Nanostructures in Therapeutic Medicine Series

Nanostructures for Drug Delivery

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Foreword of the Series

Material science and engineering at the nanoscale has brought revolutionary advances to the biomedical sciences, overturning many of the traditionally known approaches. Nanotechnology has driven many of the most successful innovative technologies, and the impressive record of accomplishments in the field make nanostructures promising candidates for medical therapy applications. The advantages that nanomaterials have already provided to therapeutics, such as targeted and controlled delivery, wide accessibility, high specificity, low side effects, improved efficiency, and impressive versatility are currently considered key elements in designing personalized medicine approaches for prophylaxis, diagnosis, and therapy.

Therapeutic nanostructures can be greatly diverse, and their unique properties have led to the development of highly specialized biosensors, more efficient drug delivery vehicles, and controlled release targeting systems to fight severe or incurable diseases, such as cancer, infections, and cardiovascular disease.

In view of the astounding progress made in the field of therapeutic nanotechnology and its rapidly progressing expansion, this book aims to collect in one place all the recent and most innovative aspects of nanomaterials in both current and future therapy. The series is organized into five volumes, covering the main areas that are relevant for the design and implementation of nanostructures in medical therapies.

The first volume, *Nanostructures for Novel Therapy: Synthesis, Characterization, and Applications*, describes methods to obtain and characterize nanosystems, emphasizing their biomedical applications. Special attention is paid in this volume to modern synthesis methods to reduce side effects and limit the toxicity of nanomaterials in biomedical applications. Numerous examples of nanostructures designed for therapy, as well as the most efficient synthesis and characterization routes for these materials, are clearly described and critically analyzed.

The second volume, entitled *Nanostructures for Drug Delivery*, covers one of the most widely utilized and investigated applications of nanomaterials in the biomedical field, namely, drug delivery. Designing nanostructures to specifically and safely carry therapeutic agents to their final destination is an intriguing approach to future targeted therapies. This approach could provide a treatment for previously incurable diseases, as well as reducing the side effects of current drugs. Many highly active drugs are severely limited by side effects related to their unspecific sites of action. This volume introduces the readers to the amazing field of nanomedicine by discussing the versatility and variety of nanovehicles for drug delivery and targeting. Moreover, readers will find numerous examples and will learn about the currently used or investigational drug delivery agents for therapy, prophylaxis, and diagnosis.

Volume 3, *Nanostructures for Antimicrobial Therapy*, highlights the impressive progress made by nanotechnology in the design of novel antimicrobial approaches. Since microbial resistance to antibiotics is a real and increasingly worrying issue across all countries, the development of more efficient antimicrobial agents to provide control of future infections is at a high priority. Antimicrobial nanosystems have proved to be remarkably efficient against drug-resistant microorganisms, plus they are able to fight biofilm-associated infections and can control the social behavior of microbial communities. Nanostructures can also reduce microbial virulence factors and reduce pathogenesis mechanisms, offering a promising alternative for future therapy.

Volume 4, entitled *Nanostructures for Cancer Therapy*, covers the applications of nanomedicine in cancer diagnosis and treatment. The use of nanoparticles for cancer therapy is not in itself a new approach, but numerous recent advances have been made in this area. The aim of this volume is to cover the most interesting new approaches in the management of this deadly disease. Nanosized drugs are currently believed to represent the most efficient approach in cancer chemotherapy, and this volume provides coverage of the latest and most novel findings, while also discussing possible improvements in more established types of nanosystems that can increase the efficiency of cancer therapy.

The final volume of this series, entitled *Nanostructures for Oral Medicine*, covers the progress made in applications of nanotechnology in treating various diseases of the oral cavity as well as progress in nanotechnology applications in dentistry. Readers can learn about the most efficient modern materials used to treat or to prevent widely encountered oral diseases such as gingivitis, periodontitis, caries, and dental plaque. Moreover, restorative dentistry also now makes wide use of nanomaterials.

Overall, this book series provides a state-of-the-art compendium of knowledge, and a crystal ball for seeing into the future of biomedical nanotechology and nanomedicine. It has appeal for researchers, clinicians, engineers, pharmacologists, pharmacists, oncologists, infectious disease experts, and dentists. In addition, interested general readers will discover the impact, current progress, and future applications of nanotechnology in therapeutics and diagnosis. Taken together, nanoscale approaches will improve the efficiency of personalized medicine for better management of diseases in the 21st century.

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Preface

ABOUT THE SERIES (VOLUMES I–V)

In our permanently changing world, novel therapeutics are constantly required to manage health and well-being of population. Although numerous diseases are currently considered incurable, massive progress made in biomedicine but also in associated fields, such as chemistry, physics, engineering, pharmacology and materials science, offers a new light to the therapeutics domain. In this context, most physicists and researchers believe that a personalized and adequate treatment may significantly improve the outcome of severe diseases and ensure a faster healing. Nanotechnology offers great perspectives for personalized medicine because nanostructured therapeutics proved their efficiency and amazing impact in improving therapy, prophylaxis, and diagnosis. The emerging field of nanosized materials has numerous applications in the biomedical field, especially in therapy. This series of five volumes came out by the need of learning about recent progress of the science of nanostructured materials to improve current therapy and lead to the next level. The books offer an interesting and updated perspective regarding applications of nanomaterials in therapy of most investigated and difficult-to-treat diseases, such as cancer and severe infections. The presentation approach of each chapter contained in those five volumes is clear and easy to understand by most readers and of a great interest for biomedical specialists, researchers, and engineers. The series is organized in an attractive manner for students and academics on the field, starting with a volume dealing with synthesis, characterization, and main applications of nanostructures, emphasizing on their impact in therapy. Next volume reveals the most recent progress made on a very investigated field, considered a key element in personalized medicine and future therapy, namely nanostructured drug delivery systems. Their impact in antimicrobial therapy is also widely discussed, and suggestive examples are given and explained. Moreover, a whole volume is dedicated to the management of the disease of the century—cancer—revealing the huge value added by the utilization of nanosystems in the therapy of this deadly disease. Important aspects related to improved diagnosis and prophylaxis are highlighted. In the last volume, the progress and novel applications of nanotechnology in oral medicine is dissected. The field of oral diseases represents an interesting and a priority field because both physicists and researchers believe that they can be prevented and treated more easily with targeting systems and nanofunctional prosthetics. All chapters are clearly illustrated to highlight most important or difficult-to-understand aspects, and suggestive examples are often enumerated in organized tables, which are explained and discussed. Overall, the series contains very recent but accessible and very interesting information regarding the progress of nanostructures in therapeutics and gives a novel perspective about future therapy of severe diseases.

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ABOUT VOLUME II

The second volume of the series *Therapeutic Nanostructures* is entitled *Nanostructures for Drug Delivery*. This volume reveals the main types of nanosized drug delivery systems, dissecting their main advantages and drawbacks in the therapy of severe and difficult-to-treat diseases. Nanosized carriers are commented in all stages of their preparation and use, starting with suitable synthesis methods, appropriate characterization, and functionalization, and ending with their application in drug delivery and therapy. A special attention is given to green nanotechnology which enables the production of natural, biocompatible and less toxic nanosystems which may be efficiently used in delivering pharmacological agents. Numerous properties of such drug delivery systems are highly appreciated for future therapy, namely longtime circulation in the bloodstream, target specificity, stimuli responsively, possibility of intracellular delivery, contrast functionality, and increased stability. Different ways for the control of the load capacity and release profile are also analyzed in many of the chapters.

Volume II contains 30 chapters, prepared by outstanding researchers affiliated in the USA, Canada, Argentina, Ireland, Italy, New Zealand, Poland, Serbia, Romania, Russia, Turkey, Egypt, Iran, Pakistan, India, and China.

In Chapter 1, entitled *Therapeutic Nanomaterials: From a Drug Delivery Perspective*, C. Ganesh Kumar et al. focus on the synthetic routes and applications of nanomaterials as potential drug delivery agents. Different nanomaterial types including polymeric nanomaterials, dendrimers, nanoparticles, carbon nanotubes, quantum dots, and their applications have been discussed and a number of case studies have been presented in this chapter.

Nily Dan, in Chapter 2, entitled *Core–Shell Drug Carriers: Liposomes, Polymerosomes, and Niosomes*, reveals the three types of main formulations used as drug nanocarriers and summarizes studies of their performance in biomedical applications such as cancer therapy (tumor targeting) or transport through the blood–brain barrier.

Chapter 3, entitled *The New Nanocarriers Based on Graphene and Graphene Oxide for Drug Delivery Applications*, prepared by Somayeh Mohamadi and Mehrdad Hamidi, gives an overview about a new carbon-based carrier for drug delivery applications. The unique properties of graphene nanosheets such as two-dimensional planar structure with sp^2 hybridation, large surface area, chemical and mechanical stability, super conductivity, and good biocompatibility provide the opportunity to design drug carriers with dual-targeting function.

In Chapter 4, entitled *Nanostructured Nanoparticles for Improved Drug Delivery*, Jean Michel Rabanel et al. provide a comprehensive view of the different types of structures found in nanoparticles intended for medical use reported so far in the literature, together with some insight regarding their fabrication processes and their physicochemical properties and how this nanoparticles deliver active compounds in a controlled fashion to the human body or developed imaging strategies.

Chapter 5, entitled *Design of Functionalized Materials for Use in Micro and Nanoscale Drug Delivery Devices and Smart Patches*, prepared by Ashleigh Anderson and James Davis, provides a critical overview of the latest developments in functional materials and nanoscale device architectures that can facilitate controlled drug delivery.

Chapter 6, entitled *Niosomes: A Novel Approach in Modern Drug Delivery Systems*, prepared by Sepideh Khoee and Morteza Yaghoobian, discusses about new drug delivery vehicles and gives a brief description on the preparation, applications, advantages and disadvantages of particular delivery system—niosomes.

Fatemeh Zamani et al., in Chapter 7, entitled *Nanofibrous and Nanoparticle Materials as Drug-Delivery Systems*, emphasize on the emerging area of nanoparticles synthesis through electrospinning technique to generate biomimetic nanofibers and nanoparticles as drug delivery devices that are responsive to different stimuli, such as temperature, pH, light, and the electric/magnetic field for controlled release of therapeutic substances.

Yun Yu et al., in Chapter 8, entitled *Brush Polymer-Based Nanostructures for Drug Delivery*, give an overview on the advantages of brush polymer (BP)-based drug delivery systems. Also, future research directions of BP-based drug delivery systems are highlighted.

Magdalena Jarosz et al., in Chapter 9, entitled *Drug Delivery Systems Based on Titania Nanostructures*, focus on different titanium (TiO_2) nanostructures used as drug delivery systems, such as nanotubular and nanoporous TiO_2, TiO_2 nanoparticles, and nanowhiskers.

Houman Alimoradi et al., in Chapter 10, entitled *Redox Activated Polymeric Nanoparticles in Tumor Therapy*, focus on the biochemical basis for oxidative stress in tumors, its role in cell-signaling, the pathophysiology of tumor vasculature, and the differences in the redox-metabolism between cancer cells and nonmalignant tissues. The recent developments toward designing redox responsive drug delivery systems which have been classified as polysulfide, polyselenide, quinones, metal complexes, arylboronic esters, aryl oxalate, and other miscellaneous examples are also discussed.

Chapter 11, entitled *Polymeric Micro- and Nanoparticles for Controlled and Targeted Drug Delivery*, prepared by Magdalena Stevanović, reports the production and applications of polymeric micro- and nanoparticles with a special emphasis on obtaining polyester particles, the incorporation of different active substances within polymer matrix, the degradation and release process of active substances from the polymeric particles, the physiochemical and biological properties of such obtained systems, as well as their application as drug delivery systems.

Chapter 12, entitled *Novel Gels: Implications for Drug Delivery*, prepared by Swarnali D. Paul et al., describes all the emerging prospects of novel gels along with their formulation aspects, manufacturing technologies, and current applications, focusing on therapeutic potential.

Chapter 13, entitled *Nanosuspension Drug Delivery System: Preparation, Characterization, Post-production Processing, Dosage Form, and Application*, prepared by Jiuhong Zhang et al., gives an overview about nanosuspension drug-delivery system (DDS) discussing preparation methods, characterization methods, postproduction process including the solidification techniques and surface modification process, common dosage forms, and clinical applications of nanosuspension DDS.

Chapter 14, entitled *Polymer-Based Nanocarriers for Therapeutic Nucleic Acids Delivery*, prepared by Weien W. Yuan and Hui H. Li, describes the challenges, advantages, and recent progress of polymer-based nanocarriers for therapeutic nucleic acids delivery. Considerations for manufacturing, safety issues, and regulatory requirements for these novel nanocarriers are also discussed.

Chapter 15, entitled *Multifunctional Therapeutic Hybrid Nanocarriers for Targeted and Triggered Drug Delivery: Recent Trends and Future Prospects*, prepared by Gulbin Kurtay et al., presents new generation and promising hybrid nanocarriers based on noble metal, porous silica, polymer, and core/shell therapeutics which exhibit active targeting, triggered release of cargo, and imaging capability for in vivo studies.

Ragwa M. Farid et al., in Chapter 16, entitled *Lipid-Based Nanocarriers for Ocular Drug Delivery*, give an up-to-date overview about lipid-based nanocarriers that can enhance the corneal absorption of both hydrophilic and lipophilic drugs and improve their ocular bioavailability. Nanostructured lipid carriers (NLCs) and lipid drug conjugates (LDCs) have emerged as a new generation of solid lipid nanoparticles (SLNs) to overcome problems of low entrapment efficiency and drug expulsion during storage.

Rajeev Sharma et al., in Chapter 17, entitled *Nanoparticulate Carrier(s): An Emerging Paradigm in New Generation Vaccine Development*, summarize the cutting edge technologies of nanoparticulate-carrier-based new generation and vaccine development, including design, trials, and clinical outcomes.

Chapter 18, entitled *Pathogen-Specific Nucleic Acid Aptamers as Targeting Components of Antibiotic and Gene Delivery Systems*, prepared by Canan Ozyurt et al., presents an overview of current cell-specific aptamer-conjugated nanoparticles. Also, the authors address two issues: nanoparticle-based antimicrobial gene delivery and modification of nanocarriers with aptamers.

Tamilvanan Shunmugaperumal et al., in Chapter 19, entitled *Multifunctional Nanosized Emulsions for Theragnosis of Life Threatening Diseases*, envision the use of the multifunctional oil-in-water (o/w) nanosized emulsions (NE) that carries imaging agents, anticancer or lipid lowering or antiatherosclerotic drug molecules and homing devices together for simultaneous imaging/diagnosing and treatment of cancer and atherosclerosis. A complete outline is given on the formulation of drug-loaded NE together with active and passive targeting moieties for accessing the unreachable organs present inside the human body.

Chapter 20, entitled *Therapeutic Nanostructures for Pulmonary Drug Delivery*, prepared by Yousef Javadzadeh and Shadi Yaqoubi, discusses about pulmonary drug delivery, inhalers, nanoparticles, and the advantages and fate of inhaled nanoparticles.

Najma Bibi et al., in Chapter 21, entitled *Nanostructures in Transdermal Drug Delivery Systems*, dissect the benefits of transdermal drug delivery over other delivery systems, arguing about the barriers in the skin to be faced by nanomaterials and their permeation pathways. Physicochemical characteristics required for the good penetration of nanostructures are also discussed.

Chapter 22, entitled *Advancement in Pulmonary Drug Delivery Systems for Treatment of Tuberculosis*, prepared by Tarun Garg et al., presents an overview about the importance of pulmonary drug delivery systems such as liposomes, niosomes, nanoparticles, microparticles, dendrimers, solid lipid nanoparticles, micelles, nanosuspensions, nanoemulsions, and microemulsions for an effective treatment of tuberculosis. The advances in delivery devices from conventional metered dose inhalers to dry powder inhalers are also discussed along with their applications.

Chapter 23, entitled *Nanosized Devices as Antibiotics and Antifungals Delivery: Past, News and Outlook*, prepared by Pio M. Furneri et al., discusses about developments in the field of (nanosized) delivery systems encapsulating antibacterial and antifungal drugs. A specific attention has been given to the pharmaceutical, microbiological, and clinical outcomes of systems for which authors have provided in vitro microbiological data and, more hopefully, in vivo results.

Chapter 24, entitled *Drug Delivery Mediated by Confined Nanosystems: Structure-Activity Relations and Factors Responsible for the Efficacy of Formulations*, prepared by Lucia Zakharova et al., presents different ways for the control of the load capacity and release profile. The chapter also discusses about the ability of formulated drug to integrate with cell membrane and penetrate through the blood-brain barrier.

Daniela Alejandra Quinteros et al., in Chapter 25, entitled *Therapeutic Use of Monoclonal Antibodies: General Aspects and Challenges for Drug Delivery*, identified and described the major issues associated with therapeutics approaches, formulating drawbacks, and delivering antibody drugs, particularly focused on the challenges and opportunities that these present for the future.

Chapter 26, entitled *Targeted Drug Delivery Via Chitosan-Coated Magnetic Nanoparticles*, prepared by Gozde Unsoy and Ufuk Gundu, presents an up-to-date review about polymer-coated magnetic nanoparticles, characterized by high surface-to-volume ratios, which are excellent scaffolds for loading targeting moieties, permeation enhancers, imaging tags, and drugs, simultaneously providing diagnostic and therapeutic capabilities.

Narinder Singh et al., in Chapter 27, entitled *Drug Delivery: Advancements and Challenges*, elaborate an updated idea regarding the effect of various drug delivery systems in contrast to their toxicity with a focus on nanocarriers and nanosystems.

Chapter 28, entitled *Stimuli-Responsive Liposome and Control Release Drug*, prepared by Xueqin An and Rijun Gui, presents an up-to-date review about the relative thermal, light, magnetism, and pH stimuli responsive properties of liposomes. Also, the mechanism of controlled drug release is discussed.

Chapter 29, entitled *Nanotechnology to Enhance Transdermal Delivery of Hydrophilic Humectants for Improved Skin Care: A Model for Therapeutic Applications*, prepared by Steven Dominguez et al., presents current status on research and development of some of the most promising agents, including nanotropocollagen and hyaluronic acid, which can serve as models for nanotechnology employed for transcutaneous active pharmaceutical ingredients (APIs) delivery.

Chapter 30, entitled *Nanostructures for Drug Delivery: Pharmacokinetic and Toxicological Aspects*, prepared by Adrian G. Ciucă et al., offers an extensive and updated report of the recent progresses and degree of toxicity that could be generated by a number of new medical therapies, with a great impact on medicine, namely “therapeutic devices” based on nanoparticles.

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CHAPTER

1

THERAPEUTIC NANOMATERIALS: FROM A DRUG DELIVERY PERSPECTIVE

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CHAPTER OUTLINE

1 INTRODUCTION

Nanotechnology is an emerging interdisciplinary field having confluence of various disciplines, such as physics, chemistry, material science and engineering devoted to the construction of structures in the nanometer regime (often 100 nm or smaller) with diverse physical and chemical properties. Although nanoscience and nanotechnology are new research areas, the use of nanomaterials by mankind was known since antiquity. Red colloidal gold tinctures as drugs for longevity, the so-called "Makaradhwaja" and "Jin Tu" were used in India and China, respectively, since ancient times (Hayat, 1989; Mahdihasan, 1985). The use of noble nanomaterials by glassmakers dates back to the Roman Empire, which is evidenced by the exotic Lycurgus Cup of 4th century AD that exhibited dichroic effect due to the presence of colloidal silver and gold particles (Barber and Freestone, 1990). Similar examples exist on the use of noble metallic nanomaterials in stained-glass windows of old European cathedrals and for coloring ceramic vases and ornaments by the Chinese (Burda et al., 2005). In the early 19th century, antibacterial preparations based on colloidal silver, such as Collargol (Argentum Crede) and Protargol (Argenti proteinatum) were marketed in Europe (Kolthoff, 1925). Paul Ehrlich first presented the concept of drug targeting or site-specific drug delivery in 1909. The "magic bullet" concept was put forth by him and his colleagues when they synthesized the first man-made antibiotic, arsphenamine, for the treatment of syphilis. This molecule after some chemical modifications inhibited the pathogens without affecting the host cells and acted as a "magic bullet." Furthermore, he also introduced the concepts, such as chemoreceptor and chemotherapy, and linked the chemical structure of the compound to their pharmacological activity (Bosch and Rosich, 2008).

In 2004, the concept of nanomedicine was put forth by the European Science Foundation, which represents a new area in the field of drug delivery research (Reis et al., 2007). A significant attention has been focused on the potentials of nanoscience and nanotechnology in drug delivery because they offer site-specific, time-controlled delivery of different molecular weight drugs and other bioactive molecules. The concept of drug delivery as a noninvasive system has recently emerged as a highly competitive and fast developing technology for treating medical infections and diseases. In this context, the nanomediated drug delivery systems, such as nanoparticles, dendrimers, carbon nanotubes, quantum dots, and so on are believed to have great potential to develop various drug carrier systems to address the growing burden of new diseases. One of the main challenges in drug delivery is to deliver the drug at the target site in the body to avoid potential side effects to the normal tissue. These nanomaterials can be modified for better efficiency to facilitate a large amount of drugs through nanocarriers, which can eventually reach the inaccessible areas, such as brain tissues, cancer cells, and other infected tissues. According to BCC Research Report (www.bccresearch.com/market-research/pharmaceuticals/advanced-drug-delivery-markets-phm006j.html), the global market for advanced drug delivery systems was valued at $151.3 billion in 2013. It was forecasted that this market value will rise to reach nearly $173.8 billion in 2018 at a 5-year compound annual growth rate of 2.8%. To meet this remarkable global demand, the synthesis of nanomaterials for diverse drug delivery applications has been a burgeoning area of research in the field of nanotechnology. This chapter focuses on the synthetic routes and characterization of various nanobiomaterials, and their drug delivery applications have been reviewed.

2 GENERAL METHODS OF SYNTHESIS OF NANOMATERIALS

Two types of approaches are generally applied for the fabrication of different types of nanomaterials (Fig. 1.1), namely the top–down approach, a process of stable division of bulk material into nanoparticles and the bottom–up approach, in which the nanoparticles are built up from the atomic level to nanolevel through clusters (Fig. 1.2). In top–down approach, the dissolution of metal from its respective bulk material is the basic principle. Several methods adopted in the top–down approach include laser ablation, solvated metal atom dispersion (Lin et al., 1986), high vacuum evaporation (Aiyer et al., 1994), electric arc reduction (Bradley, 1994), and electrochemical reduction (Reetz and Helbig, 1994). The combination of atoms or clusters to form nanoparticles is called bottom–up approach, which has gained popularity in recent years because there is a precise control over size and monodispersity of the nanoparticles (Toshima and Yonezawab, 1998). In this method, different reducing agents, such as

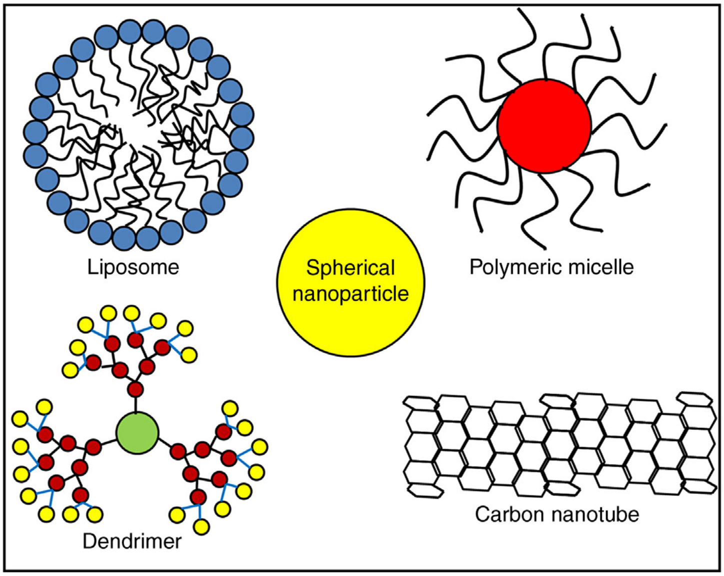

FIGURE 1.1 Different Types of Nanomaterials

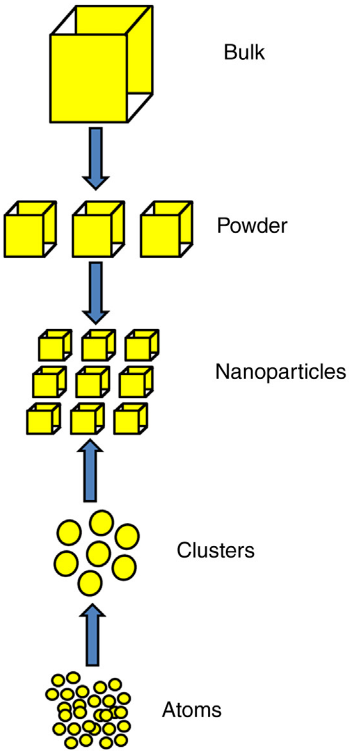

FIGURE 1.2 Top–Down and Bottom–Up Approach for Nanomaterial Synthesis

sodium borohydride, trisodium citrate, tannic acid, hydrazine, ascorbic acid, and tartaric acid were used to reduce the metal ions to form nanoparticles (Cushing et al., 2004). Metal nanoparticles, such as Au, Ag, Pt, Pd, and Rh can be prepared using mild reducing agents under ordinary conditions. The synthetic strategies of nanomaterials integrate both synthesis and assembly into a single method with better control over size, shape, and structure. The size, morphology, stability, and other properties of the nanomaterials are strongly influenced by the experimental conditions, interaction of reducing agents, and stabilizing agents. Therefore, the selection and design of a synthetic route plays a key role for determining the properties, stability, and applications of nanomaterials (Sharma et al., 2009). Currently, the techniques available for the production of nanomaterials essentially fall into three categories, such as physical, chemical, and biological methods.

2.1 PHYSICAL METHODS

A wide range of nanoparticles can be produced using different metals by employing physical methods with minor modifications. Several physical methods, such as sputter deposition, laser ablation or cluster beam deposition, microwave, evaporation–condensation, mechanical milling and pulsed wire discharge (PWD) are employed for the nanomaterial fabrication. Laser ablation and ball milling are the most commonly used methods for the preparation of nanoparticles using different kinds of solvents (Marine et al., 2000). However, the major limitation is that it is very difficult to produce ultrafine particles using these methods. Further, the physical synthetic methods involve costly equipments or vacuum systems for the preparation of nanomaterials. In case of mechanical milling, the main advantages are the simple operation, low cost of production and the possibility to scale up the process to produce large quantities (McCormick and Froes, 1998). Further, the important factors that affect the quality of the nanoparticles include the mill type, milling speed, temperature, time, atmosphere, shape, and size distribution of the grinding medium, weight ratio of ball to powder and the amount required for filling the vial (Suryanarayana, 2001). Sonolysis is also an efficient method for the synthesis of nanomaterials. For example, the iron oxide nanoparticles can be synthesized by decomposition (thermolysis or sonolysis) of organometallic precursors. Very high temperature hot spots generated by the rapid disintegration of sonically generated cavities allows the conversion of ferrous salts into magnetic nanoparticles. In this case, the different polymers, organic stabilizing agents, or structural hosts are used to limit growth of the nanomaterial (Dinega and Bawendi, 1999; Osuna et al., 1996; Puntes et al., 1999, 2002; Verelst et al., 1999). Some of the major advantages of physical methods include the use of no toxic chemicals, it is comparatively fast, lack of solvent contamination and the uniformity of nanomaterial distribution; however, the major disadvantage of these methods is the lesser quantity and poor quality of the nanomaterials produced as compared to chemical methods. These methods are also time-consuming and still under developmental stage.

2.2 CHEMICAL METHODS

Various chemical approaches have been employed for the fabrication of large amounts of nanomaterials within a shorter time period with fairly good control on the size distribution. Using chemical synthetic routes, different shapes of nanomaterials could be achieved by adjusting the concentration of the reacting chemicals and controlling the reaction environment (Murray et al., 2000). For metal nanoparticle synthesis, the most common approach employed is the chemical reduction method, which involves the reduction of an ionic metal salt in an appropriate medium in the presence of reducing agents. Different