



A Review: “Nanoparticles for Drug Delivery: Design, Development & Therapeutic Application”

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ABSTRACT -

Nanoscience is now used in many clinical and medical domains, including the treatment of cancer. On the other hand, there are many people who suffer from cancer and its variants, which have been rumored to be inclusive. In actuality, despite the therapeutic impact, patients have uncomfortable side effects from modern treatment procedures like chemotherapy, radiation, etc. To address this serious sickness, researchers and scientists are also trying to develop and improve treatment alternatives and approaches. These days, nanotechnology and nanoscience are widely used. Their various fields, such as nanoparticles, are frequently employed for a variety of purposes, particularly in imaging and drug delivery as well as diagnostic devices. The release of cancer is significantly impacted by release mechanisms centered on nanotechnology.[1]The precision medicine age has led to bottlenecks in traditional medications, including decreased solubility, absorption, and particularly ineffective organ or cell targeting. To address the aforementioned flaws, it is critically necessary to find and implement new techniques or tactics to alter existing medications or develop new ones. Although there are still numerous shortcomings, the solubility, absorption, and targeting of conventional medications have been significantly enhanced with the use of nanotechnology through the modification and fabrication of different kinds of nanoparticles. [2]

Keywords –Drug delivery; nanomedicine; nanoparticles; personalized medicine, nanocarriers.

Introduction –

Background –

The European Science Foundation’s Forward Look Nanomedicine defines nanomedicine as “the use of nano-sized tools for disease diagnosis, prevention, and treatment, as well as to better understand the intricate underlying patho-physiology of disease.” Enhancing quality of life is the ultimate objective.[3] The word nano means “dwarf” in Greek, while the SI prefix stands for 10^{-9} or 0.000000001.[4] In order to increase life expectancy by transforming medication delivery methods, drug development and delivery have moved from the micro to the nano level over the past few decades (Figure 1) The concept of nanotechnology was first presented by physicist Feynman in his 1959 lecture “There’s Plenty of room at the Bottom.” Significant advancements in the field of nanotechnology were sparked by this idea.[5]This was how the idea of contemporary technology was born. He is therefore frequently regarded as the founder of contemporary nanotechnology. It’s possible that Norio Taniguchi coined the word “nanotechnology” in 1974.[6] Nanomaterials have been utilized by humans for a long time. The earliest known account of nanomaterials’ existence was found in 5000-year-old Ayurvedic literature. The development of different bhasmas, or ashes, such as Suvarna Bhasma, Rajat Bhasma, Tamra Bhasma, etc., is thoroughly explained in Ayurveda. Dr. Samuel Hahnemann developed homeopathy, a novel medical treatment.[7]Since the 1990s, the number of FDA-approved products and nanotechnology-based clinical trials has increased dramatically.[8]There is great potential for enhanced illness detection and therapy specificity with engineered nanomaterials. The limits of traditional delivery methods, ranging from large-scale problems like biodistribution to smaller-scale obstacles like intracellular trafficking, may be addressed by nanotechnology through methods like cell-specific targeting and molecular transport to certain organelles.[9]The ability to target tumors by functionalizing their surface with ligands unique to tumors (such as transferrin, aptamer, peptides, antibodies, etc.) is another example of smart nanoparticles.[10]

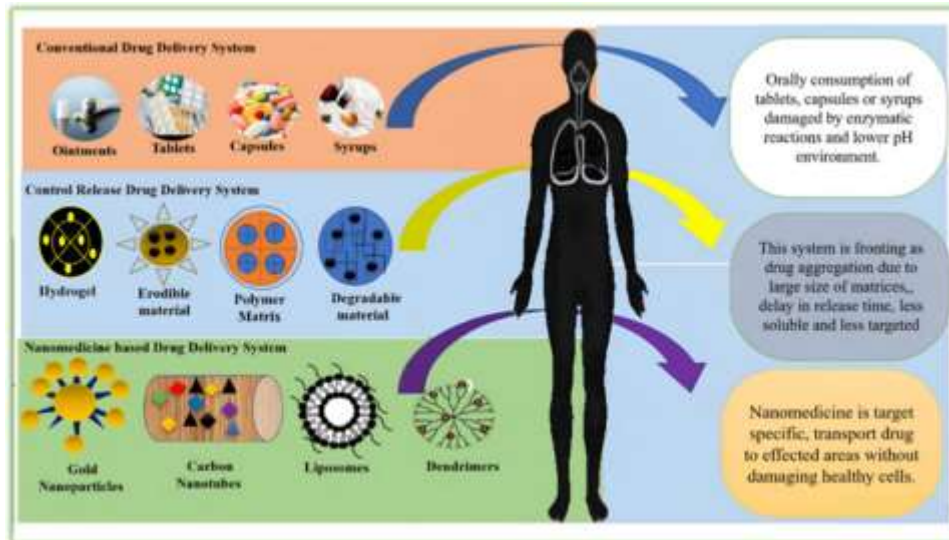


Figure 1. Illustration of how traditional medications were administered without the use of carriers and harm was done to healthy organs or cells. In contrast, modern procedures use nanotechnology to transport medications to specific parts of the body.[11]

Advantages –

1. Precision medicine: One of nanomedicine’s greatest benefits is its capacity to deliver medications and other therapeutic agents straight to the illness site. By using precision medicine, the therapeutic impact of the medication is maximized while the danger of adverse effects is decreased.
2. Early diagnosis: Imaging methods based on nanotechnology, such as computed tomography (CT) scans and magnetic resonance imaging (MRI), enable earlier and more precise treatment of illnesses like cancer.
3. Targeted therapy: It is possible to design nanoparticles to specifically target particular body tissues or cells, which is especially helpful in cancer treatment. This method of focused therapy lowers the possibility of harming healthy tissues and cells.
4. Better drug delivery: By making drugs more soluble, bioavailable, and stable, nanoparticles can help improve drug delivery. This lowers the risk of toxicity and adverse effects by enabling the use of lower dosages of medications.
5. Regenerative medicine: Growth factors and other regenerative medicines can be delivered to injured tissues using nanoparticles, facilitating tissue regeneration and repair.

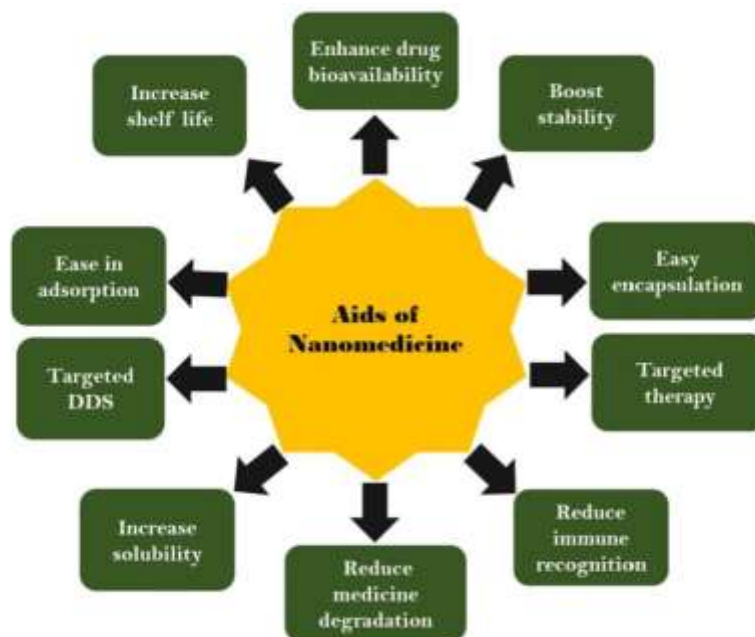


Figure 2. Aids of using nanomedicine platform for delivering drugs to the tumor complex.[11]

Disadvantages-

1. **Toxicity:** The long-term toxicity of nanoparticles is not well understood, and their application in medicine is still in its infancy. Certain nanoparticles can build up in the body and harm tissues and organs, according to studies.
2. **Cost:** The creation and manufacturing of nanoparticles can be costly, which may restrict their accessibility and affordability.
3. **Regulatory obstacles:** The development and use of novel treatments may be slowed down by the stringent regulatory approval requirements for the use of nanomedicine in people.
4. **Ethical concern :**The use of nanomedicine raises ethical questions as well, especially when it comes to fields like genetic editing and enhancement.
5. **Limited understanding:** The ways in which nanoparticles and the human body interact are yet mostly unknown. The possible advantages and hazards of nanomedicine require further investigation.[12]

Size -

The body's cells "see" nanoparticles differently depending on their size and shape, which determines their distribution, toxicity, and ability to target.[13]As previously mentioned, nanoparticles are tiny particles with a high surface area to volume ratio that range in size from 1 nm to 100 nm. Some ordinarily inert particles, like gold, become reactive in the nanoscale range due to this characteristic, which gives nanoparticles a higher surface area of contact per mass unit than more bulky particles.[14]Despite all of the progress made thus far, nothing is known about the molecular level of interactions between cells and nanostructures of specific sizes.[15]Pits covered with clathrin were implicated in the internalization of microspheres smaller than 200 nm in diameter. As particles grew larger, a mechanism based on internalization mediated by caveolae became evident, and this became the main entry point for particles with a size of 500 nm.[16]

Surface Chemistry

Nanoparticles' surface chemistry, including charge or attached chemical groups, plays a significant role in determining their reactivity and, eventually, their ability to influence function. To serve certain functions, the surface chemistry of several nanoparticles has been altered. Since DNA and rod-shaped gold nanoparticles (AuNPs) are charged, they are difficult to penetrate or enter cells. In order to increase uptake, the surfaces of both AuNP and DNA have been coated with lipid layers. Additionally, DNA has been electrostatically coupled to cationic liposomes to aid in their transport into the cell.[17,18,19]

Shape –

Compared to both spherical and short-rod nanoparticles, found that long-rod nanoparticles have a longer bioavailability in addition to being able to incorporate more particles. Although there are other shapes, such nanoflowers and nanoprisms, these could not be as active as nanorods and nanospheres because of their distinct geometries.[20]

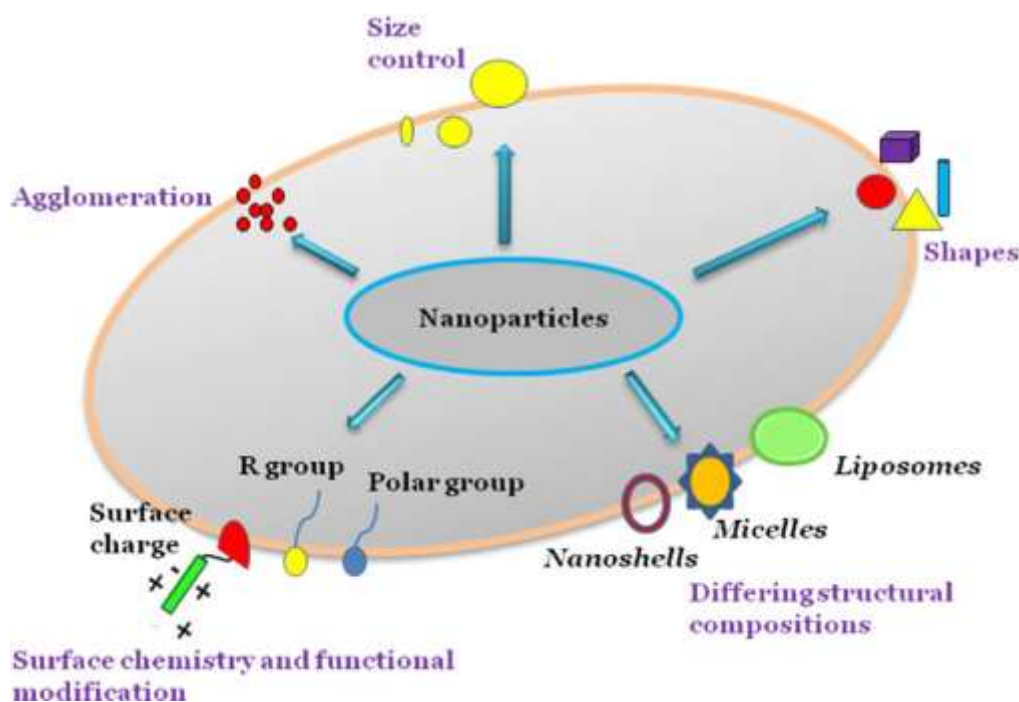


Figure 1. Physicochemical properties of nanoparticles.[14]

Design & Development

1) Material use in synthesis of NPs-

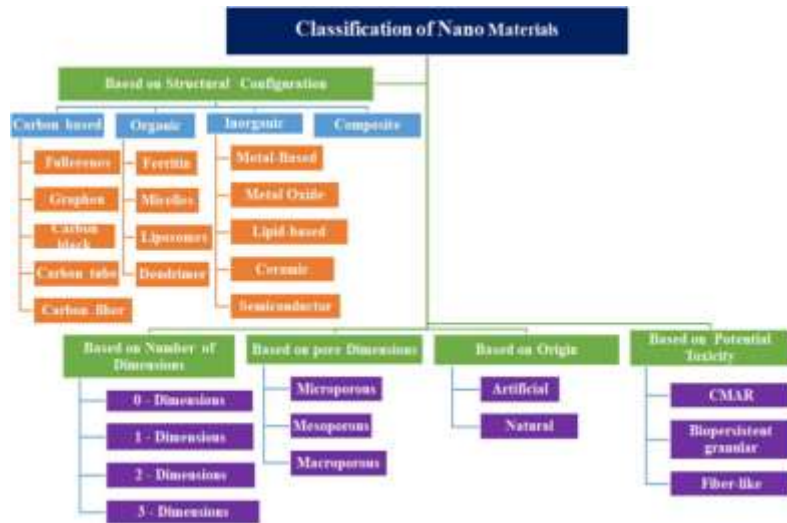


Fig. 3: Material use in nanoparticles synthesis [21]

2) Synthesis technique of Nanoparticles –

- A) **Biological Synthesis:** The simplest, most sustainable, nontoxic, and environmentally benign method of creating nanoparticles of the required quality is biological synthesis. Plants, bacteria, yeast, and fungi are used in this method to create nanoparticles. Nanoparticles can be synthesized both intracellularly and extracellularly using unicellular and multicultural methods.
- Biological synthesis of nanoparticles using bacteria
 - Biological Synthesis of nanoparticles using yeast
 - Biological Synthesis of nanoparticles using fungi.
- B) **Chemical Synthesis** -In chemical synthesis, the capping and stabilizing agent determines the size and characteristics of the nanoparticles. Three methods are employed for the chemical production of the nanoparticles:
- Dispersion of preformed polymers
 - Polymerization of monomers
 - Ionic chelation or coacervation of hydrophilic polymers[22]
- C) **Physical Synthesis** -The two physical methods that are most crucial are evaporation-condensation and laser ablation. Physical synthesis techniques have two advantages over chemical processes: the produced thin films are free of solvent contamination, and the distribution of NPs is uniform.[23]

Application

• Nanoparticles have special mechanical, magnetic, thermal, and optical qualities in addition to their other physical and chemical characteristics. Because of its distinctiveness, it has been used in several fields. The following section discusses some of the noteworthy uses of NPs:[24]

1. **Nanoparticles in Medicine** - Clinical medicine has benefited greatly from nanoparticles in the fields of drug/gene delivery and medical imaging. Most frequently used in biomedical applications are iron oxide particles like magnetite (Fe₃O₄) or their oxidized counterpart, hematite (Fe₂O₃). Because of their antibacterial properties, Ag NPs are being utilized more and more in catheters, wound dressings, and other home products.
2. **Nanoparticles in food** - Food packaging has increasingly included nanoparticles to regulate the surrounding air and keep food fresh and free from microbiological contamination (Bhardwaj M. & Saxena D.C., 2017). Since inorganic and metal nanoparticles (NPs) can directly incorporate antimicrobial compounds onto the coated film surface, they are now widely used as alternatives to petroleum plastics in the food packaging business.
3. **Electronics** -One-dimensional semiconductors and metals are the essential building blocks for a new generation of electronic, sensor, and photonic materials due to their distinct structural, optical, and electrical characteristics.

4. Environmental Remediation: Since nanoparticles can be applied both in situ and ex situ in aquatic environments, they are frequently utilized for environmental cleanup. Because of their antiviral, antifungal, and antibacterial properties, silver nanoparticles (AgNPs) have found widespread usage as water disinfectants (Zhang, C., Hu, Z., Li, P., & Gajaraj, S., 2016).[24]

5. Targeted drug delivery –

Selective NP therapies have demonstrated a high tendency for treating cancer because to their increased efficacy and reduced adverse effects (Chatelut et al., 2003). There are two possible approaches to NP medication distribution: active and passive. NP transfer by passive diffusion or convection via leaky tumor capillary fenestrations through the interstitial tumor and cells is referred to as passive delivery (Carroll et al., 2011). Selective accumulation of NP and medication is then produced by the previously mentioned features of the tumor microenvironment.[25]

6. Nanoparticles in cancer treatment –

The second most common cause of mortality globally is still cancer. Cancer is diverse, and in part, this complexity makes it extremely difficult to design effective cancer treatments. Targeted chemotherapy has been created to treat patients who express particular biomarkers, and precision medicine has emerged as a potential strategy.[25]

7. Nanoparticles for genome editing -

Engineering the genome for broad application in gene therapy, drug development and discovery, and biomedical research is becoming easier thanks to recent developments in CRISPR, transcription activator-like effector nuclease (TALEN), and zinc-finger nuclease (ZFN) technologies.[25]

• A list of some of the applications of nanomaterials to biology or medicine is given below:

- Fluorescent biological labels [26]
- Drug and gene delivery .[27]
- Bio detection of pathogens[28]
- Detection of proteins [29]
- Probing of DNA structure [30]
- Tissue engineering [31]
- Tumour destruction via heating (hyperthermia)[32]
- Separation and purification of biological molecules and Cells [33]
- MRI contrast enhancement [34]
- Phagokinetic studies [35]

Future perspectives –

The “technology of the future” that can fix a lot of issues is nanotechnology. A revolution in nanotechnology is even mentioned by some. Nanotechnology undoubtedly has a lot to offer in terms of prospective profits and advantages, but everyone should be aware that even the newest technologies have risks and that this area is still relatively unexplored.[36] It is anticipated that nanotechnology, an emerging science, will advance quickly and significantly in the future. Over the next few decades, it is expected to play a major role in the EU’s economic expansion and job creation.[37] This review has covered a wide range of nanoparticle designs that are tailored for therapeutic delivery and designed to get past the biological barriers that vary among patient demographics and illnesses. Unique physiologies, different stages of disease progression, and patient comorbidities all aggravate these delivery hurdles. Using nanoparticles made for various patient populations, diseases, or the combination of the two, this wide range of requirements can be satisfied.[25]

Conclusion:

Nanoparticles-based drug delivery systems have emerged as a promising approach for improving the efficacy and reducing the toxicity of various therapeutic agents. The development of these systems involves the design and engineering of nanoparticles with specific properties, such as size, shape, and surface chemistry, to optimize their interactions with cells and tissues.

This review has highlighted the recent advances in the development of nanoparticles-based drug delivery systems, including the use of various materials, such as lipids, polymers, and metals, and the application of different fabrication techniques, such as solvent evaporation, emulsion, and 3D printing.

In conclusion, nanoparticles-based drug delivery systems have the potential to revolutionize the field of pharmacology and improve patient outcomes. Further research and development are needed to fully realize the promise of these systems

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