
Current Trends in Drug Formulation and Delivery Systems

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Abstract:

The landscape of drug formulation and delivery systems is rapidly evolving, driven by advancements in technology and a deeper understanding of pharmacokinetics and patient needs. One significant trend is the development of personalized medicine, where drug formulations are tailored to individual genetic profiles, improving efficacy and minimizing side effects. Nanotechnology has also made significant strides, allowing for the creation of nanoparticles that enhance drug solubility, stability, and targeted delivery. This approach not only improves the bioavailability of poorly soluble drugs but also facilitates the delivery of therapeutics directly to diseased tissues, thereby increasing treatment effectiveness and reducing systemic toxicity. Another emerging trend is the integration of smart delivery systems, which utilize sensors and programmable mechanisms to release drugs in response to specific physiological conditions. These systems can provide controlled release profiles, improving patient compliance and therapeutic outcomes. Additionally, the rise of biologics and biosimilars has influenced formulation strategies, as these complex molecules often require specialized delivery methods to maintain stability and efficacy. Furthermore, advances in 3D printing technology are enabling the production of customized dosage forms, allowing for on-demand drug manufacturing that can cater to unique patient requirements. Overall, the focus on innovative delivery systems and formulations is paving the way for more effective and patient-centered therapies.

Keywords: Personalized medicine, Nanotechnology, Drug solubility, Targeted delivery, Smart delivery systems, Controlled release, Biologics, Biosimilars, 3D printing, Patient compliance.

Introduction:

The field of pharmaceutical science is undergoing a transformative evolution, driven by advancements in technology, a deeper understanding of disease mechanisms, and the increasing demand for personalized medicine. As researchers and healthcare professionals strive to improve therapeutic outcomes, the formulation and delivery of drugs have emerged as critical components in the development of effective treatments. The intricate interplay between drug formulation and delivery systems not only influences the bioavailability and

efficacy of pharmaceutical compounds but also plays a pivotal role in enhancing patient compliance and minimizing adverse effects. This introduction aims to explore the current trends in drug formulation and delivery systems, highlighting the innovative approaches that are shaping the future of pharmacotherapy [1].

One of the most significant trends in drug formulation is the shift towards targeted and personalized therapies. With the advent of genomics and proteomics, researchers are now able to tailor drug formulations to the individual characteristics of

patients, including their genetic makeup, disease state, and metabolic profiles. This personalized approach aims to maximize therapeutic efficacy while minimizing side effects, a paradigm shift from the traditional "one-size-fits-all" model of drug development. For instance, the formulation of biopharmaceuticals, such as monoclonal antibodies and gene therapies, has gained traction due to their ability to target specific molecular pathways involved in disease processes. These biologics require sophisticated delivery systems to ensure their stability, bioavailability, and controlled release, thus driving innovation in formulation strategies [2].

Nanotechnology represents another significant trend in drug formulation and delivery systems. The development of nanocarriers, such as liposomes, dendrimers, and nanoparticles, has revolutionized the way drugs are delivered to target sites within the body. These nanocarriers can encapsulate therapeutic agents, protecting them from degradation and facilitating their transport across biological barriers, such as cell membranes and the blood-brain barrier. Additionally, the surface modification of nanocarriers allows for targeted delivery, enhancing the accumulation of drugs in specific tissues or tumors while reducing systemic exposure and associated toxicity. The versatility of nanotechnology has opened new avenues for the formulation of poorly soluble drugs, enabling the development of novel therapies for chronic diseases, including cancer and neurodegenerative disorders [3].

Moreover, the integration of advanced drug delivery systems, such as implantable devices and transdermal patches, is gaining momentum in the pharmaceutical industry. These systems are designed to provide controlled and sustained release of therapeutic agents, improving patient adherence and therapeutic outcomes. Implantable drug delivery systems, for example, can deliver medications over extended periods, reducing the frequency of dosing and enhancing patient convenience. Similarly, transdermal drug delivery systems offer a non-invasive route for drug administration, bypassing the gastrointestinal tract and first-pass metabolism, thereby improving bioavailability. The development of microneedle technology has further enhanced transdermal delivery by allowing for painless penetration of the skin, facilitating the delivery of macromolecules, such as vaccines and peptides [4].

In addition to these advancements, the role of artificial intelligence (AI) and machine learning in drug formulation and delivery is becoming increasingly prominent. These technologies enable researchers to analyze vast datasets, predict drug interactions, and optimize formulation parameters with unprecedented accuracy. AI-driven simulations and modeling can accelerate the drug development process, reducing the time and cost associated with bringing new therapies to market. Furthermore, machine learning algorithms can assist in identifying patient populations that are most likely to benefit from specific formulations, thereby enhancing the precision of treatment strategies [5].

As we navigate the complexities of drug formulation and delivery, the importance of regulatory considerations cannot be overlooked. Regulatory agencies, such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), are adapting their frameworks to accommodate the rapid pace of innovation in this field. The establishment of guidelines for the evaluation of novel drug delivery systems and the implementation of risk-based approaches to regulatory oversight are crucial for ensuring patient safety while fostering innovation [6].

Advancements in Personalized Medicine and Tailored Therapies:

In recent years, the field of medicine has undergone a paradigm shift characterized by a growing emphasis on personalized medicine and tailored therapies. This innovative approach to healthcare seeks to customize treatment strategies to individual patients based on their unique genetic, biomolecular, and phenotypic profiles rather than employing a one-size-fits-all method. The advancements in personalized medicine represent not only a technological evolution but a profound change in the way healthcare is conceptualized and delivered [7].

At its core, personalized medicine relies on the understanding that every patient is unique. Factors such as genetics, lifestyle, environment, and individual health history can significantly influence how a patient responds to specific treatments. Traditional healthcare approaches typically adhere to generalized models, often resulting in trial-and-error methods to determine the efficacy of treatments. In contrast, personalized medicine leverages advances in genomics, proteomics, metabolomics, and other "omics" technologies to

create a more nuanced understanding of a patient's health [8].

The Human Genome Project, completed in the early 2000s, marked a pivotal moment in the field of genetics, providing a comprehensive map of human DNA and illuminating the pathways by which genetic variation can influence disease. The subsequent advancements in high-throughput sequencing technologies have greatly facilitated the analysis of individual genetic profiles, enabling healthcare providers to identify genetic predispositions to diseases, susceptibility to certain conditions, and potential responses to medications [9].

Recent technological innovations have propelled the field of personalized medicine forward in remarkable ways. Key among these advances is the advent of next-generation sequencing (NGS), which allows for the rapid and cost-effective sequencing of entire genomes. This technology not only enables researchers to identify genetic mutations associated with specific diseases but also aids in the development of targeted therapies designed to address these mutations [10].

Additionally, bioinformatics plays a crucial role in personalized medicine by providing the computational tools necessary to analyze vast quantities of genomic data. Machine learning algorithms can identify patterns and predict outcomes more accurately than traditional statistical methods. For instance, predictive analytics can assess an individual's risk for diseases such as cancer, allowing for earlier interventions that can significantly improve prognoses [11].

Moreover, the integration of electronic health records (EHRs) has revolutionized the way healthcare providers access and utilize patient information. EHRs can consolidate genetic data, clinical history, and treatment responses, ultimately supporting the decision-making process regarding personalized treatment approaches.

The impact of personalized medicine is particularly evident in the realm of oncology. Traditional cancer treatments often involve chemotherapy, which, while effective for some patients, can cause significant adverse effects and may not yield results in others. With the advent of targeted therapies, clinicians can now prescribe treatments that are specifically designed to attack cancer cells based on their unique genetic characteristics. For example,

cancers with mutations in the epidermal growth factor receptor (EGFR) can be treated with EGFR inhibitors, leading to improved outcomes [12].

Another illustrative case is that of cystic fibrosis (CF), a genetic disorder caused by mutations in the CFTR gene. The development of CFTR modulators, which target specific mutations within the CFTR gene, has dramatically transformed the treatment landscape for CF patients. These tailored therapies not only improve lung function but also enhance the quality of life, demonstrating the tangible benefits of personalized medicine [13].

Outside oncology and genetic disorders, advancements in pharmacogenomics have redefined how medications are prescribed. By analyzing an individual's genetic makeup, healthcare providers can make informed decisions about drug selection and dosing, minimizing adverse drug reactions and optimizing efficacy. For instance, variations in the CYP2D6 gene influence how patients metabolize certain medications, making it crucial to consider these genetic factors when determining appropriate drug therapies [14].

Despite the tremendous promise of personalized medicine, numerous challenges remain in its widespread implementation. One of the primary hurdles is the cost associated with genomic sequencing and targeted therapies. As technology advances, the price of sequencing has decreased; however, it can still be a significant barrier to access for many patients, particularly in low-resource settings [14].

Additionally, the interpretation of genetic data presents challenges. The sheer volume of genetic information can overwhelm healthcare providers, and the clinical significance of certain genetic mutations remains poorly understood. Furthermore, ethical concerns surrounding genetic testing, privacy, and potential discrimination based on genetic information need to be thoughtfully addressed [15].

Another obstacle lies in the need for interdisciplinary collaboration. Personalized medicine requires the integration of diverse knowledge areas including genomics, pharmacology, and bioinformatics. On the healthcare provider side, there is often a lack of sufficient education and training in these domains, which can hinder the appropriate application of personalized approaches [16].

Looking ahead, the future of personalized medicine and tailored therapies remains bright, although it will require concerted efforts from stakeholders in healthcare, research, and policy. With ongoing advancements in artificial intelligence and machine learning, the potential to analyze patient data more deeply and accurately is vast. Moreover, the expansion of biobanks and genomic databases can facilitate more extensive research and support the development of new targeted therapies [17].

The integration of personalized medicine into routine clinical practice will also necessitate legislative support and policy development to ensure equitable access to genetic testing and targeted therapies. Educational initiatives aimed at healthcare providers will be essential in improving confidence in utilizing personalized approaches to patient care [17].

Nanotechnology in Drug Delivery: Enhancing Bioavailability:

Nanotechnology, the manipulation of matter on an atomic or molecular scale, has emerged as a transformative force across multiple fields, particularly in medicine. One of its most promising applications lies in drug delivery systems, where it addresses the pervasive challenge of bioavailability—the degree and rate at which an administered drug reaches its target site in the body. Conventional drug delivery methods often suffer from limited bioavailability, resulting from factors like poor solubility, degradation during the absorption process, and rapid clearance from the bloodstream. The advent of nanotechnology in drug delivery offers innovative solutions to these challenges, enhancing the therapeutic efficacy of medications and revolutionizing treatment strategies [18].

Bioavailability is a crucial pharmacokinetic parameter that directly impacts the efficacy of therapeutic agents. It is defined as the fraction of an administered dose of unchanged drug that reaches the systemic circulation. A variety of factors influence bioavailability, including drug formulation, the route of administration, and physiological barriers within the body, such as the gastrointestinal tract and blood-brain barrier. Drugs that have low bioavailability may require higher doses to achieve desired therapeutic effects, which can increase the potential for side effects and toxicity [19].

Nanotechnology operates at the nanoscale, typically defined as dimensions ranging from 1 to 100 nanometers. At this scale, materials exhibit unique physical and chemical properties compared to their bulk counterparts. These unique properties allow for enhanced drug solubility, controlled release, and targeted delivery, which can significantly improve bioavailability. Various nanocarriers, such as nanoparticles, liposomes, dendrimers, and nanocrystals, serve as vehicles to transport therapeutic agents. These carriers can encapsulate drugs, protect them from degradation, and facilitate their transport to specific tissues or cells [20].

Mechanisms of Enhanced Bioavailability

1. **Improved Solubility and Stability:** One of the major challenges in the formulation of drugs, especially those that are hydrophobic, is poor solubility. Nanoparticles and nanocrystals increase surface area and promote dissolution, thereby enhancing the drug's solubility. For instance, using lipid-based nanocarriers, such as solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs), can significantly enhance the stability and solubility of lipophilic drugs [21].
2. **Targeted Drug Delivery:** Targeted therapy aims to deliver drugs directly to the desired site of action while minimizing exposure to healthy tissues. Nanotechnology allows for the functionalization of nanocarriers with specific ligands, antibodies, or peptides that can recognize and bind to target cells or tissues. This targeting mechanism reduces off-target effects and enhances bioavailability at the desired site—as demonstrated in cancer therapeutics, where targeted nanoparticles can preferentially deliver chemotherapy agents to tumor tissues [21].
3. **Controlled Release Mechanisms:** Nanocarriers can be designed to provide controlled release of drugs over prolonged periods. This approach minimizes the peaks and troughs in drug concentration, leading to improved therapeutic outcomes. For instance, polymer-based nanoparticles can be engineered to release their drug payload in response to specific physiological conditions such as pH

changes (in the case of tumor tissue) or the presence of certain enzymes.

4. **Overcoming Biological Barriers:** The human body has evolved various barriers to protect itself from foreign substances. These include the intestinal epithelium, the blood-brain barrier (BBB), and various cellular membranes. Nanoparticles can be engineered to enhance permeability through these barriers, facilitating drug delivery. For example, certain nanoparticles can exploit receptor-mediated endocytosis to penetrate cellular membranes effectively [22].
5. **Improved Pharmacokinetics:** Nanotechnology can significantly alter the pharmacokinetic profile of drugs. By prolonging the circulation time of a drug in the bloodstream (often referred to as improved half-life), nanocarriers reduce the frequency of dosing required, enhancing patient compliance and treatment effectiveness. Pegylation of nanoparticles, which involves attaching polyethylene glycol (PEG) chains, is one strategy used to create stealth particles that evade the immune system and remain in circulation longer [22].

Current Applications and Future Directions

Several nanoparticles have already advanced into clinical applications, with ongoing research continuously expanding their use. For instance, liposomes containing the chemotherapy drug doxorubicin have been successfully used in treating various cancers. Similarly, the use of iron oxide nanoparticles is being investigated for targeted drug delivery in the treatment of diseases such as rheumatoid arthritis [22].

The future of nanotechnology in drug delivery appears promising, with advancements paving the way for novel treatment modalities. Researchers are exploring multifunctional nanoparticles that can combine imaging and therapy, known as theranostics, enabling simultaneous diagnosis and treatment of diseases. Moreover, the integration of artificial intelligence and machine learning in nanotechnology has the potential to personalize drug formulations based on individual patient profiles [23].

Despite its potential, the implementation of nanotechnology in drug delivery systems faces several challenges. Regulatory hurdles, safety concerns, and the need for extensive research to understand the long-term effects of nanomaterials in the human body are significant barriers to widespread adoption. Additionally, issues related to the scalability of production and the economic feasibility of nanocarriers must be addressed to ensure they can be manufactured sustainably and made accessible to patients [24].

Smart Drug Delivery Systems: Innovations and Applications:

In recent decades, the field of drug delivery has undergone significant transformations fueled by advancements in biomedical sciences, materials science, and engineering technology. At the forefront of these transformations is the emergence of smart drug delivery systems. These systems are designed to enhance the effectiveness and safety of drug therapies by intelligently releasing medications in response to specific biological triggers [25].

Smart drug delivery systems, often referred to as "intelligent" or "responsive" drug delivery systems, are characterized by their ability to control and modify the release profile of therapeutics. Unlike traditional drug delivery methods that typically release medications at a constant rate, smart systems are engineered to respond dynamically to physiological conditions, external stimuli, or disease-specific markers. These systems utilize various mechanisms to enhance drug solubility, bioavailability, and targeted delivery, making them particularly promising in addressing the limitations of conventional therapies [26].

Innovations in Smart Drug Delivery Technologies

1. **Nanotechnology:** One of the most significant innovations in drug delivery is the application of nanotechnology. Nanoscale carriers, such as liposomes, micelles, and dendrimers, can encapsulate drugs and provide controlled release mechanisms. These nanocarriers improve drug solubility and stability, protect the drug from degradation, and enable targeted delivery to specific tissues or cells. For example, nanoparticles can be engineered to recognize cancer cells through surface modifications, allowing for selective drug

release that minimizes side effects on healthy cells [27].

2. **Stimuli-Responsive Systems:** Smart drug delivery systems often respond to various stimuli, including pH, temperature, light, magnetic fields, and enzymatic activity. For instance, pH-sensitive drug release systems can exploit the differences in pH levels between healthy tissues and diseased areas (such as tumors) to release therapeutic agents specifically at the target site. Similarly, thermoresponsive hydrogels can alter their swelling behavior in response to temperature changes, enabling controlled drug release in response to the body's temperature [28].
3. **Biodegradable Polymers:** Advances in biodegradable polymers have led to the development of drug delivery systems that minimize long-term toxicity and accumulation in the body. These polymers can be designed to degrade over time, releasing the encapsulated drug gradually. Biodegradable microspheres and nanoparticles made from materials like polylactic-co-glycolic acid (PLGA) are widely studied for their applications in sustained drug release, particularly in therapies requiring prolonged dosing intervals [29].
4. **Smart Hydrogels:** Hydrogels are network-like structures that can retain large amounts of water, making them ideal for drug delivery applications. Smart hydrogels can be engineered to respond to environmental changes, such as changes in pH, temperature, or ionic strength, to control drug release. These systems are particularly useful in applications like wound healing, where the hydrogel can release growth factors or antimicrobial agents in response to the local environment [30].
5. **Gene Delivery Systems:** Smart drug delivery systems also play a crucial role in gene therapy. Innovative vector systems, including viral and non-viral carriers, have been developed to deliver nucleic acids to target cells efficiently. These systems are designed to protect the genetic material from degradation and facilitate cellular

uptake, enabling the targeted delivery of therapeutic genes for conditions like genetic disorders and cancers [31].

Applications of Smart Drug Delivery Systems

1. **Cancer Therapy:** One of the most promising areas for smart drug delivery systems is cancer treatment. Conventional chemotherapy is often limited by systemic toxicity and suboptimal drug distribution to tumors. Smart delivery systems enhance the therapeutic index by delivering higher concentrations of drugs directly to tumor sites while minimizing exposure to healthy tissues. This targeted approach has shown to improve treatment outcomes and reduce side effects in various cancer modalities [32].
2. **Chronic Disease Management:** Conditions such as diabetes, hypertension, and cardiovascular diseases require consistent and reliable drug delivery methods. Smart delivery systems that provide controlled release or on-demand dosing can improve patient adherence, achieve therapeutic drug levels, and simplify treatment regimens. For example, implantable devices that release insulin in response to glucose levels represent a significant advancement in diabetes management [33].
3. **Vaccination:** Innovations in drug delivery systems extend to vaccine development. Smart carriers can protect antigens from degradation, enhance immune responses, and provide controlled release, facilitating the development of more effective vaccines. Research into nanoparticle-based vaccine delivery systems has shown promise, particularly in eliciting robust and long-lasting immune responses [34].
4. **Regenerative Medicine:** In regenerative medicine, smart drug delivery systems can deliver growth factors, stem cells, or other therapeutic agents to promote tissue repair and regeneration. Biodegradable scaffolds that release bioactive molecules in response to specific physiological conditions can enhance the healing process and support tissue engineering applications [35].

5. **Pain Management:** Smart drug delivery systems are increasingly being explored for pain management applications. Advanced systems capable of delivering analgesics in response to patient-initiated cues can provide on-demand relief. By offering localized treatment and reducing systemic side effects, these systems can enhance pain management strategies [36].

Future Directions and Challenges

While smart drug delivery systems hold immense potential, several challenges must be addressed before they can be widely integrated into clinical settings. Standardization of manufacturing processes, regulatory approval pathways, and long-term safety assessments remain critical factors influencing the successful translation of these technologies into practice. Additionally, comprehensive studies exploring the interactions between smart delivery systems and biological environments are essential for understanding their efficacy and safety profiles [37].

Research into combination therapies integrating smart delivery systems with other therapeutic modalities, such as immunotherapy, holds promise for optimizing treatment outcomes. The increasing use of machine learning and artificial intelligence to design personalized drug delivery strategies tailored to individual patients may further revolutionize the field [38].

Formulation Strategies for Biologics and Biosimilars:

Biologics and biosimilars represent a rapidly growing segment of modern medicine, providing ground-breaking treatments for a variety of diseases including cancers, auto-immune disorders, and metabolic diseases. Biologics are products derived from living organisms, utilizing complex biological processes for their development. Conversely, biosimilars are biologic products designed to be highly similar to an already approved biologic reference product. The formulation strategies for biologics and biosimilars are crucial for their efficacy, stability, and safety, influencing their pharmacokinetics and pharmacodynamics [39].

Biologics are typically large, complex molecules or mixtures of molecules such as proteins, nucleic acids, or living cells. They can include monoclonal

antibodies, therapeutic proteins, vaccines, and cell and gene therapies. The production of biologics involves sophisticated biological systems, which lead to product variability and challenges in characterization, stability, and manufacture [40].

Biosimilars are regarded as copies of biologics that are not identical, as the manufacturing processes can result in differences in structure and efficacy. Therefore, it is crucial that formulation strategies for both biologics and biosimilars account for their unique properties and the nuances of the regulatory landscape [40].

Key Considerations in Formulation Strategies

Several critical factors influence the formulation strategies of biologics and biosimilars, including stability, solubility, delivery method, and regulatory guidelines.

1. Stability and Shelf Life

Biologics are generally more sensitive to environmental conditions such as temperature, pH, and light compared to traditional small-molecule drugs. Ensuring stability through adequate formulation is paramount. Strategies such as lyophilization (freeze-drying), the use of stabilizers (such as sugars or amino acids), and the selection of suitable excipients are implemented to enhance shelf life while maintaining the bioactivity of the product [40].

For example, proteins can undergo denaturation, aggregation, or oxidation during storage, leading to loss of efficacy. Thus, protective agents are often included in the formulation to mitigate these risks, with extensive stability testing performed during development to determine optimal conditions for product integrity [41].

2. Solubility and Concentration

Achieving the appropriate solubility and concentration is another core consideration for formulators. Many biologics are prone to aggregation, particularly at higher concentrations which can be necessary for achieving therapeutic doses. Thus, formulators often work with surfactants, buffering agents, and osmolality modifiers to optimize solubility without compromising protein activity [41].

3. Delivery Mode

The route of administration significantly impacts formulation design. Common delivery methods for biologics include subcutaneous, intravenous, or intramuscular injections. Each route has its own unique requirements regarding formulation. For instance, intravenous formulations often demand sterile, isotonic solutions with low viscosity for ease of administration, while subcutaneous formulations may require features that enhance absorption and reduce pain such as controlled-release mechanisms [41].

4. Biocompatibility and Immunogenicity

Incorporating biologic compounds into formulations raises the risk of eliciting an immune response, which can manifest as immunogenicity. It is critical to assess the biocompatibility of excipients and to minimize the potential for adverse immunological reactions. This entails rigorous preclinical testing to evaluate both local and systemic safety profiles, which are vital for patient acceptance and commercial success [42].

Regulatory Considerations

The regulatory pathway for biologics and biosimilars adds another layer of complexity to formulation strategies. Authorities such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have strict guidelines for approving both biologics and biosimilars. For instance, the regulatory framework emphasizes the need for extensive comparability studies for biosimilars, which demonstrate similarity to their reference counterpart in terms of safety, efficacy, and quality [42].

This necessitates a robust formulation strategy that enables clear and reproducible results in these studies. The use of analytical techniques such as high-performance liquid chromatography (HPLC), mass spectrometry, and bioassays plays a significant role in characterizing the fundamental properties of these products [43].

Recent advancements in formulation technologies are transforming the landscape of biologics and biosimilars. Biopharmaceutical companies are increasingly embracing innovative techniques such as nanotechnology, which can enhance bioavailability and therapeutic effects. Nanoparticle formulations, for instance, can facilitate targeted delivery and controlled release of biologics,

improving patient adherence and therapeutic outcomes [44].

In addition, the application of microfluidics in formulation development presents new opportunities for optimizing biologic product attributes and manufacturing processes by allowing for precise control over formulation parameters [44].

Emerging Trends in Controlled Release Mechanisms:

The field of drug delivery systems has experienced transformative advancements over the past few decades, particularly with the advent of controlled release mechanisms. Controlled release mechanisms refer to technologies designed to release therapeutic agents at predetermined rates, times, or locations, enhancing the efficacy and safety of treatment regimens. As the demand for more sophisticated drug delivery systems increases, emerging trends in controlled release mechanisms are shaping the future of pharmaceuticals, targeting a myriad of applications from chronic disease management to oncology [45].

One of the most significant trends in controlled release mechanisms is the utilization of biodegradable polymers. These materials offer myriad advantages, including biocompatibility and reduced toxicity, crucial for long-term drug delivery applications. Polymers such as polylactic acid (PLA) and polyglycolic acid (PGA) are frequently employed due to their ability to degrade in physiological environments, releasing drugs in a controlled manner over extended periods. Recent advancements have led to the synthesis of novel biodegradable polymers tailored to specific release profiles, thereby customizing drug delivery to suit individual patient needs. Research into copolymers with varying hydrophilicity and hydrophobicity allows for precise modulation of drug release rates, enabling tailored therapeutic interventions [46].

Nanotechnology has emerged as a crucial player in the realm of controlled release mechanisms. Drugs are encapsulated in nanoparticles, allowing for increased surface area and enhanced drug solubility, particularly for hydrophobic compounds. Nanoparticles can be engineered to respond to environmental stimuli such as pH, temperature, or specific enzymes, offering on-demand drug release capabilities. For example, pH-sensitive nanoparticles can selectively release their payload in tumor environments where the pH level is often

more acidic than in healthy tissues. Furthermore, the use of lipid-based nanoparticles, such as liposomes and solid lipid nanoparticles, has gained traction due to their ability to encapsulate both hydrophilic and hydrophobic drugs, providing a versatile platform for controlled release applications [47].

The concept of ‘smart’ drug delivery systems represents a shift towards responsive mechanisms that adapt to physiological conditions. These systems use stimuli-responsive materials that change their behavior in response to specific changes in the environment. For instance, hydrogels engineered to swell or shrink in response to changes in pH or temperature offer primary examples of how drug release can be fine-tuned. Smart delivery mechanisms can also incorporate bio-sensors that detect biomarkers, triggering drug release when required. This intelligent approach to drug delivery not only optimizes therapeutic efficacy but also minimizes side effects by ensuring that drugs are only released when necessary [48].

The application of 3D printing technologies in medicine has grown exponentially, offering new avenues for the creation of personalized drug delivery systems. 3D printing allows for the design and production of complex structures that can release drugs at controlled rates. This technology facilitates the inclusion of multi-material components, allowing for the encapsulation of multiple drugs within a single device, potentially addressing polypharmacy issues in chronic disease management. Moreover, 3D-printed drug delivery systems can be customized to specific patient needs, providing healthcare providers with tools to create bespoke therapies that enhance treatment adherence and efficacy [49].

Emerging trends in controlled release mechanisms increasingly emphasize the importance of combination therapies. By pairing different therapeutic agents—such as chemotherapeutics and immunotherapeutics—controlled release systems can improve overall treatment outcomes while reducing individual drug doses. Multi-modal delivery systems that sequentially release multiple agents or release them simultaneously are gaining traction in cancer therapy, where the targeted delivery of chemotherapeutic agents alongside immunotherapies can synergistically enhance antitumor efficacy. This approach reduces the potential for drug resistance and allows for more

comprehensive management of complex disease states [50].

Controlled release mechanisms are also making significant strides in the field of gene therapy and RNA delivery. The quest for effective methods to deliver nucleic acids—such as DNA, mRNA, and siRNA—has led to the development of novel carriers, including lipid nanoparticles, polymeric carriers, and viral vectors. Controlled release systems facilitate the safe and efficient delivery of these macromolecules, enabling targeted expression of therapeutic genes while minimizing off-target effects. Advances in delivery technologies aim to enhance cellular uptake and achieve controlled release profiles that mimic the physiological dynamics of gene expression, continuously evolving the future of genetic and molecular therapies [51].

As the landscape of controlled release mechanisms continues to evolve, regulatory frameworks are adapting to ensure drugs are developed and delivered safely. Regulatory bodies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) are increasingly recognizing the importance of innovative drug delivery systems in accelerating drug approval processes. The integration of quality-by-design (QbD) principles is becoming essential, prompting developers to adopt a systematic approach to product design that ensures robustness and reproducibility in controlled release profiles [52].

Impact of 3D Printing on Drug Formulation and Customization:

In recent years, 3D printing, also known as additive manufacturing, has emerged as a revolutionary technology across various industries. Its applications extend far beyond the conventional realms of manufacturing and engineering, delving into the complexities of biomedicine, particularly in drug formulation and customization. The integration of 3D printing technology in pharmaceutical practices promises to reshape the landscape of drug development, delivery, and patient-centric healthcare [53].

At its core, 3D printing involves the process of creating a three-dimensional object from a digital model by layering materials in a sequential manner. In pharmaceutical settings, this technology allows for the fabrication of various dosage forms, including tablets, capsules, and bespoke drug

delivery systems. The versatility of 3D printing caters to the unique requirements of individual patients, enabling tailored pharmacotherapy that considers personal health factors such as genetic makeup, age, gender, and concomitant medical conditions [54].

A prominent form of 3D printing used in pharmaceuticals is fused deposition modeling (FDM), where thermoplastic materials are extruded to form precise shapes. Another technique, selective laser sintering (SLS), employs a laser to fuse powdered materials, allowing for more complex designs with varied mechanical properties. Additionally, inkjet printing has gained traction in developing drug formulations by depositing liquid formulations onto a substrate in controlled patterns [55].

One of the key advantages of 3D printing in drug formulation is the ability to produce personalized medications. Traditional pill formulations often involve a one-size-fits-all approach, which can lead to therapeutic inefficacy or adverse effects in certain populations. However, by leveraging 3D printing technology, pharmaceutical companies can create customized drugs that meet specific patient requirements. For instance, specific dosages can be tailored for pediatric patients, elderly patients, or individuals with unique metabolic profiles, enhancing therapeutic outcomes [56].

Moreover, 3D printing facilitates complex drug delivery mechanisms that are not feasible with conventional manufacturing techniques. This capability allows for the design of multi-layered tablets with varying release profiles, enabling controlled or sustained drug release. This approach not only improves therapeutic effectiveness but also optimizes patient adherence to treatment regimens by reducing dosing frequency [57].

Another remarkable advantage is the reduction of production time and costs associated with drug formulation. Traditional manufacturing processes require extensive time and resource investment, from formulation development to production and quality control. In contrast, 3D printing allows for rapid prototyping and production, enabling quicker iterations based on clinical feedback. This efficiency can significantly reduce the time-to-market for new drugs, ultimately benefiting patients who may be waiting for novel therapies [58].

Despite its promising benefits, the integration of 3D printing in drug formulation is not without its challenges. One primary concern is the regulatory landscape governing the production and distribution of pharmaceutical products. Regulatory agencies, such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), require stringent testing and validation of any new drug formulation processes to ensure safety, efficacy, and quality. The dynamic nature of 3D printing complicates this process, as each printed batch can vary based on machine calibration, material properties, and environmental factors. Hence, establishing reproducibility and consistency remains a significant hurdle [59].

Additionally, the selection of printing materials suitable for pharmaceutical applications presents its own challenges. Materials must not only be biocompatible but also capable of maintaining the stability of the active pharmaceutical ingredient throughout the printing process and during storage. The optimization of these materials for specific drugs requires extensive research and development, which can be resource-intensive [60].

Moreover, there is a need for robust clinical evidence supporting the efficacy and safety of 3D-printed drugs. As clinical trial protocols evolve, pharmaceutical manufacturers must adapt their processes to gather data that demonstrate the benefits of customized drugs compared to traditional formulations. This need for evidence can slow down the adoption of 3D printing technologies in pharmaceutical applications [61].

Looking ahead, the impact of 3D printing on drug formulation and customization is poised to expand significantly. As technological advances continue to enhance the capabilities of 3D printing, it is likely that we will see an increase in the variety of printable drugs and dosage forms. For example, the integration of bio-printing methods could allow the creation of complex tissue-engineered constructs for drug testing and development, providing insights into pharmacokinetics and toxicity in a more biologically relevant context [62].

Furthermore, the potential for point-of-care manufacturing using portable 3D printers could transform healthcare delivery. This innovation would enable pharmacies or healthcare facilities to produce customized medications on-site, reducing lead times and ensuring that patients receive their medications in a timely manner [63].

Additionally, the wealth of data generated through the use of 3D printing in pharmaceuticals represents an opportunity for integrating artificial intelligence and machine learning algorithms. By analyzing patient data, medical professionals can predict individual responses to medications, allowing for even more refined customization in drug formulation [64].

Regulatory Considerations and Future Directions in Drug Delivery:

The landscape of drug delivery has witnessed significant evolution over recent decades, driven by advancements in technology, a growing understanding of pharmacokinetics and pharmacodynamics, and an increasing demand for more efficient therapeutic interventions. As the pharmaceutical industry innovates in drug delivery systems (DDS), it must also navigate a complex web of regulatory considerations that ensure the safety, efficacy, and quality of new therapeutic modalities. As we look towards the future, it is crucial to examine the regulatory framework governing drug delivery, the emerging trends influencing the field, and the potential directions for future development. [65]

Regulatory agencies play a critical role in the drug delivery ecosystem, with the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), and other international bodies serving as gatekeepers to ensure that new drug delivery systems meet safety and efficacy standards. These agencies operate under stringent guidelines that address various aspects of drug development, including preclinical testing, clinical trial design, and post-marketing surveillance [65].

Before a new drug delivery system can be tested in humans, it must undergo rigorous preclinical evaluations. This stage involves assessing the pharmacokinetics, toxicity, and biocompatibility of the drug delivery method. Regulatory considerations at this stage include adherence to Good Laboratory Practices (GLP) and the necessity for comprehensive risk assessments to evaluate any potential risks associated with the new technology. The goal is to gather sufficient data to support the transition to human trials [66].

When it comes to clinical trials, the design must comply with the standards set forth by regulatory bodies. The FDA and EMA provide guidelines that stipulate the number of participants, duration, and

endpoints for clinical studies. Innovative drug delivery systems, especially those involving nanotechnology, gene therapy, or biologics, often present unique challenges concerning trial design. These include considerations surrounding the route of administration, dosing regimens, and the potential for immune responses [66].

Moreover, the regulatory approval process for combination products, such as drug-device combinations or biologic-drug systems, necessitates a multidisciplinary approach that incorporates insights from multiple regulatory domains. This complexity underscores the need for clear communication between sponsors and regulatory agencies to ensure that developments adhere to regulations while also fostering innovation [67].

Once a drug delivery system has passed clinical trials and received regulatory approval, the focus shifts to the manufacturing process. Ensuring product quality requires strict adherence to Current Good Manufacturing Practices (cGMP). Regulatory authorities conduct inspections and audits to verify that manufacturing processes are capable of consistently producing high-quality products. For advanced drug delivery systems, particularly those that are personalized or tailored to individual patient needs, this aspect presents unique regulatory challenges [67].

Key Considerations in Regulation

As drug delivery continues to evolve, there are several regulatory considerations that require ongoing attention:

1. Enhanced Regulatory Pathways

To keep pace with the rapid advancement of drug delivery technologies, regulatory agencies are also adapting their frameworks. The FDA, for example, has established expedited pathways for breakthrough therapies and regenerative medicines, which can include innovative drug delivery systems. Similarly, adaptive trial designs are emerging, allowing for modifications based on interim results, thereby enhancing the efficiency of clinical development [68].

2. Emerging Technologies

The rise of artificial intelligence (AI) and machine learning (ML) in drug delivery is reshaping traditional models. Algorithms can now optimize drug formulations, predict therapeutic outcomes,

and inform personalized medicine approaches. Regulatory frameworks need to embrace these technologies, requiring new guidelines and standards to assess AI-driven drug delivery systems [68].

3. Patient-Centric Approaches

Future regulatory considerations will increasingly focus on patient-centric drug delivery systems, which require an understanding of patient needs and preferences. In this context, regulatory frameworks must evolve to encompass real-world evidence, integrating patient-reported outcomes into the evaluation process [69].

Future Directions in Drug Delivery

As we look ahead, the future of drug delivery will likely be characterized by several key trends:

1. Personalized and Precision Medicine

Personalized medicine aims to tailor treatments based on individual patient characteristics, including genetics, lifestyle, and disease state. The potential for drug delivery systems to provide targeted therapies, such as using nanoparticles to deliver chemotherapeutic agents directly to tumor cells, signifies a shift towards more effective and individualized treatments. Regulatory agencies will need to develop frameworks that accommodate these personalized approaches, ensuring that the benefits of tailored therapies are balanced against potential risks [69].

2. Biologics and Biosimilars

The rise of biologics and biosimilars presents both opportunities and challenges for drug delivery systems. Biologics often require advanced delivery solutions due to their complex structures and sensitivities. Regulatory bodies must navigate the intricacies of assessing the safety and efficacy of these products, particularly as the market for biosimilars expands [70].

3. Advanced Drug Delivery Systems

Continuing innovation in drug delivery technologies, such as microneedles, implants, and smart delivery systems, promises to enhance therapeutic outcomes. However, each of these technologies presents unique challenges related to formulation, stability, and patient compliance. Regulatory agencies will need to establish guidelines that support the development of these

advanced systems while ensuring rigorous oversight [71].

Conclusion:

In conclusion, the study of current trends in drug formulation and delivery systems reveals a dynamic landscape characterized by innovation and a focus on patient-centered approaches. The integration of personalized medicine, driven by advancements in genomics and biotechnology, is reshaping how therapies are developed and administered, ensuring that treatments are tailored to individual patient needs. Additionally, the application of nanotechnology and smart delivery systems is revolutionizing drug bioavailability and targeting, enhancing therapeutic efficacy while minimizing side effects.

As the pharmaceutical industry continues to evolve, the emergence of biologics, biosimilars, and 3D printing technology further underscores the importance of adaptive formulation strategies that can meet the complexities of modern therapeutics. However, these advancements also bring challenges, particularly in regulatory frameworks and ensuring consistent quality across novel delivery systems. Looking ahead, ongoing research and collaboration among scientists, clinicians, and regulatory bodies will be essential in harnessing these trends to improve patient outcomes and streamline drug development processes. The future of drug formulation and delivery systems promises to be increasingly innovative, efficient, and aligned with the needs of diverse patient populations.

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