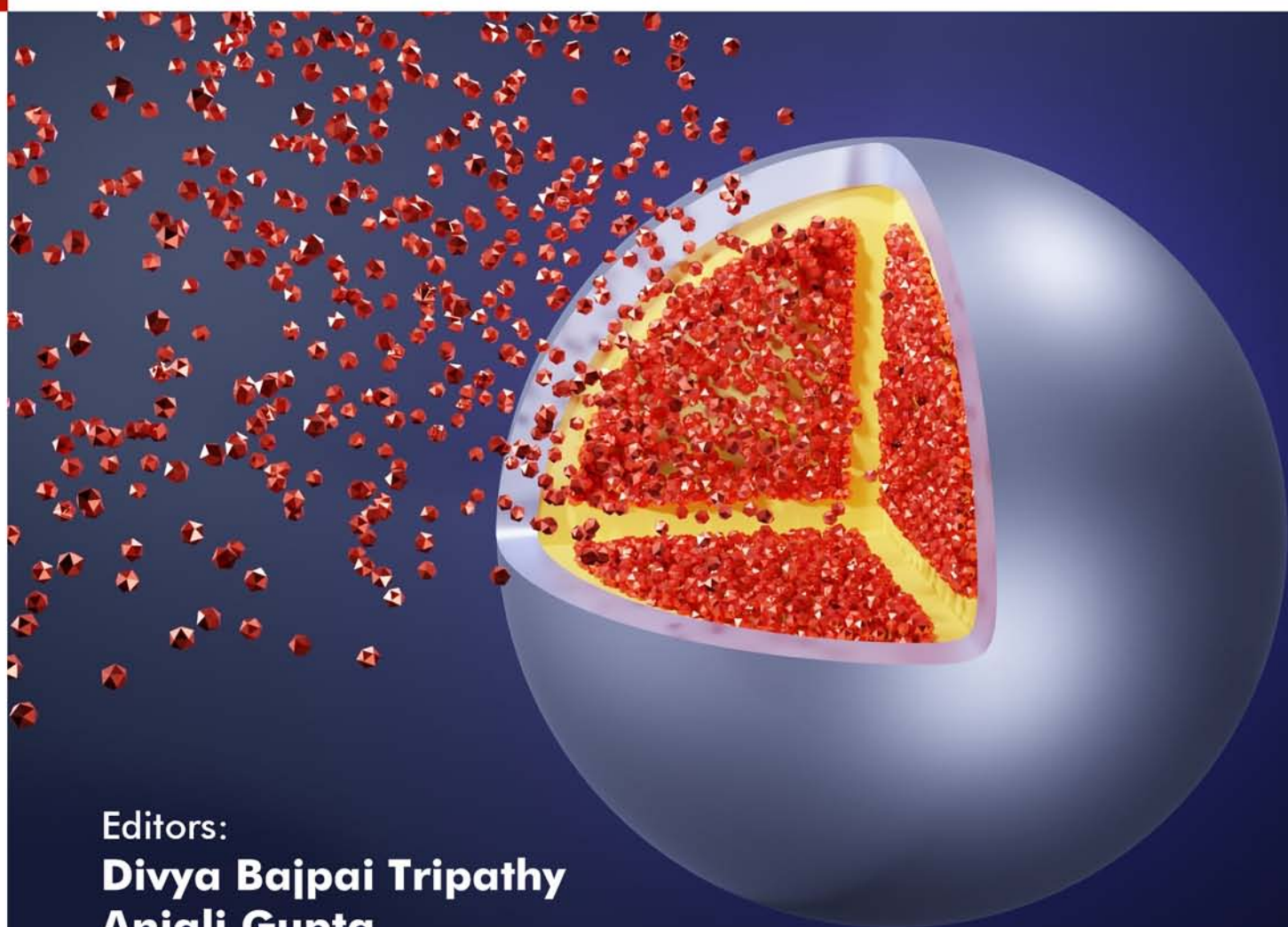


# APPLICATIONS OF NANOPARTICLES IN DRUG DELIVERY AND THERAPEUTICS



Editors:

**Divya Bajpai Tripathy**

**Anjali Gupta**

**Arvind Kumar Jain**

**Pooja Agarwal**

**Bentham Books**

# **Applications of Nanoparticles in Drug Delivery and Therapeutics**

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## PREFACE I

In recent years, the world of medical science has witnessed a remarkable transformation with the integration of nanotechnology into drug delivery and therapeutic applications. This book, titled "Applications of Nanoparticles in Drug Delivery and Therapeutics" stands as a testament to the groundbreaking strides made in this field.

Nanoparticles, as the building blocks of nanotechnology, have revolutionized the way we approach medical diagnostics, drug delivery, and disease treatment. The chapters within this volume delve into an array of captivating topics, each shedding light on the dynamic and diverse landscape of nanotherapeutics.

From novel synthesis methods of nanomaterials for cutting-edge nanodevices in medical diagnostics to exploring the synergistic relationship between nanotechnology and nutraceuticals, the chapters provide an insightful journey into the ever-evolving realm of nanomedicine. The concept of enzyme-responsive nanoparticles opens new doors for targeted drug delivery, enhancing therapeutic precision while minimizing side effects.

Cancer treatment, one of the most challenging fronts in modern medicine, benefits immensely from nanotherapeutics. The book's exploration of the application of nanoparticles in cancer treatment underscores the potential to revolutionize how we combat this formidable disease. Similarly, the chapters addressing HIV and Alzheimer's disease reflect the wide-reaching implications of nanotechnology, even in areas once considered insurmountable.

Beyond the confines of traditional medicine, the application of nanotherapeutics in skin therapy showcases the aesthetic dimensions of this technology, amplifying its impact on enhancing the well-being and confidence of individuals. Moreover, the discussions on the economical and environmental aspects of nanomaterials highlight the responsible and sustainable journey of these innovations from laboratory marvels to real-world industry solutions.

"Applications of Nanoparticles in Drug Delivery and Therapeutics" stands as a testament to human ingenuity and collaborative effort, a guiding light illuminating the path toward a healthier future. As the book delves into the patent landscape of nanotechnology in healthcare, it becomes evident that the rapid progress in this field is not only transformative but also holds potential for significant intellectual property development.

This compilation serves as a vital resource for researchers, practitioners, and enthusiasts alike, offering a glimpse into the remarkable strides made in harnessing the power of nanoparticles for the betterment of human health and well-being.

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## PREFACE II

In the rapidly evolving landscape of modern medicine, the convergence of nanotechnology and pharmaceutical sciences has given rise to a revolutionary paradigm in drug delivery and therapeutic interventions. The utilization of nanoparticles, with their unique physicochemical properties and versatile applications, has opened up new avenues for addressing complex healthcare challenges. This book, "Applications of Nanoparticles in Drug Delivery and Therapeutics", endeavors to provide a comprehensive exploration of the diverse and dynamic field of nanotherapeutics.

The chapters presented within this volume offer an in-depth analysis of how nanoparticles are being harnessed to revolutionize various aspects of healthcare, ranging from antibacterial and antiviral interventions to targeted cancer treatments. Each chapter delves into a specific application of nanotechnology, highlighting the innovative strategies, methodologies, and breakthroughs that are propelling the field forward.

In Chapter 1, "Nanotherapeutics as Antibacterial and Antiviral Agents: Approach Beyond Antibiotics", we venture beyond conventional antibiotics, showcasing how nanoparticles are redefining the fight against microbial threats.

Chapter 2, "Novel Approaches for the Synthesis of Nanomaterials for Nanodevices in Medical Diagnostics", explores the cutting-edge techniques employed in the creation of nanomaterials tailored for diagnostic purposes, underscoring their potential to revolutionize medical diagnostics.

Chapter 3, "Application of Nanotechnology in Nutraceuticals and Functional Foods", uncovers the intersection of nanotechnology and nutrition, revealing how nanoparticles are enhancing the bioavailability and therapeutic potential of nutraceuticals. The concept of enzyme-responsive nanoparticles is the focus of Chapter 4, elucidating their pivotal role in intelligent drug delivery systems that respond to specific biochemical cues.

In Chapter 5, "Application of Nanotherapeutics in Cancer Treatment", the spotlight shifts to oncology, where nanoparticles are emerging as potent tools for precise cancer targeting and therapy.

Chapter 6, "Anti-HIV Nanotherapeutics and their Challenges in the Future", takes on the formidable challenge of combatting HIV, exploring the promises and hurdles associated with nanotechnology-based HIV interventions.

The ongoing battle against Alzheimer's Disease takes center stage in Chapter 7, "Current Perspectives of Nanotherapeutics for the Treatment of Alzheimer's Disease", revealing how nanoparticles may offer novel avenues for therapeutic intervention.

Chapter 8, "Nanotherapeutics in Skin Therapy", turns attention to dermatology, showcasing the transformative potential of nanoparticles in skincare and dermatological treatments.

The socioeconomic dimensions of nanomaterials find their place in Chapter 9, "Economical and Environmental Aspects of Nanomaterials: Journey of Sustainable and Cost-Effective Nanoparticles from Lab to Industry", where we explore the transition of nanotherapeutics from research laboratories to industrial applications, considering both economic viability and environmental sustainability.

Finally, Chapter 10, "Patent Landscape of Nanotechnology in Healthcare", offers a comprehensive overview of the patent landscape surrounding nanotechnology applications in healthcare, shedding light on the innovations and intellectual property shaping the field.

Collectively, these chapters endeavor to provide a panoramic view of the multifaceted landscape of nanoparticle applications in drug delivery and therapeutics. They celebrate the strides made thus far while also acknowledging the challenges that lie ahead. As we embark on this journey through the realm of nanotherapeutics, we invite readers to explore the potential of these minuscule agents to effect monumental changes in the way we approach and conquer complex medical challenges.

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## CHAPTER 1

# Nanotherapeutics as Antibacterial and Antiviral Agents: Approach beyond Antibiotics

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**Abstract:** The field of nanotherapeutics has evolved over the last few decades, and the scientific community has become increasingly interested in exploring and developing versatile biomaterial nanosystems for clinical medicine. Antimicrobials, despite their many advances, have been plagued by an ever-growing problem of antimicrobial resistance. This threat has been labeled the “post-antibiotic era” by the WHO and other organizations. Nanoparticles (NPs)-based therapeutics have recently emerged as new tools for combating deadly bacterial infections. Traditional antimicrobials face challenges, such as antibiotic resistance, which nanoparticle-based strategies can overcome. This chapter discusses various nanotherapeutics and their essential roles in antimicrobial therapy. This book chapter delves into the burgeoning field of nanotherapeutics, focusing on their potential as innovative solutions to combat bacterial and viral infections. With the escalating threat of antimicrobial resistance and the ongoing challenge of emerging viral pathogens, traditional treatment modalities are increasingly inadequate. Nanotechnology offers a promising avenue for the development of novel antibacterial and antiviral agents, presenting unique advantages such as enhanced drug delivery, improved bioavailability, and targeted action. The chapter provides an overview of the mechanisms by which nanotherapeutics exert their antimicrobial effects, including direct disruption of bacterial and viral structures, inhibition of essential cellular processes, and modulation of host immune responses. Various types of nanoparticles, such as liposomes, polymeric nanoparticles, and metallic nanoparticles, are explored for their ability to encapsulate and deliver antimicrobial agents to target sites with precision. Furthermore, the chapter discusses the potential applications of nanotherapeutics in addressing key challenges associated with conventional antibiotics and antiviral drugs, including drug resistance, adverse effects, and limited efficacy. By leveraging the unique physicochemical properties of nanoparticles, researchers aim to develop therapeutic strategies that minimize off-target effects, reduce the likelihood of resistance development, and enhance patient outcomes.

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Despite the promising advancements in nanotherapeutics, several hurdles remain on the path to clinical translation, including standardization of manufacturing processes, evaluation of safety profiles, and regulatory approval. The chapter underscores the importance of interdisciplinary collaboration among scientists, clinicians, and regulatory agencies to overcome these challenges and realize the full potential of nanotherapeutics in clinical practice.

**Keywords:** Nanotherapeutics, antimicrobial resistance, biomaterial nanosystems, antibacterials, antivirals.

## 1. INTRODUCTION

Nanomedicine utilizes engineered nanomaterials and nanostructures for highly targeted medical intervention at the molecular scale. It includes the design, development, regulation, and application of nanotherapeutics, drugs, and devices based on nanoparticles typically under 100nm in size. Nanotherapeutics provide opportunities to enhance the safety, efficacy, and delivery of conventional therapies. Nanoparticles themselves can serve as therapeutic agents through properties such as the generation of reactive oxygen species. Photodynamic therapy uses light-activated nanoparticle photosensitizers for targeted cancer cell destruction [1].

Nanotherapeutics offer novel opportunities to improve the safety and efficacy of conventional treatments. Nanoparticles themselves can be used as therapeutic agents. Metal nanoparticles have prompted research on nanotherapeutic prospects through covalent bonding with biological molecules such as peptides, proteins, and antibodies. Amphiphilic polymer nanoaggregates also have selective antimicrobial effects and can enable on-demand antibiotic delivery or reinvigorate outdated antibiotics. Polymeric nanoparticles can deliver intracellular antibiotics to sites that are otherwise inaccessible, such as macrophages. For antiviral applications, the nanomaterial design is tailored based

on the delivery route. Vascular permeability or ligand functionalization determines their targeting mechanism. Nanomaterials have the potential to boost existing antiretrovirals by preventing nonspecific interactions and reducing toxicity.

## 2. FORMULATION OF NANOTHERAPEUTICS

Nanotherapeutic formulations offer promising opportunities to combat bacterial infections using novel delivery mechanisms. Nanotherapeutic formulations utilize various nanomaterials, including liposomes, polymers, proteins, drug nanocrystals, and inorganic nanoparticles. These nanomaterials facilitate innovative

drug delivery systems with enhanced safety, efficacy, and stability compared to conventional formulations.

For treating bacterial infections, nanotherapeutics can simultaneously target pathogen invasion and host immune response pathways. This dual targeting approach creates opportunities to develop new treatments that can overcome antimicrobial resistance. The versatility of nanoparticle-based delivery systems offers tremendous potential for transforming the treatment of bacterial infections if clinical translation challenges can be overcome through further research [2 - 5].

### 3. CLASSIFICATION OF NANOTHERAPEUTICS

Nanotherapeutics can be classified according to their constituents (Fig. 1). The classification highlights the diverse types of nanotherapeutics on the basis of their composition, therapeutic applications, and mechanisms of action. The field of nanotherapeutics continues to evolve, with ongoing research and development aimed at improving drug delivery, enhancing therapeutic efficacy, and addressing challenges related to safety and regulatory guidelines.

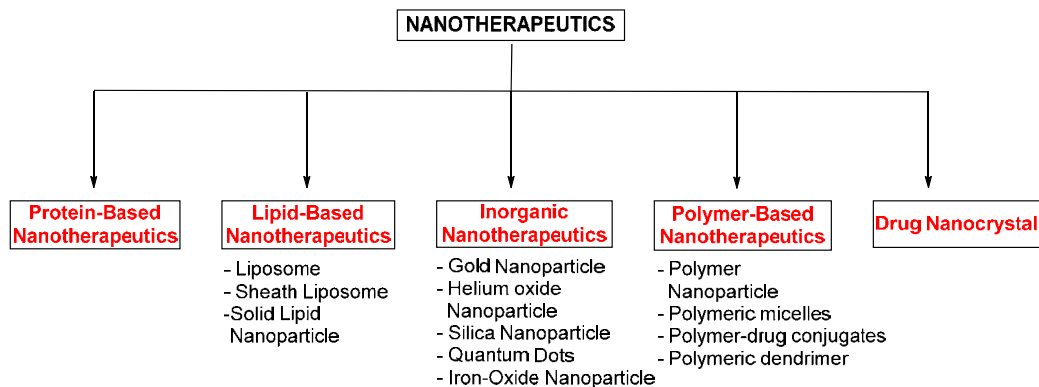


Fig. (1). Classification of nanotherapeutics.

#### 3.1. Protein-Based Nanotherapeutics

Many industries and the food industry have long relied on protein-based nanoparticles. Jeong and colleagues reported near-infrared (NIR) light-responsive vanadium-doped adhesive proteinic nanoparticles (NP) as multimodal cancer nanotherapeutics with enhanced therapeutic efficacy and high specificity [6].

Numerous emerging nanotechnology-based interventions, such as antiviral nanoparticles and nanoparticle-based DNA and mRNA vaccines, have become crucial in the fight against fatal severe acute respiratory syndrome coronavirus 2

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**CHAPTER 2**

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**Novel Approaches for the Synthesis of Nanomaterials for Nanodevices in Medical Diagnostics****Nidhi Puri<sup>1,\*</sup>**<sup>1</sup> *IILM University, Greater Noida, Uttar Pradesh, India*

**Abstract:** In recent years, the field of nanotechnology has witnessed significant advancements in the synthesis of nanomaterials tailored for applications in medical diagnostics. Nanodevices, characterized by their miniature size and exceptional properties, hold tremendous potential for revolutionizing healthcare by enabling rapid and precise diagnosis of various diseases. This chapter provides an overview of innovative strategies employed in the synthesis of nanomaterials specifically designed for integration into nanodevices for medical diagnostics. The synthesis of nanomaterials for nanodevices necessitates the development of precise and reproducible methods capable of producing materials with desired properties such as size, shape, composition, and surface functionalization. Traditional synthesis techniques, including chemical vapor deposition, sol-gel processes, and physical vapor deposition, have been augmented by novel approaches leveraging principles from chemistry, physics, and materials science. One such approach is bottom-up synthesis, which involves the self-assembly of atoms or molecules into nanoscale structures, enabling precise control over size and morphology. Techniques such as molecular beam epitaxy (MBE) and atomic layer deposition (ALD) offer atomic-level precision, facilitating the fabrication of nanomaterials with tailored properties for specific diagnostic applications. Additionally, advancements in nanomaterial synthesis have been driven by the emergence of green synthesis methods, which utilize natural sources such as plants, microbes, and biomolecules to produce nanomaterials with minimal environmental impact. Green synthesis techniques not only offer a sustainable alternative to conventional methods but also afford opportunities for the development of biocompatible and biofunctionalized nanomaterials suitable for biomedical applications. Furthermore, the integration of nanomaterials into functional nanodevices requires precise control over material properties to ensure compatibility with diagnostic platforms. Surface modification techniques, including functionalization with biomolecules, polymers, and ligands, play a crucial role in enhancing the stability, biocompatibility, and targeting capabilities of nanomaterials for diagnostic applications. The chapter also discusses recent advancements in the synthesis of multifunctional nanomaterials capable of simultaneous detection, imaging, and therapy, offering integrated solutions for personalized medicine and point-of-care diagnostics.

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By harnessing the synergistic properties of nanomaterials, researchers are developing next-generation nanodevices capable of revolutionizing medical diagnostics by providing rapid, sensitive, and cost-effective solutions for disease detection and monitoring.

**Keywords:** Medical diagnostics, Nanomaterials, Nanodevices, Nanotechnology, Pharmaceuticals.

## 1. INTRODUCTION

Global healthcare is required for a healthy and disease-free human life on our planet Earth. Individual medicinal therapy and precise treatment for particular diseases are the normal trend of pharmaceuticals. However, the scientific community has shifted its interest from traditional procedures to the smart pharmaceuticals' treatment of chronic or non-communicable diseases. Nanoscience, being the most booming field, covers almost every scientific and engineering discipline for improving human life. The potential applications of nanomaterials (ranging from 1 to 100 nm in dimension) can be seen in diverse fields of physics, chemistry, medicine, biology, and computer science. The last two decades have witnessed significant scientific research on the applications of nanomaterials in biomedical fields. Hence, new processes, nanodevices and nanomaterials have come into the picture to support disease remedies for patient benefit.

Nanomaterials help in identifying the problem in the biological system *via* biosensors and then in rectifying it by being the carrier for providing a cure to the target specific location in the human body. The wide-ranging and advanced applications of nanomaterials in diagnostics and therapeutics help in enlightening their special role in disease-free human life [1]. The novel and unique characteristics of nanomaterials, such as high surface area to volume ratios because of their ultra-small sizes, enhanced mechanical properties, tunable optical emissions, and superparamagnetic behaviors, make them extraordinary in various scientific applications [2]. The nanomaterials made up of organic or inorganic material or their nano-composites also include nanoparticles (NPs), nanopores, nanorods, nanowires, nanoribbons, nanotubes (NTs), nanoscaffolds, and nanopatterns. The higher selectivity, sensitivity, and cost-effectiveness are some of the main reasons behind their potential usage in the rapid diagnosis with the latest clinical imaging technologies such as computer tomography, MRI, and ultrasound for non-communicable diseases in humans as well as animals. The nanoscale materials are very useful in the fabrication of the latest pharmaceutical nanodevices, such as defibrillators, pacemakers, SPO2 pulse oximeters, and ECG monitors [3, 4]. In this chapter, the various emerging techniques for the synthesis

of nanoscale materials for nanodevice formations are broadly covered. The ongoing mechanisms are also discussed comprehensively to give a vibrant picture of diverse, innovative research models in the emerging field of medical diagnostics.

## 2. APPROACHES FOR THE PRODUCTION OF NANOMATERIALS

Nanomaterials are very useful in different scientific fields. These nanomaterials can be formed by using two different approaches named top-down and bottom-up approaches. These approaches are schematically shown in Fig. (1). In both approaches, the bulk material is converted into nanoparticles, and then different methods of synthesis are used for further nanomaterial formation.

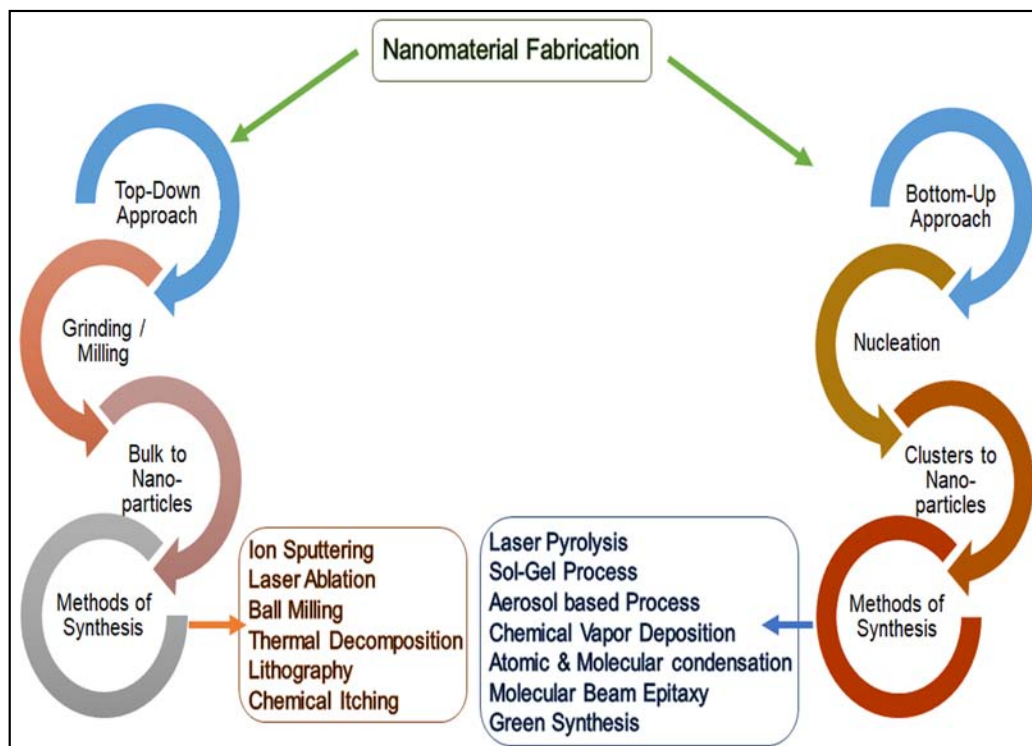


Fig. (1). Schematic explanation of the nanomaterial fabrication process.

### 2.1. Top-down Approach

In this approach, the complex bulk materials are converted into smaller nanosized materials *via* crushing, grinding or milling processes. In the top-down approach, the macroscopic complex materials are crushed into smaller nanosized particles, and then by using different techniques, the nanomaterials are synthesized, such as

## Application of Nanotechnology in Nutraceuticals and Functional Foods

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**Abstract:** In today's world, nanoscience and nanotechnology are persuading almost every field of research and development including computer science, electrical, electronics, communications, energy generation, pharmaceuticals, and many more. Similarly, the food sector is also affected by the impact of nanotechnology. Nanotechnology has a very significant role in nutraceuticals and functional foods and covers a wide range of such applications, including the development of nanoparticulate food materials like liposomes, micelles, nanosuspensions, nanoemulsions and biopolymeric nanomaterials. Similarly, while considering the production sector, nanosensors are found to be very helpful in maintaining a prime level of quality foodstuff. Some fascinating applications of nanotechnology in food industries include the protection of products due to oxidation, controlled nutrient release, taste screening, nano-encapsulated nutraceuticals delivery, detection of pathogens detection in food, food safety, better-quality packaging, an extension of shelf-life, and many more. The current chapter is based on the role of nanotechnology in nutraceutical and functional food. Various issues concerned with nanomaterial toxicity toward humans and the environment are discussed.

**Keywords:** Functional Foods, Nanotechnology, Nutraceuticals, Nanomaterials, Nano encapsulated nutraceuticals delivery.

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## **1. INTRODUCTION**

Advanced knowledge of nanotechnology has been used to understand, explain and control the particles of size in the range of  $10^{-9}$  and  $10^{-7}$ m [1]. Nanotechnology has multi-fold aspects in the field of chemical sciences, biological science, physics, and engineering and is used to generate ultra-small products and devices *via* a vast range of methods [1]. These altering characteristics are the after-effect of the distinct assembly of nanosized structures that create differences in terms of their conductance, chemical reactivity, and magnetism and have well-proven potential applications and products in several fields like medicine, electronics, and water cleansing [2].

Modeling of nanotechnology principles and structures is inspired by the element found in nature. The fact behind this is every living organism and biochemical process are based on the absence, presence, interactions, and site of nanostructures. Nature exploits various self-assembly philosophies to create nanostructures *via* a series of optimized procedures that help to reduce the free and activation energy prerequisite in this association [3].

### **1.1. Nanotechnology into Food Products: Nanofoods**

Functional constituents like vitamins, drugs, and preservatives are vital features in a broad range of products, ranging from pharmaceuticals and health care to food and cosmetics. Integrating nano-materials into food items can be done in various ways. Although some may exist naturally in food products, many can be incorporated into the food products by manufacturers. Some ways to target distinct features of the food chain are given in a research study [4]. The best-known type of example is the delivery of essential nutrients like  $N_2$  using nanomaterials as fertilizers [5]. This also helps to minimize greenhouse emissions by reducing the use of conventional fertilizers.

In food packaging, nanotechnology has provided numerous ways to generate a laminate film. Layers of nano-materials can be physically and chemically bonded to each other in 2 and 3 dimensions *via* coating charged surfaces on the interior films to manipulate electrostatic attractions among the sheets [4, 5].

The result of nanotechnology in food sectors has given rise to a new term for the group of food with specific characteristics, “nanofoods”. The food is termed nanofood when nanoparticles or nanotechnology techniques and tools are incorporated during the cultivation process of the product or/and at the time of their production, processing, or packaging [6]. In addition, the nanosized structures present in foods change their colour, odour, nutritional functionality,

and many other characteristics thus also increasing their efficiency, enhancing their flavours, customizability, and various other benefits [4].

## 1.2. Nutraceuticals

Earlier the term “Nutraceutical” was used for any food or its component with health benefits as well as have the ability to prevent and treat the ailment. A nutraceutical can be obtained either as a part of an intact edible source, as an element of refined food, or provided as a supplement [7].

Whatever food is taken in has a direct impact on human health. Here, the word ‘health’ applies to the physical, mental, and physiological condition of humans. Plant products such as fruits, vegetables, dry fruits, grains, pulses, wines, and nuts have been reported to have high beneficial values and the ability to prevent and cure age-associated disorders like cardiovascular health issues, some specific types of cancers like gastrointestinal cancer, type II diabetes, *etc.* This ability of plant products is associated with the presence of phytochemicals in them [8]. Phytochemicals are the non-nutritious types of secondary metabolites that have a vast range of biologically active compounds, hence a large range of biological activity [9]. However, this activity is relatively less effective when compared with pharmaceutical products. Therefore, their regular intake as diet supplements results in easily detectable physiological effects in long run.

Diet supplements can be explained as a product that comprises more than one nutritional ingredient such as vitamins, amino acids, and minerals. Nutraceuticals are basically diet supplements with specific bioactive compounds, being made available within a non-food medium to the health product industries. Health industries use these nutraceuticals to add known bioactive compounds from the food of their higher concentration to the normal food items to enhance human health.

## 2. TYPES OF NUTRACEUTICALS

Nutraceuticals classification is done on the basis of their origin as well as mode of action. On the basis of their sources, nutraceuticals may be of three types: plants-based nutraceuticals, animal-based nutraceuticals, and microbial-based nutraceuticals whereas, their mode of action divides them into anticancer, antioxidant, anti-inflammatory, bone protective and blood lipid profile (Fig. 1).

The most common nutraceuticals available in plants and animals are carotenoids, dietary fiber, bioactive lipids, and vitamins. Carotenoids are the orange; red and yellow pigments present in many plant parts and are considered powerful antioxidants. [10, 11]. Carotenoids can easily be altered into vitamin A after being

# Enzyme-Responsive Nanoparticles for Drug Delivery

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**Abstract:** Enzyme-responsive nanoparticles have emerged as a promising platform for targeted drug delivery, offering unparalleled control over therapeutic release in response to specific biological cues. This book chapter explores the design principles, mechanisms of action, and biomedical applications of enzyme-responsive nanoparticles in drug delivery. The chapter begins by elucidating the rationale behind the development of enzyme-responsive nanoparticles, highlighting the importance of precise drug release kinetics, site-specific targeting, and reduced off-target effects in enhancing therapeutic efficacy. Key design considerations, including choice of enzyme substrate, nanoparticle composition, and triggering mechanisms, are discussed in detail, emphasizing the versatility and tunability of these nanosystems for diverse therapeutic applications. Furthermore, the chapter delves into the underlying mechanisms governing enzyme-triggered drug release from nanoparticles, such as enzymatic cleavage, conformational changes, and degradation of nanoparticle matrices. Examples of enzyme-responsive nanomaterials, including liposomes, polymeric nanoparticles, and mesoporous silica nanoparticles, are presented, showcasing their ability to selectively release therapeutic payloads in response to specific enzymatic stimuli, such as proteases, phosphatases, and esterases. Moreover, the biomedical applications of enzyme-responsive nanoparticles are comprehensively reviewed, encompassing targeted cancer therapy, inflammation modulation, tissue engineering, and diagnostics. Case studies illustrating the efficacy of enzyme-responsive nanocarriers in overcoming biological barriers, improving drug bioavailability, and minimizing systemic toxicity are highlighted, underscoring their translational potential in clinical settings. The chapter concludes with a discussion of future perspectives and challenges in the field of enzyme-responsive nanoparticles for drug delivery, including optimization of nanoparticle stability, scalability of synthesis methods, and integration of imaging

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modalities for real-time monitoring of therapeutic responses. By harnessing the catalytic power of enzymes to orchestrate precise drug release, enzyme-responsive nanoparticles offer a paradigm shift in therapeutic precision, paving the way for personalized and targeted treatments with enhanced therapeutic outcomes.

**Keywords:** Drug delivery, Enzyme responsive, Nanomedicine, Nanocarriers.

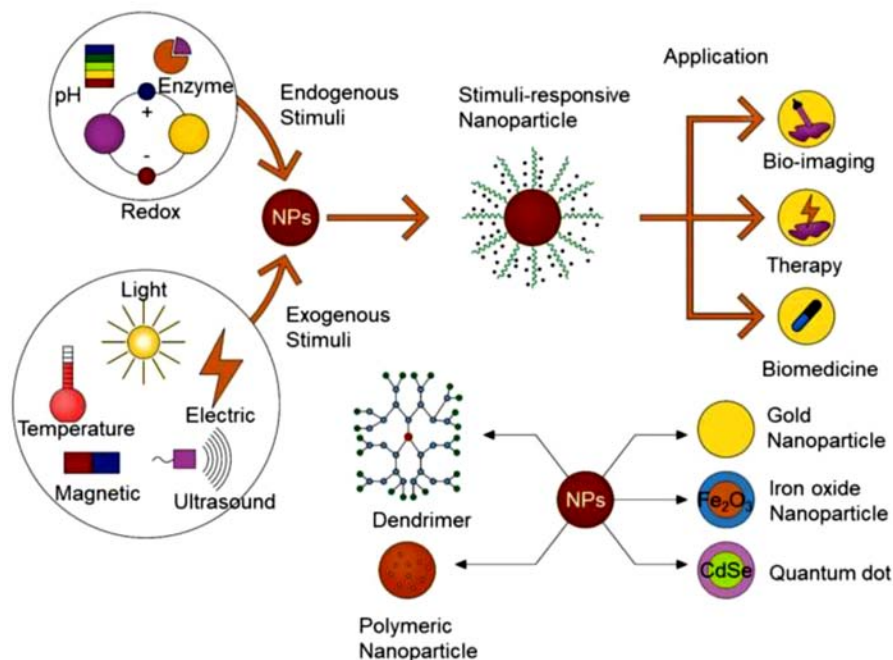
## 1. INTRODUCTION

Nanobiotechnology has been an interesting domain of research for the past few decades for its role in nanomedicine. Conventional therapeutic approaches have been associated with certain challenges, such as more therapeutic doses, permeability issues, fast degradation, efficacy, etc. The emergence of nanotechnology has helped us to overcome these issues up to a certain extent. Nanomaterials have gained considerable attention for clinical applications due to their phenomenal properties like tunable size, high loading capacity, catalytic efficiency, etc. A new approach has been developed where the combination of novel physicochemical properties of nanoscale materials are tuned with the highly specific recognizing nature of biomolecules (such as enzymes). The fabricated smart hybrid nanoformulations are successfully utilized for drug delivery where a specific tissue/diseased site is targeted based on the biocatalytic action of an enzyme. This bio-responsive physicochemical nature of smart hybrid nanoformulations has proven to be much more promising as compared to the orthodox nature of conventional nanomaterials. There are some nanoformulations that are at different phases of clinical trials and have shown promising results in cancer treatment [1, 2].

Enzymes are important targets for drug discovery and therapy because they play a crucial role in cell control. When an enzyme's activity is linked to a specific tissue or when the enzyme is found in larger concentrations at the target region, the nanomaterial can be programmed to transport pharmaceuticals *via* enzymatic carrier conversion. The exploitation of enzymes also provides advantages to work in a nominal condition such as low temperature, low pH etc., where normal chemical reactions are difficult to occur. Enzymatic processes are also more rigorous, efficient, and highly particular than other stimuli, providing extra benefits by endogenously engaging in numerous biological events that occur inside the body.

Nanomaterials are another important component of the stimuli-based drug delivery system. Nanomaterials with dimensions of <100 nm show different features and properties as compared to their bulk counterparts. Their integration with biomolecules has rendered the system with enhanced bio-specificity and selectivity, assisting in the applications pertaining to the biomedical field. For

instance, tumor targeting complex of desired nanoparticles loaded with site-specific enzymatic moieties helps in brisk movement of the complex through the vascular walls (a consequence of the size of nanoparticles) along with site-specific drug delivery with reduced non-specific drug delivery chances (a consequence of enzyme specificity). Nanovesicles, nanomicelles, nanoliposomes, and nanogels, as well as nanodendrimers, are just a few of the NPs that have been developed and tested. Polymeric NPs, mesoporous NPs, magnetic NPs, gold NPs, and other constituent components can be used to define these NPs. A variety of nanomaterials have been explored for nano-based drug delivery, as shown in Fig. (1) [3], which are responsive to several endogenous (*e.g.*, enzyme responsive, pH, redox potential) [4, 5] and exogenous (*e.g.*, light, temperature, magnetic) [6 - 8] stimuli. In this chapter, we focus on the smart drug delivery carriers in response to endogenous stimuli, particularly enzymes.



**Fig. (1).** Schematic diagram for nanomaterials responding to various stimuli used for drug delivery, bioimaging and therapy. Pham, Son H *et al. Pharmaceutics* vol. 12,7 630. 4 Jul. 2020, Copyright © 2020 by the authors.

## 2. ENDOGENOUS ENZYME AND DRUG DELIVERY

Enzymes are proteins and have essential roles in healthy metabolism and biological functioning. Hence, any change in the activity and (over- and/or

# Application of Nanotherapeutics in Cancer Treatment

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**Abstract:** For centuries, cancer has remained the leading cause of death worldwide despite the advancements in chemotherapy and immunotherapy. The challenges of tumor heterogeneity, drug resistance, and systemic toxicity have impeded effective cancer treatment. The rising number of cancer-related deaths has placed significant pressure on healthcare systems and biopharmaceutical companies to develop new therapeutic approaches. Fortunately, recent advancements in nanotherapies have shown promising results in tackling these obstacles and reducing the risk of multidrug resistance. Nanotherapies have emerged as a key player in cancer treatment by enabling targeted delivery of drugs and minimizing the side effects associated with systemic toxicity. By addressing the limitations of current treatment methods, these innovative strategies offer a new frontier in both cancer screening and treatment. In this chapter, we will explore the role of nanotherapies in cancer and their potential to overcome the challenges faced in conventional cancer treatments.

**Keywords:** Chemotherapy, Cancer, Drug delivery, Nanotherapies, Systemic toxicity.

## 1. INTRODUCTION

Nanocarriers are colloidal drug delivery devices with submicron particle sizes, generally less than 500 nm. Due to their promise in the realm of drug delivery, nanocarriers have been the subject of extensive research in recent years. Nanocarriers can alter the basic properties and bioactivity of medications because of their high surface-to-volume ratio. A few advantages that nanocarriers may provide are enhanced pharmacokinetics and biodistribution, decreased toxicities, higher solubility and stability, controlled release, and site-specific drug delivery

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[1]. Over the past three decades, nanoparticles (NPs) have been produced for new and enhanced biosensing applications due to their distinctive chemical and physical features. Cancer biomarker detection using NP-based assays, arrays, or sensors has lately gained popularity. Biomarkers can be detected using metals, metal oxides, semiconductors, polymers, lipids, and hybrid nanoparticles. The benefit of NPs is their capacity to offer extremely sensitive, selective, and quick biomarker detection methods. This makes it possible for them to be utilized in the detection of biomarker traces in a range of bodily fluids, including urine and tears. The physicochemical characteristics of the used NP influence the sensing approach; therefore, point-of-care (POC) detection and/or discrimination of ultra-low biomarker concentrations is the emerging trend—and a substantial challenge—in the development of nanotechnology-based assays [2]. Cancer is widely regarded as one of the most formidable diseases afflicting patients. In the past, it was a condition that posed significant challenges in terms of treatment and detection, often leading to untreatable and undiagnosable fatalities. With emerging technology, science and scientist have made it possible to diagnose and treat this most life-threatening disease, which is a boon to human beings [3]. Nanotechnology is an appealing option for solving several cancer therapeutic issues. Drug stability, solubility, and tumor localization/targeting are among the problems. Nanoparticles, polymers, and proteins are widely used to encapsulate or conjugate drugs to increase their solubility in aqueous physiological conditions, hence increasing the bioavailability of cancer-fighting drugs. Additionally, the “enhanced permeability and retention” (EPR) effect makes tumors healthy tissues to passively absorb nanoparticles [4]. Larger-than-average fenestrations in tumor endothelial cell layers caused by irregular angiogenesis are predicted to increase permeability (“increased permeability”), while higher retention (“enhanced retention”) is predicted to increase difficulty (“retention”). The EPR effect results in the preferential accumulation of nanoparticles in tumors, which can improve treatment efficiency, lower systemic toxicity, and lessen side effects frequently linked to chemotherapy. Liposomes, polymer micelles, albumin-bound chemotherapeutics, polymer-bound chemotherapeutics, and inorganic particles are several nanotechnologies in the field of cancer that lend themselves to being characterized by a drug delivery vehicle [4].

## **2. RISK FACTORS ASSOCIATED WITH CANCER**

Cancer encompasses a wide range of conditions characterized by abnormal cell division and the potential spread to other tissues and organs. These rapidly dividing cells can give rise to tumors and disrupt normal bodily functions. The primary cause of cancer is often attributed to mutations or changes in DNA within cells. These mutations can be inherited or acquired due to environmental factors encountered after birth [5]. Carcinogens are compounds present in the

environment that can cause cancer. These include physical agents like radiation and ultraviolet light as well as chemical molecules like those found in polluted food, water, alcohol, air pollution, asbestos, asbestos fibers, and cigarette smoke. Various bacteria, viruses, and parasites have also been classified as biological carcinogens.

Several risk factors can increase an individual's susceptibility to developing cancer. Some examples of these risk factors include:

**Age:** The likelihood of cancer increases with age, as the body's natural defenses and DNA repair mechanisms may become less effective over time.

**Family history:** Inheriting certain genetic mutations from family members can increase the risk of developing specific types of cancer.

**Lifestyle choices:** An increased risk of cancer can be brought on by elements such as the use of cigarettes and alcohol, poor nutrition, inactivity, and exposure to toxic chemicals.

**Environmental exposure:** Prolonged exposure to carcinogens in the workplace or the surrounding environment can heighten the risk of cancer development.

**Immunodeficiency:** The risk of developing certain malignancies may be higher in those with compromised immune systems, such as individuals with HIV/AIDS or organ transplant patients on immunosuppressive drugs [6].

It is crucial to emphasize that possessing one or more risk factors does not ensure the development of cancer, as many instances occur in people who have no discernible risk factors. Conversely, individuals without apparent risk factors can still develop cancer. Regular screenings, early detection, and adopting a healthy lifestyle can help reduce the risk and improve outcomes in cancer prevention and treatment.

Specific cancer types are often identified and referred to using various medical terminologies shown in Fig (1).

### 3. TYPES OF CANCER

- **Carcinoma** is a kind of cancer that begins in the epithelial cells, which coat the surfaces of organs and tissues throughout the body.
- **Sarcoma** is a kind of cancer that develops in the body's connective tissues, such as bone, muscle, fat, cartilage, or blood vessels. It includes osteosarcoma, liposarcoma, leiomyosarcoma and angiosarcoma, with unique characteristics and requiring tailored treatment approaches.



## **Anti-HIV Nanotherapeutics and their Challenges in the Future**

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**Abstract:** The human immunodeficiency virus (HIV) affects the body's immune system of the body in such a way that a minor infection, such as a cold, can become severe. The treatment of HIV is challenging due to the virus's resistance. A high dose of the drug is required to achieve viral load reduction. Current available antiretroviral therapy can improve the health of HIV patients, although systemic viral load may remain sequestered if the virus persists in anatomically privileged areas of the body. Nanotechnology-based drug delivery techniques are being developed to target the virus in various tissue compartments. Due to their durability, safety, multimodality, and multifunctionality, nanomaterials are extensively used in biological applications. However, unwanted interactions with plasma proteins in the systemic circulation, failure to cross biological barriers, and nonspecific distribution throughout the body are challenges. It is required to mitigate these challenges in the field of nanomedicine in the near future. So, the main objective of this chapter is to compile information on pathogenesis and their targets, as well as how anti-retroviral drugs improve efficacy in treatment. This chapter will provide new insight into finding nanotherapeutics for HIV.

**Keywords:** HIV, Immune system, Nanotechnology, Virus resistance.

### **1. INTRODUCTION**

Since 1981, when the first human immunodeficiency virus (HIV) infections were recorded, the rate of infection had been steadily rising [1]. After the introduction of highly active antiretroviral therapy (HAART) and multi-drug therapy, the situation of HIV-infected individuals drastically improved. On the other hand,

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HIV infection has not been cured, especially in sequestered, anatomically privileged locations such as the brain, testes, gut, liver, kidney, and secondary lymphoid tissue [2]. Currently, 37.7 million people are suffering from HIV, of which 1.7 million are children. 53% are either women or girls [3]. HIV causes Acquired Immunological Deficiency Syndrome (AIDS), which affects the body's immune system. In 2020, 36.3 million people would have died from AIDS [4]. Furthermore, the development of resistance to virus stains, as well as the adverse effects associated with long-term use, is a major challenge for effective anti-HIV treatment [5].

The US FDA authorized zidovudine as the first anti-retroviral (ART) medicine in 1987, and since then, 48 drugs have been approved for HIV treatment. These licensed medications, however, have some drawbacks, including life-threatening side effects, drug interactions, loss of efficacy over time owing to resistance, and the requirement for extremely strict medication adherence to achieve viral suppression [6]. Nanotherapeutics is a new multidisciplinary discipline with the potential to transform HIV/AIDS treatment and prevention. Nanomedicine can be utilized to create new HIV medicines that target specific cells and provide tenable and site-specific medication delivery. Nanotherapeutics have improved drug stability, increased drug penetration across the cell membrane, and increased bioavailability [7]. In this chapter, we focus on evidence-based information about HIV pathogenesis, treatments, and problems, as well as nanotherapeutics and their targets.

## **2. HIV PATHOGENESIS**

Two strands of RNA, 15 different types of viral proteins, plus a few proteins retrieved from the previous host cell, make up HIV. All of these components are encased in a lipid bilayer membrane (Fig. 1). When these pieces come together, the virus can infect immune system cells and cause them to produce new copies of the virus. Each molecule in the virus is responsible for a specific phase in the process, from the early phases of viral attachment to the budding process [8].

Dendritic cells are responsible for transmitting HIV to lymphoid organs after it has entered the body through mucosal surfaces. When HIV infection is not treated, high plasma viral loads and a steady decline in CD4<sup>+</sup> T cells occur, both of which lead to immunodeficiency later in the disease [9]. During the early stages of infection, people may appear healthy, but the virus aggressively grows in the lymph nodes and blood of those who are afflicted. The presence of CD4<sup>+</sup> molecules alone does not appear to be sufficient for viral entrance into other cell types, including monocytes and dendritic cells [10, 11].

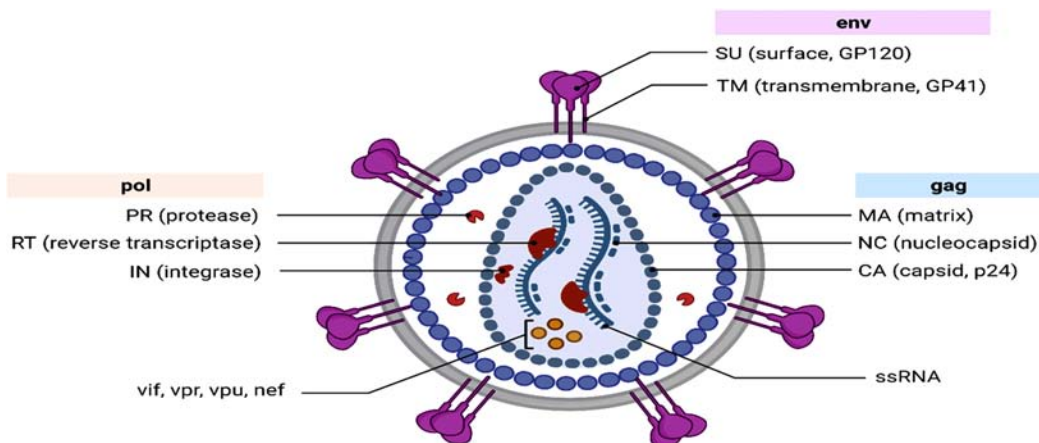


Fig. (1). Structure of HIV.

The major target of HIV is activated CD4 T cells. The virus penetrates cells through interactions between CD4 and CCR5 or CXCR4 chemokine coreceptors (shown in Fig. 2). Despite the absence of CD4+ T cells, cells can become infected with HIV, most notably astrocytes and renal epithelial cells. The pathophysiology of HIV-associated neurocognitive impairment (which is linked to astrocytes) and nephropathy is complicated by subsequent HIV gene expression (related to epithelial cells). A vast spectrum of host proteins can either hinder or increase viral replication in specific cell types depending on their interactions with HIV proteins or HIV DNA. Typically, HIV transmission across mucosal membranes is established by a single founder virus. This virus has distinct behavioral traits, such as the utilization of CCR5 rather than CXCR4 for entry, enhanced dendritic cell contact, and interferon resistance. In contrast to the mild first reaction to other chronic viral infections such as hepatitis B or C, the creation of inflammatory cytokines and chemokines after transmission of the founder virus is significant. The founder virus causes a substantial increase in inflammatory cytokines and chemokines as well as a rapid increase in HIV replication. After that, the viral load starts to decline until it reaches a set point. The majority of this level is determined by innate and adaptive immune responses [12].

Reservoirs are important because they are a source of drug-resistant viruses (due to low-level replication in the context of HAART), and they make HIV eradication and cure more difficult [13]. HIV is an encapsulated retrovirus with two copies of a single-stranded RNA genome. It is the last stage of HIV infection, which leads to acquired immunodeficiency syndrome (AIDS).

**CHAPTER 7****Current Perspectives of Nanotherapeutics for the Treatment of Alzheimer's Disease****Shruti Mishra<sup>1,\*</sup>, Dharmaraj Senthilkumar<sup>1</sup> and Vivek Kumar Yadav<sup>1</sup>**<sup>1</sup> School of Biological & Life Sciences, Galgotias University, Greater Noida, Uttar Pradesh-226003, India

**Abstract:** Alzheimer's disease (AD) is one of the most prevalent irreversible neurodegenerative disorders, contributing to approximately 50-80% of all reported cases worldwide. The majority of current treatment strategies for AD only provide symptomatic treatment. The inability of existing medications to penetrate the blood-brain barrier (BBB) is a major challenge in treating AD. The application of nanotechnology in drug delivery systems is categorized by potential medicines designed to penetrate the BBB and improve drug targeting for neurodegenerative disorders (NDDs) treatment. Nanotechnology offers a wide range of nanoparticle-based drug delivery systems with minimal systemic side effects. Nano-based gene delivery vehicles and nanocarriers such as neurotrophic factors effectively improve neuronal survival and synaptic connectivity. Thus, currently, they are being utilized as a popular therapeutic against various neurodegenerative diseases. Recently, nanotechnology has patented various novel nanostructures and developed several advanced formulations for the management and prevention of NDDs. Therefore, to combat neurodegenerative disorders, nanotechnology can be applied to neuroscience. Primary research on employing nanoparticles (NPs) to manage Alzheimer's disease has shown promising results, but additional studies are still required. In this chapter, we discuss the pathogenesis and causes of AD and also outline the role of NPs in the brain's microenvironment for treating Alzheimer's disease. Overall, this chapter focuses on newly investigated NP systems that provide unique ways of understanding AD pathophysiology and suggesting therapy to cure AD.

**Keywords:** Alzheimer's diseases, Nanomedicine, Nanotherapeutics, Neurodegenerative disorders.

**1. INTRODUCTION**

Alzheimer's disease (AD) is identified as a deadly neurodegenerative condition with complex pathological mechanisms. Moreover, AD is identified with progres-

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sive and complete cognitive impairment [1]. It leads to early memory loss along with behavioral disorders [2, 3]. Furthermore, AD steadily progresses, leading to a steady decline in brain functioning, deterioration of quality of life, and ultimately death of the patient [1]. Overall, dementia and motor impairment are severe symptoms of AD that have been categorized into three stages, as illustrated in Table 1 [4]. These symptoms further induce dysfunction of nerve synapses. Patients often die within 3–10 years after the beginning of symptoms due to complications from immobility or infections such as pneumonia, *etc* [4]. Surprisingly, epidemiologists revealed that the occurrence of AD increases with age. It is among the most prevalent causes of dementia in old age. Indeed, as the world-wide population grow old, AD becomes a major problem affecting individuals, their families, and the society. Unfortunately, Alzheimer's disease (AD) stands as a prominent contributor to death rates, exerting a significant impact on approximately 5.8 million Americans and is anticipated to pass 14 million by 2050. Additionally, as stated by Alzheimer's association, AD and other related disorders may affect 1 out of 3 elderly person, which is greater in number than cancer patients [5, 6].

**Table 1. Distinctive symptoms at different stages of AD [4].**

Stages of Alzheimer's Disease		
Early	Middle	Late
Confusion	Delusion	Severe dementia
Forgetfulness	Restlessness and anxiety	Motor impairment
Disorientation	Sleep disturbance	Highly susceptible to infections
Abrupt mood changes	Dementia	Difficulty in moving and eating
Lingual problems	Needs assistance with daily chores	Loss of bowel and bladder control

### 1.1. Outline of Pathophysiology of AD

The physiopathology of AD is extremely complicated and is controlled by numerous pathological progressions. Presently, there are diverse theories about the causes of AD, which include aggregation of  $\beta$ -amyloid ( $A\beta$ ), tau protein hyperphosphorylation, mitochondrial dysfunction (oxidative stress), neuroinflammation along with numerous other pathways that may cause AD [7, 8]. A brief overview of the main hypothesis related to the development of AD is briefly described below:

### ***1.1.1. Aggregation of A $\beta$***

One of the widely accepted assumptions of AD pathogenesis is the extracellular deposition of A $\beta$  that ultimately advances the growth of senile plaques in the brain. A $\beta$  peptide consists of 39 or 42 amino acids, which is formed as a result of hydrolysis of  $\beta$ -amyloid precursor protein (APP). Specifically, amyloid precursor protein (APP) is found intracellularly and extracellularly, and undergoes enzymatic cleavage by secretase enzymes to generate amyloid-beta (A $\beta$ ) [9, 10]. When APP metabolism is irregular, A $\beta$  production is higher, which ultimately leads to the deposition of a large amount of A $\beta$ . Furthermore, A $\beta$  is known to exist in two forms, A $\beta$ 1-40 and A $\beta$ 1-42. Amongst them, A $\beta$ 1-42 has a greater tendency for fibrillation; consequently, it is the primary element of senile plaques. The presence of these plaques destroys neurons and leads to AD [11, 12].

### ***1.1.2. Hyperphosphorylation of Tau Protein***

Research findings have demonstrated that individuals diagnosed with Alzheimer's disease exhibit a tau protein concentration that is three times greater than that observed in individuals without the disease. The key function of tau proteins is the maintenance of microtubules, specifically axons, in the phosphorylated form [13]. Therefore, under a normal state, both phosphorylation and dephosphorylation of tau protein exist in dynamic equilibrium. However, in AD, hyperphosphorylation of tau proteins results in the formation of insoluble tau protein aggregates. Subsequently, these aggregates assemble abnormally as paired spiral neurofibrillary tangles (NFTs). This ultimately advances to the failure of microscopic activity along with irrevocable damage to nerve cells [14, 15].

### ***1.1.3. Mitochondrial Dysfunction***

Mitochondria are widely distributed along with the cell with a major presence in some regions of the neurons. They play a crucial role in cell energy metabolism along with controlling cell calcium, free radical homeostasis, and apoptosis [16]. The fundamental features of mitochondrial malfunctioning are the collapse of mitochondrial oxidative respiratory sequences, decline in mitochondrial transmembrane potential, production of unstable oxygen species, and finally, cell oxidative stress [17]. Since the brain consists of highly unsaturated fatty acids, in addition to consuming large volumes of oxygen, it becomes highly susceptible to oxidative stress. Studies have concluded that excessive oxidative stress may impact the synaptic capabilities of nerve cells and apoptosis. Subsequently, mitochondrial malfunctioning leads to the degeneration of neurons and causes synapses. Moreover, mitochondrial malfunctioning also promotes the development of NFT as well as  $\beta$ -amyloid plaques in the brains of AD patients [17 - 26].

## **Nanotherapeutics in Skin Therapy**

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**Abstract:** Nanotherapeutics has emerged from nanotechnology applications and has a wide range of utilities in the medical field. Nanotherapeutics made a revolutionary change in healthcare and provided a vision to augment diagnostics and treatment solutions by managing the release of contained bioactive compounds. It has gained much research interest in today's modern world due to its implications in drug delivery and genes, which overcome lacunae prevailing in the existing therapeutic sphere by the use of engineered nanostructures and nanodevices. The interaction of nanostructures with the skin tissue at the subatomic level has significant applications in the diagnosis and treatment of dermatological conditions, especially wound healing and cosmeceutical treatment. Nanotherapies and diagnostics have the potential to improve treatment effectiveness while reducing or eliminating toxicity problems. This book chapter provides an overview of the latest advancements and applications of nanotherapeutics in skin therapy. Nanoparticles, owing to their unique physicochemical properties, have shown immense potential in enhancing drug delivery, improving skin penetration, and targeting specific cellular and molecular pathways implicated in various skin conditions. Key topics covered include the design and synthesis of nanoparticles for skin delivery, including liposomes, polymeric nanoparticles, solid lipid nanoparticles, and nanoemulsions. These nanocarriers can encapsulate a wide range of therapeutic agents, including anti-inflammatory drugs, antimicrobials, antioxidants, and gene-based therapies, enabling precise and controlled release at the site of action.

**Keywords:** Cosmeceuticals, Diagnosis, Healing, Nanostructures, Nanomedicine, Skin diseases, Therapeutics.

### **1. INTRODUCTION**

Nanotechnology, with tremendous growth, has uplifted and encouraged many researchers. The recent hype in technology is due to nanotechnology, which has

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several applications in the health and medicine sector [1]. The branch of medicine focuses on the diagnosis and treatment of diseases or illnesses using nanomaterials, referred to as nanomedicine [1, 2]. Nanomedicine is a relatively new therapy method. Drug delivery, diagnostic imaging, dental surgical applications, medical fabrics, tissue engineering (bioimplants), and radiation devices are all examples of medical applications/devices that utilize nanomaterials. In nanomedicine, diagnostic imaging demands the use of noninvasive magnetic resonance imaging (MRI) and functional imaging, such as positron emission tomography (PET). Nanomaterial emission tomography is a type of imaging that uses light. Monitoring at wide range, control, construction, repair, defense and enhancement of the management system of medicine using engineered devices and nanostructures are the main concerns of nanomedicine [1, 3]. Due to their surface-to-volume ratio and minute size, they have an increased ability to interact with microorganisms, resulting in improved microbial activity [3]. In the stratum corneum layer of the skin, nanospheres or nanocapsules demonstrate considerable drug accumulation. Lipid-based nanoparticles are a common form of nanoparticles that have been investigated extensively by scientists [4]. Liposomes, poly amphiphiles, solid-lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs) are all examples of lipid-based nanocarriers. The distribution of active ingredients of the drug to the targeted tissue is controlled by this technology [5]. There are many advances and formulations used in nanomedicines. These include nanomaterials and their different forms like nanocapsules, nanocarriers and many others. Apart from wound healing properties, nanoparticles can also be used for the treatment of several skin problems like sunburns, aches and other skin infections [6]. Such nanomaterials are known as cosmeceuticals. This chapter describes various nano derivatives that can be used in the diagnosis and treatment of skin diseases. An essential element of nanopharmaceuticals is the use of nanobiotechnologies for drug discovery and development. Some technologies will help identify targets faster, while others will develop into therapies. In the cosmetics industry, cosmeceutical is a cosmetic product infused with physiologically active ingredients that have therapeutic effects on human appearance [7, 8]. This chapter includes the knowledge of the application of nanotechnology in medicine and therapy. Besides severe wounds and diseases, nanotherapeutics can also be used in the enhancement of skin, which is more followed and focused on by people at the present time. Nanomaterials have steadily been employed in wound healing as nanotechnology and biomedicine have progressed, playing active roles in hemostasis, antibacterial inhibition, inflammation, proliferation stimulation, and so on. Antibiotic-loaded nanomaterials have the potential to enhance antibacterial effectiveness in a synergistic manner. Bionic nanofiber scaffolds made by electrospinning can



mimic the extracellular matrix seen in natural skin to encourage cell adhesion and proliferation [9].

## 2. THE STRUCTURE OF THE SKIN

The largest organ of the body is the skin. It serves as the external cover of the body. It covers an area of about 1.7m<sup>2</sup> and weighs about 15% of the total body weight. It is composed of three different layers, which are the epidermis, the dermis and the subcutaneous fat [4]. The outermost layer is called the epidermis, which is formed by the accumulation of the epidermal cells on the surface as a thin, stratified and highly specialized layer called stratum corneum. The second layer called the dermis, is formed chiefly by inter-wind elastic fibers and collagen fibers meshed in a gel-like matrix that is thicker [6]. The third layer is the subcutaneous fat layer, which provides thermal insulation for the conservation of body heat. The epidermal layer is formed of different cells and does not have any blood vessels but obtains nutrients from dermis blood vessels *via* the dermoepidermal junction [7]. About 95% of keratinocytes and other cells like Merkel cells, Langerhans cells, and melanocytes form the constituents of the epidermal layer. The layers of the epidermis are divided into the basal layer (stratum germinativum), the squamous cell layer (stratum spinosum), the granular layer (stratum granulosum), and the cornified layer (stratum corneum). The stratum malpighii and rete Malpighii are the layers that consist of living and nucleated cells of the epidermis. The epidermis is the renewing layer and origin of derivative structures such as pilosebaceous apparatus, nails, and sweat glands. Proliferation of the basal cells provides the renewal of the epidermis [7, 8]. The column-shaped keratinocytes are attached to the basement membrane zone with their axis perpendicular to the dermis, which forms the basal layer that is known as stratum germinativum. Each basal cell adheres to one another, and through the desmosome, the superficial squamous cells form a single layer [8, 9]. Mitotically active cells are located primarily in the basal layer that gives rise to the outer epidermal layer. The layer above the basal layer is formed of a variety of cells based on their location; they differ in shape, structure and subcellular properties. This layer is known as the squamous cell layer or stratum spinosum [10, 11]. There is a granular layer above the stratum spinosum, which is composed of flattened cells with abundant keratohyaline granules in the cytoplasm; this layer is known as stratum granulosum. These cells are further involved in the synthesis and modifications of the proteins that are involved in keratinization. Corneocytes form the cornified layer that provides mechanical protection to the underlying epidermis and acts as a barrier to water loss [11, 12]. This is also known as stratum corneum. The dermis is the most critical component of the body. The coarse reticular layer forms the main structural component [13]. It provides a nutritive, immune and other support system to the epidermal layer and also

## CHAPTER 9

# Economical and Environmental Aspects of Nanomaterials: Journey of Sustainable and Cost Effective Nanoparticles from Lab to Industry

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**Abstract:** In the last two decades, there has always been a hunt for reliable, cost-effective, and environmentally friendly processes for manufacturing nanomaterials to decrease the usage of dangerous chemicals affecting human life. There is always a debate about whether the industry is beneficial/nonbeneficial for human life. To answer this question, we have summarized the negative aspects of nanomaterials that have been used on numerous synthesized routes in laboratories and studied the journey of these particles from lab to industry.

**Keywords:** Carbon materials, Electrospinning, Hydrothermal, Industry, Nanomaterials.

## 1. INTRODUCTION

Renewable energy sources that are thought to be environmentally favorable are referred to as clean energy sources. The impacts of escalating global issues, including climate change, pollution of the environment, population expansion, wasteful usage, and depletion of natural resources, can be mitigated using these energy sources [1]. These issues have sparked a global concern about using methods and technology that protect natural resources while being less detrimental to the environment. Green and sustainable nanotechnology is one invention that significantly lessens the issues above. Auxiliary energy generation is required due to the growing global population and rapid economic expansion. It

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is expected that technology for renewable (green) energy will have a considerable part in sustainable energy development in conjunction with the effective adoption of green and sustainable energy technologies [2].

The development, characterization, and use of nanomaterials and nanodevices in energy generation, conversion, storage, and usage are based on clean and sustainable nanotechnologies. Supercapacitors, batteries, photovoltaics, hydrogen production, detection, storage, fuel cells, carbon capture, energy conversion (using photo- and electrocatalysts) and storage, thermoelectric devices, optoelectronic devices, flexible, integrated energy systems, and self-powered appliances are just a few examples of the various parts and processes that make up these nanomaterials-based technologies [3 - 5]. The photovoltaic device converts sunlight directly into electric power and is one of the most significant renewable energy technologies among energy storage devices [6]. Nanotechnology has been a critical component in creating solar cell devices as an electrode material. Furthermore, it is noteworthy to emphasize that fuel cell devices have demonstrated an outstanding influence of nanotechnology in directly turning chemical energy into electrical power [7].

Because of their superior electrical conductivity, extensive surface area, mesoporosity, vigorous mechanical strength, lightweight, and excellent corrosion resistance, CNTs and graphene have recently received the majority of research attention as metal-free catalysts in fuel cells. Hydrogen has a significant potential to be a future energy source [8 - 10]. Metal-organic frameworks (MOF), polymers, metal and similar complex hydrides have been researched for hydrogen storage and transportation to achieve the highest hydrogen capacity and the least amount of degradation during hydrogenation. Fossil fuels provide for almost 80% of global energy [11].

In this regard, because nanotechnology encompasses the engineering of any system at the atomic or molecular size, it can offer this option in a very practical, affordable, and environmentally benign manner. The word “nanotechnology” was initially used by Norio Taniguchi in 1974 [12]. Moreover, the concepts of nanotechnology can be used in a wide range of industries, including healthcare, fabrics, the environment, energy storage equipment (solar and fuel cells), nanocoating, *etc.*, for example, the nanoengineered, thin, flexible, and high-performance energy harvesting and storage devices, nano-enabled therapeutic and diagnostic devices, implantable biomedical devices, nano-drug delivery, and nanocoating [13 - 16]. Besides, nanotechnology finds applications in the fields directly benefiting the environment, *i.e.*, nanoparticles (NPs)-based wastewater treatment, nanomaterial-enabled renewable energy resources, anti-microbial applications, and nanomaterials for air and water purification [16 - 19]. Although

nanotechnology exhibits exceptional properties and tremendous applications, it suffers unintended environmental and health risks. Materials have extremely high reactivity and mobility at the nanoscale. This could be harmful in some situations. Due to its severe environmental devastation, this is called nano-pollution. One way to define “green technology” is the technology that is used to create environmentally beneficial nanoparticles. This technology is crucial because it can directly combat hazardous processes and contaminations. The progress of any technology is closely correlated with sustainability. These nanomaterials can potentially be necessary for environmental protection and resource preservation [1]. The advantage of using stable technology is that the use of non-renewable energy resources will be minimized. Apart from this, it can lead to a pollution-free healthy environment. This chapter's primary goal is to accomplish society's unmet needs without damaging natural resources, keeping in view sustainability. The new methods to create nanomaterials ensure manufacturing of nanomaterials without endangering the environment or human health. In short, nanomaterial synthesis requires cheap biological or plant-based raw materials. Creating nanomaterials/nanoparticles demands specialized methodologies and physical procedures employing natural instruments such as viruses, plants, microbes, *etc.* These methods produce byproducts that are safe for the environment. Many global researchers use nanotechnology to develop cost-effective and environmentally friendly products [15-21].

As discussed above, there is a need to address these issues and adopt sustainable, eco-friendly green technologies to synthesize nanomaterials. This may mitigate the risk of using nanotechnology, increase the productivity of nanomaterials, and reduce carbon footprints. In a nutshell, adopting environment-friendly and sustainable nanotechnology concepts for industrial work is of utmost importance.

## 2. TYPES AND PROPERTIES OF NMS

Materials with dimensions between 1 and 100 nm are called nanomaterials [22 - 24]. A large surface area to volume ratio is the primary element influencing how differently nanoparticles behave from bulk materials [25]. Various types of nanomaterials are produced nowadays by synthesis. Nonetheless, depending on how they are made, nanoparticles are divided into four categories: (i) carbon-based NPs, (ii) metal-based NPs, (iii) dendrimers, and (iv) composite-based NPs [26].

### 2.1. Carbon-based NMs

With a high surface area ( $\sim 2000 \text{ m}^2 \text{ g}^{-1}$ ), excellent porosity, affordability, ease of processing, strong electrical conductivity, non-toxicity, natural abundance, high stability, and environmental friendliness, carbon is a well-known electrode

**CHAPTER 10****Patent Landscape of Nanotechnology In Healthcare****Chitra Kalyanasundaram Iyer<sup>1,\*</sup> and Arvind Kumar Jain<sup>2</sup>**<sup>1</sup> Philips India Limited, Manyata Tech Park, Nagawara, Bangalore, India<sup>2</sup> School of Basic Sciences, Galgotias University, Greater Noida, Uttar Pradesh-226003, India

**Abstract:** Over the years, there has been significant research on various aspects of nanotechnology in various domains that have found applications in diverse domains. In the healthcare sector, there have been rapid advances in the application of nanotechnology for prevention, treatment and diagnosis, leading to extensive publications as well as patent filings. The patent landscape study presented in this chapter covers year-wise trends in nanotechnology-based patent filings in healthcare domains such as diagnostics, therapeutics, theranostics, drug delivery, pharmaceutical compositions, pharmaceutical preparations, *etc.* This broad and high-level overview of patent filing trends may be used to give at least an approximate indication of past, present, and future research activities, anticipated spend and expected opportunities. Given the fact that patent filing and prosecution activities are expensive and need investments beyond mere R&D in terms of patent filing, prosecuting and enforcing the patent rights in various geographies may be indicative of general interest in each of these topics, including past investments and future expectations.

**Keywords:** Composition, Diagnostics, Data, Delivery, Drug, Health, Medicine, Nanotechnology, Patents, Pharmaceutical, Preparation, Research, Technology, Theranostics, Therapeutics,.

**1. INTRODUCTION**

Over the years, there has been significant research on various aspects of nanotechnology in various domains such as nanomaterials, biotechnology, nano-electronics, *etc.*, which have found applications in several areas such as cosmetics, and healthcare, specifically those related to prevention, diagnostics, therapeutics, theranostics, drug delivery, pharmaceutical compositions, pharmaceutical preparations, *etc* [1, 2]. The research activities have been followed by both research publications and patent filings.

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Patents can be broadly described as legal monopolies that are allowed by governments, whereby the owners of certain technologies have the right to prevent any unauthorized entities (natural or legal persons) from making, using or commercializing the invention for a certain specific period (usually around 20 years from the date of filing). Further, patents are “territorial rights” conferred by respective governments, as per statutory norms developed for each country as per the unique needs of the people in those countries and as determined by the respective governing bodies, laws, and policies. These rights allow for the commercialization of new technologies and also help to prevent unauthorized entities from making, using or commercializing the invention till the patent is in force.

This chapter covers the patent landscape of nanotechnology-based patent filings in healthcare domains such as diagnostics, therapeutics, theranostics, drug delivery, pharmaceutical compositions, pharmaceutical preparations, *etc.* [3, 4].

Studies on patent filing trends are useful and important because patents are usually a leading indicator of future investments in technology. Patent filing and prosecution activities are expensive and need investments beyond mere R&D in terms of protecting the invention in markets of interest. This is followed by the development of infrastructure and engagement of human capital to support these activities. Ultimately, it leads to employment opportunities, new business creation, and expansion, further building the economy of nations.

This chapter covers some patent landscapes of nanotechnology-based patent filings in healthcare domains such as diagnostics, therapeutics, theranostics, drug delivery, pharmaceutical compositions, pharmaceutical preparations, *etc.* [3, 4].

**Diagnostics:** Relates to the diagnosis of a disease or medical condition [5].

**Therapeutics:** Relates to personalized medicine, low-cost medicines, lesser side effects [6].

**Theranostics:** Relates to novel approaches to treatment that involve devices and drugs [7]. Both are uniquely combined to seamlessly diagnose and treat medical conditions and develop a patient-specific treatment plan.

**Drug delivery:** Relates to the process or mechanism used to deliver the relevant drug to the target site [8]. Nanotechnology has the potential for targeted drug delivery and sustained release of drugs over certain periods. There is lesser risk and more chances of reaching the target molecules and dispensing the drug.

**Pharmaceutical compositions:** Relates to a composition that includes the active drug [9].

**Pharmaceutical preparations:** Relates to the appropriate development of the pharmaceutical compound and the appropriate formulation for effective delivery [10].

## 2. MATERIALS AND METHODS

A search tool called “Patseer” was used to search for relevant patents, in addition to other available free tools, such as “Google Patents”, “Espacenet”, *etc.*

### 2.1. Categories Studied

The nanotechnology healthcare-related aspects were studied for categories, such as their applications. The results were categorized in different headings, such as those related to diagnostics, therapeutics, theranostics, drug delivery, pharmaceutical compositions, and pharmaceutical preparations.

### 2.2. Period of Study

1st January 2001 to 13<sup>th</sup> September 2021 was selected as the period of patent search. The results presented in this study are also for this period

### 2.3. Jurisdiction Covered

Patents were searched across all jurisdictions.

Example: United States patent (US), Australian patent (AU), European Patent (EP), Chinese Patent (CN), Korean patent (KR), Japanese patent (JP), Indian patent (IN), Mexico patent (MX), French patent (FR), *etc.*

### 2.4. Search String Used

A number of patents under Cooperative Patent Classification [CPC] were searched [11, 12].

“The Cooperative Patent Classification (CPC) system, in force from 1st January 2013, is a bilateral system which has been jointly developed by the EPO and the USPTO. It combines the best classification practices of the two offices.”

The codes used are described hereunder (Tables. 1 and 2):

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