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ADVANCES IN NANOTECHNOLOGY FOR DRUG DELIVERY: TRENDS AND FUTURE PROSPECTS

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ABSTRACT

Inadequate solubility, inefficient bioavailability, and off-target effects remain critical obstacles to achieving optimal therapeutic outcomes in many promising new drugs. Nanotechnology, which involves manipulating materials at the 1–100 nm scale, offers strategies to address these barriers by enhancing solubility, stability, and targeted delivery. This review examines developments in nanocarrier-based drug delivery systems, focusing on liposomes, polymeric nanoparticles, dendrimers, nanocrystals, and hybrid platforms. Data were synthesized from peer-reviewed studies reporting pharmacokinetic improvements, targeting efficiency, and therapeutic outcomes across various disease models. Quantitatively, nanocrystal formulations have demonstrated up to a 4-fold increase in dissolution rate, while targeted nanocarriers have achieved 2–3-fold higher drug accumulation in tumor tissues compared to conventional formulations. In neurological applications, certain lipid nanoparticles have shown delivery efficiencies exceeding 60% across the blood–brain barrier in preclinical studies. Across oncology, infectious disease, cardiovascular, and regenerative medicine, nanotechnology-enabled delivery consistently improved drug bioavailability and therapeutic indices. These findings provide a consolidated quantitative assessment of the current performance of nanotechnology-driven drug delivery systems.

KEYWORDS: Nanotechnology, Drug Delivery, Nanocarriers, Targeted Delivery, Controlled Release, Gene Therapy.

1. INTRODUCTION

The area where drug delivery becomes a challenge in the field of pharmaceutical sciences is when there are one or more obstacles in the form of low drug solubility, low bioavailability, and off- target effects.[1] Most promising new chemical entities (NCEs) never make it into clinical practice because of these intrinsic drawbacks, requiring larger doses, which may be associated with more adverse effects and poorer adherence by the patient.[2] This is essential in surmounting these obstacles to achieve optimum therapeutic effect and reduce adverse effects.

Manipulation of matter at the atomic, molecular, and supra molecular level (where it is usually a 1-100 nanometer dimensions) i.e. nanotechnology has been a revolutionary industry in the field of pharmaceutics.[3] Nanotechnology provides the prospect of manipulating drug pharmacokinetics in a manner never before possible, by increasing solubility, enhancing stability and making drug delivery selective, by transporting drugs to the targeted site of the disease.[4] This specificity can lead to greatly enhanced therapeutic results and, at the same time, low systemic toxicity levels.

It is justified to conduct this review by the fact that nanotechnology can be critical in developing a new generation of drug delivery. The world nanotechnology drug delivery industry is already strong that is expected to touch more than USD 200 billion in 2034[5] due to rising research interest and the pressing need to find a more effective cure for chronic patients such as in the cases of cancer, cardiovascular disorders, and neuro disorders.[6] The objective of this review is to provide an overview of the recent developments, various applications, and future of nanotechnology in transforming drug delivery and how such nano scale related inventions would transform contemporary medicine.

2. Fundamentals of Nanotechnology in Drug Delivery

The pinnacle of nanomedicine is the use of materials that are designed and fabricated on the nanoscale, generally 1 to 100 nanometers.[7] Such a small scale gives nanoparticles special physicochemical characteristics dissimilar to those of their bulk sizes, and thus, they become perfect candidates of the next generation drug delivery systems.

Nanocarrier has developed a wide range of nanocarrier types that encapsulate, protect, and administer therapeutic agents. Such prominent examples are liposomes, self-assembling lipid bilayers that can accommodate both hydrophilic and hydrophobic drugs, polymeric nanoparticles, which are versatile systems made of natural or synthetic polymers, dendrimers, highly branched monodisperse macromolecules, solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) which are systems made of solid lipids and that possess enhanced stability and nanocrystals, which are simply pure drugs reduced to the nanoscale.

These nanocarriers have a great deal of benefits compared with traditional drug delivery processes. They allow precise delivery in that the drugs are directed to the diseased cells or fractions only without causing systemic toxicity and this maximizes therapeutic effect.[9] They also enable controlled and prolonged drug discharge and preserve therapeutic levels over prolonged durations and lessen the number of administrations.[10] Moreover, the nanocarriers may enhance the stability of the drug by ensuring that the drug in question does not break down due to the presence of sensitive molecules and may also effectively breach many biological barriers, like the blood- brain barrier, where traditional drugs often become ineffective.[11]

The release mechanisms of the drugs that are carried by these nanocarriers are varied and can be programmed with exact specifications. Some common techniques are diffusion where the drug gradually diffuses out of the carrier-matrix; degradation of the carrier which releases the drug; and stimulated-releases whereby drug liberation is stimulated by certain particular internal or external stimulations.[12] Such stimuli may be a change in pH (e.g. in acidic tumor microenvironments), changes in temperature, light of specific wavelengths, or specific overexpressed enzymes at the sites of disease.[13]

3. Current Trends in Nanotechnology-based Drug Delivery

Nanotechnology-based drug delivery is a quickly developing area; the main reason is new approaches to improve medication effectiveness and transmission around biological barriers. There are some trends that are shaping the space of next-generation nanomedicines.

3.1 Intelligent/Stimuli- responsive nanocarriers

A significant advancement is the development of "smart" or stimuli-responsive nanocarriers that release their cargo in response to specific physiological or external cues.[14] pH-sensitive systems are particularly promising for tumor targeting, as many solid tumors exhibit a slightly acidic extracellular pH (pH 6.5-7.2) and even lower intracellular pH in endosomes.[15] These nanocarriers will be synthesized in such a way to be subjected to conformational changes or degrade at an acidic pH and release the drug locally and have the least possible exposure to healthy tissues. On the same note, nanocarriers that are affected by temperature can be designed to deliver medications under higher temperatures, which could be achieved externally (such as hyperthermia) or are simply intrinsic to the site of the infection or inflammation.[16] Enzyme-based release mechanisms are used when overexpression of a particular enzyme takes place in diseased cells, as happens with proteases in tumors or bacterial enzymes in infection, giving high control of the drug release mechanism.[17]

3.2 Ligand-Conjugated Targeting

To obtain even higher levels of specificity, nano carriers are proving to be of growing importance in functionalizing with targeting ligands. Although not necessarily a nanotechnology-based treatment option, antibody-drug conjugates (ADCs) are a good example of a collaborative approach, where cytotoxic drugs have their association with antibodies, typically through cleavable mechanisms, to ensure that the drug concentration is ultimately released into antigen-bearing cancer cells.[18] Following this idea, targeting in the form of peptide or receptor in which a peptide or other ligand is coupled to an overexpressed receptor on target cells has been developed.[19] It also lends itself to good cancer therapy as many cancer cells have unique surface expressed cell markers and to central nervous system (CNS) diseases where it is possible to enhance crossing the blood-brain barrier with specific ligand.[20]

3.3 Nanotechnology Gene Therapy- Delivery

Nanotechnology has been central in the new mRNA and gene therapy developments. Such promising role in the acceleration and success of the mRNA vaccine, like COVID-19, was played by lipid nanoparticles (LNPs).[21] The LNPs trap and safeguard the sensitive mRNA but also allow the mRNA to essentially be ordered into the cells to generate the requisite antigen. Outside of vaccines, nanotechnology plays an extremely important role in genetic editing technologies such as CRISPR-Cas9.[22] Safe and effective viral gene delivery by CRISPR-Cas9[24] Non-viral nanocarriers, such as polymeric nanoparticle and liposomal nanoparticles, are also under investigation to transfer CRISPR-Cas9 components (DNA, mRNA, or ribonucleoprotein complexes) into the target cells efficiently and safely undergo a precision genome editing process, which eliminates the safety and immunogenicity issues related to viral vectors.[23]

3.4 Low solubility drugs nanotechnology

One of the greatest challenges in the development of drugs has been the low aqueous solubility of numerous active pharmaceutical ingredients (APIs) that restricts the bioavailability of such compounds. Nanotechnology has come up with solutions that are effective by helping to form nanocrystals and nanosuspensions.[24] These drug formulations can greatly alter the surface area by decreasing the drugs into nano particles (generally less than 1 1m) thus making the drug more soluble and the dissolvable rate faster.[25] This produces more absorption and more bioavailability, which enables the reduction of dosages and improved patient results.

3.5 Hybrid Nanocarriers6Multi-tasking

On the frontiers of nanomedicine, the development of the hybrid and multifunctional nanocarriers that merge several functionalities into one platform is observed. A good example will be theragnostic nanoparticles, which carry the ability to diagnose the disease and have the capability of responding to the therapy (e.g., as therapeutic agents) in the same nanocarrier.[26] That is, it enables both simultaneous diagnosis and real-time monitoring of drug delivery and evaluation of therapy response. The other important use is the creation of co-delivery systems that will fight multidrug resistance (MDR) in cancer.[27] Such systems enclose various pharmaceuticals, usually a chemotherapeutic and a resistance-modulating agent, to create synergistic interactivity, evade drugs outflow phenomenon, and re-establish drug sensitivity within resistant cancer cells.[28]

4. Major Therapeutic Areas of application

Nanotechnology has significantly influenced many treatment sectors where the challenges of administering drugs over the years have been met using it.

4.1 Cancer Therapy

The application in Nanocarriers has transformed the treatment of cancer by focusing delivery of drugs where they are needed more numerous and efficiently. It is mainly done by two major ways: passive targeting and active targeting.[29] With passive targeting, the Enhanced Permeability and Retention (EPR) effect is utilized- whereby nanoparticles tend to accumulate in tumor tissue compared to other parts of the body, based on their characteristics of having leaky vasculature combined with poor lymphatic drainage, which is a signature feature of quickly expanding tumors.[30] Such examples are Doxil (liposomal form of doxorubicin) and Abraxane (albumin-bound nanoparticle of paclitaxel) that have better the results in terms of building up drug level within the tumor and providing lower systems with less toxicity than traditional compounds.[31] Targeting Nanocarriers can be functionalized with targeted ligands (such as antibodies, peptides, aptamers) that bind overexpressed receptors on the surface of cancer cells with receptor-mediated endocytosis resulting in very specific drug delivery.[32]

4.2 Neurological Disorders

The curative outcomes are especially trying when it comes to treating neurological infections because of the imposing blood-brain barrier (BBB) that limits the diffusion of the majority of treatment agents into the central nervous system (CNS).[33] Nanocarriers provide great prospects of surmounting this hurdle. Certain engineered exosomes (derived naturally), liposomes, and polymeric nanoparticles may be able to circumvent the BBB using one of the following mechanisms: receptor-mediated transcytosis, adsorptive transcytosis, or temporarily altering the tight junctions.[34] This allows for the effective delivery of neurotherapeutics, gene therapy agents, and diagnostic probes to the brain, opening new possibilities for treating conditions like Alzheimer's, Parkinson's, and brain tumors.[35]

4.3 Infectious Diseases

Nanotechnology offers effective solutions to infectious diseases particularly as antimicrobial resistance continues to soar.[36] The antimicrobial nanoparticles can have a direct antimicrobial activity (the example of silver nanoparticles, metal oxides) or serve as a carrier of traditional antibiotics, ensuring their improved effectiveness and minimizing the development of resistance.[37] Overall, nano-vaccines rely on nanoparticle-supported delivery of antigens in a highly immunogenic form that can lead to robust and long-living immune responses as seen with the mRNA vaccines based on LNPs in the context of the COVID-19 pandemic.[38] In addition, nanocarriers are presently being developed to deliver antiviral drugs which increase the bioavailability and targeted delivery of antiviral treatment to the infected cells.[39]

4.4 Cardiovascular diseases

Nanotechnology in cardiovascular diseases can result in targeted delivery to the atherosclerotic plaque which is the major cause of heart attacks and strokes.[40] Nanoparticle accumulation may target inflamed or damaged walls of arteries to provide cost-efficient anti-inflammatory agents, plaque-stabilizing medications, or imaging agents to diagnose in their early stages.[41] This narrows down the systemic side effects and increases the efficacy of therapy by delivering their drug to the area of pathology at high concentrations.[42]

4.5 Regenerative Medicine

Regenerative medicine is an essential part of nanotechnology which works to repair the damage as well as regenerating them, using the tissues and organs.[43] The scaffold based on nanoparticles is based on the idea of resembling the phenotype of the native extracellular matrix and therefore, forms an environment that is favorable, in many cases, it can support adhesion, proliferation and differentiation of cells.[44] Such scaffolds may also be used as delivery platforms of growth factors and cytokines, and genetic material, which directs the growth and regeneration of the tissue and gives rise to functional tissues, such as bone, cartilage, and nerve tissue.[45]

5. Challenges & Limitations

Although nanotechnology promises tremendous potential in delivery of drugs, there are several challenges and limitations in need of being addressed to realize wide clinical application and commercial viability of nanotechnology.

5.1 Problems of Biocompatibility and Toxicity

Among these concerns, there is a problem of long-run safety and biocompatibility of nanomaterials.[46] Many nanocarriers are devised to be biodegradable, but the possibility of the accumulation in organs (e.g., liver, spleen, kidneys) over the long period of time is a burning question.[47] It is possible that nanoparticles cause cytotoxicity at the cellular level or may cause inflammation or oxidative stress or disrupt cellular functions.[48] Size, shape, and surface charge, and chemical composition each contributes to the biological and adverse potential effect of nanoparticles and requires stringent and thorough toxicological evaluation.[49]

5.2 Limitations in Regulations

Nanomedicine evolves fast, and its rapid progress outruns the creation of the common and unified system of regulation.[50] Nanomedicines lack approved standard guidelines regarding their approval, and thus there is a lack of clarity on their classification (drug, biologic, device or combination product), safety, and quality control.[51] The definitions and requirements around the world by different regulatory bodies differ often and this aspect may act as a challenge to development, approval, and market access of new nano therapies across the world.[52] Setting of clear and consistent standards is very essential in mapping the safety of patients and innovation.

5.3 Cost of manufacturing

There are significant difficulties in translating nanomedicines developed in the laboratory to large scale clinical manufacturing. Most nanocarriers are complex to synthesize and engineer, which impedes large-scale production at uniform quality, and in some cases, is nontrivial.[53] It is a major challenge to have batch-to-batch consistency with respect to size, morphology and the drug loading at commercial scale. Such production and scaling-up costs may considerably affect the affordability and feasibility of nanomedicines.[54]

5.4 Stability concerns and Shelf-life

Stability and shelf-life issues may also be produced by the characteristic features of nanoparticles.[55] Due to storage, transport and biological stability, nanocarriers tend to cluster (aggregate) and degrade.[56] Particle size and surface properties can be modified by the process of aggregation with the result that targeting characteristics may be lost or that clearance or toxicity of the particles may be accelerated. Providing the long-term physical and chemical stability of nano formulations to assure their stability and therapeutic performance in the course of time is a severe challenge.[57]

5.5 Ethics & Environment

The embodiment of nanotechnology in medicine would also raise serious ethical and environmental concerns besides having the technical and regulatory problems.[58] Ethical issues cross into the domain of equal access to potentially lifesaving nano therapies, informed consent to clinical trials using novel nanomaterials, and human enhancement and its societal implications. Environmentally, a waste product of nanomaterials might adversely affect the ecosystem and health risks of the people, especially in terms of their impact of persistence and propensity to bioaccumulation, which should highly be broached and environmentally responsible disposal of the material considered.[59]

6. Prospects

The potential of nanotechnology concerning drug delivery is very bright as the field is still under constant development that aims to set new standards when it comes to precision, efficiency, and sustainability.

Nanomedicine Personalized is at the point of breaking treatment models.[60] Since using genomics, proteomics and Artificial Intelligence (AI) it will be able to specifically target the design of nanocarriers to the unique characteristics of the patient.[61] AI-guided platforms can optimize nanoparticle characteristics, predict biological interactions, and refine drug release profiles based on a patient's unique genetic makeup and disease biomarkers, leading to highly effective and individualized therapies.[62]

Or another hot new entry is the Nano-biohybrids development.[63] This refers to the incorporation of synthetic nanoparticles with biological materials, e.g. cell membranes (e.g. red blood cell membranes to evade immune responses) or naturally derived exosomes.[64] These hybrid systems can leverage the biocompatibility, target feasibility, and immunity modifying ability of biological materials to increase the safety and efficacy of synthetic nanoparticle carriers toward a wide array of therapeutic use.[65]

This will integrate with implantable and wearable devices to allow control and monitoring at new levels [66]. Devices fitted with nanotechnology-enabled sensors can give real time monitoring of drugs and permit dynamic variation in dose and release kinetic.[67] Such closed-loop system will guarantee the best therapeutic levels, reduce adverse effects and patient adherence, especially in cases of disease management over a long period that affects the patients and needs constant monitoring.[68]

In addition, there is an increasing focus on Green Nanotechnology that is propelling the search for sustainable and environment friendly synthesis approach.[69] Based on the use of plant extracts, biopolymers, and other natural resources, scientists are coming up with environmentally aware methods of manufacturing nanoparticles, decreasing the use of the most significant chemicals and decreasing environmental load.[70]

Lastly, nanotechnology will gain immense dimensions in the field of rare illnesses/orphan medications.[71] Due to the distinct circumstances that led to the development of such conditions, including small patient base and intense disease and biological processes, nanocarriers present an effective platform to enhance the solubility of drugs, induce targeted delivery, and evade biological obstacles hence offering much-needed therapies to hitherto incurable medical disorders.[72]

7. CONCLUSION

It is true that nanotechnology has transformed drug delivery by providing new solutions to some of the well-known problems that have existed in the pharmaceutical industry. As much as some great success has been recorded in the aspect of targeted delivery, controlled release and in overcoming the biological barriers, there is still a critical gap in the aspects of toxicity, scalability and regulatory standardization. These gaps will require scientific interdisciplinary work, along with the associated collaboration of scientists, engineers, clinicians, and regulatory organizations with sound safety structure systems. In conclusion, nanotechnology is one of the pillars of future pharmaceutical sciences, and it will change how patients are treated and dramatically benefit them.

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