Comments on the Early History of the Controlled Drug Delivery Field, and the Development of “Nanopharmaceuticals”

The field of drug delivery is as old as man. Ancient man chewed natural products, or cooked them in water and drank their extracts, all to alleviate a variety of pains or other body problems. On the other hand, the field of controlled drug delivery systems (DDS) really began only about 60 years ago. The earliest controlled DDS devices appeared in the 1950s. They were called “Spansules” and were oral drug tablets with coatings that dissolved at various rates and then released the drug all at once after the coating was gone. The composition and/or thickness of the coating could be varied to control the time before drug release.

In the mid-1960s, Judah Folkman at Harvard Medical School discovered that when he circulated rabbit blood through a silicone rubber tube and exposed the tubing to anaesthetic gases on the outside, the rabbits went to sleep. So he proposed a new way to administer a drug at a controlled rate by encapsulating a drug in a sealed silicone capsule and implanting it. The wall thickness and surface area of the capsule then determined a constant rate of drug release, as long as saturated drug conditions existed within the capsule. This was really the beginning of the controlled release field.

At the same time, a pharmaceutical chemist-entrepreneur named Alejandro Zaffaroni had been thinking about starting a company around the concept of controlled DD, and in 1968 he founded Alza Corp. in Palo Alto, CA. Folkman was invited to be the Chairman of his Scientific Advisory Board. Alza was the first company dedicated to the field of controlled DD, and it led the way by patenting and getting FDA approval for a wide range of drug delivery devices. Many others soon followed with their own compositions and concepts. In this very productive period of the 1970s and 1980s, a number of new controlled DD devices and compositions were developed and clinically approved. They included a contraceptive drug-loaded poly(ethylene-co-vinyl acetate) or poly(EVA) IUD for insertion into the uterus, six contraceptive drug-loaded silicone rubber tubes for subcutaneous implantation, a drug-loaded skin patch for topical application (seven different drug skin patches...
were developed and approved), a glaucoma drug-loaded poly(EVA) sandwich wafer for insertion into the eye, a drug-loaded acrylic sandwich hydrogel for oral ingestion and so on. All of these controlled DDS were macroscopic in scale.

In the early to mid-1980s, drug-loaded, degradable microparticles composed of poly[lactic-co-glycolic]acid (PLGA) were developed for subcutaneous implantation and delivery; several were approved for clinical use. Early work on PLGA microparticles took place at the University of AL and Southern Research Institute in Alabama by Tice, Lewis, Kent, Lacey, Sanders and others. All of these DDS were microscopic in scale.

The development of nano-scale DDS began in parallel in the 1970s with the much larger size macroscopic DDS but it has taken a much longer time for nanocarrier DDS to reach the clinic. This is in part due to the fact that nanocarrier DDS are designed to be injected into the blood, and they are usually composed of both drug molecules and polymer molecules. Thus, control of the molecular weight and compatibility of the carrier molecules themselves are important regulatory issues, along with the drug itself. The injection of drug-loaded degradable polymer microspheres such as PLGA can raise similar regulatory issues.

In the early 1970s, the concept of PEGylation of protein drugs was introduced by Davis at Rutgers University. In 1976 Langer and Folkman published the delivery of active protein drugs from a protein-loaded hydrophobic polymer matrix, where the proteins dissolved from the surface into the surroundings, and created nano-sized pores in the matrix for further drug delivery. In the mid-1970s in Prague, Kopecek was developing a new polymer carrier (poly[hydroxypropyl methacrylamide], or PHPMA), and they covalently conjugated drugs to the backbone. Kopecek also introduced the concept of attaching cell-targeting ligands to the PHPMA, and along with Duncan in the UK, conjugated the drug via a lysosomal enzyme-degradable peptide linkage to the polymer backbone. Duncan has published extensively on nanocarriers for intracellular drug delivery. Other important nanocarrier DDS were subsequently developed in the 1980s and 1990s and included liposomes (Bangham “discovered” liposomes in 1965 and 30 years later, in 1995, the liposome-doxorubicin product called “Doxil®” became the first nanocarrier-drug DDS approved for clinical use). A-B diblock copolymer micelles were developed as drug carriers in Japan around 1989, especially with PEG as one of the blocks, by Kataoka and Okano. Kabanov in the USA also developed A-B-A triblock Pluronic® micelles as drug carriers. Many different block copolymer micellar drug carriers are in clinical trials today. This text brings the reader up to date with this rapidly expanding and exciting field of drug nanocarriers.

Comments on This Volume, “Fundamentals of Pharmaceutical Nanoscience”

This book is both unusual and special. It is unusual in that it covers such a broad range of topics and their sub-specialities that it is like several books combined into one. It is special because it is both comprehensive and detailed. The particular topics
and sub-specialities that are included represent the most important fundamental and practical aspects of drug delivery nanoscience. This book will be extremely useful for the beginning undergraduate students in pharmaceutical sciences, and for the graduate researchers in drug delivery technology, as well as for the research directors and leaders in this field. It is a comprehensive book that each of these scientists will want to have on his or her bookshelf.

The book is divided into three major parts: Part I—Nanomaterials Fabrication, Characterization and Use; Part II—Concepts Underpinning the Application of Biomedical Nanomaterials; and Part III—Therapeutic and Diagnostic Applications.

Part I includes chapters describing the many different and diverse drug nanocarriers that have been developed. These nanocarriers include those based on natural surfactants and carriers (e.g. liposomes and solid lipid nanoparticles), synthetic polymeric carriers (e.g. micelles, polymersomes, polymeric nanoparticles and polymer–drug conjugates), nano-scale dispersed drugs (e.g. drug nanocrystals and nanoemulsions) and inert “porous” nanocarriers (e.g. porous Si nanoparticles and carbon nanotubes).

Part II includes chapters that cover the three major delivery issues: targeting, drug loading and dissolution and biologic barriers. The last topic area includes barriers encountered in the three major drug delivery routes (e.g. transdermal, oral and mucosal) and in two important blood-related barriers (e.g. blood–brain barrier and blood–eye barrier).

Part III is a very diverse and important part of this comprehensive book. It covers applications and analytical tools of nanomedicine. The first five chapters in this part cover key drug delivery applications that are the cutting edge of the drug delivery field today: cancer chemotherapy, vaccines, anti-infectives, gene and siRNA therapy, and biomolecular drugs and ligands (peptides, proteins and antibodies). The next three chapters of Part III cover topics that are not as directly related to drug delivery as earlier chapters have been; nevertheless, these topics are growing in importance in the pharmaceutical field. They cover the emerging application areas of: tissue engineering (also called regenerative medicine); imaging, which is critical to targeted delivery of the drug, as well as to evaluation of drug efficacy; biosensors and diagnostics which are also vital to optimizing the dose and evaluating drug efficacy. The last chapter of this book is a practical discussion of the various commercialization aspects of pharmaceutical nanoscience.

In summary, this book is one of the most comprehensive books available that combines both the fundamental pharmaceutical principles of nanocarrier drug delivery plus the most important practical applications of that nanotechnology.

Seattle, WA

Allan S. Hoffman
Fundamentals of Pharmaceutical Nanoscience
Uchegbu, I.F.; Schätzlein, A.G.; Cheng, W.P.; Lalatsa, A.
(Eds.)
2013, XIV, 598 p. 155 illus., 99 illus. in color., Hardcover
ISBN: 978-1-4614-9163-7