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*Review*

# Nanotechnology importance in the pharmaceutical industry

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**During the last decades, pharmaceutical technology has taken the advantage of the advent of nanotechnology and, now days, new pharmaceutical dosage forms are under development to deliver many physicochemically different drug molecules. The present study is to investigate the role and their importance of nanotechnology in the pharmaceutical development.**

**Key words:** Nanotechnology, drug delivery, nanoparticles, cancer

## INTRODUCTION

Nanotechnology is unique in that it represents not just one specific area, but a vast variety of disciplines ranging from basic material science to personal care applications. The importance of nanotechnology in drug delivery is in the concept and ability to manipulate molecules and supramolecular structures for producing devices with programmed functions. Conventional liposomes, polymeric micelles, and nanoparticles are now called "nanovehicles," and this, strictly speaking, is correct only in the size scale. Those conventional drug delivery systems would have evolved to the present state regardless of the current nanotechnology revolution. To appreciate the true meaning of nanotechnology in drug delivery, it may be beneficial to classify drug delivery systems based on the time period representing before and after the nanotechnology revolution. To describe what nanotechnology can do to manufacture nano/micro drug delivery systems, one can use manufacturing of nano/micro particles (or capsules) as an example. The current methods of preparing nano/micro particles are mainly based on double emulsion methods or solvent exchange technique (Freitas et al., 2005; Park 2007). The main problems with the current methods are the low drug loading capacity, low loading efficiency, and poor ability to control the size distribution. Utilizing nanotechnologies, such as nanopatterning, could allow manufacturing of nano/micro particles with high loading efficiency and highly homogeneous particle sizes.

## DISCUSSION

### Types of nanoparticles as drug delivery systems

Nanoparticles can consist of a number of materials, including polymers, metals, and ceramics. Based on their manufacturing methods and materials used, these particles can adopt diverse shapes and sizes with distinct properties. Many types of nanoparticles are under various stages of development as drug delivery systems, including liposomes and other lipid-based carriers (such as lipid emulsions and lipid-drug complexes), polymer-drug conjugates, polymer microspheres, micelles, and various ligand-targeted products (such as immunoconjugates) (Liu et al., 2000; Moghimi et al., 2001; LaVan et al., 2003; Allen, 2002).

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## Characterization of nanoparticles

A good physicochemical understanding of the formulation is an absolute necessity for rational formulation design and properly interpreting *in vivo* results. Size, surface characteristics, particle morphology, structure, and drug release are all relevant topics each of which will be briefly discussed below.

### Size

Size is a central focus of nanotechnology as defined above, so its measurement is significant from that perspective. More importantly the size of a nanoparticle will determine its behavior both *in vitro* and *in vivo*, hence quantitative data on this characteristic is indispensable. Particle sizing can be broken down into three classes, ensemble, counting, and separation. Ensemble techniques, which include many of the spectroscopies such as light scattering and acoustic, make a single measurement of the system and then apply appropriate mathematics to extract a size population.

They are very useful because of their speed, accuracy, and convenience, however they are poorly suited to describing the particle population at the edge of a size distribution, and are subject to systematic errors if the data quality is poor or if required parameters such as refractive index are not available. Counting methods, such as microscopy or single particle counting, provide very quantitative results since data is collected from individual particles. However, for the same reasons such methods are slow, frequently require extensive sample preparation or dilution, and are subject to sampling errors. Finally, separation techniques give a good understanding of the shape of a size distribution, but care is required to make sure that the mechanism of separation is completely understood, i.e., is occurring in a manner quantitatively related to size rather than anomalous interaction channel walls. Analytical ultracentrifugation, various forms of field-flow fractionation and hydrodynamic fractionation are examples of such approaches. Regardless of the analyses employed, a key precept of size characterization is to use more than one method as a nanoparticle system at hand.

### Surface properties

Contact of the particle surface with its environment will determine the particles' interaction with one another and may strongly influence their *in vivo* behavior, *e.g.*, clearance. Charge, usually measured as zeta potential, is a primary descriptor and is determined most easily using techniques such as electroacoustic and electrophoretic light scattering. These particular methods are ensemble in nature and so have the same advantages and limitations as those listed above. Measurements of zeta potential based upon counting also exist. Using electrophoreses to analyze bound proteins extracted from plasma-treated nanoparticles is a useful means of better understanding the interaction of nanoparticles with blood components.

### Particle morphology

In some cases the interest is in the shape of the particle and the nature of its surface. In other cases interest focuses on the particle disposition, such as aggregation state or location within a matrix. Particularly when the objects to be analyzed have a high aspect ratio, such as the case with nanotubes, an actual picture is a valuable complement to instrumental methods.

Given the size of the particles, scanning electron microscopy, either in transmission or scanning mode, are the primary tools of the analyst. The magnifications are much higher in the former mode, but the 2-D appearance of the images and the extensive sample preparation serve as drawbacks. Freeze-fracture sample preparation, where a cast is taken of the sample of interest and then examined in turn is valuable in those instances where the sample is fragile, but it is a laborious procedure that requires a high level of skill to properly utilize. Recently there has been a great interest in applying atomic force microscopy (AFM) to the analysis of pharmaceutically relevant nanoparticles. Very high-resolution images of particles in their native environment can be obtained using AFM, albeit at the expense of time since it is a rastering method. Depending on the interaction established between the probe tip and the sample, a wide range of material characteristics can be mapped on the nano-scale, e.g., electrostatic potential or hardness. The particles must be located on a solid support like mica, so understanding the effect that the latter has on the former, flattening for example, is important, and constitutes one reason that experience of the analyst with AFM is necessary. Optical microscopy can be quite valuable, even though the size of the particles is below the resolution of the technique. For example, dark-field methods allow the presence of nanoparticles, and hence their number-weighted concentration, to be detected even though the particles themselves are not imaged directly.

### Structure

The arrangement of components within the nanoparticle can determine its behavior and stability. A number of common methods are appropriate such as differential scanning calorimetry and powder X-ray diffraction if one is interested in overall structural characteristics such as crystal form or extent of amorphous character. Given the small size of nanoparticles, particular structural features such as layers, may be on the molecular scale. In such cases, establishing the orientation of molecules requires higher energy scattering methods such as small-angle neutron and X-ray scattering. Needless to say such tech-

niques require highly specialized equipment and operators. When the nanoparticle in question has a fluid component or when there is interest in measuring free drug levels, NMR is a good technique since the magni-tude of instrumental response depends upon molecular motion. Combining chemical speciation and diffusion measurement in 2-D gradients NMR can be very informative.

**Drug release**

A central reason for pursuing nanotechnology is to deliver drugs, hence understanding the manner and extent to which the drug molecules are released is important. In order to obtain such information most release methods require that the drug and its delivery vehicle be separated. The simplest case is separating dissolved from undissolved drug in a traditional solid formulation. In this example, a filtration step is sufficient to produce the separation. However, what happens when the drug containing particles are sufficiently small to slip through the filter pores? This is easily the case with nanoparticles and the result is an inability to distinguish between free (available) and bound (unavailable) drug. In such situations the distinction can be brought about via size discrimination or spectroscopy. The former case is just an extension of conventional methodology although rather than using standard filters, diffusion membranes or ultracentrifugation can be employed instead. While effective at separating released drug from the nanoparticles, this approach takes a long time and thus makes it impossible to measure fast release rates. One can also take advantage of the fact that bound and released drug may have different spectroscopic characteristics. In this way the increase in released drug can be quantified as a measurement of release. Because of its sensitivity to molecular structure and mobility, NMR is one way of taking this approach. On the other hand, the spectroscopic method has to have a sufficient limit of quantitation. Since nanotechnology is frequently applied to poorly soluble compounds, this can become problematic. Note that in either approach it might make more sense to look for the disappearance of drug from the nanoparticle than it does to measure its appearance in the release media.

**Therapeutic applications of nanotechnology Nanotechnology era in tuberculosis**

The era of nanotechnology has allowed new research strategies to flourish in the field of drug delivery (Pandey et al., 2006 ) Nanoparticle-based drug delivery systems are suitable for targeting chronic intracellular infections such as tuberculosis. Polymeric nanoparticles employing poly lactide-co-glycolide have shown promise as far as intermittent chemotherapy in experimental tuberculosis is concerned. It has distinct advantages over the more traditional drug carriers, that is, liposomes and microparticles. Although the experience with natural carriers, e.g. solid lipid nanoparticles and alginate nanoparticles is in its infancy, future research may rely heavily on these carrier systems. Given the options for oral as well as parenteral therapy, the very nature of the disease and its complex treatment urges one to emphasize on the oral route for controlled drug delivery. Pending the discovery of more potent antitubercular drugs, nanotechnology-based intermittent chemotherapy provides a novel and sound platform for an onslaught against tuberculosis. Balasunderam et al. (2006) studied there are a number of applications requiring bone-building agents. For example, osteoporosis is a disease resulting in weak bone. However, no current effective prevention and treatment methods exist for osteoporosis. For these reasons, they studied and explained that nanotechnology (or the design of materials with 10-9 m dimensions) was used to develop novel drug-carrying systems that specifically attach to osteoporotic (not healthy) bone. Moreover, some of these novel drug carrying systems distribute pharmaceutical agents locally to quickly increase bone mass. These efforts focus on the prolonged release of bioactive agents (specifically bone morphogenetic protein-2 (BMP-2)) to efficiently regenerate enough bone for the patient to return to a normal active lifestyle. Particularly, inorganic biodegradable nanomaterials (including ceramics like hydroxyapatite or HA) were functionalized in this study with bioactive chemicals (such as RGD, a model peptide known to increase bone cell function). Such bioactive groups were placed on the outer surface of the nanoparticle systems using various techniques resulting in covalent chemical attachment. The outer coating of the embedded nanoparticle systems were also created to have different biodegradation rates for the controlled release of embedded bioactive agents to the target site. In this manner, ceramic nanoparticle drug delivery systems were developed for fighting osteoporosis.

**Nanotechnology applications in dermatology**

According to Eliana souto study the promising potential of the novel lipid nanoparticles, i.e. solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC), as new drug delivery systems for antifungal agents. To test their suitability as carrier systems within the scope of topical and dermatological purposes, intensive investigations using semi-solid formulations have also been performed. In his study two different imidazole antifungals (clotrimazole and ketoconazole) have been used as model drugs for the study of the topical features of aqueous SLN and NLC dispersions. Once the poor solubility of the drug in the carrier matrix results in a low affinity of the molecule for the carrier and, therefore, poor in vivo bioavailability, different lipid matrices have been chosen according to the solubility of the selected drugs in several lipids. This research project was also designed to assess the possi-

bility to develop SLN- and NLC-based semi-solid formulations using a well established hydrogel as topical vehicle. Investigations included the production and optimisation of the physicochemical properties of the colloidal systems containing clotrimazole and after their entrapment into carbomer-based hydrogels. In this study they found that it has been shown that lipid nanoparticles are suitable for chemicallystabilize imidazole agents, that is, clotrimazole and ketoconazole. However, lipid nanoparticles based formulations need to be optimized concerning the entrapment of labile drugs, such as ketoconazole. Based on experiences with hard fats nanoparticles, two different types of lipid nanoparticles have been investigated concerning their suitability for imidazole antifungal agents. The structure and mixing behaviour of these particles have been characterized and practical implications on controlled release properties have been tested, in comparison to commercial formulations containing one model drug in the same concentration as the developed SLN and NLC formulations. Based on solubility studies, suitable oil has been successfully incorporated in a matrix of a solid long chain acylglycerol for the production of NLC. The crystal order was therefore disturbed however, the carrier remained solid and the oil inside the particle remained in a liquid state.

## Future directions

Cancer is known to develop via a multistep carcinogennesis process and to progress using several complex survival mechanisms, such as self-sufficiency in growth signaling, insensitivity to growth inhibitory signals, evasion of apoptosis, limitless replicative potential, sustained angiogenesis, and tumor invasion and metastasis (Hanahan and Weinberg, 2000). To date, cancer treatments are performed on the basis of clinical and pathologic staging that is determined using morphologic diagnostic tools, such as conventional radiological and histopathological examinations. However, even patients suffering from cancers of the same cellular type and clinical stage respond to the same conventional treatment modalities differently and, ultimately, with variations in survival rate. This implies that cancer-associated events are unique in each patient in the development of nanotherapeutic and imaging approaches to cancer detection and treatment, it is imperative to have a better understanding of the basic principles involved in designing and applying nanoparticles for diagnosis, treatment, or the combination of imaging and therapeutics in different clinical situations.

There are certain critical questions that need to be addressed in the rational design and application of nanoparticles before further clinical development, such as how the association or conjugation of a therapeutic agent to ligand or carrier changes the pharmakinetics, biodistribution, and side effects of the nanotherapeutic drugs; how the safety profile of nanoparticles changed after conjugation, such as coating with QDs; how we can minimize the potential toxicity of polymeric nanoparticles that is inherent from the accumulation of a nonbiodegradable polymer with a size over the renal threshold (Duncan, 2003) and how side effects resulting from the ability of nanoparticles to cross the BBB can be prevented or diminished. These questions are critically important and hitherto understudied. The answers will certainly lead to more rational design of optimized nanoparticles with improved selectivity, efficacy, and safety. Attracted by the rapid and promising progress in nanotechnology, physicists, chemists, engineers, biologists, and clinicians will continue to challenge themselves to develop novel and efficacious nanosystems for the diagnosis and treatment of cancer Ray Haskell,2005; Xuwang et al., 2008)

## Conclusion

The success of a new developed pharmaceutical formulation is related to the fact that it is able to deliver the active substance to the target organ at therapeutically relevant levels, with negligible discomfort and side effects, increasing the patient compliance to the therapeutics. Regarding this respect, the route of administration is of major relevance. Topical administration of active substances offers several attractions compared to traditional routes, e.g. it avoids the hepatic first-pass metabolism, it has the potential of long-term controlled release with avoidance of the topical peak-through plasma profiles associated with frequent dosage regiments,

Several commercial opportunities exist at the intersection of nanotechnology and traditional pharmaceutical R&D. Though several companies are generating revenue today, a large degree of uncertainty remains on exactly what affects the industry will see over time. Nanotechnology is rapidly emerging as an answer to pharmaceutical industry formulation challenges, including (http://www.nanomarkets.net):

·Solubility enhancements
·Reduction of R&D and manufacturing costs
·Quicker time-to-market (TTM) for new drug candidates
·Greater targeting ability that may allow for lower dosing requirements, potentially lessened side effects, and perhaps an answer to the ever-present customer demand for increased user-friendliness and convenience.

This study would be useful for the researchers working in this field.

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