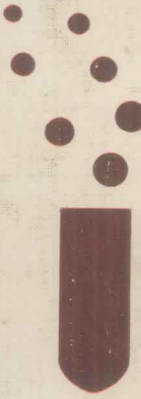
Polymeric Drugs and Drug Delivery Systems



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Polymeric Drugs and Drug Delivery Systems

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M. Joan Comstock, *Series Editor*

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Foreword

THE ACS SYMPOSIUM SERIES was founded in 1974 to provide a medium for publishing symposia quickly in book form. The format of the Series parallels that of the continuing ADVANCES IN CHEMISTRY SERIES except that, in order to save time, the papers are not typeset, but are reproduced as they are submitted by the authors in camera-ready form. Papers are reviewed under the supervision of the editors with the assistance of the Advisory Board and are selected to maintain the integrity of the symposia. Both reviews and reports of research are acceptable, because symposia may embrace both types of presentation. However, verbatim reproductions of previously published papers are not accepted.

Preface

DELIVERY OF DRUGS by means of controlled-release technology began in the 1970s and has continued to expand so rapidly that there are now numerous products both on the market and in development. These controlled-release drug-delivery products have given new life to old pharmaceuticals that either were no longer patented or had properties that prevented them from being used effectively to treat various diseases. In addition to stimulating use of these older drug products, controlled-release technology is now being directed toward the newer biopharmaceuticals produced by genetic research. It is with biopharmaceuticals that controlled-release technology may find its most important applications in medicine.

Polymers have played a major role in the development of controlled-release systems and, as expected, the earlier polymeric drug-delivery systems incorporated polymers that were commercially available and approved by the U.S. Food and Drug Administration. There are many polymers that meet this need, and they have been successfully incorporated into commercial products for oral, injectable, implantable, topical, and transdermal administration. The mechanisms by which drugs are released from these polymers and the processes for fabricating such controlled-drug-delivery devices have been well reviewed in the literature. Extensive research efforts are being made to improve both the polymers and the processes, as well as to apply them to the controlled release of a wide variety of pharmaceutical products. However, with the continued development of controlled-release technology, the need has arisen for materials with more specific drug-delivery properties. These materials include new biodegradable polymers, polymers with both hydrophilic and hydrophobic characteristics, and hydrogels that respond to temperature or pH changes. In addition, methods to overcome some of the barriers associated with current drug-delivery systems are necessary. Finally, polymers that may not only be used to deliver drugs, but that may themselves elicit biological responses are needed.

This book is divided into four sections that cover the main topics in the field of drug delivery. The first section gives an overview of the polymers and materials currently being used in drug delivery and some of the problems with and opportunities for polymeric drug delivery. The overview chapters are followed by a section on polymeric drugs and polymer–drug

conjugates. This section describes novel polymers that function as drugs themselves or that are covalently attached to drugs. This field of research offers tremendous possibilities for new materials that can be made either synthetically or by genetic engineering. The third section of the book deals with new polymers that can be used as matrices for drug delivery. Polymers described in this section are not covalently bound to a drug but rather are physically mixed or blended with the drug. Polymer–drug mixtures are currently the most widely used drug-delivery systems, and the chapters included here describe new materials that may be useful in the future. The final section covers new developments in the area of drug delivery with liposomes. This area has intrigued researchers for years, and with the development of new materials to target the liposomes, this field of research should remain prominent for the next several years.

As editors, we hope that this book will alert researchers to the problems associated with drug delivery and the opportunities for future developments. If the material presented here can stimulate new ideas and concepts for polymeric drugs and polymeric drug-delivery systems, then our efforts will have been worthwhile. We wish to thank the Division of Polymer Science, Inc., for sponsoring the symposium that served as the basis for this book, and Glaxo, Inc., Lilly Research Laboratories, and Atrix Laboratories, Inc., for providing partial funding. We also want to thank each of the authors for their participation and cooperation. Without them, this book would not have been possible. We gratefully acknowledge the staff of Atrix Laboratories and, specifically, Karen Miller and Sisca Wolff, for their assistance in the editing and production aspects of the book. Most of all, we want to thank Carol Dunn for her efforts in assembling and formatting all of the chapters and for her support throughout this endeavor.

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POLYMERIC DRUG DELIVERY

INDEXES

DRUG DELIVERY SYSTEMS

Drug Delivery Systems

The controlled delivery of drugs is a technology that draws on expertise from a number of scientific disciplines including chemistry, bioengineering, pharmacology, biology, polymer science and medicine. As the name implies, the objectives of controlled drug delivery are to disseminate a drug when and where it is needed and at the proper dose. Although mechanical devices such as pumps, syringes, and catheters can be used to deliver drugs, this book will focus on polymeric and liposomal systems for controlled delivery of drugs to the body.

In this respect, a polymer or a polymer covalently attached to a drug can have biological activity. Chapter 1 of this introductory section of the book reviews the different types of polymers that effect a biological response in the body. These include polycations, polyanions, and polynucleotides that function as polymeric drugs. Polymers that are conjugated to drugs and have activity are also described as are polymeric prodrugs and targeted polymeric drugs.

Most of the polymeric delivery systems currently being used commercially consist of an established drug physically combined with a biocompatible polymer. Chapter 2 reviews the different classes of polymers used as matrices for drug delivery and the properties of those polymers which make them suited for a particular method of drug delivery. Water-soluble, biodegradable, and nonbiodegradable polymers are discussed and examples of each which are used for drug delivery are described.

Another important method of drug delivery is by means of liposomes. Chapter 3 in this section of the book discusses the different classes of liposomes, their preparation, characterization,and unique properties for drug delivery. Liposomes that release their drug contents at specific temperatures or can be targeted to specific sites are included in this review.

The last paper in this section, Chapter 4, outlines some of the considerations that need to be made in designing any drug delivery system. These include the route of administration and the interaction of the drug with the biological system. By understanding these aspects of drug delivery, it is hoped that new methods and materials can be developed that will lead to more specific and successful controlled delivery of drugs.