); Woods and Pikaev (1994)

Conclusions

- The use of radiation processing in the bioengineering field would continue to increase
- An important advantage of radiation processing in immobilization of bioactive materials is that the substrates are not exposed to high temperatures; most bioactive materials are heat-sensitive