

Drug Formulation and Delivery Systems: Innovations and Applications

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Abstract:

Innovations in drug formulation and delivery systems have revolutionized the pharmaceutical industry, significantly improving the efficacy and safety of therapeutic agents. Advanced technologies such as nanotechnology, liposomes, and polymers have enabled the development of targeted drug delivery systems that optimize the release profiles of medications, enhance bioavailability, and minimize side effects. For instance, nanocarriers facilitate the direct delivery of drugs to specific cells or tissues, improving treatment outcomes for complex diseases like cancer and diabetes. This personalized approach enables healthcare providers to tailor therapies to individual patient needs, resulting in more effective and less invasive treatments. Moreover, the integration of digital health technologies has transformed drug delivery systems by incorporating smart devices and wearable technologies. These innovations allow for real-time monitoring of drug delivery and therapeutic effects, enhancing patient adherence and engagement in their treatment regimens. For example, implantable devices that release medication on-demand represent a significant advancement in chronic disease management. Furthermore, new formulation strategies, such as 3D printing, create opportunities for personalized medicine, enabling the production of custom dosage forms to meet specific patient requirements. Overall, the ongoing evolution of drug formulation and delivery systems promises to enhance therapeutic outcomes and improve the quality of care.

Keywords: Drug formulation, Delivery systems, Nanotechnology, Targeted drug delivery, Liposomes, Polymers, Bioavailability, Digital health technologies, Smart devices, Implantable devices, Personalized medicine, 3D printing

Introduction:

In the dynamic landscape of pharmaceutical sciences, drug formulation and delivery systems stand out as crucial components in the development of effective therapeutics. The overarching goal of drug formulation is to create a stable, effective, and safe product that delivers the active pharmaceutical ingredient (API) to its intended site of action in a manner that maximizes therapeutic effectiveness

while minimizing side effects. The recent waves of innovation in this field have transformed traditional approaches, presenting novel methodologies and technologies that not only enhance the bioavailability of drugs but also tailor the release profiles to meet patient-specific needs [1].

As the global population continues to age and the prevalence of chronic diseases escalates, the pharmaceutical industry faces a pressing challenge:

to design drug formulations that are not only more effective but also more patient-centric. A key area of focus in this context is the development of advanced drug delivery systems, which encompass a variety of modalities including nanoparticles, liposomes, micelles, and transdermal patches, among others. These systems have been instrumental in overcoming the limitations posed by conventional drug formulations, such as poor solubility, low permeability, and rapid clearance rates. By leveraging innovative materials and cutting-edge technologies, researchers aim to design formulations that ensure a more controlled and sustained release of therapeutics, thereby enhancing therapeutic outcomes [2].

The evolution of drug delivery systems is deeply intertwined with advancements in biopharmaceutical technologies, materials science, and nanotechnology. The integration of bioengineering principles has led to the emergence of targeted delivery systems that can selectively direct drugs to specific tissues or cells, thus enhancing efficacy and reducing systemic toxicity. For instance, targeted nanoparticles can be engineered to recognize and bind to specific biomarkers expressed on the surface of cancer cells, delivering chemotherapeutics directly to the tumor site. This paradigm shift not only improves the therapeutic index of cancer treatments but also spares healthy tissues, a significant concern in traditional chemotherapy regimens [3].

Another noteworthy innovation is the development of controlled and sustained-release formulations, which allow the gradual release of medication over extended periods of time. These systems are particularly beneficial for patients with chronic conditions, as they reduce the frequency of dosing and improve adherence to medication regimens. The invention of smart drug delivery systems, which utilize stimuli-responsive materials that release drugs in response to specific physiological triggers such as pH, temperature, or metabolic markers, highlights the sophistication that modern formulations can achieve. These systems promise not only to improve the pharmacokinetics of drugs but also to personalize treatment based on individual patient profiles and disease states [4].

The applications of novel drug delivery systems extend across a wide array of therapeutic areas, including oncology, cardiology, and infectious

diseases. In oncology, for example, researchers have made significant strides in creating formulations that enhance the permeability of drugs across biological barriers, ensuring that therapeutic agents can reach their targets within tumor tissues. In the realm of infectious diseases, lipid-based formulations and polymeric nanoparticles have been explored for their ability to improve the bioavailability of poorly soluble antibiotics, making them more effective in treating resistant strains of bacteria [5].

However, despite the promising advancements in drug formulation and delivery systems, several challenges remain. Regulatory hurdles, manufacturing complexities, and the need for extensive clinical validation can impede the translation of innovative formulations from the laboratory to the clinic. Furthermore, the consideration of patient variability, encompassing genetics, metabolism, and even lifestyle factors, demands a nuanced approach to formulation design, emphasizing the need for ongoing research and collaboration among scientists, clinicians, and regulatory bodies [6].

Recent Advances in Formulation Technologies:

The field of pharmaceuticals has been rapidly evolving, driven by technological advancements and an increasing understanding of drug mechanisms and patient needs. Drug formulation is a pivotal aspect of this industry, encompassing the design, development, and optimization of drug products to enhance efficacy, safety, and patient adherence. Recent years have seen significant advancements in drug formulation technologies that not only streamline the production process but also personalize treatment options, enhance drug delivery, and address the challenges posed by complex biologics and chronic diseases [7].

Nanotechnology has emerged as a groundbreaking tool in drug formulation, offering methods to enhance drug solubility, stability, and bioavailability. Nanoparticles—ranging from liposomes to polymeric nanoparticles—are engineered to improve the delivery of both small molecule drugs and large biologics. For instance, liposomal formulations, which encapsulate drugs in lipid bilayers, can enhance the pharmacokinetics of chemotherapeutics, reduce systemic toxicity, and improve patient outcomes in cancer therapy [8].

Moreover, nanoparticles can be designed for targeted drug delivery, where the drug is released precisely at the site of action. Utilizing surface modifications such as ligands or antibodies can enable selective targeting of diseased tissues while sparing healthy cells. Recent clinical trials have shown the effectiveness of nanoparticle-based therapies in treating various conditions, from cancer to infectious diseases, highlighting their potential to revolutionize traditional therapeutic approaches [8].

The advent of 3D printing technology, particularly in the pharmaceutical sector, has opened new avenues for drug formulation. 3D printing allows for the precise layering of materials to create complex drug delivery systems tailored to individual patient needs. This technology not only facilitates the production of intricate dosage forms but also enables the customization of dosage strength, drug combination, and release profiles [9].

Advancements in 3D printing have been demonstrated in the creation of oral dosage forms, particularly for pediatric patients, who often struggle with the traditional solid forms of medications. By 3D printing dissolvable tablets, caregivers can tailor the medicine's shape and size, thus improving adherence. The technology also allows for rapid prototyping and production of investigational drugs, facilitating faster clinical trials and regulatory processes. As regulatory bodies continue to adapt to these innovations, 3D printing could transform how drugs are produced and prescribed [10].

Microencapsulation is a technique that involves enclosing drug particles in a coating to control the release rate, protect the drug from degradation, and mask undesirable tastes. Recent advancements in microencapsulation technologies have led to improved methods of coating, such as the use of electrospinning and spray drying, which enhance the precision and efficiency of the encapsulation process [11].

One notable application of microencapsulation is in the field of vaccines. Advances in microencapsulation allow for better delivery of antigens, improving stability and eliciting a more robust immune response. Furthermore, microencapsulation can protect sensitive biologics from harsh gastrointestinal environments, enabling oral delivery routes for therapeutics that were previously limited to intravenous administration.

Such innovations have profound implications for vaccine distribution, especially in remote areas requiring shelf-stable formulations [12].

The formulation of biologics—large, complex molecules often derived from living systems—presents unique challenges due to their sensitivity to environmental factors such as temperature, pH, and agitation. Recent advances have focused on improving the stability and delivery of biologics. Techniques such as freeze-drying and lyophilization have gained traction to enhance the shelf life of biologics by removing moisture and preventing denaturation [13].

Continuous manufacturing processes have also been adopted to improve the production consistency and minimize the risks of contamination associated with traditional batch manufacturing. Additionally, biologics are increasingly formulated with excipients that can stabilize protein structures and maintain their activity. These advancements ensure that biologics can reach patients in their most effective form while reducing the burden of storage and transportation requirements [14].

The future of drug formulation lies in the development of smart drug delivery systems that enable on-demand release of therapeutics. Materials embedded with sensors can respond to physiological conditions such as pH, temperature, or enzymatic activity, triggering the release of the drug precisely when needed. Such systems can be particularly useful in managing chronic diseases, where adherence to a medication schedule can be challenging [15].

Smart delivery systems can be integrated with wearable technologies to monitor health parameters, allowing real-time adjustments in drug delivery. For instance, diabetic patients could benefit from insulin delivery systems that automatically regulate doses based on glucose levels. This personalized approach not only improves therapeutic outcomes but also enhances patient engagement and satisfaction [16].

Nanotechnology in Drug Delivery: Mechanisms and Applications:

Nanotechnology, the manipulation of matter at the nanoscale (1 to 100 nanometers), has revolutionized numerous fields, including electronics, materials science, and healthcare. Among its most promising applications, nanotechnology has emerged as a

powerful tool in drug delivery systems (DDS). By using nanoscale materials and devices, researchers and medical professionals can enhance the therapeutic efficacy of drugs while minimizing side effects, ultimately improving patient outcomes [17].

Mechanisms of Nanotechnology in Drug Delivery

Nanotechnology offers several mechanisms for drug delivery that target the release and distribution of therapeutic agents within the body. Among these mechanisms, the following are pivotal:

1. **Targeted Drug Delivery:** One of the primary advantages of nanotechnology is its ability to selectively deliver drugs to specific cells or tissues. This targeted approach can be achieved through the functionalization of nanoparticles, which involves attaching ligands (such as antibodies or peptides) to the nanoparticle surface that can bind to receptors overexpressed in certain diseased cells, such as cancer cells. This specificity enables higher drug concentrations at the target site while reducing systemic toxicity, a significant disadvantage of conventional drug administration methods [18].
2. **Controlled Release Systems:** Nanocarriers can be engineered to achieve controlled release of their drug payloads. This is essential in maintaining therapeutic drug levels in the bloodstream, improving drug stability, and permitting sustained drug action. Controlled release mechanisms can be triggered by various stimuli, including pH changes, temperature fluctuations, or the presence of specific enzymes, allowing for customized drug delivery as per the physiological environment [18].
3. **Enhanced Permeability and Retention (EPR) Effect:** Nanoparticles can exploit the EPR effect, a phenomenon observed in tumor tissue characterized by hyper-permeable vasculature and impaired lymphatic drainage. The size and nature of nanoparticles allow them to preferentially accumulate in tumor sites, creating a localized concentration of the therapeutic agent that enhances its efficacy and diminishes side effects.

4. **Nanocarriers for Intracellular Delivery:** Many conventional drug molecules struggle to enter cells due to their size, charge, or hydrophilicity. Nanotechnology enables the encapsulation of drugs in nanocarriers, whereby these carriers facilitate cellular uptake through endocytosis or membrane fusion. For instance, liposomes, dendrimers, and polymeric nanoparticles can encapsulate hydrophilic drugs, improving bioavailability and therapeutic outcomes [19].

Types of Nanomaterials in Drug Delivery

Nanomaterials used in drug delivery systems can be broadly classified into several categories based on their composition and structure. Each type offers unique properties and mechanisms that facilitate effective drug delivery:

1. **Liposomes:** These are spherical vesicles composed of lipid bilayers that can encapsulate both hydrophilic and hydrophobic drugs. Liposomes can enhance the solubility and stability of drugs while enabling controlled release [20].
2. **Polymeric Nanoparticles:** Composed of biodegradable polymers, these nanoparticles are particularly advantageous in drug delivery. They can be custom-designed to release drugs at a predetermined rate and respond to specific environmental stimuli.
3. **Dendrimers:** Dendrimers are highly branched, tree-like structures with functional surface groups that can be modified to encapsulate drugs. Their uniform size and shape enable precise control over drug delivery, and they can enhance drug solubility and pharmacokinetics.
4. **Inorganic Nanoparticles:** Various inorganic materials, such as gold, silica, and iron oxide, are employed in drug delivery applications. These nanoparticles are stable, can be easily functionalized, and often exhibit unique optical or magnetic properties that can be exploited for imaging and therapeutic purposes.

5. **Nanocrystals:** These are solid drug particles reduced to nanoscale dimensions, enhancing dissolution and bioavailability. Nanocrystals can improve the delivery of poorly soluble drugs, which poses significant challenges in pharmacotherapy [20].

Advantages and Limitations of Nanotechnology in Drug Delivery

The integration of nanotechnology in drug delivery provides several significant advantages:

1. **Improved Efficacy:** By targeting specific sites, controlled release, and enhanced absorption, nanotechnology can improve drug efficacy, resulting in lower drug dosages and minimized side effects [21].
2. **Reduced Toxicity:** By mitigating systemic exposure to drugs, targeted and controlled delivery can help reduce the adverse effects often observed in conventional therapies, particularly in cancer treatment.
3. **Versatility:** Nanotechnology allows for the design of multifunctional platforms capable of delivering various payloads, including traditional small molecule drugs, biologics, peptides, and genes [21].

Despite these advantages, there are also limitations and challenges associated with nanotechnology in drug delivery:

1. **Manufacturing Complexities:** The scale-up production of nanoparticles remains complex and costly. Ensuring reproducibility and consistency in nanoparticle characteristics is essential for clinical applications [22].
2. **Biodistribution and Biocompatibility:** The behavior of nanoparticles in the body can be unpredictable, and their long-term safety is not yet well-established. Potential toxicity, immunogenic responses, and biodistribution mechanisms require thorough investigation.
3. **Regulatory Challenges:** The unique properties of nanomaterials necessitate the development of comprehensive regulatory frameworks to ensure the safety and

efficacy of nanotechnology-based drug delivery systems [22].

Current and Potential Applications in Medicine

Nanotechnology's versatility allows for a wide range of applications in medicine, with numerous research studies and clinical trials underway. Some notable applications include:

1. **Cancer Therapy:** Targeted drug delivery systems are being developed to deliver chemotherapeutic agents directly to tumor sites. For instance, formulations that utilize albumin nanoparticle systems have shown promise in delivering paclitaxel for breast cancer treatment [23].
2. **Gene Therapy:** Nanoparticles facilitate the delivery of nucleic acids, such as siRNA or DNA, which can modulate gene expression. This approach holds great potential for treating genetic disorders and cancers.
3. **Vaccines:** Nanoparticles can encapsulate antigens or adjuvants, enhancing immune responses while controlling release rates. Nanoparticle-based vaccines have shown increased immunogenicity and stability for infectious diseases.
4. **Antibiotic Delivery:** Nanotechnology can improve the efficacy of antibiotics, targeting bacterial infections more effectively and potentially overcoming antibiotic resistance.
5. **Diagnostic Applications:** Beyond therapeutic applications, nanoparticles are also utilized in diagnostics, particularly in imaging and biosensing. They can be used as contrast agents in magnetic resonance imaging (MRI) and can enhance the sensitivity of diagnostic assays [23].

Innovative Delivery Systems: Liposomes, Micelles, and Beyond:

In the realm of modern pharmacology, the delivery of therapeutic agents to target sites in the body is as crucial as the drugs themselves. Effective delivery systems are essential for ensuring that medications have the desired impact while minimizing adverse effects. Traditional delivery methods often face significant limitations, such as poor solubility,

instability, and non-specific distribution of drugs. Consequently, innovative delivery systems have emerged, revolutionizing how drugs are administered and enhancing their therapeutic efficacy. Among these innovations, liposomes, micelles, and other nanocarriers have garnered substantial attention for their unique properties and potential applications [24].

Liposomes are spherical vesicles composed of lipid bilayers, which encapsulate a hydrophilic core. Due to their biocompatible nature, liposomes can be engineered to deliver both hydrophilic and hydrophobic drugs effectively. The outer lipid layer allows for the encapsulation of water-soluble drugs, while the inner core can accommodate lipophilic agents. This versatility enables liposomes to be customized for specific delivery needs based on the pharmacological profile of the drug [24].

One of the primary advantages of liposomes is their ability to enhance the bioavailability of poorly soluble drugs. For instance, in chemotherapy, liposomal formulations of cytotoxic agents have been developed to improve their therapeutic index by selectively targeting cancer cells while minimizing toxicity to healthy tissues. Doxorubicin encapsulated in liposomes, known as Doxil, has demonstrated significant improvements in patient outcomes and reduced side effects, showcasing the potential of liposome technology in oncology [25].

Moreover, liposomes can be modified to achieve passive or active targeting. Passive targeting relies on the enhanced permeability and retention (EPR) effect, where nanoparticles preferentially accumulate in tumor tissues due to their leaky vasculature. Active targeting involves the functionalization of liposomal surfaces with ligands, antibodies, or peptides that specifically bind to receptors on target cells. This precise targeting mechanism enhances therapeutic efficacy while sparing normal tissues, contributing to a more favorable side effect profile [26].

Micelles are another form of innovative drug delivery systems, primarily utilized for the delivery of hydrophobic drugs. These nanoparticles are formed by the self-aggregation of amphiphilic surfactants in aqueous solutions. The hydrophilic heads of the surfactant molecules orient toward the solvent, while the hydrophobic tails cluster together, forming a core that sequesters lipophilic drugs. This

structure enhances the solubility and stability of hydrophobic compounds in physiological environments [27].

Micelles exhibit several advantages as drug carriers, including their small size, which facilitates cellular uptake through various endocytotic pathways. Additionally, their formation from FDA-approved surfactants makes them a potentially safe option for clinical applications. However, the versatility of micelles extends beyond simple drug encapsulation; they can be engineered to release drugs in a controlled manner. By adjusting the composition of the surfactants or incorporating stimuli-responsive materials, researchers can achieve targeted and sustained release profiles [28].

A particularly interesting application of micelles is in the treatment of cancer. Many anticancer drugs, such as paclitaxel, have poor water solubility, necessitating the development of solubility-enhancing formulations. Micelles provide an effective means of improving drug delivery while also reducing adverse effects associated with high doses of free drugs in circulation. The encapsulation of paclitaxel in micelles has demonstrated improved pharmacokinetics and safety, paving the way for advancements in chemotherapy [29].

Other Nanocarrier Systems

Beyond liposomes and micelles, several other innovative drug delivery systems have emerged, each presenting unique benefits in therapeutic applications. These innovations often incorporate varying materials, methods, and mechanisms to optimize drug delivery [30].

Dendrimers are highly branched, tree-like macromolecules that can encapsulate drugs and facilitate their transport to target sites. Their precise structure allows for tailored size and surface properties, making them versatile carriers for both small molecules and large biologics, such as proteins and genes. Dendrimers have shown promise in gene therapy, where they can deliver nucleic acids effectively into cells, thereby enhancing gene expression and knocking down undesired genes [31].

Nanospheres and nanocapsules represent another approach, wherein polymers create a solid matrix (nanospheres) or a hollow shell (nanocapsules) that can encapsulate drugs. These systems can be

designed for prolonged drug release, which is particularly advantageous in chronic conditions requiring consistent therapeutic levels of medication over time.

Inorganic nanoparticles, such as gold nanoparticles and silica-based carriers, have also attracted attention in drug delivery. Their unique physical and chemical properties allow them to carry a wide range of therapeutic agents. Gold nanoparticles, for instance, can be used for photothermal therapy alongside drug delivery, where localized heating can enhance drug release at target sites [32].

Targeted Drug Delivery: Principles and Strategies:

The advent of modern medicine has ushered in a new era of therapeutic interventions, and among the most significant developments in pharmaceutical science is the concept of targeted drug delivery (TDD). This innovative approach seeks to maximize the efficacy of treatments while minimizing side effects, thereby enhancing the overall therapeutic outcomes for patients. Targeted drug delivery systems have emerged as a critical area of research, offering intricate methods to deliver drugs to specific sites within the body. Understanding the principles and strategies involved in TDD is essential for the advancement of personalized medicine and the management of various diseases, especially cancer [33].

Principles of Targeted Drug Delivery

The primary goal of targeted drug delivery is to preferentially deliver therapeutic agents to diseased tissues or cells while sparing healthy tissues. This is achieved through the application of biological and chemical principles that exploit the distinctive characteristics of target tissues [34].

1. Pathophysiological Characteristics of Target Tissues:

Targeted drug delivery strategies often take advantage of the unique biological environment surrounding diseased cells. For instance, tumor cells may exhibit enhanced permeability due to abnormal vascular architecture and leaky blood vessels, a phenomenon known as the Enhanced Permeability and Retention (EPR) effect. This property allows

nanoparticles to accumulate preferentially in tumor sites, facilitating localized drug action while reducing systemic exposure [35].

2. Biochemical Specificity:

Effective targeting also involves leveraging the biochemical markers that are overexpressed on the surface of target cells. For instance, certain receptors, antigens, or proteins may be found in elevated levels in cancerous cells compared to normal ones. Targeting agents (ligands) such as antibodies, peptides, or small molecules can be conjugated to drugs or drug carriers, promoting selective binding and uptake by the targeted cells via receptor-mediated endocytosis [35].

3. Drug Formulation and Delivery Systems:

The design and formulation of drug delivery systems are vital components of TDD. Various formulations, including nanoparticles, liposomes, dendrimers, and micelles, can encapsulate therapeutic agents and facilitate their delivery to target cells. These systems can be engineered to improve the solubility, stability, and bioavailability of poorly soluble drugs, enhancing their therapeutic effectiveness [35].

Strategies for Targeted Drug Delivery

Several strategies have been developed to implement targeted drug delivery in clinical practice, each with its unique mechanisms and applications. Below are some prominent methodologies employed in this field [36].

1. Passive Targeting:

Passive targeting relies on the natural distribution of drug carriers within the body, taking advantage of the EPR effect as previously discussed. Nanoparticles, due to their size and surface characteristics, can accumulate more in tumors than in normal tissues. This strategy is commonly used in the formulation of liposomal drugs and polymeric nanocarriers.

2. Active Targeting:

With active targeting, drug carriers are

functionalized with specific targeting ligands that recognize and bind to receptors on the surface of target cells. This strategy requires a detailed understanding of the biological mechanisms underlying the disease and the expression profile of cellular markers. For example, antibodies can be engineered to bind to tumor-associated antigens, thereby directly directing the drug payload to cancer cells. Active targeting is advantageous in increasing the specificity of drug delivery, resulting in reduced off-target effects [37].

3. **Smart Drug Delivery Systems:**

Advances in nanotechnology have paved the way for the development of smart drug delivery systems that respond to specific stimuli such as pH, temperature, or enzymatic activity. These systems can release drugs in a controlled manner when they encounter the desired conditions typical of the target site. For example, pH-sensitive nanoparticles may remain stable in the bloodstream but disaggregate in the acidic microenvironment of tumors, thereby releasing their drug content precisely where it is needed [37].

4. **Mechanically Targeted Drug Delivery:**

Another innovative approach involves utilizing various physical methods to achieve targeted delivery. Techniques such as ultrasound, magnetic fields, or focused radiation can enhance the accumulation of drug carriers at the desired site. For example, magnetic drug delivery utilizes magnetic nanoparticles that can be directed to the tumor site using an external magnetic field, intensifying localized treatment while minimizing systemic exposure [38].

5. **Combination Therapies:**

Combining targeted drug delivery systems with other therapeutic modalities, such as chemotherapy, radiotherapy, or immunotherapy, can enhance treatment efficacy. By delivering multiple agents in conjunction, TDD can improve the overall therapeutic response. For example, pairing targeted nanoparticles carrying chemotherapy drugs with immune checkpoint inhibitors may lead to a

synergistic effect, improving patient outcomes in certain cancers [38].

Challenges and Future Directions

Despite the significant advancements in TDD, several challenges remain before it can reach its full potential in clinical practice. Issues such as the heterogeneity of tumors, difficulties in predicting the biodistribution of drug carriers, and the potential for developing resistance in cancer therapies are prominent concerns. Moreover, the regulatory landscape for the approval of nanomedicine products poses another hurdle, as safety and efficacy must be meticulously demonstrated [39].

Looking ahead, future research in targeted drug delivery will likely focus on the integration of artificial intelligence and machine learning to better predict drug behavior in vivo and to identify optimal drug combinations and delivery strategies. Personalized medicine, where therapies are tailored to the individual patient's molecular and genetic profile, will play a pivotal role in shaping the future of TDD [39].

Smart Drug Delivery: The Role of Digital Health Technologies:

The landscape of healthcare is undergoing a paradigm shift, propelled by the advances in digital health technologies. Among the many innovative applications of these technologies is smart drug delivery, a concept that is revolutionizing the way medications are administered and monitored in patients. As we delve into the realm of smart drug delivery, it becomes imperative to understand how digital health technologies are transforming therapeutic interventions, enhancing patient outcomes, and streamlining healthcare delivery mechanisms [40].

The Evolution of Drug Delivery Systems

Traditionally, drug delivery systems have relied on conventional methods such as oral tablets, injections, and intravenous infusions, which are often fraught with challenges. The inability to ensure consistent drug absorption, the risk of adverse side effects, and the cumbersome nature of managing medication regimens can detract from the efficacy of treatment protocols. The advent of smart drug delivery systems signifies a move toward more efficient, targeted, and adjustable medication delivery.

Smart drug delivery is characterized by its ability to adapt to the changing needs of patients, utilizing technology to deliver medications in a precise and controlled manner. This evolution stems from the confluence of several fields—including pharmacology, nanotechnology, materials science, and digital health technologies—working together to innovate therapeutic strategies [41].

Digital Health Technologies: An Overview

Digital health technologies encompass a broad array of tools and solutions that leverage information technology to aid healthcare delivery. These include wearable devices, mobile health applications, telemedicine services, electronic health records (EHRs), and artificial intelligence (AI) analytics, all of which contribute to a more interconnected and efficient healthcare system.

These technologies enable the collection and analysis of real-time patient data, fostering a proactive rather than reactive approach to healthcare. As a result, healthcare providers can tailor interventions to individual patients, anticipating their needs and adapting treatment plans accordingly. The implications for drug delivery are profound, allowing for a more synchronized relationship between medication, patient adherence, and health outcomes [42].

Enhancing Drug Delivery with Digital Technologies

1. **Precision and Personalization:** Smart drug delivery systems harness the power of data to individualize treatments. For instance, the integration of biomarkers and patient-specific data can guide the dosing and timing of drug administration based on a patient's unique metabolic responses. Digital health technologies enable real-time monitoring of patient adherence and therapeutic efficacy, allowing for timely adjustments to treatment regimens [43].
2. **Wearable Technologies:** The proliferation of wearable devices is a pivotal development in drug delivery. These devices can monitor various physiological parameters, such as heart rate, glucose levels, and other biomarkers, providing healthcare providers with vital insights into a patient's condition. In conjunction with

smart drug delivery systems, wearables can initiate drug release automatically upon detection of certain physiological triggers, such as heightened glucose levels in diabetic patients [44].

3. **Remote Monitoring and Telehealth:** With the rise of telehealth services, healthcare providers can maintain continuous communication with patients, even from a distance. Remote monitoring systems can capture a plethora of data, including medication adherence and side effects, ensuring that caregivers are promptly informed and can make necessary adjustments to therapeutic strategies. This real-time information flow enhances the capability of smart drug delivery systems, as they can adapt to patients' needs dynamically [45].
4. **Artificial Intelligence and Machine Learning:** AI and machine learning play a crucial role in the functioning of smart drug delivery systems. These technologies can analyze vast datasets collected from patients to uncover patterns and insights that facilitate decision-making processes. Predictive analytics, for instance, can forecast how a patient is likely to respond to a particular treatment regimen, allowing for tailored drug delivery that maximizes efficacy and minimizes adverse effects.
5. **Internet of Medical Things (IoMT):** The IoMT refers to a network of interconnected devices that communicate and exchange data related to healthcare. This ecosystem of smart devices includes drug delivery pumps, smart inhalers, and connected syringes. Through IoMT, these devices can relay real-time information about drug administration, patient vitals, and adherence to treatment protocols, significantly improving the monitoring and effectiveness of drug delivery systems [45].

Challenges and Considerations

Despite the remarkable potential of smart drug delivery systems supported by digital health technologies, numerous challenges remain. Privacy and security concerns associated with the collection

and transmission of patient data are considerable. It is vital to implement stronger regulatory frameworks and cybersecurity measures to protect sensitive health information from breaches [46].

Moreover, there is a need for standardization in the development and deployment of these technologies to ensure interoperability across platforms and devices. The integration of smart drug delivery technologies into existing healthcare systems may encounter resistance from healthcare professionals due to the learning curve and necessary adaptation to new workflows [47].

Additionally, the long-term implications of using advanced technologies in medication delivery must be thoroughly investigated. The ethical considerations surrounding the use of AI in decision-making processes, the potential for bias in algorithms, and the implications of over-reliance on technology in clinical settings must be addressed to safeguard patient welfare [48].

Personalized Medicine through Advanced Formulation Techniques:

The rapid advancements in the field of medicine have paved the way for the emergence of personalized medicine, a revolutionary approach aimed at tailoring medical treatments to individual characteristics, needs, and preferences. At the heart of this evolution lies advanced formulation technologies that enhance drug efficacy, safety, and patient compliance. By integrating genomic data, biomarker identification, and sophisticated drug delivery systems, personalized medicine is transforming therapeutic strategies, making them more precise and effective [49].

Personalized medicine, often referred to as precision medicine, is an innovative approach that customizes healthcare by considering an individual's genetic makeup, environment, and lifestyle. This paradigm shift moves away from the traditional 'one-size-fits-all' model to a more tailored form of treatment. This approach utilizes diagnostic testing to determine how specific genetic variations affect an individual's response to drugs, allowing clinicians to predict which treatments will be most effective for specific patient profiles.

For instance, in oncology, targeted therapies are designed to attack cancer cells while sparing healthy tissue. These treatments often depend on the

presence of specific biomarkers—molecules that indicate the presence of disease and can guide doctors in selecting the right treatment for the right patient at the right time. By identifying these unique characteristics, personalized medicine aims to improve therapeutic outcomes and minimize adverse effects, ultimately leading to a more efficient healthcare system [50].

Advanced formulation technologies play a critical role in enabling personalized medicine. These technologies encompass a wide range of methods and processes used to design, develop, and manufacture pharmaceutical products. Key technologies include nanoformulations, smart drug delivery systems, and advanced biopharmaceuticals, each of which enhances drug performance and patient-specific customization [51].

Nanoformulations involve the use of nanotechnology to develop drugs at the molecular and nanoscale level. By manipulating drug particles at this scale, researchers can improve the solubility, stability, and bioavailability of poorly water-soluble drugs. Additionally, nanocarriers can be engineered to deliver drugs directly to targeted sites within the body, minimizing systemic side effects and enhancing therapeutic efficacy. For example, in the treatment of cancer, nanoparticles can be designed to release chemotherapeutic agents in the vicinity of tumor cells, thereby limiting the impact on healthy tissues and reducing toxicity [52].

Smart drug delivery systems are engineered platforms designed to release therapeutic agents in a controlled and targeted manner. Such systems are responsive to specific stimuli, such as pH, temperature, or the presence of specific biomarkers. This responsiveness ensures that drugs are released precisely when and where they are needed. For instance, some drug delivery systems can be activated in the acidic environment of a tumor, thereby facilitating localized drug release. This technology not only improves drug efficacy but also minimizes adverse effects associated with systemic circulation, reinforcing the principles of personalized medicine [53].

Biopharmaceuticals, including monoclonal antibodies, therapeutic proteins, and gene therapies, represent a significant shift towards targeted therapies in personalized medicine. Advanced formulation technologies have enabled the

development of these complex molecules, which can be tailored to the individual genetic and molecular profile of patients. For instance, monoclonal antibodies can be designed to precisely target specific antigens on cancer cells or immune cells, thus enhancing the body's immune response against cancer. The use of biopharmaceuticals is an exemplary demonstration of how advanced formulation technologies facilitate the transition to personalized medicine, providing customized treatments that align with individual patient profiles [54].

Benefits of Personalized Medicine

The integration of advanced formulation technologies into personalized medicine presents numerous advantages:

1. **Enhanced Efficacy:** Targeted therapies demonstrate higher success rates, as they are tailored to meet individual patients' needs based on their genetic profiles.
2. **Improved Safety Profile:** Personalized medicine can reduce the incidence of adverse drug reactions by ensuring that patients receive only those medications that are compatible with their genetic makeup.
3. **Higher Patient Compliance:** Formulations that enhance drug absorption or employ controlled release can improve patient adherence to treatment regimens, ultimately leading to better health outcomes.
4. **Cost-effective Healthcare:** Although personalized medicine may involve initial investment in genetic testing and advanced formulations, it can lead to long-term healthcare savings by minimizing ineffective treatments and hospitalizations due to adverse effects [55].

Challenges Facing Personalized Medicine

Despite its numerous benefits, several challenges must be addressed for personalized medicine to reach its full potential:

1. **High Costs:** The development of personalized therapies often involves advanced research and technology, which can drive up costs, making access limited for certain populations.

2. **Regulatory Hurdles:** The regulatory framework for assessing the safety and efficacy of personalized therapies is still evolving and can pose challenges in ensuring timely access to new treatments.
3. **Data Privacy Concerns:** The utilization of genetic and personal data raises ethical considerations regarding patient privacy and the handling of sensitive information.
4. **Educational Gaps:** There is a need for healthcare professionals to become increasingly educated in the principles of personalized medicine, genetics, and advanced drug formulation to properly implement these innovative approaches in clinical practice [56].

Future Perspectives

The future of personalized medicine, bolstered by advanced formulation technologies, looks incredibly promising. As research continues to advance our understanding of genetics and molecular biology, the possibilities for developing therapies tailored to individual patients will expand. Innovations in artificial intelligence (AI) and machine learning can aid in analyzing large datasets to identify patterns in genetic variations and treatment responses, further enhancing the precision of personalized treatments [57].

Moreover, as technology continues to evolve, the cost of genetic testing and advanced formulation technologies is likely to decrease, making personalized medicine more accessible to a broader population. The intersection of biotechnology and nanotechnology will continue to yield novel drug delivery systems and formulations that are fine-tuned to meet the unique needs of patients [58].

Regulatory Challenges and Future Directions in Drug Delivery Systems:

Drug delivery systems have revolutionized the landscape of pharmacotherapy, providing innovative ways to administer drugs that enhance therapeutic efficacy while minimizing side effects. With the rapid evolution of drug delivery technologies — from liposomes and nanoparticles to implantable devices and biologics — the regulatory framework surrounding these systems has come under intense scrutiny. Regulatory agencies, primarily the U.S. Food and Drug Administration

(FDA) and the European Medicines Agency (EMA), are tasked with ensuring that these technologies are safe, effective, and manufactured in a consistent manner. However, the complexity and diversity of drug delivery systems pose unique challenges that regulatory bodies must navigate [59].

The regulation of drug delivery systems is multifaceted, encompassing not only the pharmacokinetics and pharmacodynamics of the drug itself but also the design, formulation, and delivery mechanisms involved. Traditionally, drug delivery systems are classified under the broader categories of pharmaceutical products, including new drugs, biologics, and devices. As a result, the regulatory pathway can often be convoluted, involving multiple guidelines, depending on the specific characteristics of the drug delivery system [60].

The FDA, for instance, employs two main regulatory paths: the New Drug Application (NDA) for small molecule drugs and the Biologics License Application (BLA) for biologics. Moreover, combination products that involve both a drug and a delivery device may require a hybrid approach that engages both drug and device regulatory frameworks. The EMA follows a similar yet distinct protocol within the European Union. This complexity often leads to confusion among developers and can delay the time-to-market for potentially groundbreaking therapies [60].

One of the primary challenges in regulating drug delivery systems stems from their inherent complexity. Modern delivery systems often involve sophisticated materials and engineering that can influence the drug release profile, stability, and bioavailability. The use of nanotechnology, for instance, brings about several variables that can impact the safety and efficacy of a product. Assessing the physical and chemical properties of nanoparticles, such as size, shape, and surface characteristics, poses a significant challenge for regulators. These variables may not only affect pharmacokinetics but also trigger unintended immunological responses [60].

The data required for the regulatory approval of drug delivery systems is often inconsistent or insufficient. Preclinical data must demonstrate compatibility between the drug and the delivery system, but existing guidelines do not always standardize testing

protocols across various delivery technologies. Furthermore, clinical data must be robust enough to demonstrate safety and efficacy. Regulators frequently face gaps in knowledge related to long-term effects, particularly for advanced therapies involving biologics and gene editing technologies, complicating the approval process [60].

Ensuring that drug delivery systems are manufactured with consistent quality remains an ongoing issue. The emergence of novel materials and manufacturing techniques necessitates new quality control measures that may not yet be established within the existing regulatory framework. Variability in Good Manufacturing Practices (GMP) compliance can lead to discrepancies in product quality, which regulators are tasked with monitoring. With the rise of personalized medicine, where therapies are tailored to individual patient profiles, maintaining quality across different batches of delivery systems further exacerbates these regulatory challenges [61].

The rapid pace of scientific advancement often outstrips the ability of regulatory agencies to adapt. The introduction of innovative drug delivery platforms such as RNA-based therapies, CRISPR technologies, and smart drug delivery systems with external triggers introduces uncertainties in established regulatory pathways. Current regulatory frameworks may not adequately capture the nuances associated with these next-generation therapies, leading to potential inefficiencies and delays in product approval [61].

As we look toward the future, several strategic directions can be pursued to address the regulatory challenges associated with drug delivery systems.

One of the most significant steps forward would involve international collaboration aimed at harmonizing regulatory guidelines across different jurisdictions. Organizations such as the International Council for Harmonisation (ICH) could play an essential role in developing universally accepted guidelines for the evaluation of drug delivery systems. Such an approach would provide clearer directives for researchers and developers, streamline the approval process, and ultimately benefit patients by expediting their access to innovative therapies [61].

The establishment of more defined preclinical and clinical testing frameworks is critical for ensuring

that drug delivery systems are subjected to rigorous evaluation. Regulatory agencies should consider adopting tiered approaches that allow for more flexible study designs, particularly for early-phase trials. This framework could promote the use of adaptive trial designs, which permit modifications based on interim results, thereby advancing our understanding of the systems while maintaining patient safety [62].

Implementing a Quality by Design approach could facilitate better control over manufacturing processes for drug delivery systems. By focusing on designing quality into the product from the beginning stages of development, manufacturers can enhance consistency and reliability. Regulatory agencies can support this initiative by providing more specific guidelines on how to implement QbD principles effectively across various delivery platforms [62].

The incorporation of Real-World Evidence into regulatory assessments is another promising direction for drug delivery systems. RWE can provide valuable insights into the effectiveness and safety of products once they are in widespread use, complementing traditional clinical trial data. By leveraging data from electronic health records, patient registries, and insurance claims, regulators can make more informed decisions regarding the continued use and monitoring of these delivery systems [63].

Conclusion:

In conclusion, the field of drug formulation and delivery systems is undergoing rapid transformation, driven by technological advancements and increased understanding of disease mechanisms. Innovations such as nanotechnology, targeted delivery systems, and digital health integration are not only enhancing the effectiveness of therapies but also optimizing patient outcomes through personalized medicine. These developments allow for more precise targeting of drug action, improved bioavailability, and reduced adverse effects, thereby addressing some of the significant challenges associated with conventional drug delivery methods.

Looking ahead, the continued evolution of these systems holds great promise for the future of healthcare. As researchers and clinicians work to overcome regulatory, manufacturing, and scalability

challenges, the potential for these innovations to improve the management of chronic and complex diseases becomes increasingly apparent. Embracing these advancements will be essential for creating more effective, safe, and patient-centered therapeutic strategies, ultimately advancing the field of medicine and improving the quality of life for patients worldwide.

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