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Nanoparticle-based drug delivery systems: An efficient system for the treatment of chronic diseases

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Abstract

Nanoparticle-based drug delivery systems form an integral component in modern medicine since they respond to major problems undermining traditional pharmacotherapeutic techniques, such as poor bioavailability, toxicity, and poor targeting of the desired drug location. This review also looks into the different types of nanoparticles: liposomes, polymeric nanoparticles, dendrimers and solid lipid nanoparticles, and how they work such as: targeting, drug delivery, release of drug, and tissue penetration. Some of the FDA-approved drugs that incorporated nanotechnology are Doxil; Abraxane; Onivyde; Vyxeos and two COVID-19 vaccines— Comirnaty and Spikevax that uses lipid nanoparticles to activate the immune system against COVID-19. By comparing the nanoparticle to the conventional drug delivery physical systems, we can see that nanoparticle possess following advantages which include; targeting, bioavailability, controlled release and cross biological barriers like the blood brain barrier. However, the following challenges are still present: numerous manufacturing steps, problems in scaling up, and regulatory limitations that can affect clinical use of the technology. This review also underlines that nanoparticle-based drug delivery systems will have a very bright future in the field of personalized medicine and will change the strategy of the disease treatment such as cancer and some neurological diseases. Further development in this area is critical in order to provide thorough eradication of the existing challenges and make the best utilization of the nanoparticles for therapies.

Keywords: Nanoparticles; Drug Delivery; Bioavailability; Targeted Therapy; Nanotechnology; Personalized medicine; Nanotechnology in pharmaceuticals

1. Introduction

A novel drug delivery system (NDDS) refers to advanced techniques aimed at optimizing use of medicinal agents, increasing their bioavailability and reducing toxicity. These are targeted drug delivery wherein drugs are delivered to targeted tissues; prolonged and controlled release systems for long acting; liposomes and nano systems for encapsulation of drugs; transdermal systems for non-invasive administration; ocular and pulmonary systems to deliver drugs to the eye and lungs respectively; bio erodible polymers for rates release; stimuli sensitive systems which work on a preset stimulus; and gene delivery systems for carrying therapeutic genes. Combined, these approaches all share the goal of enhancing patients' adherence and effectiveness of treatment in today's medicine. [26]

Nanoparticle-based drug delivery systems have been developed as the new transformation in medicine for overcoming the major limitations associated with traditional approaches to drug delivery. H Panel methods of drug delivery which include oral tablets, injections and topical formulations, have some drawbacks, which include low bioavailability, random distribution of drugs, and or clearance through systemic action and toxicity. Such issues can reduce the levels of effectiveness of numerous medications and lead to negative side effects on patient care, especially those with cancer or chronic diseases. These problems can be solved by nanoparticles with size between 1-100 nm. These structures can

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be designed for increasing the solubility of drugs, for increasing targeting properties or for operating as a controlled release of therapeutic agents. Liposomal, polymeric, dendritic, and solid lipid nanoparticles characterized by their unique features for drug delivery. For example, its liposomal formulation, Doxil (liposomal doxorubicin), illustrates an effective way of decreasing cardiotoxicity but increases on-target drug delivery of chemotherapy agents. Likewise, Abraxane (albumin-bound paclitaxel) has improved solubility and increases effectiveness of paclitaxel used in the treatment of metastatic breast cancer. Examples include Onivyde, a liposomal formulation of irinotecan liposome injection for the chemotherapy of pancreatic cancer; and Vyxeos a liposomal product of cytarabine and daunorubicin for the treatment of acute myeloid leukaemia. This idea has been boosted by the recent success of using lipid nanoparticles in delivering vaccines like Comirnaty and Spikevax to deliver mRNA in the Figureht against the COVID 19 pandemic as they have an enhanced ability to encapsulate mRNA vaccines and deliver them to the appropriate site to trigger an immune response. [21,22]

However, nanoparticle-based systems also have some major benefits, mainly the possibility to home nanoparticle-carried agents to a director tissue or cell type, thus increasing the selectivity of treatment. This targeted delivery approach is also most useful in oncology, as the therapies required have to be delivered specifically to the tumour regions and not the rest of the surrounding tissue. Also, nanoparticles have the great ability to cross biological barriers, for instance the BBB for drug delivery for neurological disorders, like Alzheimer disease and Parkinson disease. However, there are certain drawbacks associated with these systems that need to be resolved to make an effective use of nanoparticle-based drug delivery systems in practice. The fabrication of nanoparticles is not always an easy process and as a result there can be challenges in scaling up production of these particles, as of the biological treatments nanoparticles are there known to follow a longer route to approval compared to the conventional drugs due to their newness in the market. It is the intention of this review to present an outline of current nanotherapeutic systems for drug delivery and their comparison with conventional techniques. This paper reviews the role of different formulation of nanoparticles that is utilized in approved products and their mode of action to demonstrate the capacity of these advanced delivery systems in overhauling treatment methodologies and enhancing patient care in multiple specialties. [10,20]

2. Types of Nanoparticles in Drug Delivery Systems

2.1. Liposomes

Liposomes are preferred encapsulation systems among all the used nanoparticles and refer to spherical vesicles made of lipid bilayers. It is biocompatible and capable of entrapping both hydrophilic and hydrophobic drugs; the carriers are thus very flexible. Doxil, the first and only liposomal drug approved by the FDA at the time this review was written, showed the prospect of liposomes in the delivery of chemotherapeutic agents with reduced cardio toxic profile. Nonetheless, issues like stability, manufacturing for large scale production, and MPS clearance have formed major drawbacks and restricted the broad clinical applications of liposomes to a great extent. [1,10]

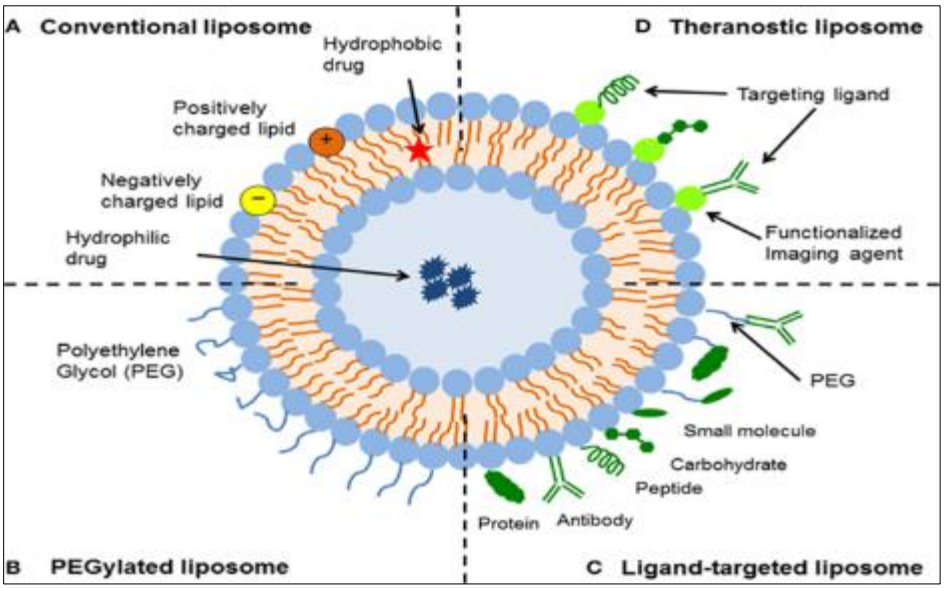

Figure 1 Different Types of Liposomes

New trends in the liposomal technology have been on the ability to increase circulation time and targeting properties of these nanoparticles. For instance, Reticuloendothelial system (RES) targeting can be alleviated by attaching polyethylene glycol (PEG) molecules to the liposome surface which not only increases circulation time but also has a shielding effect against molecules that otherwise will fix to liposomes and facilitate their clearance by the MPS. Further, oh-sensitive liposomes coupled with cell surface receptor binding through ligand conjugation to have better targeting and therapeutic efficiency in cancer treatment has been investigated. Nonetheless, the high adaptability, comparatively low biotoxicity and strong biocompatibility testify to the liposomes as an efficacious system for various therapeutic applications such as gene delivery, vaccines and antimicrobial agents. make them versatile carriers. The first FDA-approved liposomal drug, Doxil, demonstrated the potential of liposomes in delivering chemotherapeutics with reduced cardiotoxicity. However, challenges such as stability, manufacturing scalability, and clearance by the mononuclear phagocyte system (MPS) have limited the widespread clinical use of liposomes. [16]

Recent advancements in liposomal technology have focused on improving the circulation time and targeting capabilities of these nanoparticles. For example, PEGylation, the attachment of polyethylene glycol (PEG) to the liposome surface, has been used to extend the blood circulation time by reducing opsonisation and subsequent clearance by the MPS. Moreover, targeted liposomes that can bind to specific cell surface receptors through ligand attachment have been explored to enhance the selectivity and efficacy of drug delivery in cancer therapy. The versatility and relatively low toxicity of liposomes continue to make them an attractive platform for a wide range of therapeutic applications, including gene delivery, vaccines, and antimicrobial therapies. [22]

2.2. Polymeric Nanoparticles

Another formed class of Nano carriers in drug delivery is polymeric nanoparticles which consist of mainly biodegradable and biocompatible polymers including poly (lactic-co- glycolic acid) (PLGA) and polycaprolactone (PCL). [9]

As for the latter, they can release the drugs which are applicable to chronic diseases gradually and over a long time. The release profile of drugs can therefore be controlled through manipulation in the polymer matrix type, molecular weight and degradation profile. [25]

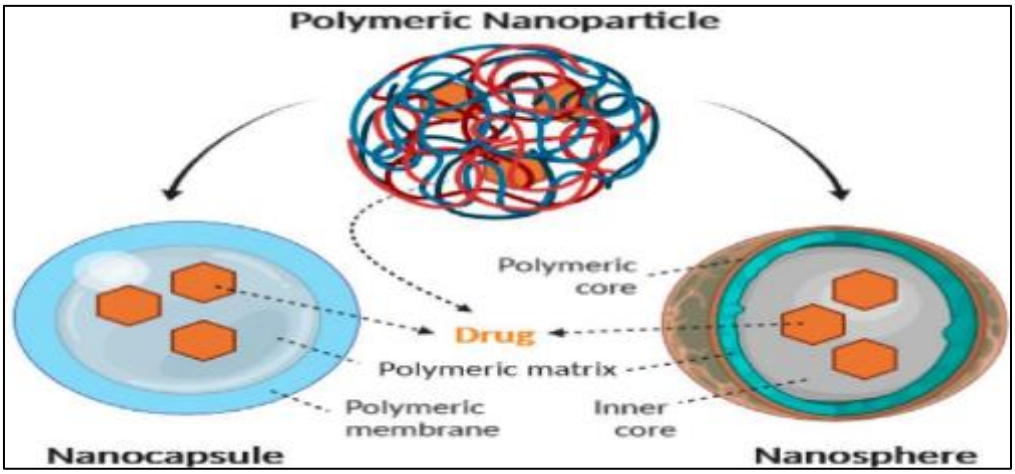

Figure 2 Polymeric Nanoparticle

Polymeric nanoparticles are now employed mainly in anticancer drug delivery, protein, peptide, and nucleic acids delivery. They offer a shield to drugs that are not very stable such that their bioavailability as well as therapeutic effectiveness is enhanced. Another benefit of polymeric nanoparticles is that the system can encapsulate drugs with poor solubility so that it can be easily distributed throughout the body. However, some issues like drug loading capacity, batch to batch reproducibility and the toxicity arising from degradation products of the polymer system, are still other issues that have to be resolve to maximize their applications in clinical practice. [15]

2.3. Dendrimers

Dendrimers are hyper branched, tree like macromolecules, they are characterized by a very compact structure, monodispersity which is the presence of one strongly branched layer concentrically arranged and symmetrically radiated out from the central core. It offers possibility for multi-surface alteration and can be conjugated with

therapeutic agent, targeting ligand, and diagnostic agent. This is suitable for small molecules, nucleic acid and protein delivery because of nature of dendrimers, which has highly branched structure like a tree. [20]

The main disadvantage arises with dendrimers, which results from toxicity due to the cationic nature of the polymers. This toxicity is due to the fact that these particles, once internalised, can cause cell damage and cell death; thus, potential surface modification strategies such as PEGylation or acetylation have been employed to increase their biocompatibility. Dendrimers have been studied extensively for cancer treatment, gene delivery and imaging but there are challenges associated with dendrimers; including the amount of drug that can be encapsulated and safety concerns. Surface modifications of dendrim These materials [small molecules, nucleic acids, and proteins] may be effectively delivered using dendrimers, because of the high ratio of surface area to volume of dendrimers. [25]

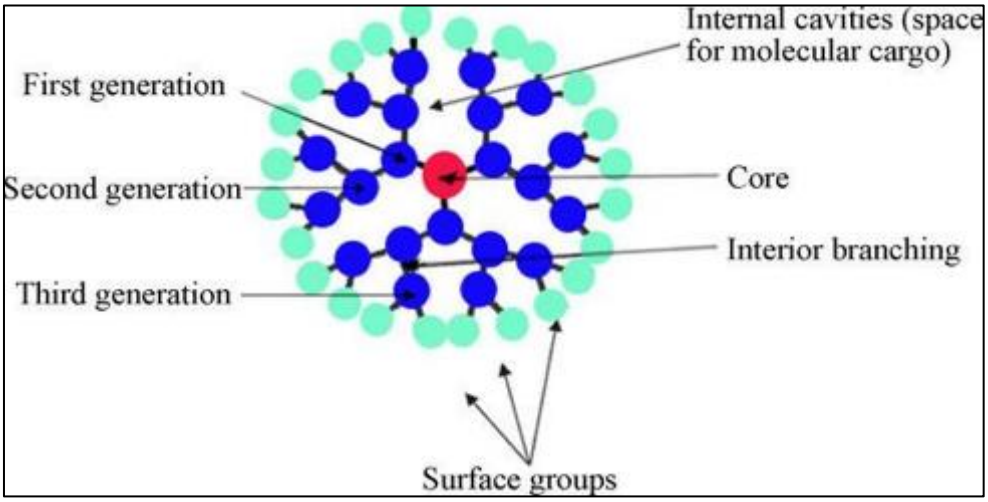

Figure 3 Structure of Dendrimers

However, one of the main difficulties associated with the applying dendrimers is the fact that they can be toxic to cells, and this property is considered to be linked to their cationic character. This toxicity has led to different approaches being implemented in an effort to modify the surface of these nanoparticles, for instance through PEGylation or acetylation. Dendrimers have been considered as potential candidates for drug delivery, cancer treatment, gene delivery, and imaging, but their safety issues and drug-loading problem needs to be address. core. Their structure provides for the multi-surface alteration and can be conjugated with therapeutic agents, targeting ligands, and diagnostic agents. This is ideal for delivering small molecules, nucleic acids, and protein owing to the nature of dendrimers in resembling highly branched trees.

One disadvantage arises from dendrimers; it is toxicity attributed to cationic character of dendrimers. This toxicity is because after internalization, these particles may bring about cell death and damage, though some potential surface modification techniques such as PEGylation or acetylation of these particles has been utilized in a bid to increase their biocompatibility. Cancer therapy, gene delivery and imaging are some of the major applications were dendrimers have been fully developed, however the drug loading capacity of dendrimers as well as their safety are limited. Surface functionalization is flexible and permits the conjugation of therapeutic analytes, targeting ligands, and imaging agents. Dendrimers proffers better vehicle system for small molecules, nucleic acids and proteins due to its high surface area compared to its volume.

Cytotoxicity is one of the main factors that make it hard to use dendrimers since their toxicity is normally attributed to charges which are normally cationic. This toxicity has been reported to be due to the surface of the nanoparticles, and efforts have been made to modify the surface by, for example, PEGylation or acetylation. Dendrimers and their applications in cancer, gene therapy, and imaging has been proposed but safety concerns and increase in drug capacity is needed. [15]

2.4. Solid Lipid Nanoparticles (SLNs)

SLNs are formed from solid lipids and have benefits including high drug encapsulation potential; stability and sustained release. A major advantage of the SLNs is that they are suitable for embedding lipophilic drugs that are, in any case,

scarcely soluble in water. These nanoparticles can also be surface functionalized for increased targeting ability and therefore can be used to deliver drug molecules across biological barriers like the blood brain barrier (BBB). [21]

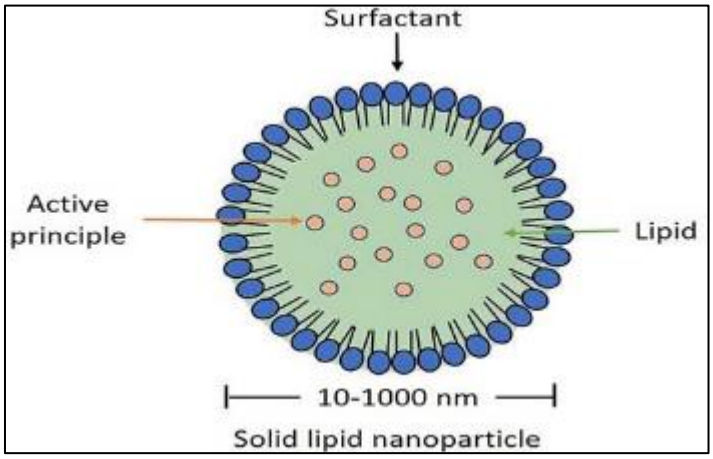

Figure 4 Solid Lipid Nanoparticles

Nevertheless, the application of SLNs is limited by some drawbacks, including low efficiency of drug encapsulation for hydrophilic drugs and the possibility of drug expulsion during storage due to lipid crystallization. But, with time the stability of the SLN and the release of drugs into the body has increased due to changes in the formulation of the SLN. SLNs are under further research for the delivery of anticancer agents, vaccines and therapeutic peptides. [16]

2.5. Metallic Nanoparticles

Nanoparticles which have metallic characteristic including gold, silver and iron oxide hold remarkable optical, electrical and magnetic characteristics that makes them suitable in both therapeutic and diagnostic applications. Gold nanoparticles (AuNPs) are perhaps some of the most studied in cancer therapy due to their unique property of Hyper thermal effect when illuminated with near Infra-red light for phototherapy. Nevertheless, questions about their chronic toxicity and ability to accumulate in tissues have not been fully addressed and persist as the primary impediment to application in clinical practice. [9,15]

3. Methods for Synthesis of Nanoparticle

Figure 5 Different Method of Synthesis for Nanoparticles

3.1. Top-Down Methods

3.1.1. Mechanical Milling

This method uses high energy ball mills to pulverize the solid materials into small size of nanoparticles. The mechanical forces disintegrate the materials down to the form of nanoparticles.

- Advantages: Ideal for use with heavy manufacturing and does not require any forms of chemicals.
- Limitations: Complex shapes and high polydispersity coefficients.
- Example: Titanium dioxide (TiO_2) nanoparticles.

3.1.2. Laser Ablation

In this method, a pulsed laser is applied to a surface of the material so as to cause the evaporation of material. There is a creation of nanoparticles because of condensation of the vapor.

- Advantages: It gives highly pure nanoparticles; does not need modification when used with different materials.
- Limitations: High costs of equipment and the problem of size control.
- Example: Gold nanoparticles.

3.1.3. Lithography

A technique of synthesising nanoparticles using moulds in which material is engraved.

Thus, to be put into particular forms and dimensions.

- Advantages: Some of the advantages include; Very high accuracy in size and shape.
- Limitations: Expensive and a limited availability of bulk orders.
- Example: Silicon nanoparticles.

3.2. Bottom-Up Methods

3.2.1. Chemical Reduction

Metal salts are then reduced into nanoparticles by using reducing agents.

- Advantages: Delivers highly polished nanoparticles, which create a uniform dispersion.
- Limitations: Some toxic reagents may be used.
- Example: Gold and silver nanoparticles.

3.2.2. Sol-Gel Synthesis

Metal precursors in solution form a gel that is dried to produce nanoparticles.

- Advantages: High purity and homogeneity.
- Limitations: Slow process.
- Example: Silica nanoparticles.

3.2.3. Co-Precipitation

Metal ions are precipitated into nanoparticles using a base.

- Advantages: Simple and cost-effective.
- Limitations: Limited control over particle size.
- Example: Iron oxide nanoparticles.

3.3. Green Synthesis

3.3.1. Biological Methods

Nanoparticles are synthesized using biological agents like plants, bacteria, or fungi.

- Advantages: Eco-friendly and sustainable.
- Limitations: Difficult to control size and shape.
- Example: Silver nanoparticles.

3.3.2. Plant Extracts

Metal salts are reduced using plant extracts, avoiding toxic reagents.

- Advantages: Low cost and environmental impact.
- Limitations: Purification challenges.
- Example: Silver nanoparticles using neem extract.

3.4. Template-Assisted Methods

3.4.1. Porous Templates

Nanoparticles are synthesized within a porous material and later extracted.

- Advantages: High control over size and shape.
- Limitations: Complex template removal process.
- Example: Gold nanoparticles.

3.4.2. Micelle-Based Templates

Nanoparticles form within micelles, which act as templates during synthesis.

- Advantages: Simple method for producing uniform particles.
- Limitations: Requires precise control over surfactant concentration.
- Example: Platinum nanoparticles.

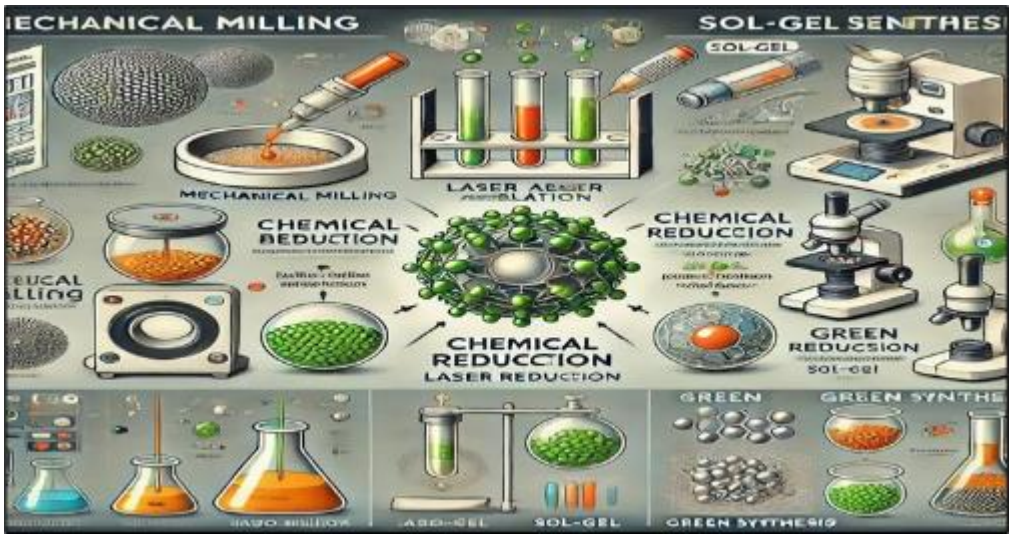

Figure 6 Different Method of Synthesis for Nanoparticles

Factors Influencing Nanoparticle Synthesis

- Reaction Conditions (Temperature, Pressure, pH):

These factors tend to have a very significant influence in determining the size, shape and crystallinity of the nanoparticles.

- Surface Modification

Functionalization and capping agents are used for avoiding agglomeration of nanoparticles and to improve the stability of the system.

Characterization Techniques

- Transmission Electron Microscopy (TEM):

Employed for the determination of the size and shape of nanoparticles/ Utilized for the purpose of visual representations of the nanoparticles.

- X-Ray Diffraction (XRD)

Determines the crystalline structure of nanoparticles.

- Dynamic Light Scattering (DLS):

Characterises a liquid suspension in terms of nanoparticle size.

- UV-Vis Spectroscopy

Traditionally applied to validate the formation of metal nanoparticles through identification of prerequisite absorption bands.

Scale-Up Considerations

- Reproducibility and Cost Efficiency

One issue with scaling up synthesis methods is that it creates an issue of uniformity and especially size control of particles.

Such as green synthesis, and thus are relatively cheaper as well as ideal for commercial production.

Applications

- Therapeutic Uses

Nanoparticles can penetrate biological barriers, target specific tissues, and release drugs in a controlled manner. Diagnostics:

Gold and silver nanoparticles are used in imaging and diagnostic tools for their sensitivity and specificity.

- Environmental Applications

Nanoparticles like titanium dioxide and zinc oxide are used in water treatment and air purification for their photocatalytic properties. [16]

4. Mechanisms of Drug Delivery Using Nanoparticles

4.1. Targeted Drug Delivery

This makes one of the biggest advantages of using nanoparticles to delivery drugs is that nanoparticles can be engineered to selectively accumulate in certain tissues or even cells. There are two types of targeting: active and passive; the later one is EPR effect; while the active targeting is based on functionalization of nanoparticles surface with ligands, antibodies or peptides which could bind to certain cell receptors. [20]

Doxil is an example of a nanoparticle-based therapeutic system that has employed active targeting whereby liposomal doxorubicin is targeted at HER2+ BC cells through an antibody that recognizes the HER2 protein. [1]

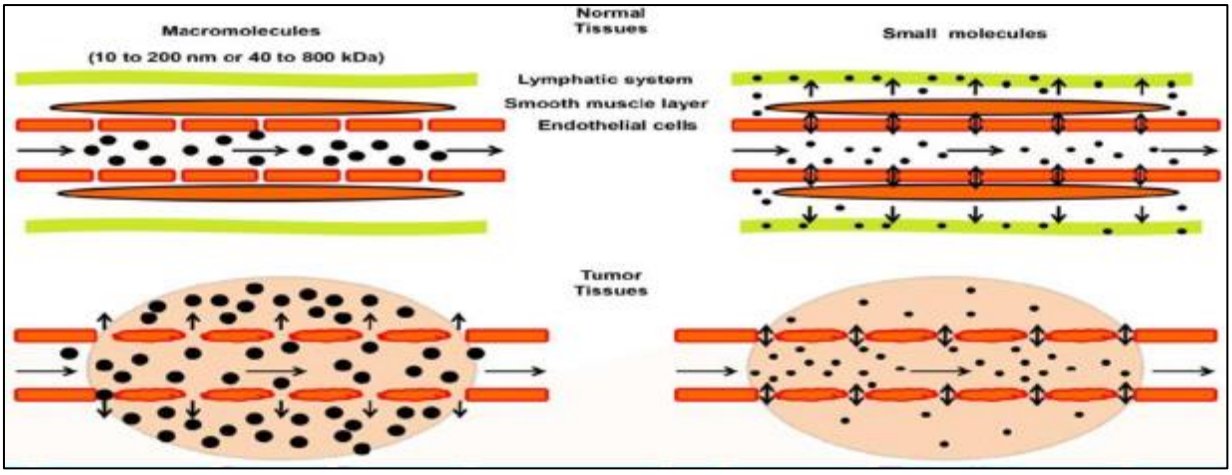

Figure 7 Targeted Drug Delivery System

4.2. Controlled and Sustained Drug Release

It also allows for development of particles that release their therapeutic cargo to the target tissue over a long period, and therefore enables treatment of patients with chronic diseases. There are various mechanisms by which a drug release can be affected from the polymeric system: diffusion, degradation, or effect of stimuli like pH, temperature or enzymes. [9]

4.3. Overcoming Biological Barriers

The small size and rational to alter the surface chemistry of nanoparticles to allow them to cross barriers that are normally impermeable to large molecules such as the BBB. LNPs have been also used as an efficient method for overcoming the BBB in order to deliver small molecules and genetic material to the treatment of NDPs. [16,23]

5. Advantages of Nanoparticle-Based Drug Delivery

5.1. Increased Bioavailability

Nanoparticles increase dissolution rate, reduce the likelihood of enzymatic hydrolysis, and increase bioavailability in the GI or other regions. For example, Abraxane a nanoparticle albumin bound formulation of paclitaxel improved solubility and biopharmaceutical availability of paclitaxel resulting to high therapeutic index.

5.2. Reduced Toxicity

Through targeted delivery, nanoparticles minimize side effects caused by the distribution of the drug through the bloodstream to the site of action. This is particularly so in cancer where chemotherapy agents are extremely toxic to normal tissues as well. Anti-inflammatories have also been encapsulated in nanoparticles that can be targeted to the site of inflammation to lessen the dose of the drug required to alleviate inflammation whilst minimizing the drug's toxicity. [20]

5.3. Enhanced Stability and Longevity

Nanoparticles also avoid early release and elimination of the encapsulated drug providing extended circulation half-life. PEGylation and other surface modifications can lead further circulation time of the nanoparticles; thus, clients will pay for less frequency of dosing. [15]

6. Challenges and Limitations

6.1. Toxicity and Biocompatibility

Non-biodegradable nanoparticles such as metallic nanoparticles are still a subject of debate as to the level of biocompatibility and safety they afford over times. Most of the nanoparticles may get targeted and remain in important organs such as the liver, spleen or lungs thus in the long run can cause some sort of toxicity. [9]

6.2. Manufacturing and Scalability

Several difficulties of nanoparticle development have been described, with the key limitations referring to the manufacturing process and cost. Challenges also arise in controlling size, shape and encapsulated drug load when manufacturing nanoparticles for large scale production from laboratory scale. [1]

6.3. Regulatory and Ethical Challenges

The process of receiving recognition for nanoparticle-based drugs is challenging since these systems are considered to be a combined product that is not only pharmaceutical but also a device. They include; However, another reason why the approval of the system is hampered is the lack of clear measures that one can use to measure the safety and efficiency of these systems. Other consideration is the ethical questions like; application of nanotechnology on people and implications of spending long time in the community. [21]

7. Recent Advances in Nanoparticle-Based Drug Delivery

7.1. Cancer Therapy

Exploitation of nanoparticles for cancer treatment based on targeted and controlled release of chemotherapeutic agents has revolutionized the therapy of cancer. EPR effect allows nanoparticles to be trapped in the tumour site thus lowering systemic hazards and enhancing treatment returns. Beside small molecule delivery, nanoparticles have been employed in delivering nucleic acids including, siRNA and mRNA for gene silencing and cancer immunotherapy. Some targeted nanoparticles are also under development as theragnostic agents, meaning that they are designed to perform the dual function of therapy and of imaging to monitor how well treatments are working. [9,12]

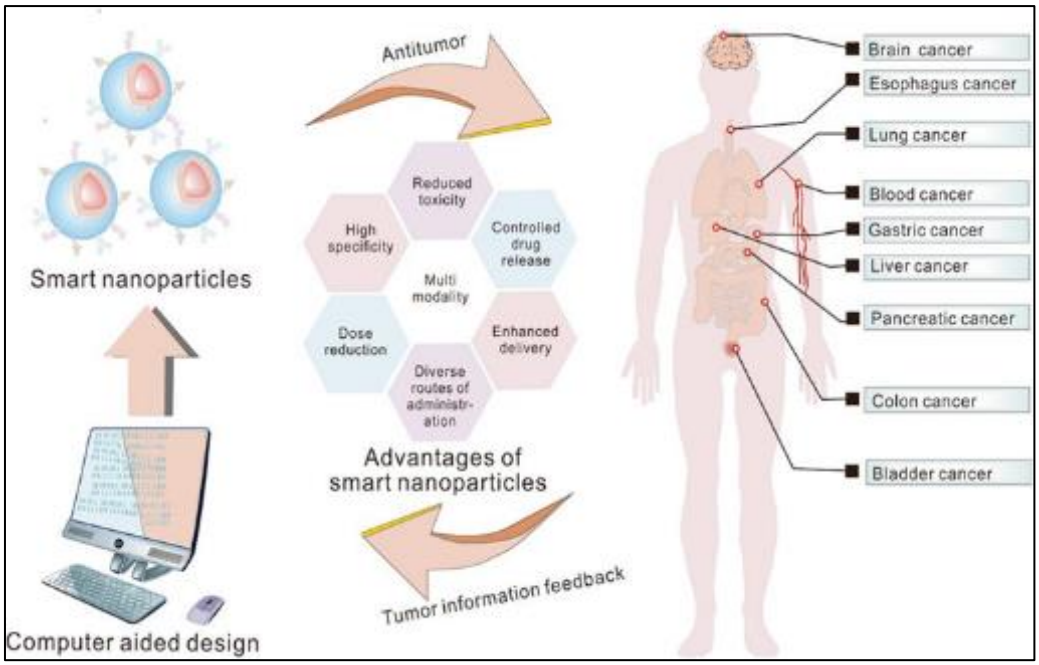

Figure 8 Cancer Therapy for Nanoparticles

Oncology is the field where nanoparticle-based drug delivery has been most advanced. By using nanoparticles, the chemotherapeutic drugs can be accumulated at cancerous tissue with the least diffusion into the rest of the body and thus enhancing therapeutic ratios. Some developments are smart nanoparticles for drug delivery which treats tumor by releasing drugs in an acidic environment. [22]

7.2. Gene Therapy and Nucleic Acid Delivery

It is suggested that nanoparticles hold great potential to be used in delivery of nucleic acids, including DNA, RNA and CRISPR based systems to the nucleus of target cell. LN based systems were instrumental for the mRNA vaccines during the COVID -19 pandemic and the ongoing trials in gene therapy for diseases such as cystic fibrosis and Duchenne

muscular dystrophy. Some of the undue merits of nanoparticles include their ability to shield nucleic acids from degradation as well as enhance their uptake in cells, which afford them the potentials for gene therapy. [15]

7.3. Vaccination

Lipid nanoparticles to deliver nucleic acids in vaccines has emerged as a trend as the world grappled with the COVID-19 pandemic and the rollout of mRNA vaccines. LNPs are for mRNA, which protect the latter and transports it into cells. The success experienced with the Pfizer BioNTech and Moderna vaccines means that more light will be shed to nanoparticles in delivering of other infectious diseases and eventually Cancer. [16]

7.4. Nanoparticles in Neurological Disorders

Use of nanoparticles in the management of neurological disorders including Alzheimer's and Parkinson is currently under investigation. They enable the transportation of drugs that protect the nerves, enzymes or gene therapies into the brain across the BBB. Approaches for targeting these therapies differently can reduce the consequences and enhance the effectiveness of treating Neurological disorders. [23]

8. Examples of Drugs Utilizing Nanoparticle-Based Drug Delivery Systems

Several drugs currently use nanoparticle-based drug delivery systems, and they span a wide range of therapeutic areas, especially in cancer therapy and vaccines. Here are a few examples of drugs utilizing nanoparticles for drug delivery:

8.1. Doxil (Doxorubicin HCl Liposome Injection) Type: Liposomal formulation

- Uses: Treatment of ovarian cancer, multiple myeloma, and AIDS-related Kaposi's sarcoma.
- Nanoparticle Delivery System: Liposomes.
- Advantage: Reduces cardiotoxicity of the drug and allows for targeted delivery to cancer cells, increasing drug accumulation in tumours while minimizing damage to healthy tissues. [5]

8.2. Abraxane (Paclitaxel Albumin-bound) Type: Albumin-bound nanoparticles

- Uses: Treatment of metastatic breast cancer, non-small cell lung cancer, and pancreatic cancer.
- Nanoparticle Delivery System: Albumin-bound nanoparticles (nanoparticle albumin-bound or NAB technology).
- Advantage: Improves the solubility and bioavailability of paclitaxel, a poorly water-soluble drug, and enhances drug delivery to tumor through the enhanced permeability and retention (EPR) effect.

8.3. Onivyde (Irinotecan Liposome Injection) Type: Liposomal formulation

- Uses: Treatment of metastatic pancreatic cancer.
- Nanoparticle Delivery System: Liposomes.
- Advantage: Prolongs circulation time of irinotecan, allowing for enhanced delivery to tumours and better control over drug release.

8.4. Vyxeos (Cytarabine and Daunorubicin Liposome Injection)

- Type: Liposomal formulation.
- Uses: Treatment of acute myeloid leukaemia (AML).
- Nanoparticle Delivery System: Liposomes.
- Advantage: Co-encapsulates two chemotherapy agents, allowing for optimized delivery of both drugs directly to cancer cells and improving the overall therapeutic index.

8.5. Comirnaty (Pfizer-BioNTech COVID-19 Vaccine) Type: Lipid nanoparticle formulation

- Uses: COVID-19 prevention.
- Nanoparticle Delivery System: Lipid nanoparticles (LNPs).
- Advantage: Encapsulates and protects mRNA, allowing for efficient delivery into cells for expression of the viral spike protein, which triggers an immune response.

8.6. Moderna COVID-19 Vaccine (mRNA-1273) Type: Lipid nanoparticle formulation

- Uses: COVID-19 prevention.

- Nanoparticle Delivery System: Lipid nanoparticles (LNPs).
- Advantage: Protects the mRNA from degradation, facilitating its delivery into cells, and enhances the immune response to the encoded protein.

8.7. Rapamune (Sirolimus) Type: Nanocrystal formulation

- Uses: Immunosuppressant used to prevent organ transplant rejection.
- Nanoparticle Delivery System: Nanocrystals.
- Advantage: Nanocrystals enhance the solubility and bioavailability of sirolimus, improving its therapeutic effects.

8.8. Feraheme (Ferumoxytol)

- Type: Iron oxide nanoparticle formulation.
- Uses: Treatment of iron deficiency anaemia in patients with chronic kidney disease.
- Nanoparticle Delivery System: Superparamagnetic iron oxide nanoparticles.
- Advantage: Allows for controlled release of iron and reduces the risk of iron overload, providing a safe alternative for iron supplementation. [21]

9. Comparison of nanoparticle-based drug delivery systems with other drug delivery systems

Introduction to Drug Delivery Systems: Portrayal of drugs is crucial in medicine since it aid the correct delivery of the drugs to their respective destinations in the body. There are various systems which have evolved specifically for the purpose of enhancing the effectiveness of the delivery of drugs while at the same time diminishing adversative response to the drugs. This section of the paper compares nanoparticle based pharmaceutical systems with the conventional systems of delivering drugs and shows the distinct advantages and drawbacks.

Table 1 Comparison of Nanoparticle-Based Drug Delivery Systems with Other [12,15]

Feature	Nanoparticle Drug Deliverysystem	Conventional Drug DeliverySystem
Size	Nano-scale (1-100 nm)	Micro to macro-scale
Targeting capability	High precision targeting (active/passive)	Low to no targeting, mainlysystemic distribution
Drug Release Control	Controlled, sustained, or triggered release	Often uncontrolled andimmediate release
Efficacy	High due to targeted delivery and reduced side effects	Lower due to broader distribution and higherpotential for side effects
Bioavailability	Enhanced bioavailability, even for poorly soluble drugs	May have low bioavailability,especially for poorly soluble drugs
Stability	Can improve the stability ofsensitive drugs	Lower stability, especially for drugs prone to degradation
Side Effects	Reduced due to targeteddelivery	Higher due to non-specific action and systemic exposure
Administration Routes	Can be administered via multiple routes, including oral, inhalation, and IV	Primarily oral or intravenous
Cost	Generally higher due to complexity of formulation andproduction	Generally lower due to simpler formulations

9.1. Detailed Comparison

- Targeting: One of the important aspects of the possibility of using nanoparticle-based systems in drug delivery is the fact that such systems permit selective targeting. This makes them highly customizable based on colour, size and shape, to seek out cancer cells or any other affected tissues for medication delivery. Conventional

methods on the other hand, disperse medication all over the body with little or no focusing indicating where the drug should affect, this leads to unnecessary side effects.

- Bioavailability: Nanoparticles can enhance the dissolution rate properties of drugs that are poorly soluble hence increase the absorption rate of the drug into the body. For instance, Abraxane with albumin-bound nanoparticles is intended to improve the delivery of paclitaxel which is normally a solubility challenged chemotherapy drug. Conventional formulations of these drugs, however, may present problems which decrease the bioavailability of the drug and, therefore, its efficacy.
- Controlled Release: The other benefit of nanoparticles is that they have the capacity to release their drug concentrations in a time-bound manner. This constant release is especially helpful for patients with chronic diseases that need to take the drug repeatedly. On the other hand, conventional drug delivery systems normally offer an immediate or an early release which may not be tome appropriate for all patients. –
- Tissue Penetration: They penetrate biological barriers such as the Blood-Brain Barrier (BBB), and as a result are potential for the delivery of neurological disorders. Standard approaches to the administration of drugs are not effective for getting drugs across the blood-brain barrier which, in turn, puts a damp on treatment regarding ailments that affect the brain. –
- Side Effects: Nanoparticles also reduce the impact of drugs on other body tissues because they deliver the drugs precisely at the intended tissue. A good example of this is liposome formulation of doxorubicin known as Doxil which has more reduced cardiotoxicity than regular doxorubicin formulation. On the other hand, conventional delivery systems lead to increased systemic toxicity, because the drugs cause an impact not only on the targeted region, but also on a healthy tissue.
- Stability: Stability of products, particularly the drugs undergoing degradation, can be improved by nanoparticle formulations. However, some types of nanoparticles may still require improvement to their stability, for instance, tendency to agglomerate. The difference between the two main kinds of formulations is that the more customary versions are usually long-lasting, but may not necessarily offer solutions similar to bioavailability.
- Manufacturing Complexity: Most nanoparticles are produced through complex techniques and this becomes a challenge in terms of up-scaling and batch to batch reproducibility.
- Conventional drug formulations in comparison are typically less complex in their preparation and where the formulation process is more standardized, it is more reliable.
- Regulatory Hurdles: Regulation of nanoparticle-based system may be difficult as these are relatively new systems hence taking a long time to gain approval. Traditional drugs have clear regulatory frameworks, which, however, may take a lot of time to proceed. [12,15]

10. Future Directions and Speculative Insights

10.1. Smart and Stimuli-Responsive Nanoparticles

Significant interest has been paid to the stimuli sensitive smart nanoparticles, where stimuli include pH, temperature, or enzymes, etc. Such nanoparticles can be designed to deliver their cargo in regard to changes in the tumor microenvironment or other pathological circumstances. For example, certain nanoparticles can release drug only if the surrounding environment has certain pH, for example, lower pH is related to performance of a tumor, so the accuracy of drug delivery would be enhanced and side effects reduced. load in response to changes in the tumor microenvironment or other pathological conditions. For example, pH-responsive nanoparticles can release drugs in the acidic environment of a tumor, enhancing drug delivery specificity and reducing off-target effects. [12,20]

10.2. AI and Machine Learning in Nanoparticle Design

AI and Machine Learning in Nanoparticle Design artificial intelligence (AI) and machine learning (ML) have recently paved their way to the world of designing nanoparticles. AI can also be used to determine the most suitable core and shell materials, as well as the interaction of drugs with nanoparticles and pharmacokinetics/pharmacodynamics of nanoparticle-based systems. AI could also help step up the design of bespoke nanoparticles for patients depending on the genetic makeup or other aspects of the disease. [16]

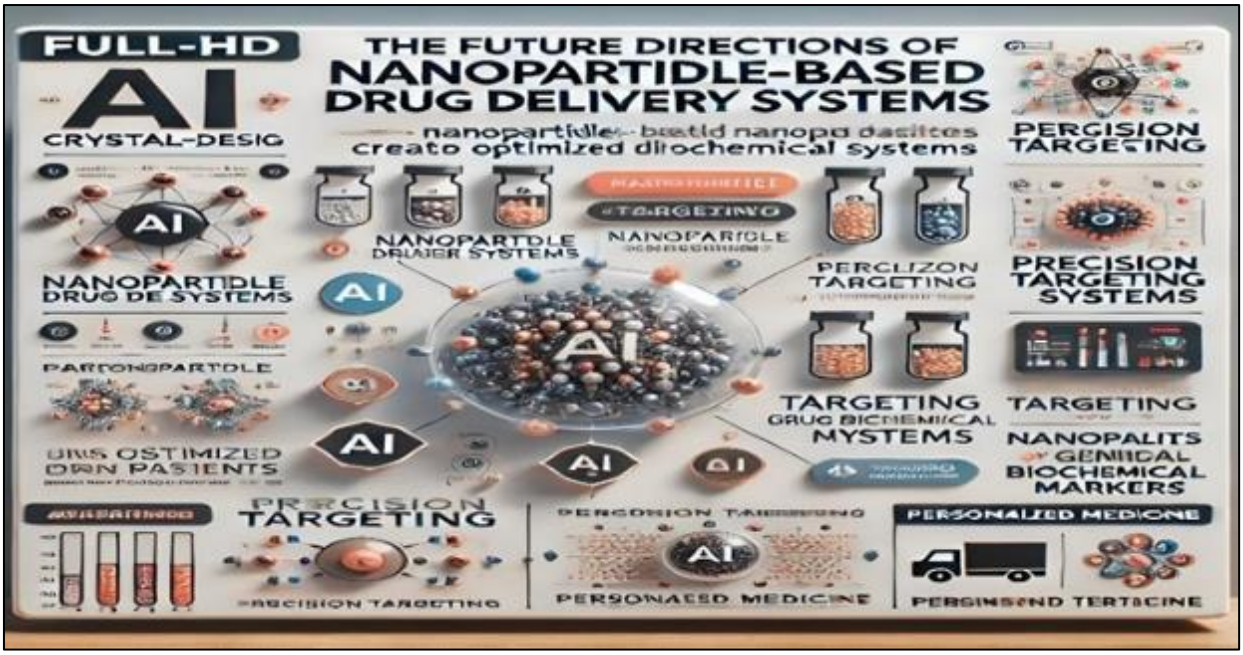

Figure 9 AI and Machine Learning in Nanoparticle Design

10.3. Nanoparticles for Personalized Medicine

Nanoparticles are anticipating to take significant position in personalized medicine. To be more specific, the results suggest that by formulating nanoparticles depending on genetic and biochemical markers of patients, one can achieve better penetration of the active ingredient into the locality of action and therefore, higher efficacy. Specialized nanoparticles can be developed to penetrate and attack exact mutations or biomarkers implying that diseases like cancers, autoimmune diseases and genetic diseases can be more efficiently treated. [9,20]

10.4. Nanoparticle Stability and Pharmacokinetics

A major determinant of performance in the nanoparticulate systems drug delivery is the stability and pharmacokinetics. In the real biological environment, NPs must be biologically stable, or else they can be rapidly eliminated by a process known as opsonisation, by plasma proteins within the body. PEGylation and also other alterations of nanoparticle surface are widely used to enhance stability and circulation time. However, the revival of the original PEG layer in circulation over time can cause the Issue of accelerated blood clearance ABC, where the body immune system recognizes later dose of PEG nanoparticles and clears will at a faster rate. [15,23]

Pharmacokinetic models are necessary to know more about distribution, metabolism, and elimination of nanoparticles from the body and its tissues. In contrast to classical small molecules, nanoparticles have their own bio distribution patterns with a propensity to concentrate in the liver, spleen and lungs. This can cause undesired side effects, but there is also the option for targeting certain tissues with the drugs as well. Knowledge of these pharmacokinetics is paramount to directing nanoparticle development and achieving the best therapeutic results with minimum adverse reactions. [1,9]

11. Discussion

Nanoparticles for targeted delivery of therapeutic agents have gained significant attention over the recent years as next generation drug delivery systems correcting most of the shortcomings of conventional techniques. In contrast, conventional system like oral tablets, injections and topical formulations face the problems that include low bioavailability, targeted/non targeted delivery of therapeutic agents and systemic toxicity. These challenges can reduce the effectiveness of the therapeutic effects of many drugs in the body, especially for groups with sensitive ailments, including cancer and chronic diseases. [22]

Comparison with Other Drug Delivery System The current nanoparticle-based drug delivery systems have many advantages over others. The traditional drug delivery methods. Conventional systems, such as oral tablets, injections, and topical formulations, often struggle with issues like low bioavailability, non-specific distribution of therapeutic

agents, and systemic toxicity. These challenges can hinder the therapeutic efficacy of many drugs, particularly in sensitive populations, such as cancer patients and individuals with chronic diseases. [1]

Comparison with Conventional Drug Delivery Systems Nanoparticle-based drug delivery systems provide several significant advantages over traditional methods. Among them there is one of the most important – possibility to create nanoparticles with certain targeting. This results in drug targeting of affected tissues or cell, in this case minimizing side effects associated with other tissues or body cells. For instance, Doxil (liposomal doxorubicin) has clearly shown that by reducing cardiotoxicity liposomal formulations are able to deliver chemotherapeutic agents to the tumor site. On the other hand, other drug delivery system transports the medicine to any other part of the body randomly and increase the probability of undesirable side effects. The improved bioavailability is another attractive feature that nanoparticles have to offer as well as stability. MRP also limits the abilities of drugs with poor solubility to attain therapeutically relevant plasma concentrations when administered by conventional routes. Abraxane (albumin-bound paclitaxel) is particularly beneficial to metastatic breast cancer in how the nanoparticle technology enhances paclitaxel solubility and efficacy. This improvement is especially valuable for many drugs for which the displays of performance have always been challenging by using the conventional routes. Further, nanoparticle system finds applications in the ability to have either a sustained or a controlled release of the therapeutic agents. This capability is very useful for chronic diseases most of which require a steady delivery of the medications to the body. For example, Onivyde (irinotecan liposome injection) releases chemotherapy for pancreatic cancer over an extended period as opposed to conventional systems where release happens immediately and has unstable corresponding drug concentration. This sustained release can enhance people's concordance and lessen the frequency of dosing. Another advantage is the ability of nanoparticles to pass biological barriers. They can easily transverse the BBB and therefore, are very suitable for use in managing neurological disorders such as Alzheimer's and Parkinsons diseases that other delivery methods prove ill-suited for. Since nanoparticles are designed to have unique properties, it is possible to deliver therapeutics in that they interact with the central nervous system. However, like its many benefits, there are also problematic issues of nanoparticle-based drug delivery systems. One drawback of manufacturing nanoparticles is that the process is very complex and this can cause problems with scaling up perhaps because the properties and quality of the materials produced may not be uniform across batches. Moreover, the density and complexity of regulation trails associated with nanoparticle formulations are sometimes more complex than regular drugs and can slow the development of availability to clinics. This can be seen when contrasting set regulation norms for conventional drugs and developing regulation norms for nanoparticle therapies. [15,16]

Nanoparticle Based Drug Delivery Systems in Clinical Applications Some key examples of drugs using nanoparticle delivery systems include In some FDA approved drugs, approaches are pioneered nanoparticle based drug delivery systems in clinic prescriptions' drug delivery is essential. For instance, Onivyde (irinotecan liposome injection) provides prolonged delivery of chemotherapy for pancreatic cancer, contrasting with conventional systems that often result in immediate release and fluctuating drug levels. This sustained release can improve patient compliance and reduce the need for frequent dosing. The ability of nanoparticles to penetrate biological barriers represents another significant advantage. They can effectively cross the blood-brain barrier (BBB), making them ideal candidates for treating neurological disorders, including Alzheimer's and Parkinson's diseases, where traditional delivery methods are often ineffective. The innovative design of nanoparticles allows for targeted delivery of therapeutics that can directly impact the central nervous system. Despite the many advantages, nanoparticle-based drug delivery systems also face challenges that must be addressed. The complexity of manufacturing nanoparticles can lead to scalability issues, particularly in maintaining consistent quality and properties across batches. Furthermore, the regulatory pathways for nanoparticle formulations are often more intricate than those for conventional drugs, which can impede timely clinical implementation. This complexity is evident when comparing established regulatory frameworks for traditional drugs with the evolving landscape for nanoparticle therapies. [21,23]

Examples of Nanoparticle-Based Drug Delivery Systems Several FDA-approved drugs highlight the successful application of nanoparticle-based drug delivery systems in clinical practice. Vyxeos (liposomal cytarabine and daunorubicin) shows that concurrent administration of chemotherapeutic drugs in the liposomal form can enhance the efficacy of the therapy in acute myeloid leukaemia. Lipid nanoparticles are incorporated in the modern mRNA vaccines including Comirnaty and Spikevax hence providing for a perfect carrier for mRNA and a great helper in the initiation of a timely and effective immune response to COVID-19. These examples show how nanoparticle technologies could be used and are effective in numerous therapeutic fields. [23,25]

Liposomal formulation Doxil (liposomal doxorubicin) example: Reduction of cardiotoxicity and direct tumor delivery of chemotherapy Our partners have demonstrated an ability to increase the effectiveness of treatments using liposomal formulations as illustrated by Doxil which reduces cardiotoxicity and delivers doxorubicin directly to the tumor tissues. In the same manner, Abraxane (albumin-bound paclitaxel) improves solubility and efficacy of paclitaxel in treatment of

metastatic breast cancer. Other samples include Onivyde (irinotecan liposome injection), that enhances the delivery of chemotherapy for pancreatic cancer and Vyxeos (liposomal cytarabine and daunorubicin) used in treating acute myeloid leukaemia. In addition, the use of lipid nanoparticles in the development of mRNA vaccines like Comirnaty and Spikevax has shown that lipid nanoparticles could open up prospects on how vaccines can be delivered most effectively especially when used in the delivery of COVID-19 vaccines. Another benefit that gives nanoparticle systems a high level of effectiveness is the ability of the nanoparticle to traffic to portions of the body that require treatment without affecting other parts of the body negatively. This targeted delivery approach especially prove useful in cancer treatment because therapies depend on targeting a tumor of interest while leaving the rest of the body tissues intact. The ability of nanoparticles to cross biological barriers they include the blood brain barrier (BBB) for treatment of neurological diseases like Alzheimer's diseases, Parkinson's disease and so on where it could be very hard to deliver the needed drug or medical treatment. [21,22]

In the future, continuous future development in nanoparticle technologies will facilitate the progress of medicine. Some form of smart nanoparticles that are sensitive to biological signals (for instance, pH, temperature, or enzyme) are developmentally superior to drug delivery systems. Moreover, it is possible to imagine that the intelligent design system will help to develop a new kind of nanoparticles focusing on the given patient needs due to genetic or biochemical markers, which may significantly amplify the effectiveness of the therapy of complex diseases. Finally, nonetheless, they behave as the new therapeutic approaches, there are rather many challenges related to the manufacturing, regulation, and safety of the nanoparticle-based drug delivery systems expected to be faced when implementing these systems. The possibilities for such innovative systems are in portending more efficacious methodologies in the delivery of relevant patient treatments and altering the trajectory of treatments. Research should be sustained, and cooperation between people and organizations should be further developed to provide optimized forms of NPDDS for medical practice overcoming the existing challenges. [23]

12. Conclusion

Nanoparticle based drug delivery systems are amongst the most promising features of modern medical practice which offers solution to many of problems related to conventional drug delivery including low solubility, unaccomplished targeting, and toxicity. Such new compounds provide better targeting ability, raise solubility, and non-capsule or extended rail of pharmaceuticals; hence, they are appropriate for treating multi-factorial and un-complex illnesses like cancer, neurological diseases, and other chronic diseases. Presently, a number of drugs approved by the Food and Drug Administration FDA such as liposome formulations and nanocrystal drug delivery systems are the best illustrations of nanoparticle systems and their relevance in practice. The successes show the possibilities of nanotechnology in medicine and present not only higher effectiveness of treatment with less impact on the patient's body and better compliance. However, there are challenges yet to overcome especially in optimizing production techniques, obtaining license from regulatory bodies, and most importantly getting long term safety. Manufacturing nanoparticles requires huge development which can prove to be complex and the dynamic evolving demands of the legislation is another challenging factor that may require new scientific discovery, closer cooperation among stakeholders and the continuous conducts of clinical trial. Nanotechnology in healthcare has a durable outlook and much will rely on multidisciplinary approaches to address existing challenges and construct nanotechnology approaches for aspirational functional heights.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed

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