

# **Future Strategies for Drug Delivery with Particulate Systems**

edited by

**Dr. rer. nat. Julia E. Diederichs**  
Research Scientist

and

**Prof. Dr. rer. nat. Rainer H. Müller**  
Professor of Pharmaceutics & Biopharmaceutics

Department of Pharmaceutics,  
Biopharmaceutics & Biotechnology  
Free University of Berlin

The book chapters are based on the lectures  
of the 1<sup>st</sup> European Workshop on Particulate Systems (EWPS)  
Berlin-Brandenburgische Akademie der Wissenschaften,  
Berlin, 14.-16. March 1997

Organizers: Rainer H. Müller and Julia E. Diederichs  
Free University of Berlin, Faculty of Pharmacy

68 Figures and 12 Tables



**CRC Press**

**Boca Raton Boston London New York Washington, D.C.**

**medpharm** GmbH Scientific Publishers Stuttgart 1998

## Contents

### I Nanoparticles and Liposomes for drug targeting

E. Fattal, H. Alphandary, C. Weingarten, Ch. Vauthier, C. Dubernet, A. Andremont, P. Couvreur .....	1
I.1 Design of a new eye delivery system for oligonucleotide based on a liposomal dispersion in a gel A. Bochot, E. Fattal and P. Couvreur .....	5
I.2 Alginate nanoparticles as a novel carrier for antisense oligonucleotides I. Aynié, Ch. Vauthier, E. Fattal, M. Foulquier, P. Couvreur .....	11
I.3 Splenic trapping of nanoparticles: Complementary approaches for in situ studies M. Demoy, S. Gibaud, J.P. Andreux, C. Weingarten, B. Gouritin and P. Couvreur .....	17
I.4 Synthesis of a novel poly(MePEG-co-alkyl) cyanoacrylate, amphiphilic copolymer for the preparation of PEG-coated nanoparticles M.T. Peracchia, D. Desmaële, J. d'Angelo and P. Couvreur .....	23

### II Lipid based Drug Delivery Systems for Peptide and Protein Drug Delivery

S. Frokjaer, K. Jørgensen and Ch. Vermehren .....	29
II.1 Fat Emulsions Based on Structured Lipids as Delivery Systems for Intravenous Use H. Hedeman, H. Brøndsted, A. Müllertz and S. Frokjaer .....	32
II.2 Relationship Between Lipid Bilayer Micro-Structure and Functional Properties of Liposomes K. Jørgensen, M.C. Sabra, J. Risbo and O.G. Mouritsen.....	38
II.3 Medium-chain Lecithin in nasal drug delivery systems: Advantages and drawbacks Ch. Vermehren, H.S., Hansen and M.K. Thomsen.....	45

### III Interaction of plasma proteins with liposomes - Influence of surface properties on adsorption patterns and protein conformation

J.E. Diederichs .....	53
-----------------------	----

<b>IV</b>	<b>Iron oxides as contrast agents in magnetic resonance lymphography</b>	
	M. Kresse .....	63
<b>V</b>	<b>Solid Lipid Nanoparticles, nanosuspensions and liposomes for pharmaceutical and cosmetic applications</b>	
	R.H. Müller .....	71
V.1	Particulate systems for the controlled delivery of active compounds in pharmaceuticals and cosmetics	
	R.H. Müller .....	73
V.2	Solid lipid nanoparticles (SLN <sup>TM</sup> ) for oral administration - drug incorporation and degradation	
	S.A. Runge, R.H. Müller .....	91
V.3	Nanosuspensions - a novel formulation for poorly soluble drugs	
	K. Peters, R.H. Müller .....	101
V.4	Two-dimensional electrophoresis (2-DE) for the determination of plasma proteins adsorbed on model drug carriers	
	M. Lück, B.-P. Paulke, W. Schröder, R.H. Müller .....	109
V.5	Development of a liposomal formulation for hair care use	
	J. Herbort, J.E. Diederichs, R.H. Müller .....	118
<b>VI</b>	<b>Liposomes as drug carrier for diagnostics, cytostatics and genetic material</b>	
	R. Reszka .....	127
VI.1	Preparation and characterization of a new generation of cationic liposomes for gene transfer	
	D. Groth, C. Lehman, O. Keil, M. Schneider and R. Reszka .....	132
VI.3	Characterization of gene transfer vesicle by electron microscopy	
	C. Lehman, D. Groth, O. Keil, M. Schneider, M. Rudolph and R. Reszka .....	140
<b>VII</b>	<b>Strategies for site specific, time and rate controlled delivery of drugs, genes and antigens</b>	
	D.J.A. Crommelin, W.E. Hennink and G. Storm .....	147
VII.1	Development of an optimized immuno-enzymosome formulation for application in cancer therapy	
	M.J. Fonseca, M.H. Vingerhoeds, H.J. Haisma, D.J.A. Crommelin, G. Storm .....	152
VII.2	Factors influencing lymphatic disposition of liposomes after subcutaneous administration	
	C. Oussoren and G. Storm .....	158

VII.3 MHC II/Peptide liposomes as artificial antigen presenting cells A.J.M.L. van Rensen, L.S. Taams, M.C.J.T. Grosfeld-Stulemeyer, A. Besseling, W. van Eden, D.J.A. Crommelin and M.H.M. Wauben .....	164
VII.4 Targeting of Antibiotics to Bacterial Infections Using Long-Circulating Liposomes R.M. Schiffelers, G. Storm, I. A.J.M. Bakker-Woudenberg .....	167
VII.5 Optimal delivery of desferrioxamine (DFO) in the treatment of murine malaria N.S. Postma, C.C. Hermsen, W.M.C. Eling, O. Boerman, J. Zuidema .....	172
VII.6 Poly ((2-dimethylamino) ethyl methacrylate) nanoparticles for gene transfection H. Talsma, J-Y Cherrng, P. v.d. Wetering, D.J.A. Crommelin and W.E. Hennink .....	177
VII.7 Liposomal delivery of cytokines for anticancer vaccination M.L. van Slooten, F.J. Koppenhagen, J.J. Bergers, R. Kircheis, D.J.A. Crommelin, E. Wagner and G. Storm .....	184
<b>VIII Index.....</b>	<b>189</b>