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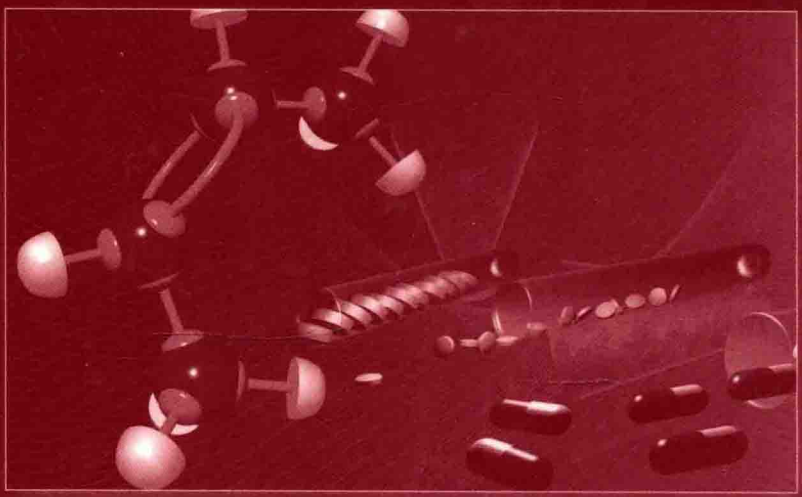
Drug Delivery Nanoparticles Formulation and Characterization



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Drug Delivery Nanoparticles Formulation and Characterization

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To the loving memories of my parents and Dr. Keshav Baliram Hedgewar, who gave a proper direction, my wife Seema, who gave a positive meaning, and my son Sarvadaman, who gave golden lining to my life.

Yashwant Pathak

I dedicate this book to my fellow scientists, my family – wife Anu, daughter Sakshi Zoya, and son Alex Om, and my parents, who taught me love, life, and compassion.

Deepak Thassu

Foreword

Drug delivery research is clearly moving from the micro- to the nanosize scale. Nanotechnology is therefore emerging as a field in medicine that is expected to elicit significant therapeutic benefits. The development of effective nanodelivery systems capable of carrying a drug specifically and safely to a desired site of action is one of the most challenging tasks of pharmaceutical formulation investigators. They are attempting to reformulate and add new indications to the existing blockbuster drugs to maintain positive scientific outcomes and therapeutic breakthroughs. The nanodelivery systems mainly include nanoemulsions, lipid or polymeric nanoparticles, and liposomes. Nanoemulsions are primarily used as vehicles of lipophilic drugs following intravenous administration. On the other hand, the ultimate objective of the other nanodelivery systems is to alter the normal biofate of potent drug molecules in the body following their intravenous administration to markedly improve their efficacy and reduce their potential intrinsic severe adverse effects.

Despite three decades of intensive research on liposomes as drug delivery systems, the number of systems that have undergone clinical trials and then reached the market has been quite modest. Furthermore, the scientific community has been skeptical that such goals could be achieved, because huge investments of funds and promising research studies have frequently ended in disappointing results or have been slow to yield successfully marketed therapeutic dosage forms based on lipid nanotechnology. Thus, the focus of the research activity has shifted to nanoparticulate drug delivery systems, as there are still significant unmet medical needs in target diseases such as cancer, autoimmune disorders, macular degeneration, and Alzheimer's disease. Most of the active ingredients used to treat these severe diseases can be administered only through the systemic route. Indeed, both molecular complexity associated with drugs and inaccessibility of most pharmacological targets are the major constraints and the main reasons behind the renewed curiosity and expanding research on nanodelivery systems, which can carry drugs directly to their site of action. Ongoing efforts are being made to develop polymeric nanocarriers capable of delivering active molecules specifically to the intended target organ. This approach involves modifying the pharmacokinetic profile of various therapeutic classes of drugs through their incorporation into nanodelivery systems. These site-specific delivery systems allow an effective drug concentration to be maintained for a longer interval in the target tissue and result in decreased adverse effects associated with lower plasma concentrations in the peripheral blood. Thus, drug targeting has evolved as the most desirable but elusive goal in the science of drug nanodelivery.

Drug targeting offers enormous advantages but is highly challenging and extremely complicated. Increased knowledge on the cellular internalization mechanisms of the nanocarriers is crucial for improving their efficacy, site-specific delivery, and intracellular targeting. Optimal pharmacological responses require both spatial placement of the drug molecules and temporal control at the site of action. Many hurdles still need to be overcome through intensive efforts and concentrated interdisciplinary scientific collaborations to reach the desired goals. However, in recent years, efforts have started to yield results with the approval by health authorities of nanoparticles containing paclitaxel (Abraxane®) for improved cancer therapy, which has rapidly become a commercial success. A large number of clinical trials are currently underway and are again raising the hopes and interest in drug nanodelivery systems.

There are various techniques to prepare drug-loaded nanoparticles, the selection of which depends on the physicochemical properties of the bioactive molecule and the polymer. The nanoparticulate drug delivery field is complex and requires considerable interdisciplinary knowledge. To facilitate the comprehension of this field, Dr. Deepak Thassu, Dr. Michele Deleers, and Dr. Yashwant Pathak co-edited their first book in a series on nanoparticulate drug delivery systems, which was published by Informa Healthcare in 2007. The book covered recent trends and emerging technologies in the field and was very well received by the scientific community. In this second volume on nanoparticulate drug delivery systems, Dr. Pathak and Dr. Thassu are covering various aspects of the field with a focus on formulations and characterization—two crucial but poorly understood issues in this technology.

The chapter authors come from a number of countries including the U.S.A., the U.K., India, Portugal, Canada, and South Korea, and represent many laboratories in the forefront of nanotechnology research. Chapters 1 to 11 cover various formulation aspects of nanoparticulate drug delivery systems. They embrace delivery of small molecules, macromolecules like therapeutic proteins, applications in gene therapy, and drug delivery systems for cancer, diabetes treatment, dermal applications, and many more. Chapters 12 to 15 cover the in vitro and in vivo evaluation as well as characterizations of the nanoparticulate drug delivery systems. The remaining chapters describe various analytical techniques used for the characterization of nanomaterials with special reference to nanomedicines. These sections highlight microscopic and spectroscopic characterization, SEM, TEM applications, structural fingerprinting of nanomaterials, mechanical characterization, and nanomaterial applications in bioimaging. Thus, a better understanding of physicochemical and physiological obstacles that a drug needs to overcome should provide the pharmaceutical scientist with information and tools needed to develop successful designs for drug targeting delivery systems. The book is therefore a timely publication that provides an opportunity for scientists to learn about the complex development issues of nanoparticulate drug delivery systems.

The book clearly and comprehensively presents recent advances and knowledge related to formulation and characterization of nanoparticulate drug delivery systems and is an excellent reference for researchers in the field of nanomedicine.

Dr. Yashwant Pathak and Dr. Deepak Thassu are to be complimented for both their judicial choice of topics in nanodelivery systems and their characterization techniques as well as for their selection of such respected and expert contributors from the field. Drs. Pathak and Thassu through their book will contribute to

advancements in designing and successfully developing new generations of nanodelivery systems.

Simon Benita
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Preface

Modern nanotechnology is an emerging and dynamic field. It is multidisciplinary in nature. It appears that *Mother Nature* was the first scientist offering nanoscale materials abundantly and they were used by the human beings from time immemorial. Several ancient practices have been developing nanoparticles through the traditional processes but these were not identified as nanosystems or nanoparticles. Ayurveda, the ancient traditional system of medicine in India, has described several "bhasmas," which have particles with sizes in nano range and have been used traditionally.

Nanotechnology employs knowledge from the fields of physics, chemistry, biology, materials science, health sciences, and engineering. It has immense applications in almost all the fields of science and human life. As generally acknowledged, the modern nanotechnology originated in 1959 as a talk given by Richard Feynman, "There's plenty of room at the bottom." However, the actual term "nanotechnology" was not coined until 1974 by Norio Taniguchi from Japan. The impetus for modern nanotechnology was provided by interest in interface and colloid science together with the development of analytical tools such as the scanning tunneling microscope (1981) and the atomic force microscope (1986).

People and scientists argue that nanotechnology is likely to have a horizontal impact across an entire range of industries and great implications on human health, environment, sustainability, and national security. The impact of nanotechnology is felt by everyone. The increasing amount of money governments are pouring worldwide in developing these technologies is an encouraging sign. It is observed that many facets of the science are impacted and people are revisiting many research areas with a nanoview to understand how the same thing can work at nano level. This phenomenon is revolutionizing pharmaceutical sciences, and many drugs are again being relooked for possibilities of delivering as a nanosystem.

We had our first volume entitled *Nanoparticulate Drug Delivery Systems: Recent Trends and Emerging Technologies*, which was edited by Drs. Deepak Thassu, Michele Deleers, and Yashwant Pathak. The book was published by Informa Healthcare in April 2007 and shares the status of nanotechnology worldwide. It has been very well received by the scientific and industrial community globally.

We are pleased to submit this second volume edited by Drs. Yashwant Pathak and Deepak Thassu. The objective of the book is to address formulation and characterization properties of nanoparticulate drug delivery systems (NPDDS) and also fulfill the void felt by the scientific community the last 2 years.

The volume comprises 20 chapters written by the leading scientists in this field. The first chapter covers the recent developments and features of NPDDS. This is followed by 8 chapters that address formulation aspects covering small molecules,

macromolecules, gene delivery, protein-based nanodelivery systems, therapeutic and diagnostic applications of gold nanoparticles, and the application of NPDDS in cancer, diabetes, and dermal and transdermal deliveries.

The following group of chapters, which includes chapters 10 to 14, deals with in vitro and in vivo characterization, covering various methods used for characterizing the NPDDS in vitro, mathematical models used in analyzing the in vitro data, in vitro characterization of the interaction of nanoparticles with cell and blood constituents, pharmacological and toxicological characterization of nanosystems, and in vivo evaluation of solid lipid nanoparticle–based NPDDS.

The final group of chapters from 14 to 20 covers various analytical techniques used for characterizing the NPDDS and nanosystems. This includes various microscopic and spectroscopic characterizations. Various advanced techniques used to characterize the nanosystems include the scanning electron microscopy, transmission electron microscopy, structural fingerprinting of the nanocrystals, mechanical properties of the nanosystems, application of fullerene nanosystems for magnetic resonance imaging analysis, and the use of nanosystems for bioimaging. The chapters are authored by experts in these fields, and they have discussed their own researches as well as the developments in their fields of interest.

It is our sincere hope that this multiauthored book covering the formulation and characterization aspects of NPDDS will be welcomed by the scientific community and get a response similar to that received for our first volume. We sincerely hope that the book will assist and enrich readers to understand various aspects of formulation of NPDDS and their therapeutic applications in different disease conditions. The book also highlights the in vitro, in vivo, and analytical characterization in depth providing an insight to the readers in characterizing the NPDDS. We deem that this book will be equally relevant to scientists from varied backgrounds working in the field of drug delivery systems representing industry as well as academia. The text is organized in such a way that each chapter represents an independent area of research and can be easily followed without referring to other chapters.

We express our sincere thanks to Evelyn Kuhn and Jamie Hampton from Creative Communications of Sullivan University for their kind help in developing appropriate figures for publications. We express our sincere thanks to Ms. Allison Koch for her kind help in manuscript development, word processing, corrections, and punctuation.

Special thanks to Ms. Carolyn Honour, Sherri Niziolek, and Sandra Beberman from Informa Healthcare for their kind help and patience in seeing this book being completed.

We will be failing in our duty if we do not express our sincere thanks to all the authors who took trouble and time from their busy schedule to write chapters and provide them in time for publication. We are grateful to Dr. Simon Benita for the wonderful foreword to this book.

We appreciate our respective families for without their continuous support this work could not have been completed.

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Contents