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## Editorial

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### Nanocarriers

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**Abstract.** The use of nanoparticulate pharmaceutical carriers to enhance the *in vivo* efficiency of many drugs well established itself over the past decade both in pharmaceutical research and clinical setting. The current level of engineering pharmaceutical nanocarriers in some cases allows for drug delivery systems (DDS) to demonstrate a combination of some desired properties. However, looking into the future of the field of drug delivery, we have to think about the development of the next generation of pharmaceutical nanocarriers combining different properties and allowing for multiple functions.

**KEY WORDS:** pharmaceutical nanocarriers.

The use of nanoparticulate pharmaceutical carriers to enhance the *in vivo* efficiency of many drugs well established itself over the past decade both in pharmaceutical research and clinical setting. The current level of engineering pharmaceutical nanocarriers in some cases allows for drug delivery systems (DDS) to demonstrate a combination of some desired properties. However, looking into the future of the field of drug delivery, we have to think about the development of the next generation of pharmaceutical nanocarriers combining different properties and allowing for multiple functions. Long-circulating immunoliposomes represent a good example of this approach, since 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 DDS. We can imagine DDS, 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 via different mechanisms, such as enhanced permeability and retention effect (EPR) and ligand-mediated recognition; (3) Respond local stimuli characteristic of the pathological site, such as abnormal pH values or temperature or respond externally applied stimuli, such as heat, magnetic field, or ultrasound, by, for example, releasing an entrapped drug or facilitating the contact between drug-loaded nanocarriers and target cells; (4) Provide an enhanced intracellular delivery of an entrapped drug in case the drug is expected

to exert its action inside the cell; (5) Provide a real-time information about the carrier (and drug) biodistribution and target accumulation as well as about the outcome of the therapy due to the presence within the structure of the carrier of a certain reporter moiety. To be able to meet the requirement listed above, drug carrier should simultaneously carry on its surface various moieties capable of functioning in a certain orchestrated order. We have to agree that systems like this still represent a challenge, although a certain work in this direction is already done.

Various pharmaceutical nanocarriers, such as nanospheres, nanocapsules, liposomes, micelles, cell ghosts, lipoproteins and some others are widely used for experimental (and already clinical) delivery of therapeutic and diagnostic agents. Surface modification of these carriers is often used to control their properties in a desirable fashion and make them to simultaneously perform several different functions. The most important results of such modification(s) include increased longevity and stability of the carrier (and carrier-incorporated drug) in the circulation, favorably changed biodistribution, targeting effect, stimuli (pH or temperature)-sensitivity, and contrast properties. Frequent surface modifiers (used separately or simultaneously) include soluble synthetic polymers (to achieve carrier longevity); specific ligands, such as antibodies, peptides, folate, transferrin, sugar moieties (to achieve targeting effect); pH- or temperature-sensitive lipids or polymers (to impart stimuli-sensitivity); chelating compounds, such as EDTA, DTPA or deferoxamine (to add a heavy metal-based diagnostic/contrast moiety onto a drug carrier). Evidently, different modifiers can present on the surface of the same nanoparticulate drug carrier in different combinations providing it with a set of useful properties required in each particular case (for example, longevity and targetability, targetability and stimuli-sensitivity, or longevity, targetability and contrast properties).

This section attempts to draw the readers’ attention to this very subject and combines two review papers and four

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original research papers covering various areas of multifunctional pharmaceutical nanocarriers. In his review paper, Dr. Davidson and co-authors address multifunctional nanoparticulate polyelectrolyte complexes, which demonstrate a variety of physical, chemical, and biological properties making them promising multitask carriers for site specific delivery of various drugs, genes and imaging agents. Multifunctional nanorods, reviewed by Dr. Salem *et al.*, represent a relatively new family of pharmaceutical nanocarriers capable of combining various properties essential for drug delivery and diagnostic application. Original papers of this section deal with different aspects of multifunctionality in pharmaceutical carriers and clearly show the advantages of the approach and various goals this approach allows to achieve. The Editor hopes this nice set of papers will not pass unnoticed by the readers.

#### INTERVIEW WITH DR. VLADIMIR P. TORCHILIN

1. What do you think holds the key to your success as a pharmaceutical scientist?

–I don't know how really big my success is, but whatever I did, I always liked what I was doing and never watched time in the lab. Fairly, I still do not watch it.

2. What do you consider to be your key research accomplishments?

–Probably, the very first polymer-modified enzyme to become a drug back in former Soviet Union.

3. What was the turning point in your career?

–I think, I had two turning points. The first one, when I decided to move from the Moscow State University to the Academy of Medical Sciences, and the second—when I decided to move from the Soviet Union to the United States.

4. Who are the individuals who most influenced your research career?

–Cannot name a single person. I had many great teachers and colleagues and never hesitated to learn.

5. Pharmaceutical scientists are faced with the dilemma of having to publish in biomedical or basic science journals. Does it mean cutting edge science will not

likely be featured in the Pharmaceutical Research?

–I think it's OK. Pharmaceutical Research publishes a lot of good papers on its own, which do relate namely to pharmaceutical research. Basic breakthrough papers should be available for the broader audience and published in general basic journals.

6. Where is the field of Multifunctional Polymeric Drug and Nucleic Acid Delivery going, and how do the articles in the theme section fill the gap?

–The field of Multifunctional Pharmaceutical Carriers is a novel one, and at this point it is hard to say where it goes. Evidently, the development will result in drug delivery systems, which will combine at least some of the following properties: longevity, targetability, stimuli-sensitivity, intracellular delivery, controlled drug release, and ability to be visualized by standard imaging techniques. What namely the first drug of this type will be, hard to say right now, but most probably these will be some anti-cancer preparations. The theme section on this topic is just supposed to attract more attention to this area.

7. What are the challenges for Polymeric Drug Delivery and how can they be overcome?

–I don't see any major challenges. The field develops fast and successfully.

8. What is the key to developing successful collaborative relationships?

–Never think who gets what. Think about the success of the project.

9. What is your philosophy of educating graduate students?

–They have to leave the lab being able to do everything—from chemical synthesis to cell culture and animal experiments and also learn how to write papers and make presentations. It is hard but it pays back.

10. What are the challenges facing the pharmaceutical sciences?

–Not to lose the basic component and become just another applied field.

11. What is the place for collaboration with industry in academia?

–It may sound naïve, but industry should be more aggressive in further pursuing the developments done by academia and not to wait that these developments go to clinical trials.