Lipospheres in Drug Targets and Delivery

Approaches, Methods, and Applications

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Claudio Nastruzzi

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Preface

Colloidal drug carriers, such as liposomes and lipid nanoparticles, are able to modify the *in vivo* distribution of associated substances. They, therefore, can be used to improve the therapeutic index of drugs by increasing their efficacy or reducing their toxicity. If these delivery systems are carefully designed with respect to the target and route of administration, they help us to overcome some of the delivery problems posed by new classes of active molecules, such as peptides, proteins, genes, and oligonucleotides. They may also extend the therapeutic potential of established drugs, such as doxorubicin and amphotericin B.

This book describes the use of lipid-based nano- and microparticulate carriers in such applications. It presents innovative methods of delivering active biochemicals to different systems, discusses lipospheres as a technical solution to problems associated with controlled release of biochemicals, covers lipospheres as carriers for vaccines, and finally provides procedures for specific applications and describes biological systems.

With the identification, characterization, and cloning of specific growth factors, recombinant proteins are now widely used in the clinic. The use of recombinant hematopoietic growth factors has, for example, allowed the clinical manipulation of the hematopoietic system. Recombinant human granulocyte colony-stimulating factor and granulocyte-macrophage colony-stimulating factor are now widely used to mobilize hematopoietic stem cells, thereby providing a source of hematopoietic stem cells for autologous or allogeneic transplantation.

However, one disadvantage associated with the use of most recombinant molecules is their rapid clearance. Because of this rapid clearance, recombinant molecules require repeated administration to achieve biological efficacy. Initially, continuous infusion was used to address this pharmacological deficiency. Continuous infusion has the advantage of delivering drugs in a controlled manner and is particularly appropriate when it is important to maintain constant plasma drug concentrations. However, the requirement for continuous venous access and the use of ambulatory pumps limits its use.

In this context, other approaches have been developed to improve the pharmacokinetic and pharmacodynamic properties of recombinant proteins *in vivo*. These have included the addition of polyethylene glycol to the recombinant molecules (PEGylation) and the use of sustained-release delivery systems. One goal of these approaches is to achieve clinical efficacy and lower the number of administrations, possibly to single injections, and thereby increase patient compliance. In addition to improving the pharmacokinetic and pharmacodynamic profile of recombinant molecules, sustained release may also increase the biological activity of specific molecules.

Moreover, it should be acknowledged that the use of an efficient carrier for nucleic acid–based medicines is considered to be a determinant factor for the successful

application of gene therapy. However, the drawbacks associated with the use of viral vectors, namely, those related to safety problems, have prompted investigators to develop alternative methods for gene delivery, with cationic lipid-based systems being the most representative systems. Despite extensive research in the last decade on the use of cationic liposomes as gene transfer vectors, and the development of elegant strategies to enhance their biological activity, these systems are still far from being viable alternatives to the use of viral vectors in gene therapy.

Finally, in this book considerations are made regarding the structure–activity relationships of cationic liposphere/DNA complexes, and the key formulations are presented and discussed in terms of their effect on biological activity.

Editor

Claudio Nastruzzi was born in Ferrara, Italy, on March 29, 1958. In 1983, he earned his undergraduate degree in pharmaceutical chemistry at the University of Ferrara, and in the late 1980s he was a fellow at the university's Department of Pharmaceutical Science, working on natural compound synthesis (prostaglandins and leukotrienes) and the characterization of isosazolic and isosazolinic nuclei reactivity. In 1988, he obtained his Ph.D. in pharmaceutical science with a dissertation on the synthesis and antitumor and antimetastatic activity of aromatic polyamidines.

During the late 1990s, Dr. Nastruzzi worked with Professor P. L. Luisi as a postdoctoral fellow at the Institute for Polymers at the Swiss Federal Institute of Technology in Zürich. As a postdoctoral fellow at the Department of Pharmaceutical Sciences at the University of Ferrara, he focused on the production and characterization of liposomes specially designed for retinoid delivery, as well as on biophysical studies and activity of *in vitro* cultured cell lines. In 1991, he obtained a researcher position in this department, where he devoted his energy to the production of microspheres, liposomes, and microemulsions for the controlled delivery of biological response modifiers.

Since 1998, Dr. Nastruzzi has been an associate professor in the Department of Chemistry and Pharmaceutical Technology at the University of Perugia, Italy. His main topics of interest include the production and characterization of innovative

dermatologic and cosmetic formulations for dermal and transdermal delivery (phospholipid-based microemulsion gels, cubic phases, liposomes, and niosomes); the production and characterization of microspheres and solid lipid microparticles; and liposome-based formulations for gene delivery.

Dr. Nastruzzi has published more than 90 papers in international journals and has presented more than 80 contributions to national and international congresses.

Contributors

Heike Bunjes
Department of Pharmaceutical Technology
Friedrich Schiller University of Jena
Jena, Germany

Rita Cortesi
Department of Pharmaceutical Sciences
University of Ferrara
Ferrara, Italy

Abraham J. Domb
Department of Medicinal Chemistry and Natural Products
Hebrew University of Jerusalem
Jerusalem, Israel

Elisabetta Esposito
Department of Pharmaceutical Sciences
University of Ferrara
Ferrara, Italy

Aviva Ezra
Department of Medicinal Chemistry and Natural Products
Hebrew University of Jerusalem
Jerusalem, Israel

Achim Göpferich
Department of Pharmaceutical Technology
University of Regensburg
Regensburg, Germany

Stephanie Könnings
Department of Pharmaceutical Technology
University of Regensburg
Regensburg, Germany

Karsten Mäder
Institute of Pharmaceutics and Biopharmacy
Martin Luther University of Halle
Halle, Germany

Wolfgang Mehnert
Department of Pharmaceutical Technology
Free University of Berlin
Berlin, Germany

Boaz Mizrahi
Department of Medicinal Chemistry and Natural Products
Hebrew University of Jerusalem
Jerusalem, Israel

R.H. Müller
Department of Pharmaceutics, Biopharmaceutics, and Biotechnology
Free University of Berlin
Berlin, Germany

Carsten Olbrich
Schering AG
Berlin, Germany

Monika Schäfer-Korting
Department of Pharmacology and Toxicology
Free University of Berlin
Berlin, Germany

Nadja Schöler
Schering AG
Berlin, Germany

Kerstin Tabatt
PenCef Pharma GmbH
Berlin, Germany

Sylvia A. Wissing
Drug Delivery Services GmbH
Kronshagen, Germany

Table of Contents