Preface

The use of various pharmaceutical carriers to enhance the in vivo efficiency of many drugs and drug administration protocols has been well established during the last decade in both pharmaceutical research and clinical setting. Surface modification of pharmaceutical nanocarriers, such as liposome, micelles, nanocapsules, polymeric nanoparticles, solid lipid particles, and niosomes, is normally used to control their biological properties in a desirable fashion and to simultaneously make them perform various therapeutically or diagnostically important functions. The most important results of such modification include an increased stability and half-life of drug carriers in the circulation, required biodistribution, passive or active targeting into the required pathological zone, responsiveness to local physiological stimuli, and ability to serve as contrast agents for various imaging modalities (gamma-scintigraphy, magnetic resonance imaging, computed tomography, ultra-sonography). Frequent surface modifiers (used separately or simultaneously) include soluble synthetic polymers (to achieve carrier longevity); specific ligands, such as antibodies, peptides, folate, transferrin, and sugar moieties (to achieve targeting effect); pH- or temperature-sensitive lipids or polymers (to impart stimuli sensitivity); chelating compounds, such as EDTA, DTPA, and deferoxamine (to add a heavy metal-based diagnostic/contrast moiety onto a drug carrier).

Certainly, new or modified pharmaceutical carriers (nanocarriers) as well as their use for the delivery of various drugs and genes are still described in many publications. However, looking into the future of the whole field of drug delivery, we have to think about the development of the next generation of pharmaceutical nanocarriers, combining variety of properties and allowing for the simultaneous performance of multiple functions. The current level of engineering pharmaceutical carriers in some cases allows for drug delivery systems, demonstrating a combination of several desired properties. Long-circulating immunoliposomes represent a good example of this approach as they combine the ability to remain in the circulation for a long time with the ability to specifically accumulate in target areas. One may add pH-sensitive long-circulating liposomes and micelles, or nanocarriers simultaneously loaded with a drug and an imaging agent, to the list. Such nanocarriers belong to the new, “smart” generation of drug delivery systems. In principle, we can

imagine drug delivery systems, which, depending on the immediate requirements, can simultaneously or sequentially demonstrate the following properties: (1) circulate long in the blood or, more generally, stay long in the body; (2) specifically target the site of the disease (accumulate there) via both nonspecific and/or specific mechanisms, such as enhanced permeability and retention (EPR) effect and ligand-mediated recognition; (3) respond local stimuli characteristic of the pathological site, such as intrinsic abnormal pH values or temperature or externally applied heat, magnetic field, and ultrasound, by, for example, releasing an entrapped drug or deleting a protective coating and facilitating the contact between drug-loaded nanocarriers and target pathological cells; (4) provide an enhanced intracellular delivery of an entrapped drug in case the drug is expected to exert its action inside the cell (gene delivery to the nuclei or delivery of proapoptotic drugs to the mitochondria surface are good examples); (5) supply real-time information about the carrier (and drug) biodistribution and target accumulation as well as the outcome of the therapy due to the presence within the structure of the carrier of a certain reporter/contrast group. Some other less significant and more exotic functions can also be "attached." Strictly speaking, the term "multifunctionality" may also be applicable to pharmaceutical carriers simultaneously loaded with more than one drug type. To meet the requirements listed above, drug carrier should simultaneously carry various moieties capable of functioning in a certain orchestrated and coordinated fashion. Thus, for example, if a system that can provide the combination of longevity (allowing for the target accumulation via the EPR effect) and specific cell binding (allowing for its internalization by target cells) has to be constructed, two requirements have to be met. First, the half-life of the carrier in the circulation should be long to fit EPR effect requirements. Second, the internalization of the carrier within the target cells should proceed fast to avoid carrier degradation and drug loss in the interstitial space. We have to agree that systems like this still represent a challenge, although a certain work in this direction has already been done and certain examples of multifunctional matrices for oral and tumoral delivery already exist.

This book attempts to cover an emerging area of multifunctional pharmaceutical carriers. It includes 15 chapters describing different aspects of this approach, from stimuli-responsive long-circulating micelles to magnetically sensitive drug carriers, which can be simultaneously used as imaging agent. Certainly, a single book cannot include all the currently available information, and the potential reader may discover that certain areas of interest are absent in this volume. Still, I feel that it is a good beginning.

I am deeply grateful to all my friends and colleagues who have contributed to this book. As an editor, I am open to comments and advices from our readers and I believe that they will find this book useful.

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