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# Preparation ,Characterization and Applications of Nanoparticles using Nanotechnology toward Advancing Personalized NanoMedicine

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**ABSTRACT**

*Nanotechnology offers many potential benefits to medical research by making pharmaceuticals more efficacious and by decreasing their adverse side-effects. Preclinical characterization of nanoparticles intended for medical applications is complicated – due to the variety of materials used, their unique surface properties and multifunctional nature. Prior to an involved discussion of protocols for nanotechnology, a definition of terms is in order. The SI prefix "nano" means a billionth ($10^{-9}$) part, and a nanometer is thus a billionth of a meter (about one hundred thousandth the thickness of a sheet of paper). An object is nanoscale, then, when it is of a size convenient to measure in nanometers – generally less in size than a micron. The nanoscale is also the size scale at which the properties of a material are often different than they are for the bulk (or "macroscale") phase. For many materials, this is approximately in the 1–300 nm size range. In this size range, properties change because as things become very small, their surfaces shrink more slowly than their volumes, causing nanoscale materials ("nanomaterials") to have far larger surface-to-volume ratios than larger objects. More surface area can mean that nanomaterials have higher reactivity; different elastic, tensile, and magnetic properties; increased conductivity; or increased tendency to reflect and refract light.*

*The Food and Drug Administration (FDA) and pharmaceutical industry have used standards to assess material biocompatibility, immunotoxicity, purity, and sterility (as well as many other properties) for several decades. Nanotechnology offers the potential to significantly transform diagnostics and therapeutics. The ability to manipulate the biological and physicochemical properties at the macromolecular size-scale allows for efficient drug targeting and delivery, which result in greater potency and decreased adverse side effects. Nanoparticles intended for clinical applications consist of a wide variety of materials, for which preclinical characterization is particularly challenging.*

*Most nanoparticle formulations include surfactants to promote dispersion (i.e., prevent agglomeration) of the primary particles. These compounds too can interfere with conventional characterization methods. Impurities and contaminants which adsorb to nanoparticle surfaces can also contribute to ambiguous analytical results. These difficulties tend to hamper the development of standards for characterization and the subsequent clinical application of nanoparticles.*

*A rational characterization strategy for biomedical nanoparticles contains three elements: physicochemical characterization, in vitro assays, and in vivo studies. Each of these is essential to a comprehensive understanding of nanoparticle safety and efficacy.*

*In spite of these difficulties Development of nanoparticles for drug delivery has progressed by leaps and bounds over the last few decades, facilitating the possibility of an efficacious therapy for some fatal diseases. This development has stemmed from either the unsuitable physicochemical characteristics of the existing drug molecules, such as limited solubility and hence poor bioavailability, or the inadequacy of the conventional delivery systems to provide safe and efficient delivery. So nanoscale materials (NSMs) are gaining attention due to their small size*

*and unique physiochemical properties.*

**Keywords: Nanoparticles, Nanoemulsions, Nanocrystals, Nanoprecipitation,Gene Delivery, Brain Delivery, Ocular Drug Delivery , Tumor-Targeted ,Dynamic light scattering, TEM, SEM, Zeta potential, Media milling, Morphology, EPR effect, Mycoplasma , Microbial contamination, Immunological potential , Toxicity**

## 1. INTRODUCTION

The last decade of drug delivery research has witnessed a boom in the development of the nano-drug delivery systems. The major drivers responsible for the initiation of this new revolution were the development of a plethora of varied nano-drug delivery systems, not only by the academic institutions but also by industrial organizations. This led to the availability of a huge database comprising several research papers and patents from all over world, describing these new dosage forms. Numerous funding agencies and industries actively promoted research into nanoparticulate drug delivery vehicles and huge investments were made to this end. All these diverse and concurrent efforts created an awareness about the immense potential of these new drug delivery systems, which were then looked upon as therapeutic regimens of the future.

There are many reasons behind the development and success of nanoparticulate drug delivery systems. A few years ago, the entire attention of pharmaceutical industry was focused on the novel developments in designing various dosage forms, primarily due to expiry of the existing patents, a surfeit of poorly soluble drug candidates and the problems of non-specificity from conventional dosage forms. Under these circumstances, the development of nanoparticulate drug delivery systems gained huge momentum due to a number of diverse factors listed in the following section.

The pharmaceutical industries were poised to provide quality products to the patient, at the same time increasing or maintaining their profitability. However, this process demanded extensive scientific innovation and financial support [1].

Research progress in the drug discovery area resulted in the development of various poorly soluble drug candidates. The solubility limitations of these drug candidates, in turn, lead to poor bioavailability and lower therapeutic efficacy [2, 3]. In such situations, formulation of these therapeutic molecules into nanoparticulate delivery systems was observed to improve their bioavailability and hence elicit the desired therapeutic effects from these candidates. The nanoparticles also received a prominence due to other probable benefi ts like biodegradability, biocompatibility, high encapsulation characteristics and probability of surface functionalization [1–3].

Nanoparticles were found to exhibit several advantages for parenteral drug delivery; counter to the aggregation phenomenon commonly observed with microparticles, the smaller size of nanoparticles endowed them with better distribution profiles during systemic administration. Nanoparticles enabled an effective systemic circulation, thus leading to better therapeutic outcomes. Better systemic circulation was found to be specifically important for cancer therapies, where nanoparticles could infiltrate through the vasculature of tumor tissue and provide targeted therapeutic effects [4].

First pass metabolism is one of the key concerns for many commercial and upcoming drugs. This phenomenon accounts for their low bioavailability and reduced efficacy at the site of action. In this regard, nanoparticulate drug delivery vehicles were particularly advantageous because of their likelihood in being modulated for site specific delivery/targeted delivery. Apart from their specificity, nanoparticles were also found to mitigate drug related side effects and dose related toxicities, resulting in enhanced bioavailability of the encapsulated agent and excellent patient compliance [1, 3, 5].

Owing to their small size, nanoparticles were found to effectively traverse many biological barriers. Of significant importance is their ability to permeate the blood brain barrier (BBB). Although brain administration is an effective route for the treatment of various brain diseases, it is severely limited due to the highly impermeable nature of the BBB. Because of their potential to cross this barrier, numerous publications have demonstrated the effectiveness of nanoparticles for targeting various central nervous system disorders [6]. Nanospectra Bioscience, Texas, USA, has initiated a clinical trial of nanoparticle based ‘nanoshells’ for the treatment of brain tumors [7].