



**A REVIEW ON NANOPARTICLES**

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Article Received on 30/08/2024

Article Revised on 19/09/2024

Article Accepted on 09/10/2024

**ABSTRACT**

Nanotechnology is being used in developing countries to help and treat disease conditions and prevent health care issues. The common term of nanotechnology is Nanomedicine. Nanomedicines is a branch of medicine which applies the knowledge and tools of nanotechnology to the prevention and treatment of disease conditions. Nanomedicine involves the use of nanoscale materials, such as biocompatible nanoparticles and nanorobots, for the diagnosis of the disease, delivery of the drug, for sensing or actuation purposes in living organisms. Nanomedicine is the application of nanotechnology, which is often described as technologies under 1000 nm, in the health care sciences. Well, the researchers have been using nanomedicine to the target microbes, with an appropriate result in vitro and as a potential innovation to the field of antimicrobials. In these studies, followed, as clinical trials started to appear, and a movement of clinical translation is initiating in the field of antimicrobial nanomedicine. An important achievement for this field is stimulating further clinical research and basic sciences and generating research questions and scientific enquiries. The trials addressing nanoparticles on catheters, hand gels, therapeutic vaccines, safety, and other issues have been conducted. As per their financial and bureaucratic restrictions, the presence of clinical trials is a great indicator of the potential in the field and is a necessary step to fight against microbes by nanomedicine.

**KEYWORDS:** Nanotechnology, nanomedicine, theragnostic, nanorobots.

**INTRODUCTION**

Nanomedicine is the medical application of nanotechnology. Nanomedicine ranges from the medical applications of nanomaterials and biological devices to nanoelectronics' biosensors, and even possible future applications of molecular nanotechnology such as biological machines. Current problems for nanomedicine involve understanding the issues related to toxicity and environmental impact of nanoscale materials (materials whose structure is on the scale of nanometers, i.e. billionths of a meter). Functionalities can be added to nanomaterials by interfacing them with biological molecules or structures. The size of nanomaterials is similar to that of most biological molecules and structures; therefore, nanomaterials can be useful for both in vivo and in vitro biomedical research and applications. Thus far, the integration of nanomaterials with biology has led to the development of diagnostic devices, contrast agents, analytical tools, physical therapy applications, and drug delivery vehicles. Nanomedicine, an interdisciplinary technology domain is attracting worldwide attention owing to its perceived advantages such as efficacy and efficiency.<sup>[1]</sup> Varied

aspects of the subject have been suitably covered earlier. Interestingly, the Indian nanomedicine market is expected to grow to a value of USD 1.6 Billion in another 10–15 years.<sup>[2]</sup> It is anticipated that India would rank among the top three healthcare markets by 2020.<sup>[3]</sup> The Indian government has been funding research and development (R&D) in the area of nanomedicine with the intention to address specific societal needs and to be a forerunner in this area. In the year 2007, the Department of Science and Technology (DST) established a Nano mission program to foster basic research, establish research infrastructure, nurture human capital, strike international collaborations, and strengthen the capacity for creating nano enabled technologies. Other government organizations, such as the Council of Scientific and Industrial Research (CSIR), Defence Research and Development Organization (DRDO), Department of Biotechnology (DBT), and Indian Council of Medical Research (ICMR), also followed suit in funding nanomedicine projects.<sup>[4]</sup> Although research in India on nanomedicine has progressed, a comprehensive landscape on Indian nanomedicine innovation activities

is currently unavailable to assess the impact of India's engagement in the field of nanomedicine.

### Current Landscape of Nanomedicine

#### A) Current uses of nanomedicine

Numerous nanomedicines have been developed and applied for disease treatment, with a particular focus on cancer therapy. Recently, nanomedicine has been utilized in various advanced fields, including diagnosis, vaccines, immunotherapy, gene delivery, and tissue engineering.

#### B) Current goals of nanomedicines

Improve unfavorable pharmacokinetics and tissue distribution of many drugs, increase therapeutic efficacy by achieving higher accumulation of a drug in the target tissue, reduce (dose-limiting) adverse effects by minimizing drug exposure to non-target tissues.

#### Innovative Diagnostic Approach

Nanomedicine has led to the development of innovative diagnostic approaches that offer improved sensitivity, specificity, and speed. Some examples include.

1. Nanoparticle-based assays: Utilize nanoparticles to detect biomarkers or pathogens.
2. Quantum dot-based imaging: Use quantum dots to visualize cellular processes or tumor margins.
3. Gold nanoparticle-based diagnostics: Employ gold nanoparticles for lateral flow assays or biosensors.
4. Magnetic nanoparticle-based diagnostics: Utilize magnetic nanoparticles for magnetic resonance imaging (MRI) or magnetoresistance-based assays.
5. Nanostructured biosensors: Leverage nanostructured materials to enhance sensor performance.
6. Point-of-care diagnostics: Develop portable, user-friendly devices for rapid diagnosis.
7. Liquid biopsies: Analyze circulating tumor DNA or other biomarkers in bodily fluids.
8. Nanopore sequencing: Use nanopores to sequence DNA or RNA molecules.
9. Synthetic biology-based diagnostics: Engineer biological systems to detect specific biomarkers.
10. Artificial intelligence-powered diagnostics: Apply AI algorithms to analyze medical images or diagnostic data.

These innovative diagnostic approaches in nanomedicine enable.<sup>[5]</sup>

- Early disease detection
- Personalized medicine
- Real-time monitoring
- Improved patient outcomes
- Enhanced drug development

By leveraging nanotechnology and innovative materials, researchers are creating cutting-edge diagnostic tools that transform healthcare and improve patient lives.

#### Recent Trends for Nanomedicine Safety

Nanomedicine has gained tremendous attention in medical professionals to its smart strategies of treatment and huge applications in healthcare. Nanomedicine is

mainly used for drug delivery with special attention to drug targeting, their excellent properties of high drug loading, sustained drug release, surface tunability, surface modification possibilities, and unique surface properties.<sup>[6]</sup> A major portion of nanomedicine has been occupied by nanocarrier systems. For diagnosis and therapeutic purposes, nanoparticles, nanoliposomes, dendrimers, and other nanoparticulate devices have been reported for treatment/diagnosis of diseases. Several nanomedicines with emerging therapeutic efficacy have been already commercially available and many more are in pipeline. Despite their impressive therapeutic benefits, some critical challenges are associated with their transition from laboratory to clinical usage.<sup>[7]</sup> Toxicity caused by nano formulated drug is the most adverse barrier for its broad range of application. In this chapter, we have reported different nanocarriers available for their diversified applications in the management of several diseases, with a special emphasis on recently published reports, clinical evidence, and their toxicity and safety concerns.

#### Theragnostic - Integrating Diagnostic and Therapeutic Potentials in Nanomedicine

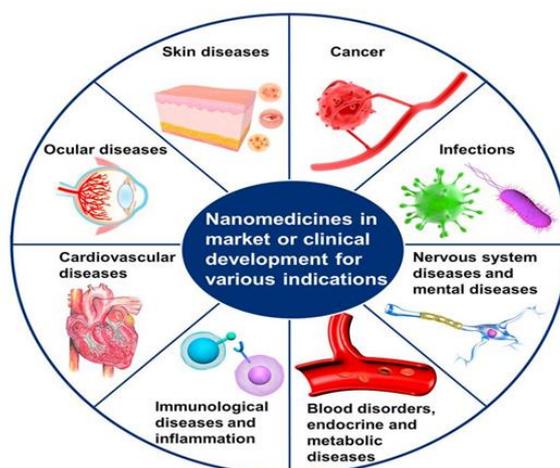
Theragnostic is a strategy that integrates therapeutics with diagnostics to develop new personalized treatments with enhanced efficacy and safety. One key component of theragnostic is diagnostic imaging with high sensitivity and molecular specificity. The advent of molecular imaging has brought revolutionary changes to conventional imaging by enabling characterization of biological processes at the cellular and molecular levels spatially and temporally. Depending on the molecular imaging modality and contrast agent used, theragnostic could be achieved by applying imaging throughout treatment planning, drug and dosage selection, and therapeutic response monitoring. Nanotechnology has led the advances in theragnostic, because of the development of a variety of fine particulate materials with size dimensions in the range of 1–200 nm, and the discovery of their unique physicochemical properties that are not found in their bulk counterparts. These properties include quantum confinement in semiconductor nanoparticles (also known as quantum dots), superparamagnetic in certain oxide nanoparticles, and surface-enhanced Raman scattering (SERS) in metallic nanoparticles, among others. These unique physical properties have expanded the potential of molecular imaging, and led to the development of extremely sensitive, and cost-effective novel molecular imaging agents.<sup>[8]</sup> These new imaging agents can be broadly categorized as optical (fluorescent, SERS, photoacoustic, etc.), magnetic, radioactive (positron or  $\gamma$ -ray emitting), X-ray opaque (nanoparticles with high electron density) and ultrasound-sensitive (nanobubbles) agents.

#### Promises and Challenges for The Future of Public Health

As the scope of nanotechnology applications in medicine evolves, it is important to simultaneously recognize and

advance contributions germane to public health.<sup>[9]</sup> A wide range of innovations in nanomedicine stand to impact nearly every medical specialty and unveil novel ways to improve the quality and extend the duration of life – these gains can be measured at both individual and population levels. For example, heart disease and cancer combined make up approximately half of all deaths in the United States per year, and already, advances in nanomedicine demonstrate great potential to reduce rates of morbidity and mortality due to these diseases. Meanwhile, public health applications of nanomedicine such as rapid and portable diagnostics and more effective vaccinations have the potential to revolutionize global

health. Research driven by innovators across disciplines such as engineering, biology, medicine, and public health should collaborate in order to achieve maximal potential impact in health for individuals and populations. In turn, knowledge gaps regarding the potential health and safety implications of exposure to engineered nanomaterials must be continuously addressed and actively researched.<sup>[10]</sup> Dynamic, proactive, and socially responsible research will drive nanomedicine as it plays an increasingly integral and transformative role in medicine and public health in the 21st century. Current approaches of nanomedicines in the market.



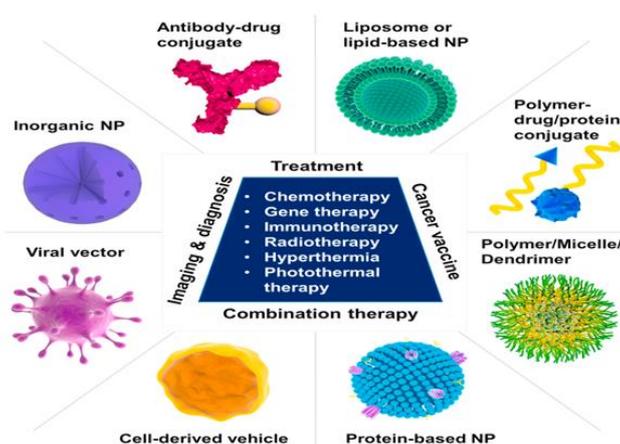
**Figure 1: Nanomedicines in the market and various stages of clinical translations for many types of diseases. The skin diagram was reprinted with permission from Ref. 13. Copyright © 2021 American Chemical Society. The eye structure was reprinted under terms of the CC-BY license with the permission from Ref. 14. Copyright © 2020 MDPI, Basel, Switzerland. The cardiovascular graphic was reproduced under terms of the CC-BY license with the permission from Ref. 15. Copyright © 2015 MDPI, Basel, Switzerland.**

## Applications of nanomedicines in various indication

### Cancer treatment

Nanomedicines have been widely used in cancer therapy due to their distinguished features, such as modulating *in vivo* distribution profiles, promoting specific tumor accumulation *via* passive or active targeting capability, delivering multiple therapeutic agents at fixed ratios, or reducing the adverse effect of loaded drugs.<sup>[11]</sup> The

passive targeting of nanomedicines mainly depends on the difference of pathophysiological characteristics between tumor and healthy tissues, such as the abnormal structures of the tumor vasculatures. In contrast, the active targeting nanomedicines can be achieved by their preferential recognition or binding to the over-expressed or specifically expressed receptors in the tumor microenvironments.<sup>[12]</sup>

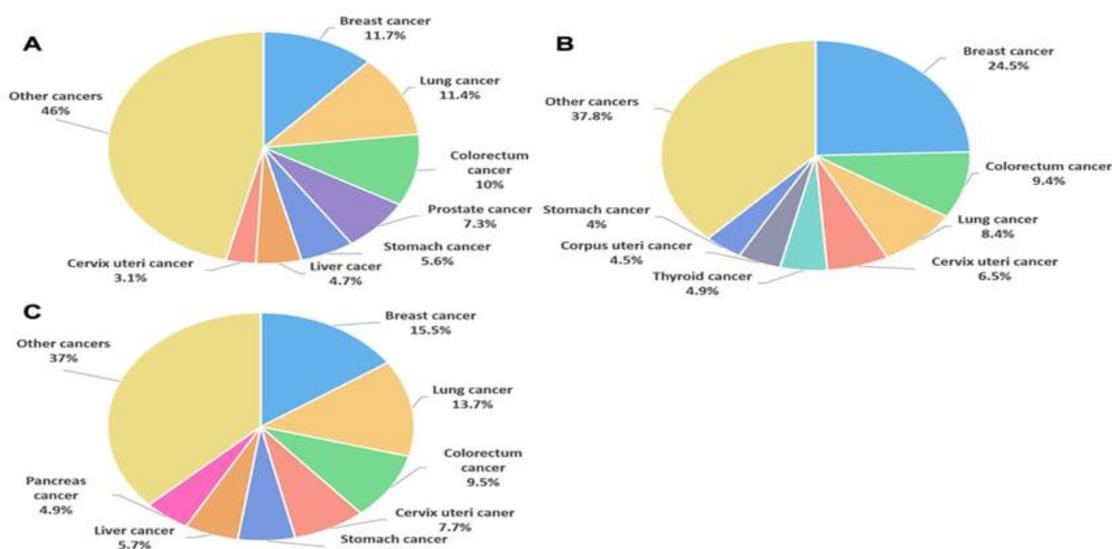


**Figure 2: Types and applications of anticancer nanomedicines on the market and under clinical trials.**

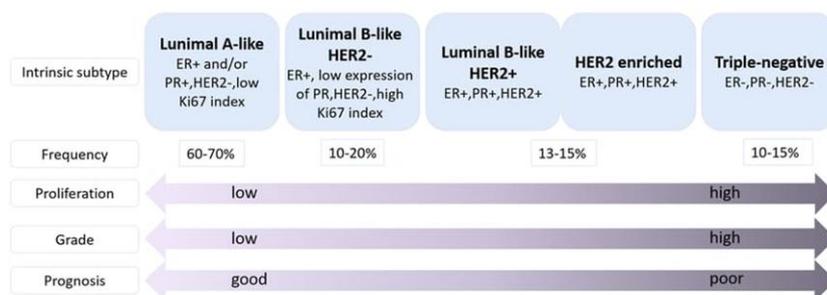
### Breast cancer

Breast cancer (BC) is the most commonly diagnosed cancer in female worldwide. There were about 2.3 million new cases of BC and the number of deaths reached 685,000 in 2020, accounting for 1 in 6 cancer deaths (Sung *et al.*, 2021). Heterogeneous cancer type and was classified into four main subtypes: luminal A, luminal B, human epidermal growth factor receptor 2 (HER2) enriched and basal-like BC. Currently, clinically relevant surrogate subtypes based on the histological and molecular characteristics included luminal A-like, luminal B-like HER2-, luminal B-like HER2+, HER2 enriched, and triple-negative type (Perou *et al.*, 2000; Cheang *et al.*, 2009; Harbeck *et al.*, 2019) (Figure 2). Generally, multidisciplinary approaches which are used to treat BC include systemic therapy (chemotherapy,

endocrine therapy, HER2 targeted therapy and soon) and local therapy (surgery and radiotherapy). The choice of therapeutic strategy depends on subtype and disease stage of BC (Waks and Winer, 2019; Shien and Iwata, 2020).<sup>[13]</sup> Although the optimization of these treatment schemes has increased the cure opportunity of about 70%–80% of early BC patients, so far, metastatic BC is still considered as incurable (Harbeck *et al.*, 2019). In addition, disadvantages of conventional anti-cancer drugs, such as lack of selectivity for tumors, poor solubility, high toxicity, multidrug resistance, short half-life and poor chemical stability, often lead to the therapeutic efficacy far from satisfactory (Fraguas-Sanchez *et al.*, 2022). Hence, the more efficient and less toxic therapeutic strategies warrant further in deep investigation to develop personalized treatment for BC.



**Figure 3: The cancer cases and deaths in 2020. (A) Percentage of new cancer cases worldwide in 2020, both sexes. (B) Percentage of new cancer cases worldwide in 2020, females. (C) Percentage of female cancer deaths worldwide in 2020. (Data source: The World Health Organization).**



**Figure 4: Classification of molecular subtypes of breast cancer (Harbeck *et al.*, 2019). ER: estrogen receptor, PR, progesterone receptor; HER2, human.**

### Future of Nanomedicine

Disease and other disturbances of function are caused largely by damage at the molecular and cellular level but current surgical tools are large and crude.<sup>[14]</sup> Even a fine scalpel is a weapon more suited to tear and injure than heal and cure. It would make more sense to operate at the cell level to correct the cause of disease, rather than chop

off large lesions because of the disturbances at cell level. Nanotechnology will enable construction of computer-controlled molecular tools that are much smaller than a human cell and built with the accuracy and precision of drug molecules. Such tools will be used for interventions in a refined and controlled manner at the cellular and molecular levels.<sup>[15]</sup> They could remove obstructions in

the circulatory system, kill cancer cells, or take over the function of subcellular organelles. Instead of transplanting artificial hearts, a surgeon of the future would be transplanting artificial mitochondrion. Nanotechnology will also provide devices to examine tissue in minute detail. Biosensors that are smaller than a cell would give us an inside look at cellular function.<sup>[16]</sup> Tissues could be analyzed down to the molecular level, giving a completely detailed “snapshot” of cellular, subcellular, and molecular activities. Such a detailed diagnosis would guide the appropriate treatment. It is expected that within the next few years, we will have a better understanding of how to coat or chemically alter nanoparticles to reduce their toxicity to the body, which will allow us to broaden their use for disease diagnosis

and for drug delivery.<sup>[17]</sup> Biomedical applications are likely to be some of the earliest. The first clinical trials are anticipated cancer therapy.

### Therapeutic Applications

Numerous nanomedicines have been developed and applied for disease treatment, with a particular focus on cancer therapy. Recently, nanomedicine has been utilized in various advanced fields, including diagnosis, vaccines, immunotherapy, gene delivery, and tissue engineering. Nanotechnology in Medicine employs minuscule materials and devices to revolutionize healthcare.<sup>[18]</sup> It offers precise drug delivery, advanced disease detection, and innovative treatments, leveraging nanoparticles and nanodevices for targeted therapy and diagnosis.

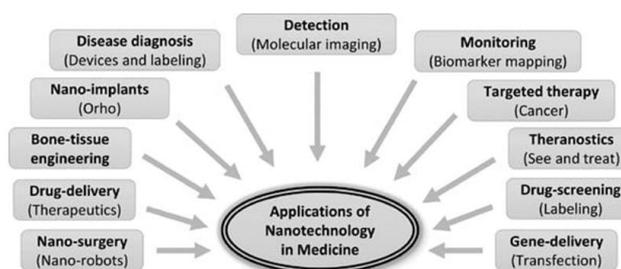


Figure 5: Application of Nanotechnology in Medicine.

### Trends In Nanomedicine

#### Stem cells

Nanoparticles are beneficial to regenerative medicine, stem cell growth, and differentiation. Pluripotent stem cells generally need to be cultured before being transferred to the human body. Due to the large surface area and low-concentration biocompatibility of the two-dimensional nanostructures, it has been proven advantageous for manufacturing a scaffold suitable for culturing pluripotent stem cells.<sup>[19]</sup> Tracking or monitoring the status of transplanted stem cells in the body can provide more useful information for precise treatment. MSNs have been widely functionalized with different imaging agents to integrate the therapeutic and diagnostic functions of nanomedicine.<sup>[20]</sup> Similarly, MSNs with imaging capabilities can also be used to label stem cells. Kempen et al. reported a biodegradable MSN

with dual-mode ultra-sound and magnetic resonance imaging capabilities and used it to label mesenchymal stem cells. Even at a high concentration of 250  $\mu\text{g/mL}$ , the detection limit reached 9000 cells.<sup>[21]</sup> The imaging capabilities of MSNs are maintained after about three weeks of implantation in the body. Chen et al. demonstrated that a new type of cup-shaped MSN can be used as a contrast agent for ultrasound imaging of stem cells.<sup>[20]</sup> They claim that the detection limit in vivo is less than  $\sim 500$  cells, and its toxicity is negligible at the concentration used. Rosenbrand et al. studied the effect of lipid and PEG modification of MSNs on stem cell tracking ability.<sup>[22]</sup> The results showed that organic modification, especially lipids, can greatly improve its labeling performance. Considering its powerful Therapeutic delivery function, MSNs may play a significant role in engineering stem cells and tissue engineering.<sup>[23]</sup>

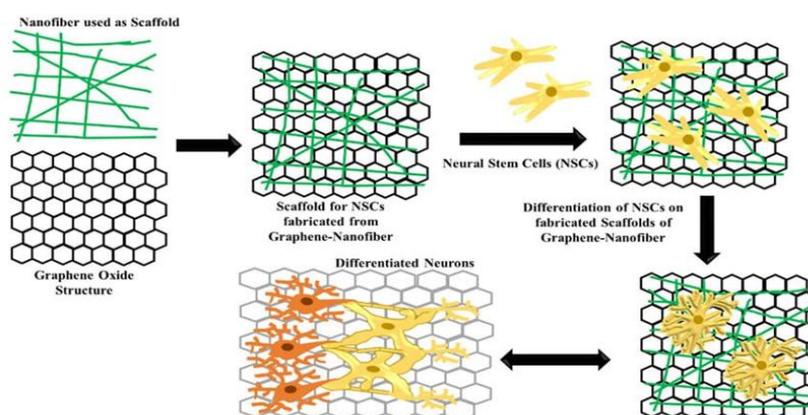


Figure 6: New Trends in Nanomedicine by Stem Cells.

### Advanced nanoparticles (NPs)

Recently, magnetic nanoparticles have emerged as a research field and have received extensive attention from researchers because they have a wide range of applications in various fields, including catalysis, data storage, environmental remediation, magnetic fluid, electronic communications, and biomedicine. Among the different types of magnetic nanoparticles (MNPs), iron oxide nanoparticles (IONPs) are the most popular.<sup>[24]</sup> They are widely used in nanomedicine due to their ease of surface modification, synthesis, and low toxicity. Current research and literature have confirmed that magnetic IONPs are often used to treat hyperthermia or as drug carriers for cancer treatment, magnetic resonance imaging (MRI) agents, biological separation, gene delivery, biosensors, protein purification, immunoassays, and to identify cells.<sup>[25]</sup> Surface coatings can improve the

stability, biocompatibility, and even solubility of IONP, greatly expanding the application of IONPs.<sup>[26]</sup>

Liu et al. developed an inexpensive titanium dioxide (TiO<sub>2</sub>) nanofiber substrate, as shown in Fig. 1.3, to efficiently and selectively capture circulating tumor cells (CTCs) from bio simulated patient samples. The titanium dioxide nanofiber substrate is made by a combination of electrospinning and calcination processes.<sup>[27]</sup> The surface of the nanofiber substrate was modified by antiadhesion molecules, bovine serum albumin (BSA), and the nuclide inducer AS1411, where the inducer AS1411 clearly binds to the nuclide protein overexpressed on the surface of the cancer cell membrane.<sup>[28]</sup> The formed TiO<sub>2</sub> nanofiber matrix exhibits high efficiency and specificity in capturing nucleotide-positive cells.

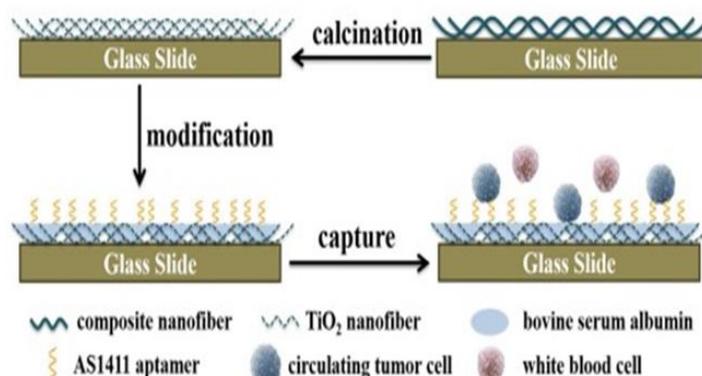


Figure 7: Advanced In Nanoparticles.

### Challenges in Pharmaceutical Development

The translation of nanotechnology forms the bench to the market imposed several challenges.<sup>[29]</sup> General issues to consider during the development of nanomedicine

products including physicochemical characterization, biocompatibility, and nanotoxicology evaluation, pharmacokinetics and pharmacodynamics assessment, process control, and scale-reproducibility.

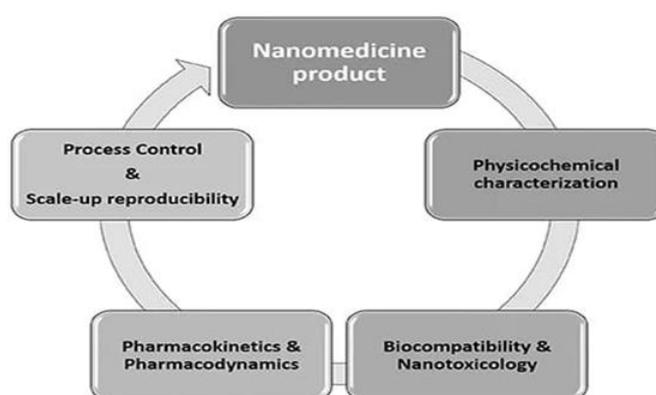


Figure 8: Schematic representation of the several “barriers” found throughout the development of a nanomedicine product.

### CONCLUSION

Nanomedicine is one of the most rapidly growing fields of translational medicine and has made marked impacts in terms of alleviation of toxicity and enhancement of efficacy for therapies. Overall, nanotechnology offers the opportunity to create functional materials and devices

with unique properties at the nanoscale, with applications in various fields and the potential for future advancements. It enables rapid detection and treatment at the cellular level. Nanoparticles improve currently used methods. Nanorobots and nanomachines have opened a new world of discoveries and feasibilities in

nanomedicine. Numerous novel nanomedicine-related applications are under development or nearing commercialization, the process of converting basic research in nanomedicine into commercially viable products will be long and difficult. Although realization of the full potential of nanomedicine maybe years or decades away, recent advances in nanotechnology-related drug delivery, diagnosis, and drug development is beginning to change the landscape medicine. New nanotechnologies may offer the only hope for systematic, affordable, and long-term improvements to the health status of our population.

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