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Use of Nanoparticles in Pharmaceutical and Drug Delivery Systems: Advances and Challenges

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ABSTRACT

Nanoparticles represent a significant innovation in pharmaceutical drug delivery, tackling essential issues such as inadequate solubility, restricted bioavailability, and systemic toxicity of medicinal medicines. Their distinctive physicochemical characteristics, such as nanoscale dimensions, elevated surface area-to-volume ratio, and adjustable surface functions, provide accurate targeting and regulated drug release, rendering them essential for contemporary medicine. This review synthesizes contemporary advances, obstacles, and emerging trends in nanoparticle-mediated drug delivery methods. This analysis focuses on essential nanoparticle types, including liposomes, polymeric nanoparticles, and lipid nanoparticles, emphasizing their applications in oncology, gene therapy, and RNA-based vaccinations. Despite significant advancements, the analysis highlights persistent limitations such as biocompatibility, stability, regulatory obstacles, and deficiencies in comprehending biodistribution and long-term toxicity. The paper examines creative strategies to tackle these issues, including stimuli-responsive nanoparticles, theranostic systems, and biomimetic designs. Moreover, it underscores the use of cutting-edge innovations, such as artificial intelligence for nanoparticle optimization and advanced manufacturing methods, to improve scalability and efficiency. Future research will be enhanced by resolving the current shortcomings and broadening the applicability of nanoparticles to fields such as regenerative medicine and brain-targeted therapeutics. This study highlights the revolutionary capacity of nanoparticles to improve pharmaceutical drug delivery and emphasizes the necessity for ongoing interdisciplinary collaboration to convert these advancements into clinical and economic success.

INTRODUCTION

Nanoparticles are being considered as a new model of technology in the pharmaceutical domain offering new approaches to old problems in drug delivery systems. Nanoscale carriers, ranging from 1 to 100 nm in size, have unique physicochemical properties such as increased surface-area-to-volume ratios, tunable surface functions, and increased solubility. Their distinct features make them an indispensable part of modern drug delivery systems (Nouri-Vaskeh et al., 2020)s. Global nanoparticle drug delivery market was estimated to be the market size of $74.64 billion in the year 2022 and forecasted to grow at a high rate to reach $156 billion by 2030, showing one sector that increased its dependence on nanoparticles for precision medicine and customized medicines. Advanced formulations of nanocarriers, encompassing lipid nanoparticles for mRNA vaccine delivery as well as polymeric carriers that provide sustained drug retention and release, have demonstrated versatility and promise for therapeutic use (Kremsner et al., 2021). However, many challenges still

exist such as biocompatible cities, scale, regulation approval, and stability (Sabouri et al., 2018). This review integrates the data available in the literature to explain how these nanoparticles operate as pharmaceutical drug delivery systems, with a particular focus on their classifications, recent progress, challenges, and future directions to address current gaps and develop advances.

New research has dramatically improved our comprehension of how nanoparticles function to improve the delivery efficiency of the therapy whilst reducing their systemic toxicities. Abstract: The rapid development and distribution of COVID-19 mRNA vaccines rely on lipid-based nanoparticles, which highlights their scalability and clinical potential (Walsh et al., 2020). Polymeric nanoparticles enable controlled drug release and dose site in cancer and other chronic disorders. However, there remain many key gaps in knowledge, including long term in vivo biocompatibility of nanoparticles, their distribution in vivo, and their elimination pathways. While studies have demonstrated that nanoparticles can successfully deliver small chemicals, proteins, and nucleic acids, few have explored how they can do the same for complex diseases like neurodegenerative diseases or rare genetic diseases. Additionally, the contradictory evidence around nanoparticle toxicity and lack of standardized evaluation methods hinders clinical translation. If these shortcomings corrected, the discipline will provide a firm footing to the rational design of safer, more effective, and scalable nanoparticle-formulation based systems, vitally required for advancement of the field (Khoobchandani et al., 2020). We systematically highlight and discuss major pitfalls with the aim of informing researchers about existing challenges and help them design better future drug delivery strategies.

This review attempts to elaborate and scrutinize the current advances, challenges and future directions of nanoparticle-based drug delivery systems with special emphasis on the gaps identified in the literature. We combined several recent findings in a complete synthesis approach to provide a comprehensive overview of the field. This review addresses the limitations of nanoparticles to offer new functions with ideas related to their design, function and scalability, and because it provides alternative perspectives on these topics, it could add to the existing knowledge in the field of nanoparticles (Sabouri et al., 2018). These explanatory principles are intended to facilitate the development of more biocompatible and clinically-translatable nanoparticle systems, therefore promoting the ultimate goal of revolutionizing oral drug delivery. Thus, the results of this study will provide an initial ground for further research and clinical applications for the purpose of personalized and regenerative medicine as well as targeted therapeutic approaches to complex diseases (Khoobchandani et al., 2020).

Types of Nanoparticles in Drug Delivery Systems

The improvements in pharmaceutical sciences brought by nanoparticles are especially noteworthy in ways to deliver medication. These nanoscale structures typically range from 1 to 100 nm and have special physicochemical properties that make them excellent candidates for solubilizing, stabilizing, and providing bioavailability of drugs (Purpura et al., 2018). Nanoparticles have different material compositions and shapes that render them versatile carriers for achieving different therapeutic goals via different methods of drug delivery as shown in figure 1(Nakano et al., 2018).

Liposomes are one of the most well-characterized and commonly used classes of nanoparticles in drug delivery applications. Due to their structure with phospholipid bilayers surrounding an aqueous core, liposomes can entrap both hydrophilic and hydrophobic drugs. Due to their biocompatibility, biodegradability, and most importantly ability to mimic biological membranes, they demonstrate a great potential for pharmaceutical applications (Khongkhunthian et al., 2018). Liposomal formulations enhance solubility, prolonged circulation time and targeted targeting (especially for anticancer agents and vaccines) (Tewari et al., 2020). Doxil® is a liposomal formulation of doxorubicin and marks an important milestone in cancer with an improved safety profile due to reduced cardiotoxicity compared to conventional formulations. Changes in liposomal architecture/characteristics, such as stealth liposomes (PEGylated liposomes) or cationic liposomes, improve their functionality due to enhanced stability and cellular uptake (Cho et al., 2019).

Polymeric nanoparticles like nanospheres and nanocapsules are made up of degradable and biocompatible polymers, such as polylactic acid (PLA), poly(lactic-co-glycolic acid) (PLGA), and chitosan. The drug release features can be tailored to achieve sustained or stimulus-responsive release of drugs from these nanoparticles (Moradi et al., 2016). Polymeric nanoparticles can encapsulate proteins, peptides, and small-molecule medicines, protecting them from degradation and enhancing their bioavailability (Boyacıoğlu et al., 2021). Functionalization of their surfaces can be achieved with selective-delivery ligands, such as PLGA nanoparticles with folic acid-modified with and directed toward cancer cells. These advantages notwithstanding, challenges such as complex production processes and immunogenicity need to be solved (Mistraletti et al., 2019).

Dendrimers, highly branched, tree-like macromolecules with well-defined architectures and tunable surfaces or end-group functionalities. The unique architecture not only allows for conjugation of drugs, targeting ligands and imaging agents, but also makes them versatile platforms for drug delivery. Dendrimers improve solubility and pharmacokinetics and also assist controlled release of drugs (Huang et al.,

2019). The dendrimer that has been most extensively researched in the all fields above is that of Polyamidoamine (PAMAM) dendrimer (Wang et al., 2019). Dendrimer–based formulations of methotrexate: better tumor penetration and lower systemic toxicity. Dendrimers have some limitations mostly in the synthesis which is sometimes complex and expensive hindering the large-scale application (Viney et al., 2021).

Solid-lipid nanoparticles are a type of nanoparticle composed of a solid-lipid matrix which can encapsulate lipophilic drugs. Solid lipid nanoparticles (SLNs) combine the advantages of lipid-based nanocarriers, such as liposomes and polymeric nanoparticles, and display excellent biocompatibility, controlled drug release, and improved stability. For oral, topical, and intravenous drug delivery these nanoparticles are particularly suitable (Zhang et al., 2020). Solid lipid nanoparticles (SLNs) can provide, among other things, a protective environment against gastric enzymes that may degrade pharmaceuticals being administered orally, thereby enhancing oral bioavailability (Nakano et al., 2018). SLNs have been to deliver compounds such as curcumin and paclitaxel, increasing the therapeutic efficacy 16,17. However, some challenges such as low drug-loading capacity and the risk of gelation during storage require further investigation (Boyacıoğlu et al., 2021).

Nanocrystals are pure pharmaceutical particles reduced to nanoscale dimensions and stabilized by surfactants or polymers. In contrast to other nanoparticles, nanocrystals operate independently of the carrier material, facilitating higher drug-loading capabilities. Their diminutive size enhances their surface area and dissolution rate, rendering them exceptionally useful in augmenting the bioavailability of poorly soluble pharmaceuticals (Kelidari et al., 2016). Nanocrystal formulations, exemplified by NanoCrystal® technology, have been effectively marketed as pharmaceuticals, including fenofibrate and sirolimus. The synthesis of nanocrystals is relatively straightforward relative to other nanoparticle systems, utilizing methods such as high-pressure homogenization and wet milling (Banzhaf et al., 2017).

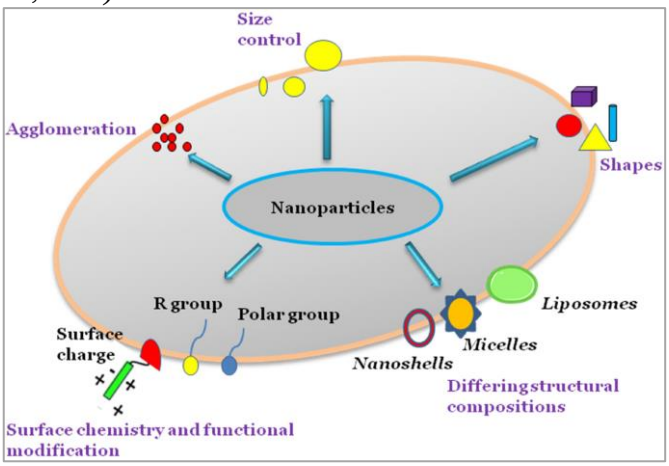
Gold and silver metallic nanoparticles have been of great interest owing to their unique optical, electronic, and bactericidal properties. Among the studied systems of drug delivery, gold particles (AuNPs) are one of the most researched, because their surface properties have a high conjugation efficiency of drugs, peptides and even DNA when functionalized and with a very scalable production173. Gold nanoparticles (AuNPs) are increasingly being used as carriers of drugs and photothermal agents for cancer therapy (Gomeni et al., 2016). AgNPs have been receiving much attention as an antibacterial phytomedicine and an antimicrobial agent for the treatment of wounds and the prevention of infections. However, concerns about long-term toxicity and environmental effects of the metallic nanoparticles remain an unsolved problem (Srichana et al., 2016).

Carbon-based drug delivery Carbons base nanoparticles e. g such as carbon nanotube (CNTs) and graphene oxide (GO) show unique structural and electronic properties for drug delivery application. Pharmaceutical drugs can also be encapsulated in their hollow structures or conjugated to their surfaces to achieve targeted and controlled release (Michotte et al., 2018). Due to the high surface area and biocompatibility of graphene oxide, it is recommended for encapsulating different drug molecules. Carbon (C) with its natural track record has tripod ashore toxicity, as it can be remained in a biological mechanism, leading to cytotoxicity and inflammation whereas the safety liferaft of such nanoparticles is currently being studied (Khalifa et al., 2019).

Hybrid nanoparticles combine two or more materials such as polymers, lipids or metals to achieve synergistic benefits." They integrate the stability and precise controllable morphology of polymeric nanoparticles with the biocompatibility and biofunctionality of the liposomes (Usmani et al., 2018). Those systems are designed to deliver the drug accurately, especially for cancer immunotherapy or mRNA vaccines. The recent development consists in the simultaneous delivery of medicines and adjuvants using hybrid nanoparticles, which has proved to enhance therefore therapeutic efficacy and reduce side effects (Lilienberg et al., 2017).

Figure 1

Physicochemical properties of nanoparticles (Yusuf et al., 2023).



Advances in Nanoparticle-Based Drug Delivery

The discovery of these nanoparticles has revolutionized the delivery system of drugs and also provides a new scope of research to overcome the limitations of conventional levels of pharmaceutical systems. The developments in drug delivery systems due to unique properties of nanoparticles such as nanoscale dimension, a higher surface-area-to-volume ratio and applicability for functionalization with a variety of biomolecules (Shi et al., 2021). Such innovative

approaches have enhanced drug therapeutic efficacy, lowered systemic toxicity, and facilitated patient compliance (Bilia et al., 2018).

Focused Pharmacological Administration

This represents a major development in nanoparticle-mediated drug delivery, specifically in the area of targeting drugs to the appropriate tissue or cellular target and thus minimizing off-target effects and improving efficacy (Sabouri et al., 2018). Based on how they operate, Targeted Delivery systems can be further divided into the passive and active system. Passive targeting relies on the enhancement of permeability and retention (EPR) effect as a consequence of the defective vasculature and low lymphatic drainage that induces a high local accumulation of nanoparticle (Shi et al., 2021 The application of this method is related with therapy of cancers. Diseased location-predictable nanoparticles such as liposomes and polymeric micelles have been designed to make delivery and aggregation of chemotherapeutics onto tumor site improved (Huang et al., 2019).

Active targeting involves modifying the surface of the nanoparticles using ligands (usually antibodies, peptides, or aptamers) that specifically recognize and bind to receptors that are over-expressed on target cells. Folic Acid-Functionalized Nanoparticles: Nanoparticles functionalized with folic acid have been applied to these types of cancer cells by discriminating those that overexpress folate receptors (Sabouri et al., 2018). A different instance is the utilization of transferrin-coated nanoparticles for brain drug delivery, as transferrin receptors are found in brain capillary endothelial cells that form the blood-brain barrier (Zimmermann et al., 2017).

Stimuli-Responsive Nanoparticles

A major yet recent development in the field of drug delivery is the use of stimuli-responsive nanoparticles which release their therapeutic payload upon specific internal/external stimuli. Such approaches enable spatiotemporal control of drug delivery, enabling improved specificity and impact (Madhi et al., 2020).

Internal stimuli: Internal stimuli responsive nanoparticles employ physiological variables like pH, redox potential, and/or enzymatic activity. Some pH-sensitive nanoparticles are designed to release drugs in an acidic environment like tumor or endosome. Similarly, the redox-responsive nanoparticles are designed to exploit the high levels of glutathione in the cancer cells and release the drug inside (Huang et al., 2019).

External Stimuli: External stimuli responsive systems will respond to stimuli (temperature, light, ultrasound or a magnetic field) (Viney et al., 2021). Thermosensitive nanoparticles release drugs by localized hyperthermia and light-sensitive nanoparticles use ultraviolet or near-infrared light to trigger controlled release. Magnetic nanoparticles such as iron oxide nanoparticles have been used for magnetically induced guided therapy [e.g. stimulation of secretion of antigens and drugs to sustain local cytokine production and magnetically guided guided drug delivery and hyperthermia therapy (Zimmermann et al., 2017).

Multifunctional Nanoparticles

One of the key features of advanced nanoparticle-based medication delivery systems is multifunctionality. Such nanoparticles combine drug and diagnostic functionalities and target capabilities, which is summarized by the term theragnostic. In personalized medicine, the combination of diagnosis and treatment makes these systems very useful especially (Sabouri et al., 2018).

Therapeutic/diagnostic integration: For simultaneous imaging and drug delivery, AuNPs and quantum dots have been used. In addition to being targeted for drug delivery, AuNPs can also serve as an anticancer medicinal carrier (Huang et al., 2019). SPIONs have also been used as MRI contrast agents for the targeted delivery of chemotherapeutics (Zimmermann et al., 2017).

Simultaneous Administration of Therapeutics: Multifunctional nanoparticles allow for simultaneous administration of numerous therapeutic agents (i.e. small-molecule drugs, genes or proteins). For instance, lipid-polymer hybrid nanoparticles have been designed as novel carriers to synergistically co-deliver chemotherapeutics and gene-silencing agents (e.g., siRNA) against cancer (Madhi et al., 2020).

Advancements in Manufacturing and Design

Advancement of synthesis and design of nanoparticles has raised its function and range of use. Unique techniques including but not limited to microfluidics, electrospraying, and nanoprecipitation have enabled production of nanoparticles with well-controlled sizes, shape, and drug incorporation capacity (Bilia et al., 2018).

Precise Design: The circulation time, cell uptake, and biodistribution of nanoparticles are strongly underlying by their size and shape (Huang et al., 2019) Spherical nanoparticles have been popular as they are quite easy to manufacture, but, it should be pointed that rod-shaped or disc-shaped nanoparticles show a better contact with cell and tissues compared to spherical particle. The engineering of nanoparticles of a certain shape has improved their potency (Zimmermann et al., 2017).

Surface Engineering: This includes application of polyethylene glycol (PEG) to surface of nanoparticles enhancing NP stability and avoiding immune system response (PEGylation). Ligand-based decoration of the nanoparticles enables active targeting and stealth

coatings increase the systemic circulation time (Viney et al., 2021).

Case Studies and Applications

Numerous nanoparticle-based drug delivery systems have attained clinical application or have progressed to advanced developmental phases, highlighting the practical significance of these innovations (Madhi et al., 2020). Liposomal formulations, such as Doxil® (doxorubicin liposome), have markedly enhanced the therapeutic index of chemotherapeutic drugs by diminishing off-target toxicity and augmenting tumor accumulation (Shi et al., 2021).

Challenges in Nanoparticle-Based Drug Delivery

Nanoparticle-based drug delivery technologies hold significant promise for the pharmaceutical industry; however, its application has significant challenges. II) However, the main issues are biocompatibility and toxicity. Nanoparticle engineering is often aimed at maximizing therapeutic effects, but this approach can also lead to cytotoxicity or unwanted immunogenicity. These metallic nanoparticles such as gold or silver, have been reported to generate oxidative stress and generation of reactive oxygen species causing damage to cells (Roh et al., 2020). Similarly, carbon-based nanoparticles, such as carbon nanotubes (CNTs) are also potentially chronically toxic due to their persistence in biological milieu. Moreover, they are vulnerable to the recognition of the immune system and can also cause hypersensitivity reactions or fast clearance (decreasing therapeutic effects of the therapy) by immune system because the nanoparticles are recognized as foreign particles (Opgenorth et al., 2020). To do so, though, surface modifications (e.g., polyethylene glycol [PEGylation]) are used, but long-term safety issues are not addressed (Beckman et al., 2016).

Stability of nanoparticles at storage and transport is big challenge. Aggregation, disintegration, or even phase separation are the mostly encountered issues with nanoparticles that substantially spoil their physicochemical properties and therapeutic effect, particularly in the face of undesirable conditions. Nanoparticles that are lipid-based, including liposomes, are specifically at risk of hydrolysis and oxidation, which may lead to changes in their structures over time (Fadaee et al., 2017). Aggregation induced by the high surface energy of nanoparticles could change their size and release properties of the loaded drug, reducing their effectiveness (Cowper et al., 2017). In order to overcome these issues, to stabilize the nanoparticle formulations, surfactants and cryoprotectants are often employed, and lyophilization processes are performed to enhance their longevity. However, such solutions add complexity and cost to the production process, imposing further barriers to commercialization of biofuels (Koga et al., 2020).

These Regulatory challenges also impede the translation of nanoparticle-based systems from fundamental research into the clinic. A wide variation of nanoparticles in size, shape, surface characteristics, and composition makes it challenging to standardize evaluation methodologies for safety and efficacy. Diverse regulatory frameworks have shown vagueness and inconsistency in the case of nanoparticle-based medicines and this in itself leads to a lengthy approval process (Mohammadi et al., 2017). One unique aspect is the difficulty of preclinical and clinical assessments of nanoparticles, because toxicity and pharmacokinetic models currently available often fail to predict there in vivo behavior (França et al., 2017). Several regulatory bodies, including the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA), have tried to establish common guidelines for nanoparticle-based therapeutics. Still, there remain considerable defects that prevent the market access of these new drugs (Nishimaki et al., 2018).

But besides regulatory hurdles, scalability of nanoparticle making will be a serious problem as well. In nanoparticles synthesis, these methods often require complex processes (including solvent evaporation, emulsification, and surface functionalization) with the need to control many parameters (Li et al., 2020). Technical hurdles exist to improving these and other similarly low-yield procedures while maintaining their fidelity, consistency, and reproducibility. Additionally, the need for high-cost resources like rare metals, functionalized polymers and ligands significantly raises production cost. Such cost factors make the development of nanoparticle-based pharmaceuticals less accessible to patients, especially in the deprived settings (Rasmussen et al., 2016). Advancements in manufacturing technologies, including microfluidic systems and automated platforms, offer early opportunities by enabling more efficient and high-throughput production. However sea-wide deployment take goal undertaken only in childhood stages of evolution (Angeles et al., 2020).

One of the most critical challenges of nanoparticle drug delivery is achieving the appropriate biodistribution and clearance properties. Nanoparticles are still prone to off-target accumulation in non-diseased organs (e.g. liver, spleen and kidneys); even though targeting strategies have advanced to improve localization. This can cause unwanted side effects and also can lower the therapeutic index of the drug. Furthermore, the mononuclear phagocyte system (MPS)—also known as the reticuloendothelial system—often quickly clears nanoparticles from the circulation, which limits their lifetime and effectiveness. Strategies to resolve these challenges entail the use of stealth coatings, for example PEGylation, to prevent detectability by the immune system and promote systemic circulation. While

zwitterionic materials and ligand-based targeting methods are being actively explored to improve biodistribution, both approaches have few fundamental limitations (Makinde et al., 2017).

Future Directions and Emerging Trends

Drug delivery through nanoparticles is rapidly evolving, with future pathways and emerging trends that will address current limitations, enhance precision medicine, and integrate emerging therapeutic technologies for better clinical outcomes. Given the expanding reach of nanoparticles in the lab and the clinic, it can be expected that new ideas and technologies in the design, operation, and utilization of nanoparticles will enter into the arsenal of drug delivery methods, further broadening the therapeutic landscape involving these agents (Khoobchandani et al., 2020).

Nanoparticles in Personalized Medicine

One future tendency in personalized medicine is the incorporation of nanoparticles. Through progress in genomics, proteomics, and metabolomics, precision drug delivery systems personalized to an individual's unique genetic and physiologic characteristics can be developed. By designing nanoparticles that interact with specific biomarkers pertinent to specific diseases, such as cancer or autoimmune disorders, targeted therapy approaches can be achieved (Khalifa et al., 2019). For instance, the formulations of nanoparticles may entail surface ligands that selectively adhere to overexpressed receptors in pathological tissues, including HER2 receptiors in breast cancer or CD44 in certain hematological malignancies. Moreover, nanoparticles can be applied to deliver gene-editing tools, like CRISPR-Cas9, that can potentially repair the genetic defects that lead to the genetic diseases (Tripathy et al., 2019).

Combining artificial intelligence (AI) and machine learning (ML) with nanoparticles are expected to greatly improve personalized therapy. AI and ML systems can use the large amounts of patient data to predict how a patient will respond to medicines based on nanoparticles, leading to more precise and effective treatment protocols. These technologies enable the optimization of NP design through the identification of ideal material compositions, surface modifications and drug-release profiles tailored to specific patient needs (Yassine et al., 2016).

Stimuli-Responsive and Smart Nanoparticles

Developing stimuli-responsive and intelligent nanoparticles is a gradually growing direction, which aims to increase the specificity and controllability of drug delivery. Such nanoparticles are designed to release their drug in response to some specific internal or external stimulus like pH, temperature, enzyme, light or magnetic field (Gomeni et al., 2016). pH-sensitive internal triggers can exploit the acidic nature of tumors to selectively release chemotherapeutic drugs into the tumor site to minimize systemic toxicity. For instance, localized therapy with few or no off-target effects can be achieved by exploiting enzyme-sensitive nanoparticles in which drugs can be released by overexpressed enzymes in pathological tissues (Weiland et al., 2017).

External stimuli (e.g., light, magnetic fields) have been explored to control drug release. Light-responsive nanoparticles ravage drug-free release by ultraviolet or near-infrared illumination to trigger drug release or photo-sensitizers activation for photodynamic therapy. Magnetic nanoparticles, such as magnetic iron oxide nanoparticles, on the other hand, enable magnetically directed drug delivery for hyperthermia therapy (Bosch et al., 2017). While tremendous progress has been made in the construction of new multi-stimuli-responsive nanoparticles that can respond to multiple stimuli, the special response of multi-stimuli-responsive nanoparticles is still limited (Leuthardt et al., 2016).

Integration with Novel Technologies

At the same time, the coalescence of nanomaterials and next generation technologies (eg, gene therapy, immunotherapy, RNA based therapies) have also enabled further progress in drug delivery. Nanoparticles have been shown to work as carriers for nucleic acid delivery including small interfering RNA (siRNA), messenger RNA (mRNA) and DNA. A key feature of mRNA-based COVID-19 vaccines from both Moderna and Pfizer-BioNTech are lipid nanoparticles (LNPs) (Nguyen et al., 2020). Nanoparticles are also being investigated as possible carrier for RNA-based medicines against genetic diseases, human infectious diseases and cancer (Srichana et al., 2016).

As adjuvants and delivery systems, nanoparticles have been explored for cancer immunotherapy. Through efficient delivery of immunostimulators like checkpoint inhibitors or tumor antigens, the potency of cancer vaccines and immunotherapy methods could be enhanced by the use of nanoparticles (Khoobchandani et al., 2020). Moreover, theranostic nanoparticles have been developed to integrate therapeutic with modalities for imaging and monitoring drug delivery and response in vivo, thus facilitating precision medicine development (Andanooru Chandrappa et al., 2020).

Addressing Present Challenges with Innovative Strategies

Eventually, about the issues of use of nanoparticles in order to deliver medicines, their biocompatibility, toxicity, and also scalability; studies will provide the solutions. A few of valid approaches include integrated design with naturally originating substances [polysaccharides (chitosan, hyaluronic acid)] and biomimetic nanoparticles for augmenting biocompatibility whilst minimizing chronic toxicity (Ahmed, 2018). Biomimetic nanoparticles such as

cloaked natural cell membrane, including red blood cells or platelets, are likely to have less recognition by the immune system and a longer circulation time, hence, represent ideal targeted delivery vehicle (Tripathy et al., 2019).

To overcome this hurdle and offer the possibility of tuning NP size, shape and drug loading, several novel fabrication techniques are being explored including microfluidics and 3D printing (Gomeni et al., 2016). This ultimately enables cheap, reproducible and scalable nanoparticle production which translates to affordable technologies to nanomedicines. Furthermore, identification of its biological properties has accelerated the computational modeling and simulation for development and design of nanoparticle (Yassine et al., 2016).

Nanoparticles for Novel Applications

Beyond classical drugs delivery, nanoparticles have been explored for several new applications such as in regenerative medicine and tissue engineering. Gold nanoparticles may serve as a drug carrier for growth factors, peptides and stem cells to repair and regenerate tissues (Andanooru Chandrappa et al., 2020). Nanoparticles loaded with vascular endothelial growth factors (VEGF) are capable of stimulating angiogenesis into ischemic tissues. Similarly, nanoparticles available have been studied towards the transport of antibacterial agents to prevent the onset of infections in wound healing and implanted devices (Nguyen et al., 2020).

One promising application is using nanoparticles for targeted delivery of drugs to the brain. Exceeding the blood-brain barrier (BBB) poses a major challenge in the treat of neurodegenerative disorders, such as Alzheimer's or Parkinson's diseases (Bosch et al., 2017). New blood-brain barrier-penetrating ligands modified nanoparticles, or nanoparticles engineered to exploit receptor mediated transcytosis, are being developed to carry medicines into the brain, offering hope for improved treatment of a range of conditions (Tripathy et al., 2019).

CONCLUSION

Nanoparticles play an important role in overcoming the hemorrhagic fever groups pharmacologically with respect to the drug design and drug carrier relationship for drug action. This review highlights some recent critical aspects including classes, progress, challenges and future trends of nanoparticles in drug delivery system. Nanoparticles have represented the new-generation tools for the improvement in drug solubility, stability, and target delivery, in which progresses in including the field of stimuli/ responsive systems, multifunctional nanoparticles, and application in the field of personalized medicine have been made into account. The revolutionary potential of such systems has been demonstrated by recent progress in the implementation of lipid nanoparticles that protect mRNA vaccines and polymeric nanoparticles that offer on-demand delivery of drugs. However, their widespread application remains a significant challenge due to biocompatibility, stability and scalability issues, as well as regulatory limitations. These findings are highly consequential for improving therapeutic innovation. Nanoparticle systems could revolutionize the delivery of therapies for cancer, genetic disorders, and infectious diseases by improving the efficiency of drug dissemination and limiting systemic toxicity. These apparent discrepancies highlight the urgent need to better integrate various lines of inquiry to overcome current limitations and enable new applications, particularly in the context of personalized medicine and future technologies, including gene editing and theragnostic. While significant progress has been made, many gaps still exist in literature. Other areas needing further exploration include inconsistent evidence on biocompatibility in the long term, poor understanding of mechanisms of biodistribution and clearance, and challenges in scaling up the manufacturing processes. Further research is needed to improve nanoparticle design, standardize evaluation strategies, and explore their use with poorly studied applications including the treatment of neurological diseases and regenerative medicine. Increasing the application of AI and machine learning in design for accurate nanoparticle specialization can lead to the development of cost-effective, biocompatible, and scalable nanoparticle production methods as a focus in further research. Addressing these shortcomings will pave the way for wider clinical indications and regulatory approvals. Although this review is one of the most in-depth on the topic, it reviews only a narrow range of literature, and novel, lesser explored nanoparticles may be missed. However, it highlights the potential such nanoparticle drug delivery systems have to fulfil unmet medical needs, closing a chapter and opening a new one for pharmaceutical sciences.

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