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Controlled Drug Delivery Systems

Towards New Frontiers in Patient Care

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Preface

Over the past 25 years many interesting biomedical uses have been proposed for polymers especially in diagnostics and drug delivery. However, medical research is often regulated by "trial-and-error" approaches, and complete theory and understanding sometimes lack. Chemical engineering, thanks to their knowledge in thermodynamics, physical chemistry, polymer chemistry, and transport phenomena, can help medicine designing smart controlled drug delivery devices. Since its very beginning (first decade of the twentieth century), chemical engineering has undergone several and fundamental transformations. Indeed, the affirmation of the concept of *unit operation* (distillation, absorption, stripping, extraction, and crystallization) marked the definitive detachment of chemical engineering from the original chemistry frame. The main idea of that time was that each unit operation was governed by its own distinct principles: this view was overcome in 1960 when some outstanding scientists (in particular Neal R. Amundson, Rutherford Aris, R. Byron Bird, Edwin N. Lightfoot, and Warren E. Stewart) proposed to combine all these single units into one single discipline that takes into account mass, energy, and momentum balance. A clear evidence of the extension of the cultural horizons of chemical engineering was felt only in the mid 1970s, the seed of biochemical engineering must be searched in the early 1960s when valuable researchers (such as Elmer L. Gaden, Arthur B. Metzner, R. Byron Bird, Edward W. Merrill) understood that the concept of balance (mass, energy, and momentum) could be profitably applied also to knowledge fields, such as medicine, biology, pharmacy, and psychology, which were, traditionally far from chemical engineering. In so doing, these researchers introduced the concept of interdisciplinary that is so important in the modern research and that represents, according to our point of view, the winning strategy also for the future. In this book, our purpose is to provide a complete understanding of these systems to address different medical needs. In addition, new highlights, from the material point of view, are analyzed over the classic well-established delivery systems.

In summary, the main innovative aspect is the definition of chemical engineering principles applied to drug delivery systems, the focus on the main problem with a

brief overview of the most recent approaches and the examination of some applications already on the market. In order to illustrate drug delivery mechanisms, devices, and applications we divided this book into five chapters:

- Chemical engineering and medicine: brief introduction and joint points between these two disciplines that seemed to be very far;
- Principles of controlled drug release: a mass transport matter. Detailed description of transport phenomena applied to drug delivery.
- Overview on polymeric drug delivery systems: updated description of different possibilities to deliver drugs.
- Device design: functional polymer for drug delivery. The possibility to modify and functionalize scaffolds with compounds that are able to improve mechanical properties or cell viability and improve their differentiation in a tailorable manner opens new opportunities for researchers.
- Applications: principles described are applied to a complete and novel design of drug-eluting stent taking into account polymer degradation, drug release, and in-stent restenosis.

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Contents

Acronyms

DES	Drug-eluting stent
HA	Hyaluronic acid
MC	Methylcellulose
NASI	*N*-acryloxysuccinimide
NPs	Nanoparticles
PAA	Polyacrylic acid
PAM	Polyamide
PCL	Poly(ε-caprolactone)
PEG	Poly(ethylene glycol)
PGA	Poly(glycolic acid)
PLA	Poly(lactic acid)
PLGA	Poly(lactide-*co*-glycolide)
PNIPAM	Poly(N-isopropylacrylamide)
RAFT	Reversible addition-fragmentation chain transfer
SCI	Spinal cord injury
SDDS	Smart drug delivery systems
SMC	Smooth muscle cells

Symbols

a_i	Thermodynamic activity of component i
C	Concentration
Cl	Clearance of the system
D	Diffusion coefficient
D_m	Mutual diffusion coefficient
E	Activation energy
F	Faraday constant
f	Free volume
J	Molar flux
k	Permeability

k_B	Boltzmann constant
K	Drug partitioning coefficient
l	Thickness
M_c	Average molecular weight between crosslinks
M_n	Average molecular weight of uncrosslinked polymer
M_t	Solvent absorbed per unit area of polymer
MW	Molecular weight
Q	Volumetric degree of swelling
R	Gas constant
R_{diff}	Solvent diffusion rate
R_h	Hydrodynamic radius
R_{relax}	Polymer relaxation rate
T_g	Glass transition temperature
V_d	Distribution volume

Greek Symbols

ΔG	Gibbs free energy
ε	Porosity
η	Solution viscosity
κ	Screening hydrodynamic interactions between the polymer and the solute in a semi-dilute polymer solution
μ	Dynamic viscosity
μ_i	The chemical potential of component i
ξ	Network mesh size
Π	Osmotic pressure
τ	Tortuosity
φ	Volume fraction of the polymer
ψ	Donnan potential