Fine Particles in Medicine and Pharmacy

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Editor

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Preface

There are several areas in medicine and pharmacy in which finely dispersed matter plays a significant role. Drugs in solid state can be produced as particles of diverse shapes and structures, in modal sizes ranging from a few nanometers to a few micrometers. Such medication is commonly combined with inactive diluents, while the pills themselves are often coated with layers which protect them from the effects of the environment, such as humidity. Both these chemically inert components in the delivery systems (diluents and shells) may also control the release of the active component.

Thus, there are many physical aspects of the medication which can affect its functionality. The first deals simply with the size of the active substance to be delivered. For example, in recent years much emphasis has been placed on the use of nanosize active materials. A recent issue of ACS NANO published several articles on the subject, including "Impact of Nanotechnology on Drug Delivery", by O.C. Farukhzad and R. Langer (3, 2009, 16–20), and "Virtual Issue on Nanomaterials for Drug Delivery" by P.T. Hammond (5, 2011, 681–684).

Another significant aspect of the drug in the pill form is the morphology of active molecules, which affects many properties of a medication, including its stability, solubility, and release. Most of the medically active compounds tend to form polymorphs, i.e., the same molecules being differently packed in the solid state, which determines their functionality. This aspect of drugs was dealt with in great detail by A.M. Rouhi in *Chemical and Engineering News* (American Chemical Society), February 24, 2003 issue, under the title "The Right Stuff: From research and development to the clinic, getting drug crystals right is full of pitfalls." It is, therefore, of great importance to produce drug delivery systems (e.g. pills) that contain the active compound in the stable state, and assure its controlled delivery.

Fine particles of different size and other properties (optical, magnetic, adhesive, etc.) play an essential role in the diagnostics, such as barium sulfate slurries in the X-ray of intestines, or well defined magnetic particles used as a biosensor, or nanodispersed gold used in bioimaging, to mention a few. Such specific uses of fine particles are described in several chapters. A short description of the contents of individual chapters is given below.

In the first chapter Vladimir Privman addresses the advancement of modeling approaches aimed at explaining morphological and geometrical features of fine particles. Specifically, discussed are certain aspects of particle shape selection and size uniformity, emerging as results of kinetics involving diffusional transport of matter in solution synthesis of nanocrystals and colloids. Processes ranging from nucleation to growth by aggregation, and mechanisms of uniform shape development are reviewed, with selected results outlined in some detail.

In the second chapter, Egon Matijević demonstrates that uniform drug dispersions can be prepared by precipitation in solutions. Indeed, in some cases, the same substance is obtained as particles of different, but uniform shapes, by altering the experimental conditions, or by varying additives. Furthermore, it is possible to coat so prepared drugs with an inorganic layer of alumina or silica, thus altering the surface reactivity and charge of the resulting particles. Such layers protect the cores and may promote specific reactions within the body.

The chapter by Silvana Andreescu, Maryna Onatska, Joseph Erlichman, Ana Estevez, and J.C. Leiter focuses on the interactions of the most widely used nanoparticles of metal oxides with cells and tissues in relation to the physico-chemical properties, biocompatibility, and cytotoxic reflexes in model biological systems, and selected biomedical applications. New and emerging uses of these particles as neuroprotective and therapeutic agents in the treatment of medical diseases related to reactive oxygen species, such as spinal cord repair, stroke, and degenerative retinal disorders are discussed. Furthermore, issues related to biocompatibility and toxicity of these nanoparticles for *in vivo* biomedical applications are dealt with in some detail.

Dan Goia and Tapan Sau contribute a comprehensive review of uniform colloidal gold, as applied in medicine and biology. Specifically, they describe how functionalized gold particles are used in bioimaging (optical, immunostaining, computed tomography, magnetic resonance, phagokinetic tracking), biosensing (optical and electrochemical), drug delivery, and therapeutic applications. Also described are additives for the preparation of highly dispersed active nanogold, including the complex (core–shell) and hierarchical structures, involving both inorganic and organic phases.

In their chapter Evgeny Katz and Marcos Pita deal with magnetic particles (microspheres, nanospheres, and ferrofluids), which are extensively used as labeling units and immobilization platforms in various biosensing schemes, mainly for immunosensing and DNA analysis, as well as in environmental monitoring. Biomolecule-functionalized magnetic particles generally exist in a ‘core–shell’ configuration through organic linkers, often organized as a polymeric ‘shell’ around the core. The state-of-the-art in the preparation, characterization, and application of biomolecule-functionalized magnetic particles and other related micro/nano-objects allows for efficient performance of various *in vitro* and *in vivo* biosensors, many of which are directed to biomedical applications.

The focus of the chapter by Devon Shipp and Broden Rutherglen is on the degradable polymer particles in drug delivery applications, based on their architectural design. Specifically, the authors consider polyanhydrides, which have the un-

usual property of undergoing surface erosion, and to predictable therapeutic agent release rates of approximate zero-order kinetics.

Artem Melman, in his contribution, describes an innovative method for the preparation of uniform nanoproteins, which involves their growth on monodispersed protein templates. This process is extensively involved in biomineralization in a multitude of living organisms, providing structures of exceptional complexity and uniformity. Current availability of pure recombinant cage shaped proteins and viruses offer limitless possibilities for their modification, and for targeted delivery on nanoparticles.

The chapter by Philip K. Hopke and Zuocheng Wang deals with the delivery and the effectiveness of medicine dosages deposited in the respiratory tract. Their study was originally driven by the concern regarding the effects of radioactive particles in this application. Empirical studies in animals and physical models of human airways have provided data which allows the prediction of regional deposition roles.

The chapter by Maria Hepel and Magdalena Stobiecka describes new bioanalytical sensing platforms, based on functionalized nanoparticles, for the detection of biomarkers of oxidative stress. These biomarkers and biomolecules indicate the diminished capacity of a biological system to counteract an invasion (or overproduction) of reactive oxygen species and other radicals. The oxidative stress has been implicated in a number of diseases, including diabetes, cancer, Alzheimer's, autism, and others. The detection methods for the oxidative stress biomarkers, such as glutathione, homocysteine, and cysteine, presented in this chapter, are based on their interactions with monolayer-protected gold nanoparticles. Such functionalized particles have also been shown to amplify the analytical signal in molecularly-templated conductive polymer sensors for the detection of biomolecules, and novel designs of molecularly-imprinted poly(orthophenylenediamine) sensor films.

In his chapter Sergiy Minko discusses the synthesis and applications of multifunctional hierarchically organized, multilevel structured, active hybrid colloidal particles, uniform in size and shape. Such particles are capable of programmed and controlled responses to changes in the environment or to external signals. Furthermore, various core–shell structures were synthesized in two steps consisting of metals, oxides, or polymers of different sizes and shapes, and functionalized with stimuli-responsive polymers. Specifically, deposition, precipitation on colloidal templates, grafting to the surface of particles, and self-assembly of amphiphilic block-copolymers, were extensively used for the synthesis of the core–shell colloids. A properly engineered combination of sensitivity to external stimuli with resulting changes in the particles' properties is critically important for drug delivery capsules, capsules for diagnostics and, particles-biosensors. The development of these stimuli-responsive colloids is driven by several important applications: including, biosensors that respond to changes in the chemical and biological environment, stimuli-responsive capsules that can release the cargo upon external stimuli for delivery of drugs and contrasting agents, and biocomposite materials that can adapt to living tissue.

In the final chapter, Richard Partch, Adrienne Stamper, Evon Ford, Abeer Al Bawab and Fadwa Odeh, deal with the incidence of overdoses of chemicals into

the body, causing either serious injury to organs or even death. The latter is more common than what is generally believed to be the case. Among such chemicals are prescription therapeutics, illicit derivatives, biotoxins, and those found in beverages and food, leached from packaging. In this chapter it is demonstrated that both oil–water microemulsions and functionalized carrier nanoparticles are capable of removing overdosed concentrations of several of the problem chemicals from liquids including blood, both *in vitro* and *in vivo*.

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Contents

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